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Applications of planar-chiral heterocycles in enantioselective catalysis: Cu(I)/bisazaferrocene-catalyzed asymmetric ring expansion of oxetanes to tetrahydrofurans

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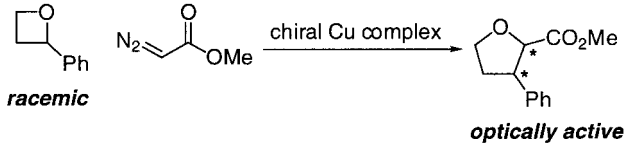
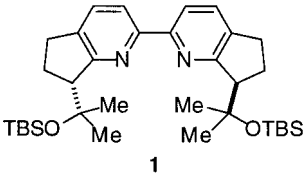
Abstract—A planar-chiral, C_2-symmetric bisazaferrocene ligand is shown to control the stereochemistry of Cu(I)-catalyzed ring expansions of oxetanes to tetrahydrofurans.

As part of their seminal 1966 study of transition metal-catalyzed enantioselective reactions, Nozaki and Noyori reported that copper catalysts can effect the asymmetric ring expansion of oxetanes to tetrahydrofurans (Eq. (1)), although they did not determine the enantiomeric excess of the products.[1]



(1)

Surprisingly, since this initial work, only Katsuki has described further investigations of this interesting transformation.[2,3] He has established that ring expansions catalyzed by CuOTf in the presence of C_2-symmetric bipyridine ligands (e.g. **1**) proceed with good stereoselectivity, and he has utilized this process as a key step in the synthesis of molecules such as *trans*-(+)-whisky lactone[2b] and (−)-avenaciolide.[2f]



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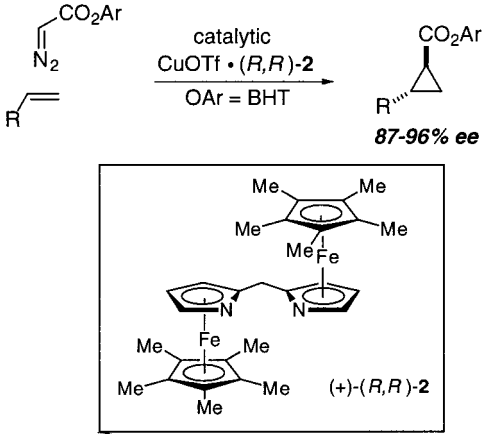
We have recently reported the application of C_2-symmetric bisazaferrocene **2** in a highly enantioselective Cu(I)-catalyzed cyclopropanation of olefins (Eq. (2)).[4,5] Based on these positive results, we decided to explore the possibility that the same CuOTf/**2** complex might also serve as an effective catalyst for another reaction of diazo esters, the asymmetric ring expansion of oxetanes to tetrahydrofurans. In this paper, we describe our investigations in this area (Eq. (3)).



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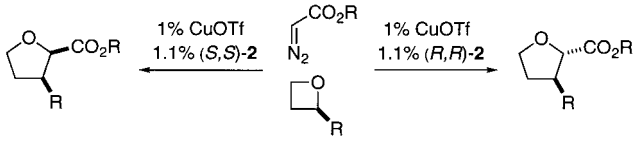

(3)

1. Results and discussion

In an early study of the copper-catalyzed ring-expansion process, we compared the selectivity of bisazaferrocene

Keywords: asymmetric synthesis; catalysis; copper and compounds; diazo compounds; oxetanes.

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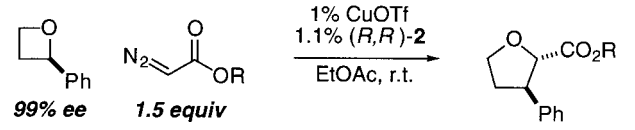
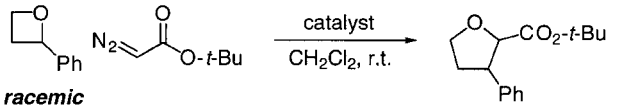
Table 1. Asymmetric ring expansions catalyzed by CuOTf/**2**: Dependence of selectivity on the diazo ester



Entry	O*R*	*trans*/*cis*	*trans* ee (%)
1	OEt	82:18	92
2	O-(D)-menthyl	90:10	95
3	O-(L)-menthyl	90:10	97
4	O-*t*-Bu	90:10	97
5	$OCMeCy_2$	95:5	98

All data are the average of two runs.

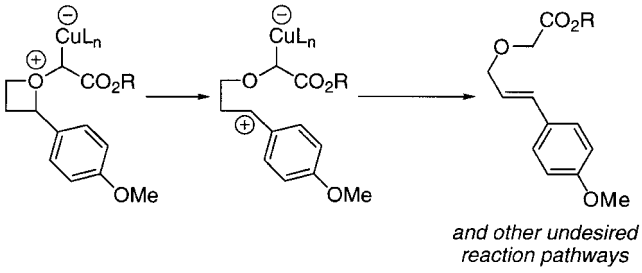
ligand **2** with Katsuki's best bipyridine ligand (**1**). Under the conditions that he had optimized for his catalyst system, we found that our ligand furnishes nearly comparable stereoselection (Eq. (4)). In accord with the report of Katsuki, no kinetic resolution of the oxetane is observed.



(4)

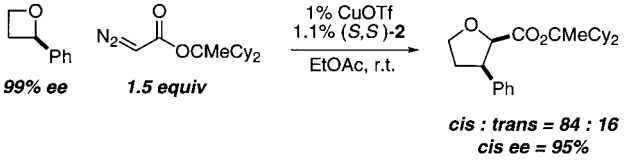
We have optimized the reaction conditions for our ligand, and we have found CuOTf to be the best copper source and EtOAc to be the best solvent, among those that we have examined. We have also determined that, as with CuOTf/**2**-catalyzed cyclopropanations,[4] the steric demand of the diazo ester has a significant impact on selectivity—as the bulk of the diazo ester increases, the stereoselection increases (Table 1). Thus, whereas ethyl diazoacetate affords 82:18 selectivity (entry 1), menthyl diazoacetates and *t*-butyl diazoacetate furnish 90:10 selectivity (entries 2–4). Interestingly, the stereochemistry of the menthyl subunit has essentially no impact on stereoselection (entry 2 vs entry 3). We obtain the highest selectivity with the most hindered diazoester (R=$CMeCy_2$; entry 5). The $CMeCy_2$ ester of the product tetrahydrofuran is readily converted into the carboxylic acid through treatment with CF_3CO_2H in CH_2Cl_2 (10 min), without cleavage of the ring or epimerization.[6]

CuOTf/**2** catalyzes the ring expansion of a range of 2-substituted oxetanes with good selectivity under our optimized conditions (Table 2). Incorporation of an electron-withdrawing substituent on the aromatic ring has no effect on stereoselection (entry 1 vs entry 2). On the other hand, incorporation of an electron-donating group leads to a poor reaction, both in terms of stereoselectivity and yield (entry 3), perhaps due to the ionization process illustrated in Eq. (5). Naphthyl- and alkynyl-substituted oxetanes undergo ring expansion with good stereoselection (entries 4 and 5).



(5)

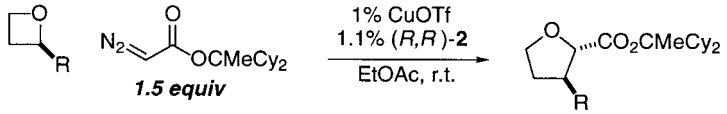
The ring expansions illustrated in Table 2 correspond to the 'matched' process, wherein the chiral catalyst and the substrate are working in concert to preferentially generate the *trans* diastereomer. When we employ the opposite enantiomer of the catalyst, we produce the *cis* isomer with good selectivity (Eq. (6)). Thus, the catalyst, not the substrate, predominantly determines the configuration of the new stereocenter (Eq. (6) vs Table 2, entry 1).



(6)

We have established that this observation is general—as illustrated in Table 3, the *cis*, rather than the *trans*, tetrahydrofuran can be obtained in the ring-expansion process simply by using the (*S*,*S*), rather than the (*R*,*R*), enantiomer of bisazaferrocene ligand **2** (cf. Table 2). The stereoselection

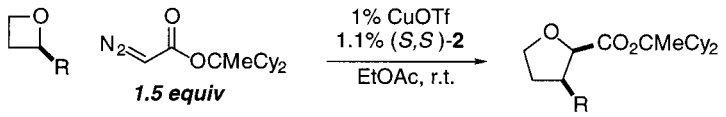
Table 2. Asymmetric ring expansions catalyzed by CuOTf/**2**



Entry	*R*	Oxetane ee (%)	*trans*/*cis*	*trans* ee (%)	Yield (%)
1	Ph	99	95:5	98	74
2	4-$(F_3C)C_6H_4$	97	94:6	98	81
3	4-$(MeO)C_6H_4$	98	75:25	69	29
4	1-Naphthyl	99	86:14	91	75
5	*n*-$C_7H_{15}C{\equiv}C$	99	89:11	97	64

All data are the average of two runs. Yields are isolated yields. The yield for entry 1 includes both diastereomers.

Table 3. Asymmetric ring expansions catalyzed by CuOTf/**2**: Catalyst control of the newly generated stereocenter



Entry	*R*	Oxetane ee (%)	*cis*/*trans*	*cis* ee (%)	Yield (%)
1	Ph	99	84:16	95	74
2	4-(F_3C)C_6H_4	97	86:14	95	52
3	4-(MeO)C_6H_4	98	58:42	82	20
4	1-Naphthyl	99	85:15	95	72
5	*n*-$C_7H_{15}C{\equiv}C$	99	84:16	94	60

Yields are isolated yields. The yield for entry 1 includes both diastereomers.

appears to be largely independent of the nature of the 2-substituent, unless it is electron-rich (entry 3).

Hydrolysis of the ester generated in entry 5 of Table 3 furnishes the carboxylic acid that is an intermediate in the Katsuki synthesis of (−)-avenaciolide.[2f] The stereoselectivity that we obtain with bisazaferrocene ligand **2** (*cis*/*trans*=84:16, *cis* ee=94%) compares favorably with that produced by bipyridine ligand **1** (*cis*/*trans*=85:15, *cis* ee=72%).[2f]

2. Conclusions

CuOTf/bisazaferrocene **2** serves as an effective catalyst for the asymmetric ring expansion of oxetanes to tetrahydrofurans. The catalyst controls the absolute stereochemistry of the newly generated stereocenter and is capable of overriding the inherent preference of the substrate for formation of the *trans*-2,3-disubstituted product. The level of stereocontrol compares favorably with other chiral catalysts that have been developed for this reaction.

3. Experimental

3.1. General

Analytical achiral GC analysis was performed on a J & W Scientific DB-1701 column (0.25 mm×30 m). Analytical chiral GC analysis was performed on either a Chiraldex G-TA column (0.25 mm×20 m) or a Chiraldex B-PH column (0.25 mm×20 m). Analytical chiral HPLC analysis was performed on a Daicel Chiralcel OD or Chiralpak AD column (4.6 mm×25 cm). Preparative achiral HPLC was performed on an Alltech Econosphere Silica 10U column (22 mm×250 mm).

