Isothiourea-Catalyzed Asymmetric O- to C-Carboxyl Transfer of Furanyl Carbonates

Caroline Joannesse, Louis C. Morrill, Craig D. Campbell, Alexandra M. Z. Slawin, Andrew D. Smith*

EaStCHEM, School of Chemistry, University of St Andrews, North Haugh, St Andrews, KY16 9ST, UK
Fax +44(1334)463806; E-mail: ads10@st-andrews.ac.uk

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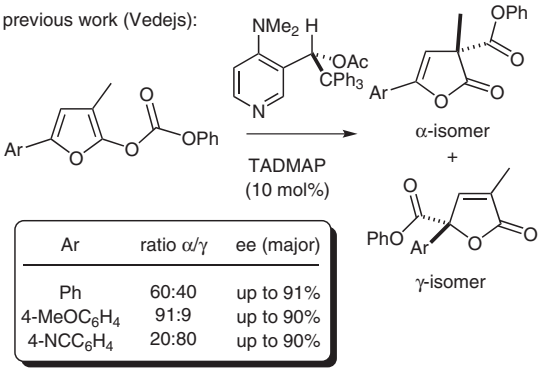
Abstract: The ability of a chiral isothiourea to promote the regio- and enantioselective O- to C-carboxyl transfer of a series of 3-alkyl-5-aryl- and 5-methyl-3-phenylfuranyl carbonates is examined, generating preferentially the α-regioisomers (α/γ up to 83:17) with high asymmetric induction (up to 83% ee).

Key words: isothiourea, organocatalysis, carboxyl transfer, furanyl carbonates, butenolides

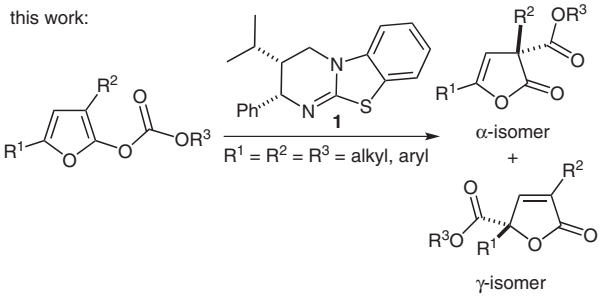
Butenolides are a common subunit of a variety of biologically active natural products,[1] with the development of methods for the enantioselective construction of quaternary stereogenic centres within these templates via organocatalysis being an active area of research. Functionalization of butenolides is commonly achieved by derivatization of a furanyl dienolate or its equivalent; for example, Deng and co-workers have reported the highly diastereo- and enantioselective vinylogous aldol reaction of 2-silyloxyfurans,[2] while MacMillan and co-workers have described the related γ-functionalization of butenolides using iminium ion catalysis.[3] As an alternative strategy, Vedejs et al. have investigated the TADMAP-promoted regio- and enantioselective O- to C-carboxyl transfer of a series of 5-aryl-3-methylfuranyl carbonates.[4] In all cases, mixtures of α- and γ-functionalized products were observed in high enantiomeric excess, with the regioselectivity dependent upon the electronic nature of the 5-aryl substituent; an electron-donating 4-$MeOC_6H_4$ substituent favoured α-functionalization (α/γ 91:9, 90% ee) while an electron-withdrawing 4-NCC_6H_4 substituent favoured γ-functionalization (α/γ 20:80, 90% ee) (Scheme 1).

Building upon our ongoing interests in Lewis base[5] catalysis,[6,7] and in particular our demonstration that chiral isothioureas promote the O- to C-carboxyl transfer of oxazolyl carbonates[8] with high enantioselectivity,[9] herein we probe the ability of isothiourea **1**[10] to promote the regio- and enantioselective rearrangement of a series of 3-alkyl-5-aryl- and 5-methyl-3-phenylfuranyl carbonates. The effect of carbonate group variation, as well as substitution at C3 and C5 within these systems, upon the regio- and enantioselectivity of this process is sequentially evaluated (Scheme 2).



Ar	ratio α/γ	ee (major)
Ph	60:40	up to 91%
4-$MeOC_6H_4$	91:9	up to 90%
4-NCC_6H_4	20:80	up to 90%

Scheme 1 Regio- and enantioselective O- to C-carboxyl transfer of furanyl carbonates by Vedejs



Scheme 2 Proposed isothiourea-catalyzed regio- and enantioselective O- to C-carboxyl transfer of furanyl carbonates

Model studies compared the regio- and enantioselective rearrangements of 5-methyl-3-phenylfuranyl carbonate **4** and its isomeric 3-methyl-5-phenylfuranyl carbonate **5**. While **5** was prepared following the literature procedure,[4] carbonate **4** was prepared from **2**[11] by sequential selenation and elimination to give **3**, followed by carbonate formation (Scheme 3).[12]

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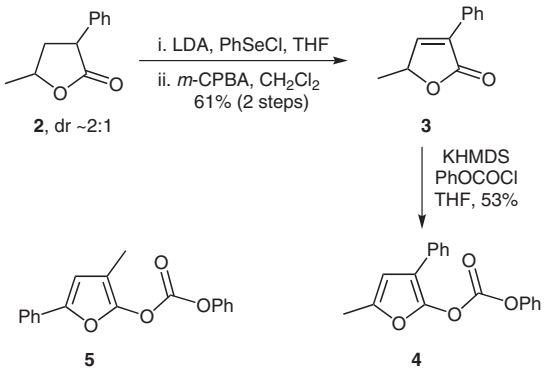


Scheme 3 Preparation of isomeric furanyl carbonates **4** and **5**

X-ray crystal structure analysis of carbonate **4** confirmed unambiguously that O- rather than C-carboxylation had occurred under these reaction conditions (Figure 1).