Solvents were distilled under nitrogen from the indicated drying agents: THF (sodium/benzophenone); Et_2O (sodium/benzophenone); CH_2Cl_2 (CaH_2). Anhydrous MeCN and EtOAc were obtained from Aldrich.

Unless otherwise stated, all reagents were purchased from commercial suppliers and used as received. The following reagents were distilled under reduced pressure from the indicated drying agents: dicyclohexyl ketone ($MgSO_4$); diketene (CaH_2). KH was purchased as a suspension in paraffin oil, and oil-free KH was obtained after repeated washing with pentane in a glove box, followed by drying in vacuo. Ethyl diazoacetate was purified by column chromatography prior to use. Ligand **2**,[4] *t*-butyl diazoacetate,[7] (D)-menthyl diazoacetate, (L)-menthyl diazoacetate,[8] (±)-2-phenyloxetane,[9] (4′-trifluoromethylphenyl)-tri-*n*-butylstannane,[10] and methanesulfonyl azide[11] were synthesized according to literature procedures.

All reactions were carried out with magnetic stirring in oven-dried glassware under an atmosphere of argon (manifold) or under an atmosphere of nitrogen (Vaccum Atmospheres glove box), unless otherwise noted. All reactions that involve the preparation of substrates are unoptimized.

3.1.1. 1′,1′-Dicyclohexylethyl 2-diazo-3-oxobutanoate. In a 100 mL round-bottom flask equipped with a condenser, 1,1-dicyclohexylethanol[12] (8.02 g, 38.1 mmol), DMAP (0.461 g, 3.77 mmol), Et_3N (0.386 g, 3.81 mmol), and methanesulfonyl azide (6.04 g, 49.8 mmol) were mixed and dissolved in MeCN (60 mL). The mixture was then brought to reflux, and a solution of diketene (6.04 g, 49.8 mmol) in MeCN (15 mL) was added by syringe over 10 min. The deep-brown reaction mixture was cooled to room temperature and stirred for another 12 h (TLC at that time indicated that there was still some acetoacetate ester). The reaction mixture was poured into Et_2O/water. The aqueous layer was extracted with Et_2O (4×100 mL), and the combined organic extracts were washed with 2 M KOH and brine, dried ($MgSO_4$), and concentrated to afford a brown oil. The crude product was then dissolved in MeCN (100 mL). Et_3N (8.0 mL, 57 mmol) and then methanesulfonyl azide (7.18 g, 59.3 mmol) were added dropwise, and the resulting mixture was stirred under air for 5 h, at which time TLC indicated that there was no acetoacetate ester. The reaction mixture was poured into Et_2O/water. The aqueous layer was extracted with Et_2O, and the combined organic extracts were washed with 2 M KOH and brine, dried ($MgSO_4$), and concentrated to afford an orange-yellow slurry. ^1H NMR (500 MHz, $CDCl_3$): δ 1.0–1.3 (m, 11H), 1.48 (s, 3H), 1.6–2.0 (m, 11H), 2.45 (s, 3H).

3.1.2. 1,1-Dicyclohexylethyl diazoacetate. The unpurified product from the previous step was dissolved in MeOH (100 mL). NaOMe (4.07 g, 75.3 mmol) was added batchwise to the stirred solution, turning the yellow-orange reaction mixture to deep brown. After 12 h, TLC indicated that there was no starting diazo ester. The reaction mixture was

diluted with water (200 mL) and saturated with NaCl. Extraction with Et_2O (4×200 mL) afforded a brown solution, which was then washed with brine, dried ($MgSO_4$), and concentrated to afford a yellow slurry. This crude product was purified by column chromatography (5/95 Et_2O/pentane), which afforded a bright-yellow liquid (7.76 g, 85% isolated yield based on 1,1-dicyclohexylethanol), which slowly solidified to a yellow solid upon storage at low temperature. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.0–1.3 (m, 10H), 1.42 (s, 3H), 1.62–1.69 (m, 2H), 1.70–1.80 (m, 8H), 1.86 (tt, 2H, J=2.9, 11.4 Hz), 4.60 (br, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 19.5, 26.6, 27.1, 27.7, 28.3, 45.1, 46.7, 91.8, 166.5. IR (KBr): 3136 (m), 2998 (m), 2955 (s), 2922 (s), 2850 (s), 2107 (s), 1693 (s), 1671 (s), 1450 (m), 1340 (s), 1244 (s), 1128 (m), 1050 (m), 997 (m), 737 (m) cm^{-1}. mp 48–49°C.

3.1.3. 3-Chloro-1-(4′-trifluoromethylphenyl)propan-1-one. A solution of P(t-Bu)$_3$ (0.612 g, 3.02 mmol) in CH_2Cl_2 (30 mL) was added to a solution of $Pd_2(dba)_3$ (1.15 g, 1.26 mmol) in CH_2Cl_2 (20 mL).[13] The reaction mixture was cooled to 0°C, and 3-chloropropionyl chloride (12.0 mL, 0.126 mol) was added, yielding an initially purple solution that then turned brown. After 15 min, degassed (4′-trifluoromethylphenyl)tri-n-butylstannane (21.8 g, 50.1 mmol) was added to the reaction mixture, which was stirred at 0°C for 12 h and then at room temperature for an additional 36 h. The reaction mixture was filtered through a plug of silica (Et_2O as the eluant), and the filtrate was concentrated, affording a red liquid. The crude product was purified by column chromatography (2.5/97.5 Et_2O/pentane), which furnished the desired product as a yellow liquid (7.79 g, 66% yield) that slowly solidified to a white solid upon standing at 0°C. ^{1}H NMR analysis showed a small amount of an organotin impurity. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.49 (t, 2H, J=6.7 Hz), 3.94 (t, 2H, J=6.7 Hz), 7.76 (d, 2H, J=8.9 Hz), 8.07 (d, 2H, J=7.9 Hz). ^{13}C NMR (126 MHz, $CDCl_3$): δ 38.4, 41.7, 123.7 (q, $^1J_{C-F}$=273 Hz), 126.0 (q, $^3J_{C-F}$=3.9 Hz), 128.6, 134.9 (q, $^2J_{C-F}$=32.6 Hz), 139.1, 195.9. IR (KBr): 1686 (s), 1513 (m), 1414 (m), 1326 (s), 1129 (s), 1067 (s), 853 (m), 834 (m), 714 (m), 653 (m) cm^{-1}. HRMS (EI, m/z): Calcd for $C_{10}H_8ClF_3O$: 236.0216 (M^+). Found: 236.0211.

3.1.4. 3-Chloro-1-(4′-methoxyphenyl)propan-1-one. Anisole (13.5 mL, 0.124 mol) and then 3-chloropropionyl chloride (12.5 mL, 0.131 mol) were added to a solution of $AlCl_3$ (20.0 g, 0.150 mol) in $PhNO_2$ (150 mL). After 2 h, TLC showed that no anisole remained. The reaction mixture was quenched by pouring it into a mixture of ice and water (300 mL). The resulting aqueous layer was extracted with CH_2Cl_2 (4×300 mL), and the combined organic layers were washed with a saturated Na_2CO_3 solution, dried ($MgSO_4$), and concentrated in vacuo (70–80°C, 2 Torr) to afford a mixture of a brown oil and a white solid. Recrystallization of this crude product from Et_2O/hexanes furnished the desired product as pale-brown crystals (13.4 g, 55% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.42 (t, 2H, J=6.9 Hz), 3.88 (s, 3H), 3.92 (t, 2H, J=6.9 Hz), 6.95 (d, 2H, J=9.2 Hz), 7.95 (d, 2H, J=8.9 Hz).[14] ^{13}C NMR (126 MHz, $CDCl_3$): δ 39.2, 41.1, 55.7, 114.1, 129.6, 130.6, 164.0, 195.4. HRMS (EI, m/z): Calcd for $C_{10}H_{11}ClO_2$: 198.0448 (M^+). Found: 198.0444.

3.1.5. 3-Chloro-1-(1′-naphthyl)propan-1-one. 3-Chloropropionyl chloride (25.7 g, 0.240 mol) was added to a suspension of $AlCl_3$ (34.2 g, 0.257 mol) in CH_2Cl_2 (300 mL). The reaction mixture was cooled to 0°C, and then naphthalene (25.7 g, 0.201 mol) was added batchwise over 15 min, resulting in the precipitation of a large quantity of a white solid, which re-dissolved over 1 h. After 12 h (total), the reaction mixture was poured onto ice, and the resulting aqueous layer was extracted with CH_2Cl_2 (3×300 mL). The combined organic layers were washed with saturated $NaHCO_3$, dried ($MgSO_4$), and concentrated to afford an emerald-green liquid. The product was purified by column chromatography (5/20/75 Et_2O/CH_2Cl_2/pentane), which furnished a yellow oil (45.6 g, 100% yield). ^{1}H NMR analysis showed a small amount of the 2-acyl naphthalene (1-isomer/2-isomer~10:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.51 (t, 2H, J=6.6 Hz), 3.97 (t, 2H, J=6.6 Hz), 7.49 (dd, 1H, J=7.3, 8.2 Hz), 7.53 (ddd, 1H, J=1.2, 6.9, 8.1 Hz), 7.59 (ddd, 1H, J=1.4, 6.7, 8.7 Hz), 7.86 (d, 2H, J=7.6 Hz), 7.99 (d, 1H, J=8.2 Hz), 8.66 (d, 1H, J=8.2 Hz). ^{13}C NMR (126 MHz, $CDCl_3$): δ 39.3, 44.4, 124.5, 125.9, 126.8, 128.2, 128.4, 128.6, 130.2, 133.5, 134.1, 135.1, 200.6. IR (neat): 3050 (w), 2968 (w), 1682 (s), 1593 (m), 1573 (m), 1508 (s), 1337 (s), 1236 (s), 1099 (s), 944 (m), 801 (s), 776 (s) cm^{-1}. HRMS (EI, m/z): Calcd for $C_{13}H_{11}ClO$: 218.0498 (M^+). Found: 218.0495.

3.1.6. (Non-1-ynyl)trimethylsilane. The title compound was synthesized according to the procedure of Hanack and Haßdentenfel for related alkynyltrimethylsilanes.[15] The crude product was distilled under reduced pressure (65–68°C, 0.6 Torr) to afford the product as a colorless liquid (12.8 g, 90% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.14 (s, 9H), 0.88 (t, 3H, J=6.9 Hz), 1.2–1.4 (m, 8H), 1.51 (qnt, 2H, J=7.3 Hz), 2.21 (t, 2H, J=7.2 Hz). ^{13}C NMR (126 MHz, $CDCl_3$): δ 0.4, 14.3, 20.1, 22.8, 28.8, 29.0, 31.9, 84.4, 108.0. IR (neat): 2958 (s), 2931 (s), 2856 (s), 2176 (s), 1466 (m), 1249 (s), 1033 (m), 841 (s) cm^{-1}. HRMS (EI, m/z): Calcd for $C_{12}H_{24}Si$: 181.1413 (M-CH_3^+). Found: 181.1409.

3.1.7. 1-Chlorododec-4-yn-3-one. A mixture of (non-1-ynyl)trimethylsilane (12.7 g, 64.7 mmol) and 3-chloropropionyl chloride (8.23 g, 64.8 mmol) was added over 10 min to a stirred suspension of $AlCl_3$ (9.50 g, 71.2 mmol) in CH_2Cl_2 (150 mL) at 0°C. The yellow suspension slowly dissolved to form a brown solution. After the addition was complete, the reaction mixture was allowed to warm to room temperature and stirred for 1 h. The solution was then poured into a mixture of ice and CH_2Cl_2. The aqueous layer was extracted with CH_2Cl_2 (2×150 mL), and the combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated, to afford a brown liquid. The crude product was purified by column chromatography (30/70→75/25 $CHCl_3$/hexanes), which furnished the product as a yellow oil (10.9 g, 68% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.89 (t, 3H, J=7.0 Hz), 1.2–1.5 (m, 8H), 1.59 (qnt, 2H, J=7.3 Hz), 2.38 (t, 2H, J=7.2 Hz), 3.01 (t, 2H, J=7.2 Hz), 3.79 (t, 2H, J=6.7 Hz). ^{13}C NMR (126 MHz, C_6D_6): δ 14.1, 19.1, 22.7, 27.7, 28.8, 28.9, 31.7, 38.0, 47.8, 80.4, 96.3, 184.0. IR (neat): 2929 (s), 2857 (m), 2212 (m), 1678 (s), 1649 (m) cm^{-1}.

3.2. Asymmetric reduction of γ-chloroketones with DIP-Cl: general procedure

3.2.1. (*R*)-3-Chloro-1-(4′-trifluoromethylphenyl)propan-1-ol. A solution of (+)-DIP-Cl (2.67 g, 8.32 mmol) in THF (15 mL) was added dropwise to a −78°C solution of 3-chloro-1-(4′-trifluoromethylphenyl)propan-1-one (2.08 g, 8.81 mmol) in THF (10 mL). The reaction mixture was warmed from −25 to −30°C and stirred for 48 h, at which time the reaction mixture was quenched with MeOH (2 mL), followed by saturated NH_4Cl solution (50 mL). The resulting aqueous layer was extracted with Et_2O (3×50 mL), and the combined organic layers were added to $HN(CH_2CH_2OH)_2$ (2.53 g, 24.1 mmol). A large quantity of a white solid slowly precipitated. The solid was removed by filtration, and the filtrate was concentrated to a white slurry. The crude product was purified by column chromatography (4/96 Et_2O/benzene), which furnished the desired product as a colorless liquid (1.46 g, 67% yield). GC analysis showed >98% ee. ^1H NMR (500 MHz, $CDCl_3$): δ 2.08 (m, 1H), 2.12 (d, 1H, *J*=3.7 Hz), 2.21 (tdd, 1H, *J*=5.4, 8.9, 14.5 Hz), 3.58 (td, 1H, *J*=5.7, 11.0 Hz), 3.78 (ddd, 1H, *J*=5.2, 8.5, 11.0 Hz), 5.05 (td, 1H, *J*=4.0, 8.9 Hz), 7.50 (d, 2H, *J*=8.2 Hz), 7.63 (d, 2H, *J*=8.2 Hz). ^{13}C NMR (126 MHz, $CDCl_3$): δ 41.6, 41.6, 70.8, 124.3 (q, $^1J_{C-F}$= 272 Hz), 125.8 (q, $^3J_{C-F}$=3.8 Hz), 126.3, 130.3 (q, $^2J_{C-F}$= 32 Hz), 147.9. IR (neat): 3369 (m, br), 2967 (w), 2916 (w), 1621 (m), 1420 (m), 1327 (s), 1167 (s), 1127 (s), 1069 (s), 1017 (s), 840 (s) cm^{-1}. HRMS (EI, *m/z*): Calcd for $C_{10}H_{10}ClF_3O$: 238.0372 (M^+). Found: 238.0367. $[\alpha]^{20}_D$= +15° (*c*=0.56, $CHCl_3$, 98% ee).

3.2.2. (*R*)-3-Chloro-1-(4′-methoxyphenyl)propan-1-ol. The general procedure was followed with 3-chloro-1-(4′-methoxyphenyl)propan-1-one as the substrate. The crude product was first purified by column chromatography (25/75 Et_2O/pentane), followed by recrystallization (Et_2O/pentane, −10°C), which furnished a white, cotton-like solid (618 mg, 24% yield). GC analysis of the acetate derivative revealed >99% ee. A ^1H NMR spectrum showed that the product was still impure, but it was carried on to the next step without further purification. A pure sample of the alcohol was obtained by repeating the recrystallization. ^1H NMR (500 MHz, $CDCl_3$): δ 1.90 (dd, 1H, *J*=0.9, 3.4 Hz), 2.06 (m, 1H), 2.24 (tdd, 1H, *J*=5.8, 8.2, 14.3 Hz), 3.54 (td, 1H, *J*=6.0, 11.0 Hz), 3.72 (ddd, 1H, *J*=5.7, 8.1, 10.8 Hz), 3.81 (s, 3H), 4.90 (ddd, 1H, *J*=3.6, 4.7, 8.2 Hz), 6.90 (d, 2H, *J*=8.9 Hz), 7.29 (d, 2H, *J*=8.5 Hz). ^{13}C NMR (126 MHz, $CDCl_3$): δ 41.5, 42.0, 55.5, 71.2, 114.2, 127.3, 136.0, 159.5. IR (KBr): 3293 (m, br), 2960 (w), 2904 (w), 1612 (m), 1516 (m), 1288 (m), 1253 (s), 1179 (m), 1032 (m), 834 (m), 652 (m) cm^{-1}. HRMS (FAB, *m/z*): Calcd for $C_{10}H_{13}ClO_2$: 200.0604 (M^+). Found: 200.0608. Mp 59–60°C. $[\alpha]^{20}_D$= +16° (*c*=1.03, $CHCl_3$).

3.2.3. (*R*)-3-Chloro-1-(1′-naphthyl)propan-1-ol. The general procedure was followed with 3-chloro-1-(1′-naphthyl)propan-1-one as the substrate. The crude product was purified by column chromatography (15/85 Et_2O/pentane), which furnished a yellow liquid (1.26 g, 39% yield). ^1H NMR showed that the product was impure, but it was carried on to the next step without further purification. An analytical sample was obtained by synthesizing and purifying the 3,5-dinitrobenzoate ester derivative, and then regenerating the alcohol (MeOH/catalytic $NaHCO_3$). HPLC analysis showed 97% ee. ^1H NMR (500 MHz, C_6D_6): δ 1.35 (dd, 1H, *J*=1.2, 3.7 Hz), 1.87 (tdd, 1H, *J*=4.7, 9.6, 14.5 Hz), 2.0 (m, 1H), 3.23 (ddd, 1H, *J*=4.6, 5.8, 10.7 Hz), 3.63 (ddd, 1H, *J*=4.7, 9.8, 10.5 Hz), 5.37 (td, 1H, J=3.4, 9.2 Hz), 7.24–7.28 (m, 2H), 7.31 (ddd, 1H, *J*=1.2, 6.7, 8.5 Hz), 7.50 (d, 1H, *J*=7.0 Hz), 7.56 (d, 1H, *J*=8.2 Hz), 7.65 (d, 1H, *J*=8.5 Hz), 8.09 (d, 1H, *J*=8.2 Hz). ^{13}C NMR (126 MHz, $CDCl_3$): δ 40.9, 42.5, 68.1, 122.9, 123.1, 125.7, 125.9, 126.5, 128.5, 129.2, 130.2, 134.0, 139.7. IR (neat): 3382 (m, br), 3051 (w), 2962 (w), 1597 (w), 1511 (m), 1281 (m), 1070 (s), 801 (s), 778 (s) cm^{-1}. HRMS (EI, *m/z*): Calcd for $C_{13}H_{13}ClO$: 220.0655 (M^+). Found: 220.0660. $[\alpha]^{20}_D$=+40° (*c*=0.64, $CHCl_3$, 97% ee).

3.2.4. (*R*)-1-Chlorododec-4-yn-3-ol. Neat (*R*)-Alpine Borane (11.5 mL, 42.2 mmol) was slowly added to 1-chlorododec-4-yn-3-one (4.52 g, 21.1 mmol) at −20°C. The reaction mixture was stirred at −15 to −20°C for 4 days and at 0°C for 1 day. Then, the reaction mixture was diluted with Et_2O and quenched by the addition of acetaldehyde (2 mL). Ethanolamine (~1.4 g) was then added to the stirring mixture, and the resulting white precipitate was removed by filtration. Concentration of the filtrate afforded the crude product, which was purified twice by column chromatography (10/90 Et_2O/pentane), resulting in an impure yellow liquid (2.09 g, 46% yield). GC analysis showed 89% ee. In order to enhance the enantiomeric excess and purify the product, the 3,5-dinitrobenzoate ester of the alcohol was synthesized. A suspension of 3,5-$(O_2N)_2C_6H_3COCl$ (3.34 g, 14.5 mmol) and DMAP (128 mg, 1.05 mmol) in CH_2Cl_2 (20 mL) was added to a solution of the alcohol in CH_2Cl_2 (50 mL). The resulting mixture was cooled to 0°C, and Et_3N (2.0 mL, 14 mmol) was slowly added, resulting in a change from a heterogeneous yellow suspension to a brown solution. After 2 h, TLC showed no starting alcohol. The reaction mixture was diluted with CH_2Cl_2 (300 mL), washed with 1 M HCl and then a saturated $NaHCO_3$ solution, dried ($MgSO_4$), and concentrated, to afford a yellow oil. Purification by column chromatography (5/95→10/90 Et_2O/pentane) furnished the 3,5-dinitrobenzoate as a pale-yellow solid (1.49 g, 37% overall yield from the ketone). Recrystallization of this yellow solid from Et_2O/pentane afforded fine white needles (1.00 g), which HPLC analysis showed was >99% ee. The ester was then transesterified back to the alcohol. The pure 3,5-dinitrobenzoate (989 mg, 2.41 mmol) was dissolved in 15 mL MeOH/2 mL CH_2Cl_2. $NaHCO_3$ (156 mg, 1.85 mmol) was added, and the reaction mixture was stirred at room temperature. After 1 h, TLC showed no starting ester. The reaction mixture was diluted with HCl (200 mL), washed with 1 M HCl, dried ($MgSO_4$), and concentrated, to afford a white solid. This was purified by column chromatography (90/10 benzene/pentane), which furnished the desired product as a colorless liquid (471 mg, 90% yield). GC analysis confirmed that the product is enantiomerically pure (>99% ee). ^1H NMR (500 MHz, C_6D_6): δ 0.89 (t, 3H, *J*=7.2 Hz), 1.15–1.30 (m, 8H), 1.38 (qnt, 2H, *J*=7.2 Hz), 1.68 (d, 1H, *J*=5.2 Hz), 1.86–2.00 (m, 2H), 2.02 (dt, 2H, *J*=2.0, 7.1 Hz), 3.38 (td, 1H, *J*=6.3, 10.8 Hz), 3.46 (ddd, 1H, *J*=6.4, 7.3, 11.0 Hz), 4.44 (m, 1H). ^{13}C NMR (126 MHz, C_6D_6): δ 14.7, 19.2, 23.4, 29.3, 29.5, 29.5,

32.4, 41.4, 41.4, 60.2, 81.4, 86.2. IR (neat): 3346 (m, br), 2930 (s), 2857 (s), 2228 (w), 1456 (m), 1285 (m), 1045 (m), 662 (m) cm^{-1}. $[\alpha]^{20}_D=-3.1°$ (c=1.09, $CHCl_3$).