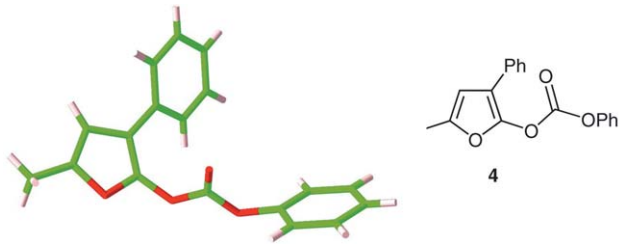
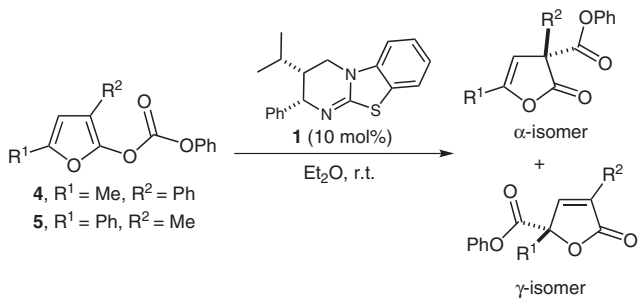


Figure 1 Molecular representation of the X-ray crystal structure of furanyl carbonate **4**

Treatment of 5-methyl-3-phenylfuranyl carbonate **4** with isothiourea **1** proceeded with moderate regio- and enantiocontrol, giving a 54:46 mixture of α/γ regioisomers **6** and **7** in 44% ee and racemic form, respectively. However, treatment of 3-methyl-5-phenylfuranyl carbonate **5** with isothiourea **1** gave an 83:17 mixture of α/γ regioisomers, with the major α-isomer **8** isolated in 75% yield and 81% ee (Table 1).

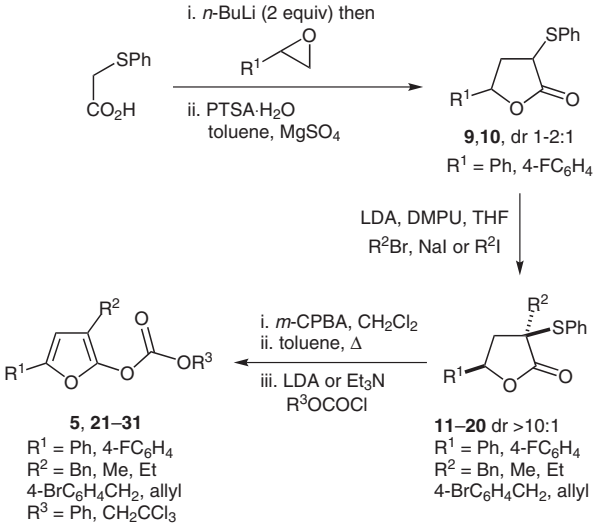
Table 1 Probing the O- to C-Carboxyl Transfer of Furanyl Carbonates **4** and **5** Using Isothiourea **1**



Entry	Carbonate	R^1	R^2	Ratio[a] α/γ	Yield[b] (%)	ee[c] (%)
1	**4**	Me	Ph	54:46	44 (α-**6**) 34 (γ-**7**)	44 (α) 0 (γ)
2	**5**	Ph	Me	83:17	75 (α-**8**)	81 (α)

[a] As shown by ^{1}H NMR spectroscopic analysis of the crude reaction product.
[b] Isolated yield of either major α-regioisomer (α) or minor γ-regioisomer (γ).
[c] Determined by chiral HPLC analysis.

Having demonstrated that rearrangement of 3-methyl-5-phenylfuranyl carbonate **5** leads to higher regio- and enantioselectivity than its 5-methyl-3-phenyl carbonate isomer **4**, a range of 3-alkyl-5-arylfuranyl carbonates **21**–**31** were prepared. Based upon literature procedures,[13] these substrates were accessed by alkylation of the dianion of (phenylthio)acetic acid, lactonization, diastereoselective alkylation to give **11**–**20** (dr typically >10:1, see Figure 2 for X-ray analysis of major diastereoisomer **11**), and subsequent oxidation and thermal elimination, followed by carbonate formation giving **21**–**31** (Scheme 4).



Scheme 4 Preparation of furanyl carbonate derivatives **5**, **21**–**31**

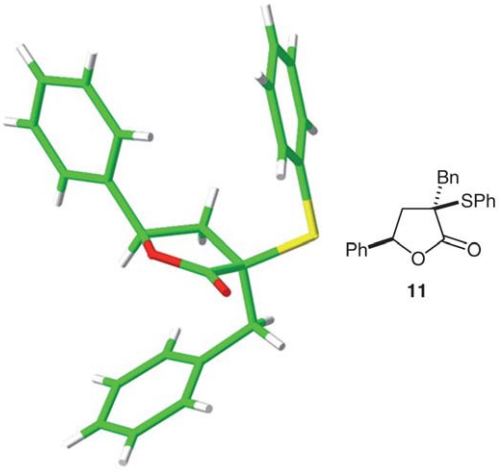
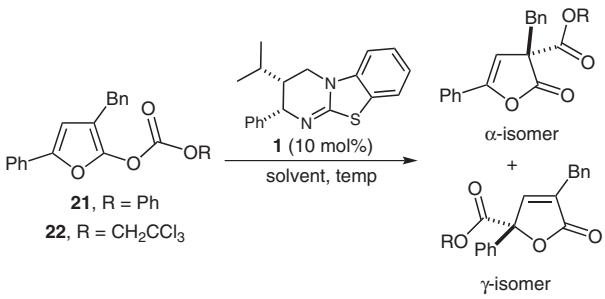


Figure 2 Molecular representation of the X-ray crystal structure of **11**

Optimization studies probed the regio- and enantioselective rearrangement of 3-benzyl-5-phenylfuranyl phenyl carbonate (**21**) catalyzed by isothiourea **1**. At room temperature in dichloromethane, isothiourea **1** gave a 63:37

ratio of α/γ products, with purification giving the major α-isomer **32** in 54% yield and 80% ee (Table 2, entry 1). No improvement in enantiomeric excess, and a noticeable decrease in reactivity,[14] was observed upon cooling the reaction temperature, while changing solvent gave a marginal improvement in regiocontrol and enantioselectivity at room temperature. Under optimal conditions, rearrangement of **21** using isothiourea **1** in diethyl ether at room temperature gave a 75:25 regioisomeric α/γ ratio, with the major α-isomer **32** isolated in 70% yield and 83% ee (entry 5). Rearrangement of the trichloroethyl carbonate **22** gave a 50:50 mixture of α/γ products **33** and **34** (entry 6) with reduced enantioselectivity in comparison with phenyl carbonate **21**, consistent with variation of the carbonate group influencing both regio- and enantiocontrol in this series.