3.3. Assignment of absolute configuration of the alcohols

The absolute configurations of the 3-chloro-1-arylpropan-1-ols obtained from (+)-DIP-Cl were assigned as (*R*), based on the model proposed by Brown,[16] and the 1-chlorododec-4-yn-3-ol from (*R*)-Alpine Borane was assigned as (*R*), based on the model proposed by Midland.[17]

3.4. Preparation of oxetanes: general procedure

3.4.1. (*R*)-2-Phenyloxetane. A solution of (*R*)-3-chloro-1-phenylpropan-1-ol (943 mg, 5.53 mmol) in THF (8 mL) was slowly added by syringe to a 0°C suspension of KH (290 mg, 7.24 mmol) in THF (70 mL). The reaction mixture was then warmed to room temperature. After 15 h of stirring, it was poured into a mixture of 200 mL Et_2O/100 mL H_2O, and the aqueous layer was extracted with Et_2O (2×100 mL). The combined organic layers was washed with brine, dried (K_2CO_3), and concentrated, to afford a yellow liquid. Purification by column chromatography (1/4/96 Et_3N/Et_2O/pentane) furnished the desired compound as a light-yellow liquid (564 mg, 76% yield). GC analysis showed that the product is enantiomerically pure (>99% ee). $[\alpha]^{20}_D=+180°$ (c=1.52, EtOH).

(*S*)-2-Phenyloxetane was prepared similarly from (*S*)-3-chloro-1-phenylpropan-1-ol in 78% isolated yield. GC analysis showed that the product is enantiomerically pure (>99% ee).

3.4.2. (*R*)-2-(4′-Trifluoromethylphenyl)oxetane. The general procedure was followed with (*R*)-3-chloro-1-(4′-trifluoromethylphenyl)propan-1-ol as the substrate. The crude product was purified by column chromatography (1/9/90 Et_3N/Et_2O/pentane), which furnished the desired product as a colorless liquid (636 mg, 54% yield). GC analysis showed 97% ee. ^{1}H NMR (500 MHz, C_6D_6): δ 1.97 (dddd, 1H, J=7.0, 7.6, 9.1, 11.0 Hz), 2.33 (dtd, 1H, J=5.8, 8.2, 11.0 Hz), 4.19 (td, 1H, J=5.8, 9.2 Hz), 4.38 (dt, 1H, J=5.8, 7.9 Hz), 5.38 (t, 1H, J=7.6 Hz), 7.10 (d, 2H, J=8.5 Hz), 7.37 (d, 2H, J=8.2 Hz). ^{13}C NMR (126 MHz, C_6D_6): δ 30.9, 68.2, 81.8, 125.4 (q, $^1J_{C-F}$=272 Hz), 125.7, 125.9 (q, $^3J_{C-F}$=3.9 Hz), 130.0 (q, $^2J_{C-F}$=32 Hz), 148.8. IR (neat): 2965 (w), 2887 (w), 1619 (w), 1325 (s), 1165 (s), 1124 (s), 1067 (s), 983 (s), 838 (m) cm^{-1}. HRMS (EI, *m*/*z*): Calcd for $C_{10}H_9F_3O$: 202.0606 (M^+). Found: 202.0609. $[\alpha]^{20}_D=+113°$ (c=2.64, EtOH, 97% ee).

3.4.3. (*R*)-2-(4′-Methoxyphenyl)oxetane. The general procedure was followed with (*R*)-3-chloro-1-(4′-methoxyphenyl)propan-1-ol as the substrate. The crude product was purified by two column chromatographies (1/10/89 Et_3N/Et_2O/pentane), which furnished the desired product as a pale-yellow liquid that solidified on standing to a white solid (265 mg, 26% yield). HPLC analysis showed 98% ee. ^{1}H NMR (500 MHz, C_6D_6): δ 2.28 (tdd, 1H, J=7.6, 9.3, 10.8 Hz), 2.43 (dtd, 1H, J=5.4, 8.0, 10.7 Hz), 3.30 (s, 3H), 4.32 (td, 1H, J=5.7, 9.2 Hz), 4.47 (dt, 1H, J=5.7, 8.0 Hz), 5.59 (t, 1H, J=7.5 Hz), 6.83 (d, 2H, J=8.5 Hz), 7.31 (d, 2H, J=8.9 Hz). ^{13}C NMR (126 MHz, C_6D_6): δ 31.3, 54.8, 67.4, 82.4, 114.1, 127.0, 136.7, 159.8. IR (KBr): 3059 (m), 2972 (m), 2881 (s), 1593 (m), 1508 (m), 1328 (m), 1048 (m), 977 (s), 927 (s), 800 (s), 781 (s) cm^{-1}. HRMS (EI, *m*/*z*): Calcd for $C_{10}H_{12}O_2$: 164.0837 (M^+). Found: 164.0840. Mp 48–49°C. $[\alpha]^{20}_D=+141°$ (c=1.04, EtOH, 98% ee).

3.4.4. (*R*)-2-(1′-Naphthyl)oxetane. The general procedure was followed with (*R*)-3-chloro-1-(1′-naphthyl)propan-1-ol as the substrate. The crude product was purified by column chromatography (1/4/95 Et_3N/Et_2O/pentane), which furnished a white solid (695 mg, 70% yield; HPLC analysis: 97% ee). This was recrystallized from Et_2O/pentane at −35°C to afford a crystalline white solid (438 mg; HPLC analysis: >99% ee). ^{1}H NMR (500 MHz, C_6D_6): δ 2.18 (tdd, 1H, J=7.3, 8.9, 10.7 Hz), 2.62 (dtd, 1H, J=5.8, 8.2, 10.7 Hz), 4.32 (td, 1H, J=5.8, 9.2 Hz), 4.52 (ddd, 1H, J=5.7, 7.5, 8.2 Hz), 6.22 (t, 1H, J=7.6 Hz), 7.2–7.3 (m, 2H), 7.35–7.42 (m, 2H), 7.59 (d, 1H, J=8.2 Hz), 7.66–7.70 (m, 1H), 8.06 (td, 1H, J=1.2, 7.0 Hz). ^{13}C NMR (126 MHz, C_6D_6): δ 30.7, 68.5, 80.8, 122.2, 123.5, 126.1, 126.3, 126.4, 128.1, 129.5, 129.8, 134.5, 140.6. IR (KBr): 2999 (w), 2958 (m), 2882 (m), 1611 (m), 1514 (s), 1250 (s), 1034 (m), 957 (m), 832 (m) cm^{-1}. HRMS (FAB, *m*/*z*): Calcd for $C_{13}H_{12}O$: 185.0966 ($M+H^+$). Found: 185.0963. Mp 73–74°C. $[\alpha]^{20}_D=+250°$ (c=1.05, EtOH).

3.4.5. (*R*)-2-(Non-1′-ynyl)oxetane. The general procedure was followed with (*R*)-1-chlorododec-4-yn-3-ol as the substrate. The crude product was purified by column chromatography (1/4/95 Et_3N/Et_2O/pentane), which furnished a yellow liquid (149 mg, 38% yield). The ^{1}H NMR matched the literature data.[2f] ^{13}C NMR (126 MHz, C_6D_6): δ 14.7, 19.5, 23.3, 29.3, 29.5, 29.5, 30.5, 32.4, 68,4, 70.5, 81.9, 89.6. HRMS (EI, *m*/*z*): Calcd for $C_{12}H_{20}O$: 180.1514 (M^+). Found: 180.1511. $[\alpha]^{20}_D=+92°$ (c=1.7, $CHCl_3$). lit.[2f] $[\alpha]^{20}_D=+33.3°$ (c=1.51, $CHCl_3$).

3.5. Reaction in Eq. (4)

A solution of (*R*,*R*)-**2** (5.4 mg, 10 μmol) in CH_2Cl_2 (2 mL) was added to CuOTf·0.5C_6H_6 (2.4 mg, 9.5 μmol) and stirred for 90 min. The resulting solution was filtered through an acrodisc to afford an orange solution. Half of this solution was transferred to a flask containing (±)-2-phenyloxetane (128 mg, 0.955 mmol), and CH_2Cl_2 was then added until the total volume was 2.5 mL. A solution of *t*-butyl diazoacetate (67.6 mg, 0.476 mmol) in CH_2Cl_2 (0.75 mL) was added to the reaction mixture by a syringe pump over 45 min. After one more hour, the reaction mixture was filtered through a plug of silica gel (1% Et_3N/Et_2O as the eluant). GC analysis showed that the product was a 55:45 *trans*/*cis* mixture and that both diastereomeric products were formed in 71% ee. The residual oxetane had an ee <1%. The reaction was repeated with (*S*,*S*)-**2**. GC analysis of the crude reaction product revealed a 55:45 *trans*/*cis* mixture, with the *trans* product formed in 71% ee and the *cis* product in 73% ee. The residual starting oxetane had an ee <1%. The ^{1}H NMR spectrum of the diastereomers matched the literature data.[2c]

***t*-Butyl (2*S*,3*R*)-3-phenyltetrahydrofuran-2-carboxylate.**

^{13}C NMR (126 MHz, $CDCl_3$): δ 28.2, 35.1, 50.1, 69.6, 81.6, 84.0, 127.0, 127.5, 128.8, 142.1, 172.1.

***t*-Butyl (2*S*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate.** ^{13}C NMR (126 MHz, C_6D_6): δ 27.7, 31.8, 48.1, 68.9, 81.2, 81.8, 127.1, 128.4, 128.6, 139.5, 170.2.

3.6. General procedure—Table 1

A solution of (*R*,*R*)-**2** (4.4 mg, 8.4 μmol) in EtOAc (2 mL) was added to CuOTf·0.5C_6H_6 (1.8 mg, 7.2 μmol) and stirred for 30 min. The catalyst solution was then filtered through an acrodisc to afford an orange solution. Half of this solution was transferred to a flask containing (*R*)-2-phenyloxetane (48.7 mg, 0.363 mmol), and EtOAc was added until the total volume was 2.5 mL. The solution was stirred for 5 min in a water bath maintained at 20°C, and then a solution of the diazo ester (0.48 mmol) in EtOAc (1 mL) was added over 5 min to the reaction mixture. After 30 min, the reaction mixture was filtered through a plug of silica gel (Et_2O as the eluant) to afford the crude product.

3.6.1. Table 1, entry 1. Run 1: 81:19 *trans*/*cis*; *trans* ee=91% ee (major enantiomer: 2*S*,3*R*). Run 2 (with (*S*,*S*)-**2**, (*S*)-oxetane): 82:18 *trans*/*cis*; *trans* ee=92% ee (major enantiomer: 2*R*,3*S*).

Ethyl (2*R*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.85 (t, 3H, *J*=7.2 Hz), 1.68 (qd, 1H, *J*=7.8, 12.4 Hz), 1.99 (dtd, 1H, *J*=4.6, 7.5, 12.2 Hz), 3.45 (dt, 1H, *J*=6.0, 7.7 Hz), 3.90 (m, 3H), 4.02 (dt, 1H, *J*=6.7, 8.2 Hz), 4.52 (d, 1H, *J*=5.8 Hz), 7.00–7.06 (m, 1H), 7.08 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 14.4, 35.1, 49.8, 61.2, 69.7, 83.6, 127.1, 127.4, 128.9, 141.9, 172.9. IR (neat): 3030 (w), 2979 (m), 2878 (m), 1747 (s), 1603 (w), 1493 (w), 1455 (w), 1266 (m), 1192 (s), 1098 (s), 759 (m), 700 (s) cm^{-1}. HRMS (FAB, *m*/*z*): Calcd for $C_{13}H_{16}O_3$: 220.1099 (M^+). Found: 220.1105. $[\alpha]^{20}_D$=−99° (*c*=0.99, EtOH, 92% ee).

3.6.2. Table 1, entry 2. Run 1: 90:10 *trans*/*cis*; *trans* ee=95% ee (major enantiomer: 2*S*,3*R*). Run 2 (with (*S*,*S*)-**2**, (*S*)-oxetane, (L)-menthyl diazoacetate): 90:10 *trans*/*cis*; *trans* ee=95% ee (major enantiomer: 2*R*,3*S*).

(L)-Menthyl (2*R*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.58 (dq, 1H, *J*=3.9, 12.7 Hz), 0.72 (d, 3H, *J*=6.4 Hz), 0.76 (d, 3H, *J*=4.9 Hz), 0.78 (d, 3H, *J*=4.9 Hz), 0.75–0.82 (m, 1H), 0.86 (q, 1H, *J*=11.6 Hz), 1.08–1.18 (m, 1H), 1.21 (tdd, 1H, *J*=3.1, 11.0, 12.3 Hz), 1.36–1.44 (m, 2H), 1.71 (ddd, 1H, *J*=8.5, 12.2, 16.5 Hz), 1.77 (dtd, 1H, *J*=2.8, 7.2, 14.4 Hz), 1.98–2.05 (m, 2H), 3.53 (dt, 1H, *J*=6.6, 8.0 Hz), 3.94 (dt, 1H, *J*=3.8, 8.0 Hz), 4.06 (dt, *J*=6.6 Hz, 1H, 8.5), 4.58 (d, 1H, *J*=6.4 Hz), 4.85 (dt, 1H, *J*=4.3, 10.8 Hz), 7.0–7.06 (m, 1H), 7.10–7.14 (m, 4H). ^{13}C NMR (126 MHz, C_6D_6): δ 16.6, 21.2, 22.4, 23.8, 26.5, 31.8, 34.7, 36.1, 41.4, 47.4, 51.0, 70.0, 74.9, 84.6, 127.4, 127.9, 129.3, 142.4, 172.8. IR (neat): 3063 (w), 3029 (w), 2954 (s), 2870 (s), 1742 (s), 1604 (w), 1494 (m), 1455 (s), 1371 (m), 1265 (m), 1193 (s), 1099 (s), 986 (m), 758 (m), 700 (s) cm^{-1}. HRMS (FAB, *m*/*z*): Calcd for $C_{21}H_{30}O_3$: 330.2195 (M^+). Found: 330.2205. $[\alpha]^{20}_D$=−135° (*c*=1.29, EtOH, 96% de).

3.6.3. Table 1, entry 3. Run 1: 91:9 *trans*/*cis*; *trans* ee=97% ee (major enantiomer: 2*S*,3*R*). Run 2 (with (*S*,*S*)-**2**, (*S*)-oxetane, (D)-menthyl diazoacetate): 90:10 *trans*/*cis*; *trans* ee=97% ee (major enantiomer: 2*R*,3*S*).

(D)-Menthyl (2*R*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.59 (dq, 1H, *J*=3.8, 12.7 Hz), 0.75 (d, 3H, *J*=6.4 Hz), 0.79 (d, 3H, *J*=4.9 Hz), 0.80 (d, 3H, *J*=4.6 Hz), 0.7–0.85 (m, 1H), 0.89 (q, 1H, *J*=11.7 Hz), 1.1–1.2 (m, 1H), 1.26 (tdd, 1H, *J*=3.1, 11.0, 12.4 Hz), 1.36–1.44 (m, 2H), 1.71 (qd, 1H, *J*=7.8, 12.4 Hz), 1.93–2.08 (m, 3H), 3.56 (dt, 1H, *J*=5.8, 7.6 Hz), 3.94 (dt, 1H, *J*=4.3, 8.1 Hz), 4.08 (dt, 1H, *J*=7.0, 8.2 Hz), 4.60 (d, 1H, *J*=5.8 Hz), 4.93 (dt, 1H, *J*=4.4, 10.9 Hz), 7.08 (tt, 1H, *J*=1.8, 6.9 Hz), 7.09–7.15 (m, 4H). ^{13}C NMR (126 MHz, C_6D_6): δ 16.8, 21.2, 22.5, 23.9, 26.8, 31.8, 34.7, 35.5, 41.5, 47.5, 50.5, 69.8, 74.8, 84.5, 127.4, 127.9, 129.3, 143.0, 172.5. IR (neat): 3063 (w), 3029 (w), 2954 (s), 2870 (s), 1743 (s), 1604 (w), 1494 (m), 1455 (s), 1370 (m), 1264 (s), 1194 (s), 1100 (s), 986 (m), 758 (m), 700 (m) cm^{-1}. HRMS (FAB, *m*/*z*): Calcd for $C_{21}H_{30}O_3$: 330.2195 (M^+). Found: 330.2202. $[\alpha]^{20}_D$=−38° (*c*=1.10, EtOH, >99.5% de).

3.6.4. Table 1, entry 4. Run 1: 90:10 *trans*/*cis*; *trans* ee=97% ee (major enantiomer: 2*S*,3*R*). Run 2 (with (*S*,*S*)-**2**, (*S*)-oxetane): 90:10 *trans*/*cis*; *trans* ee=97% ee (major enantiomer: 2*R*,3*S*).

3.6.5. Table 1, entry 5. Run 1: 95:5 *trans*/*cis*; *trans* ee=98% ee (major enantiomer: 2*S*,3*R*). Run 2 (with (*S*,*S*)-**2**, (*S*)-oxetane): 95:5 *trans*/*cis*; *trans* ee=98% (major enantiomer: 2*R*,3*S*).

1′,1′-Dicyclohexylethyl (2*R*,3*S*)-3-phenyltetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.9–1.2 (m, 10H), 1.43 (s, 3H), 1.5–1.8 (m, 11H), 1.85 (t qnt, 2H, *J*=2.8, 11.6 Hz), 2.03 (dddd, 1H, *J*=4.3, 6.7, 7.6, 11.9 Hz), 3.54 (dt, 1H, *J*=6.4, 7.9 Hz), 3.93 (dt, 1H, *J*=4.0, 8.1 Hz), 4.04 (dt, 1H, *J*=6.7, 8.5 Hz), 4.51 (d, 1H, *J*=6.4 Hz), 7.02–7.06 (m, 1H), 7.10– 7.16 (m, 4H). ^{13}C NMR (125 MHz, C_6D_6): δ 19.8, 27.2, 27.5, 27.6, 28.2, 28.2, 28.6, 28.7, 36.0, 45.5, 50.6, 69.8, 85.2, 91.1, 127.3, 128.0, 129.2, 142.9, 172.2. IR (neat): 2929 (s), 2852 (s), 1742 (s), 1449 (s), 1190 (s), 1100 (s), 755 (m), 700 (s) cm^{-1}. HRMS (FAB, *m*/*z*): Calcd for $C_{25}H_{36}O_3$: 385.2743 ($M+H^+$). Found: 385.2732. $[\alpha]^{20}_D$=−63° (*c*=1.00, EtOH, 98% ee).

3.7. General procedure—Tables 2 and 3

A solution of (*R*,*R*)-**2** (4.7 mg, 8.9 μmol) in EtOAc (1 mL) was added to CuOTf·0.5C_6H_6 (1.9 mg, 7.5 μmol) and stirred for 1 h. The catalyst solution was then filtered through an acrodisc to afford an orange solution. Half of this solution was added to a flask containing the oxetane (0.39 mmol), and EtOAc was added until the total volume was 0.8 mL. The solution was stirred for 5 min in a water bath maintained at 20°C, and then a solution of the diazoacetate (170 mg, 0.62 mmol) in EtOAc (1 mL) was added to the reaction mixture in four batches over 3 h. After one additional hour, the reaction mixture was filtered through a plug of silica gel (Et_2O as the eluant).

3.7.1. Table 2, entry 1. Run 1 was carried out using (*R*)-oxetane (77.1 mg, 0.575 mmol) and the diazoacetate (208 mg, 0.746 mmol). 1,3-Diisopropylbenzene (111 mg, 0.685 mmol) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the *trans* tetrahydrofuran was 77% (C_6D_6). NMR analysis showed that the product was a 95:5 *trans*/*cis* mixture. The crude product was purified by column chromatography (5/95 Et_2O/pentane), which afforded a mixture of *trans* (98% ee, major enantiomer: 2*S*,3*R*) and *cis* (20% ee, major enantiomer: 2*R*,3*R*) tetrahydrofurans (145 mg, 66% yield) as colorless liquids. Run 2 was carried out similarly with (*S*)-oxetane and (*S*,*S*)-**2**. NMR analysis showed that the product was a 95:5 *trans*/*cis* mixture. Column chromatography afforded a mixture of *trans* (98% ee, major enantiomer: 2*R*,3*S*) and *cis* (22% ee, major enantiomer: 2*S*,3*S*) tetrahydrofurans (146 mg, 83% yield).

3.7.2. Table 2, entry 2. Run 1 was carried out using (*R*)-oxetane (78.1 mg, 0.386 mmol) and the diazoacetate (172 mg, 0.617 mmol). 1,3-Diisopropylbenzene (69.4 mg, 0.428 mmol) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the *trans* tetrahydrofuran was 91% (C_6D_6). NMR analysis showed that the product was a 94:6 *trans*/*cis* mixture. The crude product was purified first by column chromatography (10/90 EtOAc/hexanes), and then by preparative achiral HPLC (15/85 EtOAc/hexanes), which afforded the *trans* tetrahydrofuran (139 mg, 79% yield, 99% ee, major enantiomer: 2*S*,3*R*) and the *cis* tetrahydrofuran (1% ee, major enantiomer: 2*S*,3*S*) as colorless liquids. Run 2 was carried out similarly. NMR analysis revealed that the crude product was a 94:6 *trans*/*cis* mixture and that the yield of the *trans* tetrahydrofuran was 89%. Column chromatography, followed by preparative achiral HPLC, afforded the *trans* tetrahydrofuran (171 mg, 82% yield, 98% ee, major enantiomer: 2*S*,3*R*) and the *cis* tetrahydrofuran (6% ee, major enantiomer: 2*R*,3*R*).