Table 2 Isothiourea **1** Promoted O- to C-Carboxyl Transfer of **21** and **22**

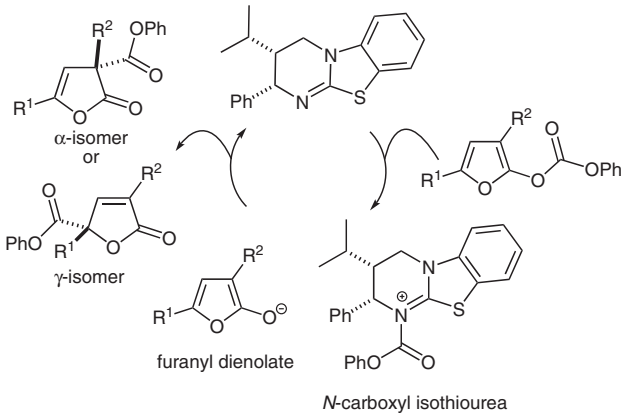


Entry	Solvent	R	Ratio[a] α/γ	Yield[b] (%)	ee[c] (%)
1	CH_2Cl_2	Ph	63:37	54 (α-**32**)	80 (α)
2	CH_2Cl_2[d]	Ph	68:32	59 (α-**32**)	71 (α)
3	toluene	Ph	75:25	64 (α-**32**)	80 (α)
4	THF	Ph	75:25	62 (α-**32**)	79 (α)
5	Et_2O	Ph	75:25	70 (α-**32**)	83 (α)
6	Et_2O	CH_2CCl_3	50:50	44 (α-**33**) 39 (γ-**34**)	62 (α) 26 (γ)

[a] As shown by ^{1}H NMR spectroscopic analysis of the crude reaction product.
[b] Isolated yield of either major α-regioisomer (α) or minor γ-regioisomer (γ).
[c] Determined by chiral HPLC analysis.
[d] Reaction temperature –78 °C to r.t.

The full scope and generality of the asymmetric process was next investigated (Table 3). Consistent trends within this series indicate that 3-alkyl-5-arylfuranyl phenyl carbonates rearrange with higher regio- and enantioselectivity [α/γ up to 79:21; up to 81% ee (α)] than the corresponding trichloroethyl carbonate derivatives [up to 59:41, up to 71% ee (α)]. Reasonable levels of asymmetric induction (76–83% ee) are observed for the major α-isomer, with only modest enantiodiscrimination observed for the minor γ-isomer. The absolute configuration of **8** obtained using isothiourea **1** was assigned by comparison of the specific rotation and HPLC retention times of a sample of (*S*)-**8** that was prepared by rearrangement of **5** with (*R*)-TADMAP.[15] This indicates that chiral isothiourea **1** generates the same sense of asymmetric induction in this preferential α-regioselective carboxyl transfer process as observed previously in the analogous O- to C-carboxyl transfer process of oxazolyl carbonates.[9]

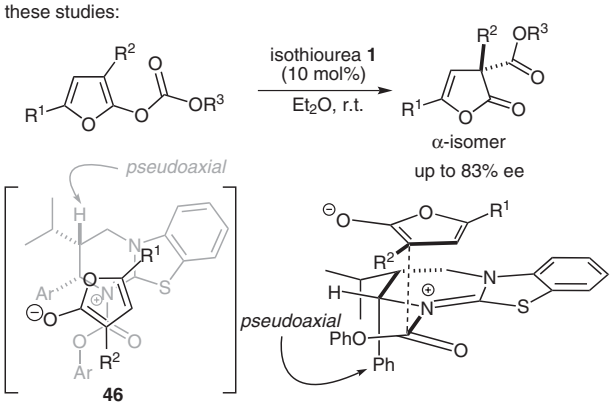
We assume this process is initiated by nucleophilic attack of the isothiourea to the furanyl carbonate carbonyl, generating a furanyl dienolate and *N*-carboxyl isothiouronium ion, with C-carboxylation of the dienolate at either the α- or γ-position generating the observed C-carboxyl products (Scheme 5).



Scheme 5 Assumed mechanism for the asymmetric O- to C-carboxyl transfer of furanyl carbonates with chiral isothiourea **1**

By analogy to our previous transition state modelling for the analogous O- to C-carboxyl transfer process of oxazolyl carbonates, a simple model to account for the high enantioselectivity observed for α-functionalization in the O- to C-carboxyl transfer of furanyl carbonates is schematically outlined below (Scheme 6).[9] This model assumes the *N*-carboxyl group of the isothiouronium intermediate lies co-planar with the heterocycle, forcing the adjacent C2-phenyl unit pseudoaxial in order to minimize 1,2-strain.[16] Preferential α-C-carboxylation of the dienolate subsequently takes place *anti*- to this stereodirecting axial unit, through a transition state such as **46**, in which interactions with the axial C3-H of the tetrahydropyrimidinium ion are minimized. Although this simple model accounts for the observed sense of induction observed for the major α-isomer in the majority of these transformations, this rationale cannot account for the reduced level of regio- and enantioselectivity noted in the rearrangement of 5-methyl-3-phenylfuranyl carbonate **4**, nor the low enantioselectivity observed for formation of the minor γ-isomer in these rearrangement processes. However, the lower enantioselectivity observed upon rearrangement of **4** is consistent with the typically moderate enantioselectivity observed upon rearrangement of the analogous C4-aryl substituted oxazolyl carbonates.[4,8j]

In conclusion, we have shown that isothiourea **1** promotes the O- to C-carboxyl transfer of furanyl carbonates with



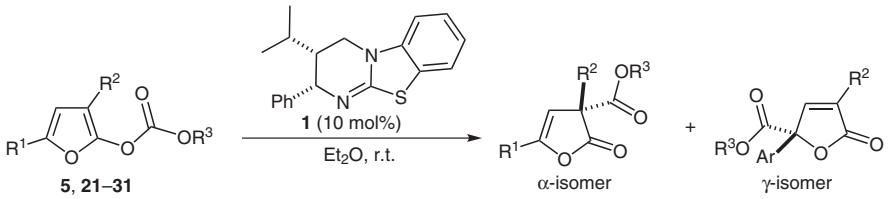
Scheme 6 Proposed simplistic model for the asymmetric O- to C-carboxyl transfer of furanyl carbonates with chiral isothiourea **1**

preferential α-regiocontrol (up to 83:17) and with good levels of enantiocontrol (up to 83% ee). Ongoing studies within this laboratory are directed toward the demonstration of alternative catalytic asymmetric reaction protocols using isothioureas and other Lewis bases in asymmetric catalysis.