1′,1′-Dicyclohexylethyl (2*S*,3*R*)-3-(4″-trifluoromethylphenyl)tetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.9–1.2 (m, 10H), 1.41 (s, 3H), 1.50–1.75 (m, 13H), 1.94 (dtd, 1H, *J*=4.4, 7.5, 12.0 Hz), 3.40 (dt, 1H, *J*=6.4, 7.9 Hz), 3.86 (dt, 1H, *J*=4.0, 8.1 Hz), 3.99 (dt, 1H, *J*=6.9, 8.3 Hz), 4.35 (d, 1H, *J*=6.1 Hz), 6.93 (d, 2H, *J*=7.9 Hz), 7.31 (d, 2H, *J*=7.9 Hz). ^{13}C NMR (126 MHz, $CDCl_3$): δ 19.3, 26.6, 26.7, 27.0, 27.0, 27.0, 27.6, 27.6, 28.1, 28.2, 35.8, 44.9, 44.9, 49.9, 69.5, 83.9, 92.3, 124.3 (q, $^1J_{C-F}$=272 Hz), 125.8 (q, $^3J_{C-F}$=3.8 Hz), 127.9, 129.4 (q, $^2J_{C-F}$=32.3 Hz), 146.3, 171.7. IR (neat): 2933 (s), 2854 (s), 1745 (s), 1620 (m), 1449 (s), 1327 (s), 1165 (s), 1124 (s), 1069 (s), 1017 (m), 834 (m) cm^{-1}. HRMS (FAB, *m*/*z*): Calcd for $C_{26}H_{35}F_3O_3$: 452.2538 (M^+). Found: 452.2546. $[\alpha]^{20}_D$=+52° (*c*=1.05, EtOH, 99% ee).

3.7.3. Table 2, entry 3. The general procedure was used to prepare the catalyst solution. In a 4 mL vial, the (*R*)-oxetane (39.0 mg, 0.238 mmol) and the diazoacetate (99.4 mg, 0.357 mmol) were dissolved in EtOAc (0.5 mL) and stirred for 5 min in a water bath maintained at 20°C. The catalyst solution was added to the stirring reaction mixture, and after 1 h the reaction mixture was filtered through a plug of silica with Et_2O as the eluant. 1,3-Diisopropylbenzene (51.4 mg, 0.317 mmol) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the *trans* tetrahydrofuran was 32% (C_6D_6). NMR analysis showed that the product was a 75:25 *trans*/*cis* mixture. The crude product was purified first by column chromatography (10/90 Et_2O/pentane) and then by preparative achiral HPLC (10/90 EtOAc/hexanes), which afforded the *trans* tetrahydrofuran (25.9 mg, 26% yield, 68% ee, major enantiomer: 2*S*,3*R*) and the *cis* tetrahydrofuran (53% ee, major enantiomer: 2*R*,3*R*) as colorless liquids. Run 2 was carried out similarly. NMR analysis revealed that the crude product was a 76:24 *trans*/*cis* mixture and that the yield of the *trans* tetrahydrofuran was 36%. Column chromatography, followed by preparative achiral HPLC, afforded the *trans* tetrahydrofuran (32.0 mg, 32% yield, 70% ee, major enantiomer: 2*S*,3*R*) and the *cis* tetrahydrofuran (52% ee, major enantiomer: 2*R*,3*R*).

1′,1′-Dicyclohexylethyl (2*S*,3*R*)-3-(4″-methoxyphenyl)tetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.95–1.2 (m, 10H), 1.45 (s, 3H), 1.55–1.61 (m, 2H), 1.63–1.94 (m, 11H), 2.04 (dddd, 1H, *J*=4.0, 7.0, 7.6, 11.9 Hz), 3.31 (s, 3H), 3.54 (dt, 1H, *J*=6.7, 8.1 Hz), 3.96 (dt, 1H, *J*=3.8, 8.0 Hz), 4.06 (dt, 1H, *J*=6.7, 8.5 Hz), 4.50 (d, 1H, *J*=6.4 Hz), 6.76 (d, 2H, *J*=8.8 Hz), 7.08 (d, 2H, *J*=8.5 Hz). ^{13}C NMR (126 MHz, C_6D_6): δ 19.8, 27.2, 27.2, 27.6, 27.6, 28.2, 28.3, 28.7, 28.7, 36.2, 45.5, 50.0, 55.1, 69.8, 85.4, 91.0, 114.7, 129.0, 134.6, 159.4, 172.3. IR (neat): 2929 (s), 2852 (s), 1741 (s), 1613 (m), 1514 (s), 1448 (m), 1249 (s), 1180 (s), 1098 (s), 1036 (m), 827 (m) cm^{-1}. HRMS (FAB, *m*/*z*): Calcd for $C_{26}H_{38}O_4$: 453.2407 ($M+K^+$). Found: 453.2417. $[\alpha]^{20}_D$=+43° (*c*=0.86, EtOH, 70% ee).

3.7.4. Table 2, entry 4. Run 1 was carried out using (*R*)-oxetane (69.5 mg, 0.377 mmol) and the diazoacetate (170 mg, 0.610 mmol). Anisole (81.1 mg, 0.750 mmol) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the *trans* tetrahydrofuran was 74% (C_6D_6). NMR analysis showed that the product was an 86:14 *trans*/*cis* mixture. The crude product was purified first by column chromatography (10/90 Et_2O/pentane) and then by preparative achiral HPLC (1/99 *i*-PrOH/hexanes), which afforded the *trans* tetrahydrofuran (126 mg, 77% yield, 91% ee, major enantiomer: 2*S*,3*R*) and the *cis* tetrahydrofuran (7% ee, major enantiomer: 2*S*,3*S*) as colorless liquids. Run 2 was carried out similarly. NMR analysis revealed that the crude product was an 86:14 *trans*/*cis* mixture and that the yield of the *trans* tetrahydrofuran was 72% (C_6D_6). Column chromatography, followed by preparative achiral HPLC, afforded the *trans* tetrahydrofuran (146 mg, 73% yield, 91% ee, major enantiomer: 2*S*,3*R*) and the *cis* tetrahydrofuran (14% ee, major enantiomer: 2*S*,3*S*).

1′,1′-Dicyclohexylethyl (2*S*,3*R*)-3-(1″-naphthyl)tetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.8–1.2 (m, 10H), 1.44 (s, 3H), 1.5–1.9 (m, 13H), 2.27 (tdd, 1H, *J*=6.6, 7.9, 13.1 Hz), 4.02 (dt, 1H, *J*=5.8, 7.9 Hz), 4.24 (dt, 1H, *J*=6.6, 8.0 Hz), 4.41 (td, 1H, *J*=5.0, 8.2 Hz), 4.79 (d, 1H, *J*=4.3 Hz), 7.23 (t, 1H, *J*=7.6 Hz), 7.28 (ddd, 1H, *J*=1.2, 6.9, 8.1 Hz), 7.32 (d, 1H, *J*=6.4 Hz), 7.37 (ddd, 1H, *J*=1.4, 6.9, 8.5 Hz), 7.55 (d, 1H, *J*=8.2 Hz), 7.66 (d, 1H,

J=7.9 Hz), 8.21 (d, 1H, J=8.5 Hz). ^{13}C NMR (126 MHz, C_6D_6): δ 19.4, 26.8, 26.8, 27.1, 27.2, 27.2, 27.8, 27.9, 28.3, 28.4, 34.0, 45.1, 45.1, 45.3, 69.3, 84.0, 90.9, 123.7, 123.8, 125.8, 125.8, 126.3, 127.7, 129.4, 132.3, 134.6, 138.7, 172.1. IR (neat): 3048 (m), 2926 (s), 2852 (s), 1738 (s), 1598 (m), 1512 (m), 1383 (s), 1279 (s), 1193 (s), 1106 (s), 1086 (s), 933 (m), 778 (s) cm^{-1}. HRMS (FAB, *m/z*): Calcd for $C_{29}H_{38}O_3$: 434.2828 (M^+). Found: 434.2828. $[\alpha]^{20}_D$= +32.8° (c=1.02, EtOH, 91% ee).

3.7.5. Table 2, entry 5. Run 1 was carried out using (*R*)-oxetane (46.3 mg, 0.257 mmol) and the diazoacetate (108 mg, 0.386 mmol). 1,3-Diisopropylbenzene (23.2 mg, 0.143 mmol) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the *trans* tetrahydrofuran was 68% (C_6D_6). NMR analysis showed that the product was an 87:13 *trans*/*cis* mixture. The crude product was purified by column chromatography (4/96 Et_2O/pentane), which afforded the *trans* tetrahydrofuran (65.2 mg, 59% yield, 96% ee, major enantiomer: 2*S*,3*R*) and the *cis* tetrahydrofuran (17% ee, major enantiomer: 2*R*,3*R*) as colorless liquids. Run 2 was carried out similarly. NMR analysis revealed that the crude product was a 90:10 *trans*/*cis* mixture and that the yield of the *trans* tetrahydrofuran was 76% (C_6D_6). Column chromatography afforded the *trans* tetrahydrofuran (135 mg, 69% yield, 97% ee, major enantiomer: 2*S*,3*R*) and the *cis* tetrahydrofuran (8% ee, major enantiomer: 2*R*,3*R*).

1′,1′-Dicyclohexylethyl (2*S*,3*R*)-3-(non-1″-ynyl)tetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.89 (t, 3H, J=7.0 Hz), 1.0–1.4 (m, 18H), 1.41 (m, 2H), 1.47 (s, 3H), 1.60 (m, 2H), 1.65–2.0 (m, 12H), 2.07 (dt, 2H, J=2.3, 7.1 Hz), 3.30 (ttd, 1H, J=2.0, 5.6, 9.7 Hz), 3.84 (m, 2H), 4.58 (d, 1H, J=6.1 Hz). ^{13}C NMR (126 MHz, C_6D_6): δ 14.7, 19.5, 19.8, 23.4, 27.3, 27.3, 27.6, 27.6, 27.7, 28.3, 28.3, 28.8, 28.8, 29.5, 29.6, 29.6, 32.5, 34.7, 36.1, 45.5, 45.5, 69.3, 80.6, 83.0, 84.5, 91.4, 171.4. IR (neat): 2927 (s), 2853 (s), 1745 (s), 1449 (s), 1380 (m), 1283 (m), 1251 (m), 1191 (s), 1098 (s) cm^{-1}. $[\alpha]^{20}_D$=+72° (c=1.11, EtOH, 97% ee).

3.7.6. Table 3, entry 1. Run 1 was carried out using (*R*)-oxetane (61.5 mg, 0.458 mmol) and the diazoacetate (166 mg, 0.597 mmol). NMR analysis showed that the product was an 84:16 *cis*/*trans* mixture. The crude product was purified by column chromatography (5/95 Et_2O/pentane), which afforded a mixture of *trans* (24% ee, major enantiomer: 2*R*,3*S*) and *cis* (95% ee, major enantiomer: 2*R*,3*R*) tetrahydrofurans (120 mg, 68% yield) as colorless liquids. Run 2 was carried out similarly with (*S*)-oxetane and (*R*,*R*)-**2**. 1,3-Diisopropylbenzene (135 mg, 0.832 mmol) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the *cis* tetrahydrofuran was 74% (C_6D_6). NMR analysis showed that the product was an 84:16 *cis*/*trans* mixture. Column chromatography afforded a mixture of *trans* (23% ee, major enantiomer: 2*S*,3*R*) and *cis* (95% ee, major enantiomer: 2*S*,3*S*) tetrahydrofurans (181 mg, 81% yield).