Reactions involving moisture-sensitive reagents were carried out under an argon atmosphere using standard vacuum line techniques. All glassware used was flame dried and cooled under vacuum. Solvents (THF, CH_2Cl_2, toluene, hexane, and Et_2O) were obtained anhydrous and purified by an alumina column (Mbraun SPS-800). PE is defined as petroleum ether 40–60 °C. All other solvents and commercial reagents were used as supplied without further purification unless stated otherwise. Room temperature (r.t.) refers to 20–25 °C. Temperatures of 0 °C and –78 °C were obtained using ice/water and CO_2(s)/acetone baths, respectively. Temperatures of 0 °C to –50 °C were obtained using an immersion cooler (Haake EK 90). Reflux conditions were obtained using an oil bath equipped with a contact thermometer. In vacuo refers to the use of a Büchi Rotavapor R-2000 rotary evaporator with a Vacubrand CVC_2 vacuum controller or a Heidolph Laborota 4001 rotary evaporator with a vacuum controller. Analytical TLC was performed on pre-coated aluminium plates (Kieselgel 60 F_{254} silica). TLC visualisation was carried out with UV (254 nm), followed by staining with a 1% aq $KMnO_4$ soln. Flash column chromatography was performed on Kieselgel 60 silica in the solvent system stated.

^{1}H and ^{13}C NMR spectra were acquired on either a Bruker Avance 300 (300 MHz, ^{1}H, 75 MHz ^{13}C) or a Bruker Avance II 400 (400 MHz, ^{1}H, 100 MHz ^{13}C) spectrometer at r.t. in the deuterated solvent stated with the residual solvent as the internal standard. Infrared spectra were recorded on a Perkin-Elmer Spectrum GX FT-IR spectrophotometer using either thin films on NaCl plates or KBr

Table 3 Isothiourea **1** Promoted O- to C-Carboxyl Transfer of Furanyl Carbonates **5** and **21**–**31**



Entry	Substrate	R^1	R^2	R^3	Ratio[a] α/γ	Yield[b] (%)	ee[c] (%)
1	**5**	Ph	Me	Ph	83:17	75 (α-**8**)	81 (α)
2	**21**	Ph	Bn	Ph	75:25	70 (α-**32**)	83 (α)
3	**22**	Ph	Bn	CH_2CCl_3	50:50	44 (α-**33**) 39 (γ-**34**)	62 (α) 26 (γ)
4	**23**	4-FC_6H_4	Bn	Ph	80:20	64 (α-**35**)	83 (α)
5	**24**	4-FC_6H_4	Me	Ph	79:21	64 (α-**36**)	81 (α)
6	**25**	4-FC_6H_4	Me	CH_2CCl_3	59:41	49 (α-**37**) 27 (γ-**38**)	71 (α) 0 (γ)
7	**26**	Ph	Et	Ph	64:36	39 (α-**39**)	83 (α)
8	**27**	4-FC_6H_4	Et	Ph	62:38	55 (α-**40**)	81 (α)
9	**28**	Ph	4-BrBn	Ph	76:24	57 (α-**41**)	82 (α)
10	**29**	4-FC_6H_4	4-BrBn	Ph	80:20	66 (α-**42**)	81 (α)
11	**30**	Ph	allyl	Ph	72:28	56 (α-**43**) 16 (γ-**44**)	81 (α) 16 (γ)
12	**31**	4-FC_6H_4	allyl	Ph	75:25	62 (α-**45**)	76 (α)

[a] As shown by ^{1}H NMR spectroscopic analysis of the crude reaction product.
[b] Isolated yield of either major α-regioisomer (α) or minor γ-regioisomer (γ).
[c] Determined by chiral HPLC analysis.

discs. Only the characteristic peaks are quoted. Melting points were recorded on an Electrothermal apparatus and are uncorrected. HPLC analyses were obtained on a Gilson HPLC consisting of a Gilson 305 pump, Gilson 306 pump, Gilson 811C dynamic mixer, Gilson 805 manometric module, Gilson 401C dilutor, Gilson 213XL sample injector and sample detection was performed with a Gilson 118 UV/vis detector. Separation was achieved using a Chiralcel OD-H, Chiralpak AD-H, or Chiralpak AS-H column. MS data were acquired by electrospray ionisation (ESI), electron impact (EI) or nanospray ionisation (NSI) either at the University of St Andrews or the EPSRC National Mass Spectrometry Service Centre, Swansea. At the University of St Andrews, low and high resolution ESI MS were carried out on a Micromass LCT spectrometer. At the EPSRC National Mass Spectrometry Service Centre, low resolution NSI MS was carried out on a Micromass Quattro II spectrometer and high resolution NSI MS on a Thermofisher LTQ Orbitrap XL spectrometer. Optical rotations were measured on a Perkin Elmer Precisely/Model-341 polarimeter operating at the Na D line with a 100-mm path cell.

Crystallographic data (excluding structure factors) for compounds **4** and **11** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 822214 and 822213. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44(1223)336033 or e-mail: deposit@ccdc.cam.ac.uk].

Butyrolactones; General Procedure A

To a soln of *i*-Pr_2NH (2.21 equiv) in THF at 0 °C was added 2.5 M *n*-BuLi in hexanes (2.21 equiv). After 15 min, the soln of LDA was cooled to –78 °C and (phenylthio)acetic acid (1 equiv) was added as a soln in THF. After 1 h, the requisite epoxide (1.20 equiv) was added in one portion and the mixture was allowed to warm to r.t. over 16 h. The mixture was quenched with H_2O and extracted with Et_2O (3 ×). The aqueous layer was acidified with aq 10 M HCl and extracted with EtOAc (3 ×) and the combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The hydroxy acid formed was converted into the butyrolactone by stirring in toluene with catalytic PTSA·H_2O (~1 mol%) at r.t. for 16 h followed by concentration in vacuo.

Alkylation of Butyrolactones; General Procedure B

To a soln of *i*-Pr_2NH (1.3 equiv) in THF at 0 °C was added 2.5 M *n*-BuLi in hexanes (1.3 equiv). After 15 min, the soln of LDA was cooled to –78 °C and a soln of the requisite lactone (1 equiv) in THF was added over 15 min. After 30 min, a soln of the requisite halide (1.1 equiv) in DMPU was added in one portion and the mixture allowed to warm to r.t. over 16 h. The reaction was quenched with sat. aq NH_4Cl and extracted with Et_2O (3 ×). The combined organic extract was washed with H_2O and brine, dried ($MgSO_4$), filtered, and concentrated in vacuo.