1′,1′-Dicyclohexylethyl (2*R*,3*R*)-3-phenyltetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.71 (dq, 1H, J=3.4, 12.4 Hz), 0.86–1.16 (m, 9H), 1.24 (s, 3H), 1.4–1.5 (m, 2H), 1.5–1.7 (m, 9H), 1.73–1.9 (m, 2H), 2.29 (qd, 1H, J=8.7, 11.9 Hz), 3.27 (q, 1H, J=8.1 Hz), 3.74 (q, 1H, J=7.8 Hz), 4.26 (dt, 1H, J =3.7, 8.4), 4.58 (d, 1H, J= 7.6 Hz), 7.05 (m, 1H), 7.14 (t, 2H, J=7.6 Hz), 7.20 (d, 2H, J=8.2 Hz). ^{13}C NMR (126 MHz, C_6D_6): δ 19.5, 27.2, 27.2, 27.6, 27.6, 27.7, 27.8, 28.2, 28.2, 28.6, 31.6, 45.3, 45.4, 48.6, 68.8, 83.0, 91.0, 127.4, 128.8, 129.2, 139.5, 170.6. IR (neat): 2930 (s), 2852 (s), 1732 (s), 1449 (s), 1381 (m), 1243 (s), 1193 (s), 1101 (s), 1083 (s), 698 (s) cm^{-1}. HRMS (FAB, *m/z*): Calcd for $C_{25}H_{36}O_3$: 385.2743 ($M+H^+$). Found: 385.2735. $[\alpha]^{20}_D$=−44° (c=0.65, EtOH, 95% ee).

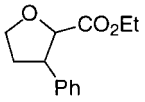
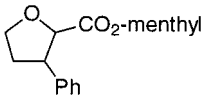
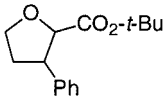
3.7.7. Table 3, entry 2. The reaction was carried out using (*R*)-oxetane (32.5 mg, 0.161 mmol) and the diazoacetate (70.8 mg, 0.254 mmol). 1,3-Diisopropylbenzene (32.9 mg, 0.203 mmol) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the *cis* tetrahydrofuran was 62% (C_6D_6). NMR analysis showed that the product was an 86:14 *cis*/*trans* mixture. The crude product was purified first by column chromatography (10/90 EtOAc/hexanes) and then by preparative achiral HPLC (15/85 EtOAc/hexanes), which afforded the *trans* tetrahydrofuran (17% ee, major enantiomer: 2*R*,3*S*) and the *cis* tetrahydrofuran (37.8 mg, 52% yield, 95% ee, major enantiomer: 2*R*,3*R*) as colorless liquids.

1′,1′-Dicyclohexylethyl (2*R*,3*R*)-3-(4″-trifluoromethylphenyl)tetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.63 (dq, 1H, J=3.3, 12.3 Hz), 0.8–0.9 (m, 2H), 0.95–1.1 (m, 7H), 1.18 (s, 3H), 1.3–1.4 (m, 2H), 1.5–1.8 (m, 11H), 2.07 (qd, 1H, J=8.4, 12.0 Hz), 3.10 (q, 1H, J=7.9 Hz), 3.68 (q, 1H, J=7.9 Hz), 4.17 (dt, 1H, J=4.0, 8.4 Hz), 4.45 (d, 1H, J=7.6 Hz), 7.05 (d, 2H, J=7.9 Hz), 7.36 (d, 2H, J=8.2 Hz). ^{13}C NMR (126 MHz, C_6D_6): δ 19.0, 26.8, 26.8, 27.1, 27.1, 27.2, 27.2, 27.4, 27.8, 27.9, 28.2, 31.3, 44.9, 45.0, 47.8, 68.3, 82.3, 91.3, 125.0 (q, $^1J_{C-F}$= 272 Hz), 125.4 (q, $^3J_{C-F}$=3.8 Hz), 129.2, 129.3 (q, $^2J_{C-F}$= 32.2 Hz), 143.6, 169.7. IR (neat): 2932 (s), 2854 (s), 1733 (s), 1619 (m), 1449 (m), 1327 (s), 1165 (s), 1125 (s), 1070 (s), 849 (m) cm^{-1}. HRMS (FAB, *m/z*): Calcd for $C_{26}H_{35}F_3O_3$: 452.2538 (M^+). Found: 452.2528. $[\alpha]^{20}_D$= −32° (c=0.62, EtOH, 95% ee).

3.7.8. Table 3, entry 3. The same procedure as for Table 2, entry 3 was followed, using (*R*)-oxetane (19.7 mg, 0.120 mmol) and the diazoacetate (50.3 mg, 0.181 mmol). 1,3-Diisopropylbenzene (18.3 mg, 0.113 mmol) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the *cis* tetrahydrofuran was 29% (C_6D_6). NMR analysis showed that the product was a 58:42 *cis*/*trans* mixture. The crude product was purified first by column chromatography (10/90 Et_2O/pentane) and then by preparative achiral HPLC (10/90 EtOAc/hexanes), which afforded the *trans* tetrahydrofuran (36% ee, major enantiomer: 2*S*,3*R*) and the *cis* tetrahydrofuran (9.8 mg, 20% yield, 82% ee, major enantiomer: 2*R*,3*R*) as colorless liquids.

1′,1′-Dicyclohexylethyl (2*R*,3*R*)-3-(4″-methoxyphenyl)-tetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.73 (dq, 1H, J=3.5, 12.5 Hz), 0.9–1.2 (m, 9H), 1.29 (s, 3H), 1.4–1.5 (m, 2H), 1.5–1.7 (m, 9H), 1.75–1.85 (m, 2H), 2.31 (qd, 1H, J=8.7, 11.8 Hz), 3.28 (q, 1H, J=

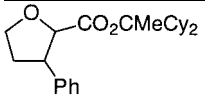
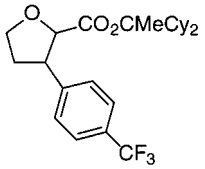
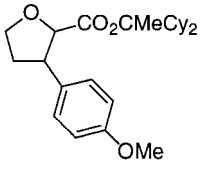
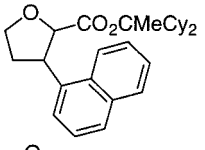
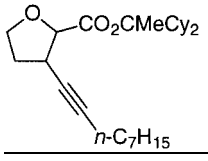
Table 4. GC data (DB-1701)

Compound	Temperature (°C)	Carrier gas flow (mL/min)	*trans* t_R (min)	*cis* t_R (min)
	130	He, 1.0	33.2	31.2
	180	He, 1.0	47.7, 48.0	44.2, 44.8
	130	He, 1.0	40.3	39.3

9.2 Hz), 3.34 (s, 3H), 3.77 (q, 1H, *J*=7.8 Hz), 4.29 (dt, 1H, *J*=3.7, 8.4 Hz), 4.59 (d, 1H, *J*=7.6 Hz), 6.78 (d, 2H, *J*=8.5 Hz), 7.14 (d, 2H, *J*=8.6 Hz). ^{13}C NMR (126 MHz, C_6D_6): δ 19.5, 27.2, 27.2, 27.6, 27.6, 27.7, 27.8, 28.2, 28.2, 28.6, 31.8, 45.3, 45.5, 47.9, 55.1, 68.9, 83.1, 91.0, 114.3, 130.2, 131.4, 159.5, 170.8. IR (thin film): 2929 (s), 2851 (s), 1733 (s), 1613 (w), 1514 (s), 1448 (m), 1248 (s), 1181 (m), 1096 (m), 1073 (m), 1036 (m), 840 (w), 806 (w) cm^{-1}. HRMS (ESI, *m*/*z*): Calcd for $C_{26}H_{38}O_4$: 437.2662 ($M+Na^+$). Found: 437.2649. $[\alpha]^{20}_D=-33°$ (*c*=0.91, EtOH, 82% ee).

3.7.9. Table 3, entry 4. The reaction was carried out using (*R*)-oxetane (29.5 mg, 0.160 mmol) and the diazoacetate (71.4 mg, 0.256 mmol). Anisole (28.1 mg, 0.260 mmol) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the *cis* tetrahydrofuran was 70% (C_6D_6). NMR analysis showed that the product was an 85:15 *cis*/*trans* mixture. The crude product was purified first by column chromatography (10/90 Et_2O/pentane) and then by preparative achiral HPLC (1/99 *i*-PrOH/hexanes), which afforded the *trans* tetrahydrofuran (18% ee, major enantiomer: 2*R*,3*S*) and the *cis* tetrahydrofuran (49.9 mg, 72% yield, 95% ee, major enantiomer: 2*R*,3*R*) as colorless liquids.

Table 5. NMR data

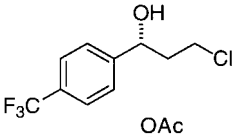
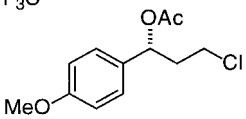
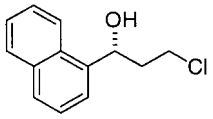
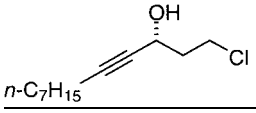
Compound	Solvent	δ (*trans*)	δ (*cis*)
	C_6D_6	4.51 (d)	4.58 (d)
	C_6D_6	4.35 (d)	4.45 (d)
	C_6D_6	3.54 (dt) [H on 5-position]	4.59 (d)
	C_6D_6	4.79 (d)	4.96 (d)
	C_6D_6	4.58 (d)	4.45 (d)

1′,1′-Dicyclohexylethyl (2*R*,3*R*)-3-(1″-naphthyl)tetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.11 (dq, 1H, *J*=3.5, 12.5 Hz), 0.47 (dq, 1H, *J*=3.2, 12.4 Hz), 0.7–1.1 (m, 10H), 1.02 (s, 3H), 1.1–1.2 (m, 1H), 1.35–1.6 (m, 8H), 1.69 (tt, 1H, *J*=2.7, 11.9 Hz), 1.75–1.8 (m, 1H), 2.73 (tt, 1H, *J*=9.0, 11.0 Hz), 3.86 (td, 1H, *J*=7.6, 8.4 Hz), 4.00 (td, 1H, *J*=7.3, 10.7 Hz), 4.41 (dt, 1H, *J*=2.6, 8.2 Hz), 4.96 (d, 1H, *J*=7.6 Hz), 7.22–7.34 (m, 3H), 7.52 (d, 1H, *J*=7.3 Hz), 7.54 (d, 1H, *J*=8.2 Hz), 7.63 (d, 1H, *J*=7.9 Hz), 7.84 (d, 1H, *J*=8.5 Hz). ^{13}C NMR (126 MHz, C_6D_6): δ 19.5, 26.9, 27.1, 27.4, 27.4, 27.6, 27.7, 27.7, 28.1, 28.5, 30.2, 44.8, 45.1, 45.5, 68.6, 81.4, 90.5, 124.3, 125.0, 126.0, 126.1, 126.6, 128.3, 129.4, 133.7, 134.5, 134.7, 171.1. IR (neat): 3045 (w), 2928 (s), 2852 (s), 1732 (s), 1447 (m), 1212 (m), 1192 (m), 1077 (m), 778 (m) cm^{-1}. HRMS (FAB, *m*/*z*): Calcd for $C_{29}H_{38}O_3$: 473.2458 ($M+K^+$). Found: 473.2450. $[\alpha]^{20}_D=-140°$ (*c*=0.60, EtOH, 95% ee).