Note: If using a reactive alkyl halide, such as BnBr, only DMPU was required to promote the alkylation. If not activated, Finklestein catalysis should be employed using NaI (0.2–1 equiv).

Butenolides; General Procedure C

To a soln of lactone (1 equiv) in $CHCl_3$ at 0 °C was added *m*-CPBA (1 equiv) portionwise. After 1 h, sat. aq $NaHCO_3$ (excess) was added and the soln was extracted with EtOAc (3 ×). The combined organic extract was washed with brine, dried ($MgSO_4$), filtered, and concentrated in vacuo to afford the crude sulfoxide. The crude sulfoxide was dissolved in toluene and heated at reflux for 16 h before concentration in vacuo.

Carbonates; General Procedure D

To a soln of *i*-Pr_2NH (1.3 equiv) in THF at 0 °C was added 2.5 M *n*-BuLi in hexanes (1.3 equiv). After 15 min, the soln of LDA was cooled to –78 °C and a soln of butenolide (1 equiv) in THF was added dropwise. After 30 min the dienolate soln was added dropwise to a soln of the requisite chloroformate (1.3 equiv) in THF at –78 °C then allowed to warm to r.t. The mixture was poured into 0.5 M HCl, and extracted with Et_2O (3 ×). The organic fraction was washed with brine, dried ($MgSO_4$), filtered, and concentrated in vacuo.

General Lewis Base Promoted Rearrangement; General Procedure E

To a soln of carbonate (1 equiv) in THF (~1 mL per 100 mg of carbonate) was added isothiourea 1 (10 mol%). The mixture was stirred for 1 h, then concentrated in vacuo.

Alternative Preparation of Carbonates; General Procedure F

To a soln of butenolides in THF at 0 °C was added Et_3N. After 15 min, the requisite chloroformate was added dropwise then allowed to warm to r.t. overnight. The mixture was poured into H_2O and extracted with Et_2O (3 ×). The combined organic extracts were washed with aq 0.1 M HCl, aq sat. $NaHCO_3$, and brine, dried ($MgSO_4$), filtered, and concentrated in vacuo.

5-Methyl-3-phenyldihydrofuran-2(3*H*)-one (2)

Phenylacetic acid (12.0 g, 88.1 mmol) in THF (80 mL) was slowly added at –78 °C to a solution of LDA (176 mmol, 2 equiv) in THF (40 mL). The mixture was stirred for 30 min at 0 °C and cooled again to –78 °C. The dianion mixture was added at –78 °C via cannula to a flask containing 2-methyloxirane (6.17 mL, 88.1 mmol) and LiCl (3.74 g, 88.1 mmol) in THF (80 mL) and then the mixture was stirred for 16 h at r.t. The reaction was quenched with H_2O and the mixture extracted with Et_2O (3 ×). The aqueous layer was acidified under ice-bath cooling by careful addition of concd HCl and then extracted with EtOAc (3 ×). The organic layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated in vacuo to give a residue which gave, after chromatographic purification (EtOAc–PE, 25:75), an inseparable mixture of both diastereomers of lactone (±)-**2** (13.25 g, 85%) as a colourless oil. Data are in accordance with the literature.[7b]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.52 (d, *J* = 5.6 Hz, 3 H, CH_3), 1.55 (d, *J* = 6.1 Hz, 3 H, CH_3), 2.00–2.14 (m, 1 H, CH), 2.33–2.45 (m, 1 H, CH), 2.52–2.64 (m, 1 H, CH), 2.77–2.87 (m, 1 H, CH), 3.89–4.02 (m, 2 H, CH), 4.61–4.74 (m, 1 H, CH), 4.79–4.91 (m, 1 H, CH), 7.28–7.45 (m, 10 H, H_{Ar}).

5-Methyl-3-phenylfuran-2(5*H*)-one (3)

To a cooled (0 °C) soln of *i*-Pr_2NH (6.74 mL, 47.7 mmol) in THF (75 mL) was added 2.5 M *n*-BuLi in hexanes (6.74 mL, 50.0 mmol). After 20 min at 0 °C, the LDA soln was cooled to –78 °C, and a soln of lactone (±)-**2** (8.00 g, 45.5 mmol) in THF (15 mL) was added. The reaction temperature was maintained at –78 °C for 30 min, and a soln of PhSeCl (13.1 g, 68.2 mmol) in THF (40 mL) was added. The resultant mixture was slowly allowed to warm to r.t. (over 2 h), diluted with EtOAc, washed with sat. aq NH_4Cl, dried ($MgSO_4$), filtered, and concentrated in vacuo. Chromatographic purification (CH_2Cl_2–PE, 50:50) gave the selenyl intermediate as a white solid, which was used immediately without characterisation. To a cooled (0 °C) soln of the phenylselenyl intermediate in $CHCl_3$ (75 mL) was added *m*-CPBA (70% purity, 16.8 g, 68.2 mmol) portionwise at 0 °C and the mixture was allowed to warm to r.t. over 15 min. A further portion of $CHCl_3$ (75 mL) was added along with 5% aq Na_2CO_3 (150 mL). The layers were separated, the organic phase was washed with 5% aq Na_2CO_3 (150 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo. Chromatographic purification (EtOAc–PE, 15:85) gave butenolide (±)-**3** (4.86 g, 61%) as a white solid; mp 45–46 °C [Lit.[12] 45–46 °C]. Data are in accordance with the literature.[12]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (d, *J* = 6.8 Hz, 3 H, CH_3), 5.09 (qd, *J* = 6.8, 1.8 Hz, 1 H, CH), 7.29–7.38 (m, 3 H, H_{Ar}), 7.47 (d, *J* = 1.8 Hz, 1 H, CH), 7.76–7.80 (m, 2 H, H_{Ar}).

5-Methyl-3-phenylfuran-2-yl Phenyl Carbonate (4)

To a soln of butenolide (±)-**3** (1 g, 5.75 mmol) in THF (45 mL) at –78 °C was added 0.45 M KHMDS in hexanes (14.1 mL, 6.32 mmol). The soln was allowed to stir for 30 min before phenyl chloroformate (0.80 mL, 6.32 mmol) was added in one portion and the mixture was allowed to warm to r.t. over 1 h. The mixture was quenched with sat. aq NH_4Cl and extracted with Et_2O (3 ×). The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a residue which gave, after chromatographic purification (EtOAc–PE, 2.5:97.5), carbonate **4** (896 mg, 53%) as a white solid; mp 72–73 °C.

IR (KBr): 3050, 2936 (C–H), 1790 (C=O), 1658 (Ar C=C), 1586, 1555 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.34 (d, *J* = 1.1 Hz, 3 H, CH_3), 6.32 (br q, *J* = 1.1 Hz, 1 H, CH), 7.24–7.33 (m, 4 H, H_{Ar}), 7.40–7.46 (m, 4 H, H_{Ar}), 7.51–7.55 (m, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7, 106.8, 109.0, 120.8, 126.5, 126.8, 127.0, 128.9, 129.8, 131.2, 144.3, 146.4, 150.7, 151.0.

MS (CI^+): *m*/*z* (%) = 295 ([M + H]$^+$, 100).

HRMS (CI^+): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{15}O_4$: 295.0970; found: 295.0969.

3-Methyl-5-phenylfuran-2-yl Phenyl Carbonate (5)

Following general procedure C using *m*-CPBA (1.17 g, 4.75 mmol) and lactone **17** (1.35 g, 4.75 mmol) in $CHCl_3$ (40 mL) gave the crude sulfoxide, which was heated in toluene (40 mL). NMR crude shows 11:1 mixture of 5*H*/3*H* isomers. Purification by chromatography (silica gel, EtOAc–PE, 5:95–10:90) gave 3-methyl-5-phenylfuran-2(5*H*)-one (**47**) (0.65 g, 79%) as a white solid with spectroscopic data in accordance with the literature.[17]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.02 (t, *J* = 1.8 Hz, 3 H, CH_3), 5.91 (app. s, 1 H, C*H*Ph), 7.15–7.16 (m, 1 H, CH=C), 7.27–7.30 (m, 2 H, H_{Ar}), 7.39–7.42 (m, 3 H, H_{Ar}).

Following general procedure F using Et_3N (0.95 mL, 6.84 mmol), butenolide **47** (0.596 g, 3.42 mmol), THF (10 mL), and phenyl chloroformate (0.86 mL, 6.84 mmol) gave, after purification by chromatography (silica gel, CH_2Cl_2–PE, 10:90), **5** (0.250 g, 25%) as a white solid; mp 96–98 °C. Spectroscopic data in accordance with the literature.[4]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.02 (s, 3 H, CH_3), 6.52 (s, 1 H, CH), 7.23–7.26 (m, 1 H, H_{Ar}), 7.30–7.32 (m, 2 H, H_{Ar}), 7.34–7.38 (m, 2 H, H_{Ar}), 7.42–7.46 (m, 2 H, H_{Ar}), 7.58–7.61 (m, 2 H, H_{Ar}).

Phenyl (*R*)-5-Methyl-2-oxo-3-phenyl-2,3-dihydrofuran-3-carboxylate [(*R*)-6] and Phenyl 2-Methyl-5-oxo-4-phenyl-2,5-dihydrofuran-2-carboxylate (7)

Following general procedure E using carbonate **4** (29.4 mg, 0.1 mmol) and chiral isothiourea **1** (3.08 mg, 0.01 mmol) in THF (0.3 mL) heated at reflux overnight, after chromatographic purification (CH_2Cl_2–PE, 50:50), gave **6** (13 mg, 44%) as a white solid and **7** (10 mg, 34%) as a colourless oil.

Compound (*R*)-6

Mp 56–58 °C; 15% ee; chiral HPLC (Chiralpak AS-H, 5% *i*-PrOH–hexane, flow rate 1 mL min^{-1}): t_R = 15.8 (*R*), 19.4 min (*S*).

$[\alpha]_D^{20}$ –52.0 (*c* 0.1, CH_2Cl_2).

IR (KBr): 3118, 3062, 2924 (C–H), 2854, 1809 (C=O), 1742 (C=O), 1686, 1590 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.11 (d, *J* = 1.5 Hz, 3 H, CH_3), 5.72 (q, *J* = 1.5 Hz, 1 H, CH), 6.97–7.00 (m, 2 H, H_{Ar}), 7.14–7.18 (m, 1 H, H_{Ar}), 7.26–7.38 (m, 5 H, H_{Ar}), 7.49–7.52 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 53.5, 103.6, 121.0, 126.4, 127.1, 128.9, 129.0, 129.5, 134.4, 150.4, 155.2, 166.2, 172.1.

MS (NSI^+): *m*/*z* (%) = 312 ([M + NH_4]$^+$, 100).

HRMS (NSI^+): *m*/*z* [M + NH_4]$^+$ calcd for $C_{18}H_{18}O_4N$: 312.1230; found: 312.1230.

Compound 7

Racemic; chiral HPLC (Chiralpak AS-H, 5% *i*-PrOH–hexane, flow rate 1 mL min^{-1}): t_R = 26.5 (*R*), 37.6 min (*S*).

IR (thin film): 3522, 3076, 2938 (C–H), 1770 (C=O), 1592 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.87 (s, 3 H, CH_3), 7.01–7.05 (m, 2 H, H_{Ar}), 7.17–7.21 (m, 1 H, H_{Ar}), 7.29–7.39 (m, 5 H, H_{Ar}), 7.59 (s, 1 H, CH), 7.83–7.86 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.6, 84.1, 121.0, 126.6, 127.4, 128.6, 128.9, 129.6, 130.1, 132.4, 145.9, 150.2, 167.0, 170.2.

MS (NSI^+): *m*/*z* (%) = 312 ([M + NH_4]$^+$, 62).

HRMS (NSI^+): *m*/*z* [M + NH_4]$^+$ calcd for $C_{18}H_{18}O_4N$: 312.1230; found: 312.1234.

Phenyl (*S*)-3-Methyl-2-oxo-5-phenyl-2,3-dihydrofuran-3-carboxylate [(*S*)-8]

Following general procedure E using carbonate **5** (59.0 mg, 0.200 mmol), Et_2O (0.6 mL), and **1** (6.0 mg, 10 mol%) gave, after 1 h at r.t. NMR of the crude shows a mixture α/γ 83:17. and purification by chromatography (silica gel, CH_2Cl_2–PE, 50:50), (*S*)-**8** (44.0 mg, 75%) as a white solid;[4] mp 62–64 °C; 81.0% ee; HPLC (Chiralpak AS-H column, 5% *i*-PrOH–hexanes, flow rate 1.0 mL min^{-1}): t_R = 10.8 (*S*), 12.3 min (*R*).