3.7.10. Table 3, entry 5. The reaction was carried out using (*R*)-oxetane (28.0 mg, 0.155 mmol) and the diazoacetate (70.0 mg, 0.251 mmol). 1,3-Diisopropylbenzene (20.6 mg, 0.127 mmol) was added to the crude product as an internal NMR standard, and the NMR yield thus determined for the *cis* tetrahydrofuran was 62% (C_6D_6). NMR analysis showed that the product was an 84:16 *cis*/*trans* mixture. The crude product was purified by column chromatography (4/96 Et_2O/pentane), which afforded the *trans* tetrahydrofuran (15% ee, major enantiomer: 2*R*,3*S*) and the *cis* tetrahydrofuran (39.9 mg, 60% yield, 94% ee, major enantiomer: 2*R*,3*R*) as colorless liquids.

1′,1′-Dicyclohexylethyl (2*R*,3*R*)-3-(non-1″-ynyl)tetrahydrofuran-2-carboxylate. ^{1}H NMR (500 MHz, C_6D_6): δ 0.89 (t, 3H, *J*=7.0 Hz), 1.1–1.4 (m, 18H), 1.49 (qnt, 2H, *J*=7.3 Hz), 1.60 (s, 3H), 1.61–2.2 (m, 14H), 2.14 (dt, 2H, *J*=2.1, 7.2 Hz), 2.95 (tq, 1H, *J*=2.2, 7.9 Hz), 3.58 (q, 1H, *J*=7.5 Hz), 4.16 (dt, 1H, *J*=4.9, 8.2 Hz), 4.45 (d, 1H, *J*=7.3 Hz). ^{13}C NMR (126 MHz, C_6D_6): δ 14.3, 19.4, 19.6, 23.0, 27.0, 27.0, 27.3, 27.4, 27.4, 27.9, 28.1, 28.3, 28.4, 29.3, 29.3, 32.1, 33.2, 34.6, 45.4, 45.5, 68.6, 77.9, 81.5, 84.1, 90.8, 170.2 IR (neat): 2927 (s), 2853 (s), 1732 (s),

Table 6. Assay conditions for enantiomeric γ-chloroalcohols

Compound	Column	Conditions	Illustrat. config. t_R (min)	Opposite config. t_R (min)
	GC Chiraldex B-PH	120°C, He, 1.0 mL/min	70.9	73.8
	GC Chiraldex B-PH	130°C, H_2, 1.0 mL/min	59.4	57.0
	HPLC Chiralcel OD	10% *i*-PrOH/hexanes 1.0 mL/min	27.0	10.0
	GC Chiraldex G-TA	120°C, H_2, 1.0 mL/min	48.4	52.2

1449 (s), 1379 (m), 1300 (m), 1210 (m), 1097 (s) cm^{-1}. HRMS (FAB, *m/z*): Calcd for $C_{28}H_{46}O_3$: 469.3084 ($M+K^+$). Found: 469.3068. $[\alpha]^{20}_D=+5.8° \pm 0.3°$ (*c*= 0.95, EtOH, 94% ee).

3.8. Assay of diastereoselectivity

Table 4 summarizes the GC (achiral) conditions for the diastereomeric tetrahydrofurans.

The diastereomeric ratios of the tetrahydrofurans that cannot be analyzed by GC were determined by integration of the ^1H NMR spectra (delay time=30 s). Table 5 lists the peaks used for integration.

3.9. Assignment of relative stereochemistry

The assignment for *t*-butyl 3-phenyltetrahydrofuran-2-carboxylate is based on comparison with the NMR data of Katsuki.[2c] The other assignments are based on analogy. It appears that all of the diastereomers possess the following properties:

(a) $(J_{2,3})_{trans}<(J_{2,3})_{cis}$;
(b) The ester group of the *cis* diastereomer is more shielded than the ester group of the *trans* diastereomer;
(c) With the (*R*)-oxetane and the (*R*,*R*)-ligand, the *trans* diastereomer is formed preferentially.

3.10. Assay of enantioselectivity

The enantiomeric excess of the γ-chloroalcohols was assayed either directly or as the acetate derivative (Ac_2O/pyridine/Et_3N in CH_2Cl_2). Table 6 summarizes the assay conditions.

Table 7 summarizes the assay conditions for the oxetanes.

The ee's of the tetrahydrofurans were assayed by one of three methods:

(a) reduction to the alcohol ($LiAlH_4$), followed by acetylation (Ac_2O/pyridine);

Table 7. Assay conditions for enantiomeric oxetanes

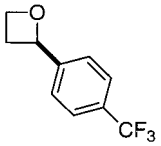
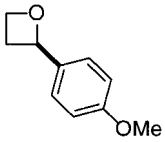
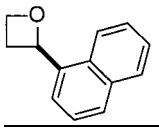
Compound	Column	Conditions	Illustrat. config. t_R (min)	Opposite config. t_R (min)
	GC Chiraldex G-TA	120°C, He, 1.5 mL/min	6.1	7.7
	GC Chiraldex G-TA	100°C, He, 1.0 mL/min	7.8	8.4
	HPLC Chiralcel OD	1% *i*-PrOH/hexanes, 1.0 mL/min	14.1	13.2
	HPLC Chiralcel OD	3% *i*-PrOH/hexanes, 1.0 mL/min	18.9	8.4

Table 8. Assay conditions for enantiomeric tetrahydrofurans

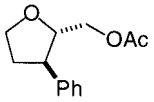
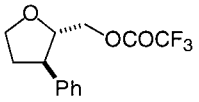
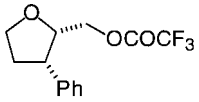
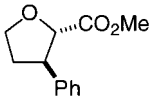
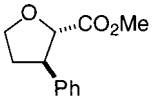
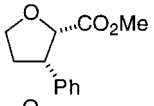
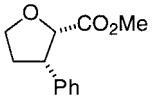
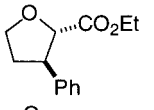
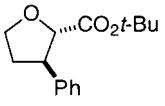
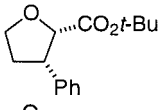
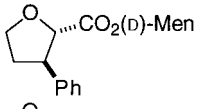
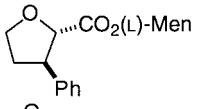
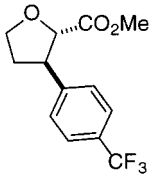
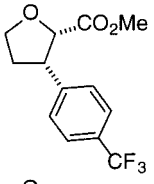
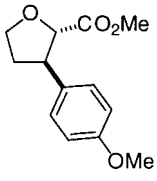
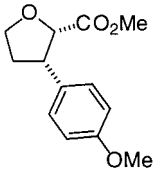
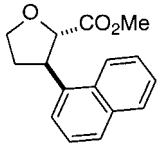
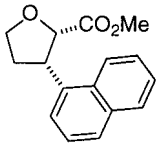
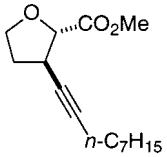
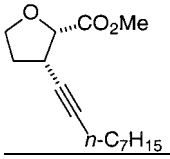
Substrate	Column	Conditions	Illustrat. config. t_R (min)	Opposite config. t_R (min)
	GC Chiraldex B-PH	110°C, H_2, 2.0 mL/min	57.4	59.5
	GC Chiraldex G-TA	90°C, He, 1.0 mL/min	81.7	77.5
	GC Chiraldex G-TA	90°C, He, 1.0 mL/min	74.1	83.2
	GC Chiraldex G-TA	120°C, He, 0.5 mL/min	67.7	58.9
	HPLC Chiralcel OD	1% *i*-PrOH/hexanes, 1.0 mL/min	19.1	24.6
	GC Chiraldex G-TA	120°C, He, 0.5 mL/min	64.3	56.1
	HPLC Chiralcel OD	1% *i*-PrOH/hexanes, 1.0 mL/min	23.0	37.6
	GC Chiraldex B-PH	110°C, He, 1.0 mL/min	68.3	70.4
	GC Chiraldex B-PH	120°C, H_2, 1.0 mL/min	41.6	44.0
	GC Chiraldex B-PH	120°C, H_2, 2.0 mL/min	50.1	51.3
	GC Chiraldex B-PH	150°C, He, 1.0 mL/min	134.0	138.0
	GC Chiraldex B-PH	150°C, He, 1.0 mL/min	131.8	135.6
	GC Chiraldex G-TA	130°C, He, 1.0 mL/min	31.3	24.2
	GC Chiraldex G-TA	130°C, He, 1.0 mL/min	21.8	19.6
	GC Chiraldex G-TA	130°C, He, 1.0 mL/min	92.9	86.3

Table 8
(*continued*)

Substrate	Column	Conditions	Illustrat. config. t_R (min)	Opposite config. t_R (min)
	GC Chiraldex G-TA	130°C, He, 1.0 mL/min	73.2	70.6
	HPLC Chiralpak AD	1% EtOH/hexanes 1.0 mL/min	19.6	15.2
	HPLC Chiralpak AD	1% EtOH/hexanes 1.0 mL/min	21.6	27.4
	GC Chiraldex G-TA	120°C, He, 1.0 mL/min	110.4	92.3
	GC Chiraldex G-TA	120°C, He, 1.0 mL/min	105.8	95.4

(b) reduction to the alcohol ($LiAlH_4$), followed by trifluoroacetylation ($(CF_3CO)_2O$);
(c) hydrolysis to the acid (CF_3CO_2H), followed by methylation with $TMSCHN_2$ (for tetrahydrofurans that bear an ester derived from a tertiary alcohol).

Table 8 summarizes the assay conditions for the tetrahydrofurans.

3.11. Assignment of absolute configuration

The sign of the optical rotation of the *trans* tetrahydrofuran derived from the reaction of (*S*)-2-phenyloxetane and *t*-butyl diazoacetate in the presence of (*S*,*S*)-**2** is negative; the absolute configuration of the predominant enantiomer of the *trans* tetrahydrofuran is therefore (2*R*,3*S*).[2c] The absolute configurations of the other products (Table 1) were assigned by correlation (reduction or hydrolysis of the ester). The absolute configurations of the products illustrated in Table 2 were assigned by analogy.

The sign of the optical rotation of the *cis* tetrahydrofuran derived from the reaction of (*S*)-2-phenyloxetane and *t*-butyl diazoacetate in the presence of (*R*,*R*)-**2** is positive; the absolute configuration of the predominant enantiomer of the *cis* tetrahydrofuran is therefore (2*S*,3*S*).[2c] The absolute configurations of the products illustrated in Table 3 were assigned by analogy.

Acknowledgements

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equivalents of TMSI at 0°C. Use of a larger excess of TMSI leads to the destruction of the THF ring.
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