$[\alpha]_D^{20}$ +121.8 (*c* 0.60, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.82 (s, 3 H, CH_3), 6.03 (s, 1 H, CH), 7.10–7.13 (m, 2 H, H_{Ar}), 7.25–7.27 (m, 1 H, H_{Ar}), 7.38–7.42 (m, 2 H, H_{Ar}), 7.46–7.49 (m, 3 H, H_{Ar}), 7.69–7.72 (m, 2 H, H_{Ar}).

5-Phenyl-3-(phenylthio)dihydrofuran-2(3*H*)-one (9)

Following general procedure A using 2.5 M *n*-BuLi in hexanes (52 mL, 130 mmol), *i*-Pr_2NH (18 mL, 130 mmol), THF (170 mL), (phenylthio)acetic acid (10.0 g, 59.0 mmol) in THF (50 mL), styrene oxide (8.1 mL, 71.0 mmol) and PTSA·H_2O (0.450 g, 2.36 mmol) in toluene (100 mL) gave, after purification by chromatography (silica gel, 100% CH_2Cl_2), an inseparable mixture of both diastereomers (~1:1.5 dr) of lactone **9** (12.7 g, 80%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.25 (ddd, *J* = 13.4, 11.4, 10.2 Hz, 1 H, CH*H*), 2.60–2.76 (m, 2 H, CH_2), 3.02 (ddd, *J* = 13.2, 8.7, 6.2 Hz, 1 H, CH*H*), 4.04 (dd, *J* = 7.8, 4.5 Hz, 1 H, CH), 4.14 (dd, *J* = 11.4, 8.7 Hz, 1 H, CH), 5.39 (dd, *J* = 10.1, 6.0 Hz, 1 H, CH), 5.49 (t, *J* = 7.5 Hz, 1 H, CH), 7.17–7.20 (H_{Ar}), 7.31–7.43 (H_{Ar}), 7.60–7.67 (H_{Ar}).

5-(4-Fluorophenyl)-3-(phenylthio)dihydrofuran-2(3*H*)-one (10)

Following general procedure A using *n*-BuLi (26.3 mL, 65.6 mmol), *i*-Pr_2NH (9.26 mL, 65.6 mmol), THF (85 mL), (phenylthio)acetic acid (5.00 g, 29.7 mmol) in THF (25 mL), 4-fluorostyrene oxide (4.22 mL, 35.7 mmol), and PTSA·H_2O (200 mg, 1.05 mmol) in toluene (50 mL) gave, after chromatographic purification (100% CH_2Cl_2), an inseparable mixture of both diastereomers of lactone (±)-**10** (6.66 g, 78%) as a white solid; mp 60–62 °C.

IR (KBr): 3062, 3005 (C–H), 1895, 1767 (C=O), 1607, 1512.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.16–2.25 (m, 1 H, CH), 2.57–2.71 (m, 2 H, CH), 2.97–3.04 (m, 1 H, CH), 4.02 (dd, *J* = 8.1, 3.7

Hz, 1 H, CH), 4.12 (dd, *J* = 11.3, 8.8 Hz, 1 H, CH), 5.35 (dd, *J* = 9.9, 6.3 Hz, 1 H, CH), 5.45 (dd, *J* = 8.8, 6.3 Hz, 1 H, CH), 7.02–7.15 (m, 5 H, H_{Ar}), 7.28–7.32 (m, 3 H, H_{Ar}), 7.38–7.42 (m, 6 H, H_{Ar}), 7.59–7.64 (m, 4 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 38.3, 38.6, 45.3, 46.7, 78.4, 79.0, 115.7, 115.8, 127.3, 127.6, 128.8, 129.0, 129.4, 129.4, 131.6, 131.6, 133.7, 134.1, 134.3, 134.3, 162.8, 162.9, 174.0, 174.2.

MS (NSI$^+$): *m*/*z* (%) = 306 ([M + NH_4]$^+$, 100).

HRMS (NSI$^+$): *m*/*z* [M + NH_4]$^+$ calcd for $C_{16}H_{17}O_2NFS$: 306.0959; found: 306.0962.

3-Benzyl-5-phenyl-3-(phenylthio)dihydrofuran-2(3*H*)-one (11)

Following general procedure B using 2.5 M *n*-BuLi in hexanes (9.2 mL, 23.1 mmol), *i*-Pr_2NH (3.2 mL, 23.1 mmol) in THF (40 mL), lactone **9** (4.80 g, 17.8 mmol) in THF (20 mL) and, BnBr (2.7 mL, 23.1 mmol) and NaI (0.540 g, 3.60 mmol) in DMPU (11 mL) gave crude product. NMR crude shows 6:1 mixture of diastereomers. Purification by chromatography (silica gel, CH_2Cl_2–PE, 20:80–100:0) gave the major diastereomer (4.76 g, 74%) as a white solid; mp 110–112 °C.

IR (KBr): 2978, 1770 (C=O), 1488, 1439, 1172 (C–O), 1070, 980, 752, 697 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.33 (ABX, J_{AB} = 14.1 Hz, J_{AX} = 9.0 Hz, 1 H, CH*H*), 2.80 (ABX, J_{BA} = 14.1 Hz, J_{BX} = 7.5 Hz, 1 H, CH*H*), 3.02 (ABq, J_{AB} = 13.2 Hz, 1 H, CH*H*), 3.47 (ABq, J_{BA} = 13.2 Hz, 1 H, CH*H*), 4.03 (ABX, J_{XA} = 9.0 Hz, J_{XB} = 7.5 Hz, 1 H, CH), 6.58–6.61 (m, 2 H, H_{Ar}), 7.11–7.22 (m, 3 H, H_{Ar}), 7.34–7.41 (m, 7 H, H_{Ar}), 7.44–7.49 (m, 1 H, H_{Ar}), 7.62–7.65 (m, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.9, 43.7, 58.4, 78.2, 126.0, 128.3, 128.8, 128.9, 129.4, 129.8, 130.4, 130.5, 130.6, 135.6, 137.8, 139.4, 177.6.

5-(4-Fluorophenyl)-3-methyl-3-(phenylthio)dihydrofuran-2(3*H*)-one (12)

Following general procedure **B** using *n*-BuLi (5.42 mL, 13.5 mmol), *i*-Pr_2NH (1.90 mL, 13.5 mmol), THF (10 mL), lactone (±)-**10** (3.00 g, 10.4 mmol) in THF (10 mL), and MeI (0.71 mL, 11.5 mmol) in DMPU (7 mL) gave a mixture of both diastereomers of lactone (±)-**12** (94:6 ratio). Chromatographic purification (EtOAc–PE, 15:85), gave lactone (±)-**12** (2.49 g, 79%) as a yellow solid.

Major diastereomer

Mp 42–44 °C.

IR (KBr): 2977 (C–H), 1769 (C=O), 1488 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.69 (s, 3 H, CH_3), 2.40 (dd, *J* = 13.7, 9.0 Hz, 1 H, CH), 2.64 (dd, *J* = 13.7, 7.0 Hz, 1 H, CH), 5.34 (dd, *J* = 9.0, 7.0 Hz, 1 H, CH), 6.92–7.01 (m, 4 H, H_{Ar}), 7.38–7.42 (m, 2 H, H_{Ar}), 7.45–7.49 (m, 1 H, H_{Ar}), 7.60–7.62 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.7, 44.0, 52.8, 76.6, 115.6, 127.5, 129.3, 129.9, 130.3, 134.6, 137.1, 162.7, 177.2.

MS (NSI$^+$): *m*/*z* (%) = 320 ([M + NH_4]$^+$, 100).

HRMS (NSI$^+$): *m*/*z* [M + NH_4]$^+$ calcd for $C_{17}H_{19}O_2NFS$: 320.1115; found: 320.1118.

3-Ethyl-5-(4-fluorophenyl)-3-(phenylthio)dihydrofuran-2(3*H*)-one (13)

Following general procedure B using *n*-BuLi (7.22 mL, 18.0 mmol), *i*-Pr_2NH (2.53 mL, 18.0 mmol), THF (10 mL), lactone (±)-**10** (4.00 g, 13.9 mmol) in THF (10 mL), and EtI (1.23 mL, 15.3 mmol) in DMPU (10 mL) gave a mixture of both diastereomers of lactone (±)-**13** (96:4 ratio). Chromatographic purification (EtOAc–PE, 10:90), gave lactone (±)-**13** (2.87 g, 65%) as a white solid.

Major diastereomer

Mp 48–50 °C.

IR (KBr): 3066, 2971 (C–H), 2941, 1765 (C=O), 1606, 1512 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3), 1.96–2.07 (m, 2 H, CH_2CH_3), 2.35 (dd, *J* = 14.1, 8.4 Hz, 1 H, CH), 2.77 (dd, *J* = 14.1, 7.6 Hz, 1 H, CH), 5.29 (t, *J* = 8.0 Hz, 1 H, CH), 6.83–6.87 (m, 2 H, H_{Ar}), 6.92–6.97 (m, 2 H, H_{Ar}), 7.37–7.42 (m, 2 H, H_{Ar}), 7.45–7.50 (m, 1 H, H_{Ar}), 7.59–7.61 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.4, 29.8, 41.2, 57.6, 77.0, 115.5, 127.5, 129.3, 129.9, 130.3, 135.1, 137.3, 162.6, 176.7.

MS (NSI$^+$): *m*/*z* (%) = 334 ([M + NH_4]$^+$, 100).

HRMS (NSI$^+$): *m*/*z* [M + NH_4]$^+$ calcd for $C_{18}H_{21}O_2NFS$: 334.1272; found: 334.1274.

3-(4-Bromobenzyl)-5-(4-fluorophenyl)-3-(phenylthio)dihydrofuran-2(3*H*)-one (14)

Following general procedure **B** using *n*-BuLi (5.42 mL, 13.5 mmol), *i*-Pr_2NH (1.90 mL, 13.5 mmol), THF (10 mL), lactone (±)-**10** (3.0 mg, 10.4 mmol) in THF (10 mL), and 4-bromobenzyl bromide (2.86 mL, 11.5 mmol) in DMPU (7 mL) gave a mixture of both diastereomers of lactone (±)-**14** (96:4 ratio). Chromatographic purification (CH_2Cl_2–PE, 40:60) gave lactone (±)-**14** (2.45 g, 51%) as a white solid.

Major diastereomer

Mp 104–106 °C.

IR (KBr): 3065, 2926 (C–H), 1775 (C=O), 1604, 1509 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.23 (dd, *J* = 14.3, 8.5 Hz, 1 H, CH), 2.69 (dd, *J* = 14.3, 7.6 Hz, 1 H, CH), 2.91 (ABq, *J* = 13.4 Hz, 1 H, CH_AH_B), 3.32 (ABq, *J* = 13.4 Hz, 1 H, CH_AH_B), 4.14 (t, *J* = 8.1 Hz, 1 H, CH), 6.52–6.55 (m, 2 H, H_{Ar}), 6.75–6.79 (m, 2 H, H_{Ar}), 7.10–7.13 (m, 2 H, H_{Ar}), 7.30–7.34 (m, 2 H, H_{Ar}), 7.38–7.44 (m, 3 H, H_{Ar}), 7.52–7.54 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.2, 42.5, 57.5, 77.0, 115.4, 122.1, 127.4, 129.5, 129.9, 130.2, 131.7, 132.2, 134.1, 134.7, 137.5, 162.6, 176.7.

MS (NSI$^+$): *m*/*z* (%) = 476 ([M + NH_4]$^+$, 100).

HRMS (NSI$^+$): *m*/*z* [^{79}BrM + NH_4]$^+$ calcd for $C_{23}H_{22}O_2N^{79}BrFS$: 474.0533; found: 474.0528.

3-Allyl-5-(4-fluorophenyl)-3-(phenylthio)dihydrofuran-2(3*H*)-one (15)

Following general procedure **B** using *n*-BuLi (7.22 mL, 18.0 mmol) and *i*-Pr_2NH (2.53 mL, 18.0 mmol) in THF (10 mL), lactone (±)-**10** (4.00 g, 13.9 mmol) in THF (10 mL) and allyl bromide (1.32 mL, 15.3 mmol) and NaI (0.42 g, 2.78 mmol) in DMPU (10 mL) gave a mixture of both diastereomers of lactone (±)-**15** (95:5 ratio). Chromatographic purification (EtOAc–PE, 10:90) gave lactone (±)-**15** (2.83 g, 65%) as a white solid.

Major diastereomer

Mp 56–58 °C.

IR (KBr): 3077, 2981 (C–H), 2934, 1771 (C=O), 1640, 1607, 1513 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.33 (dd, *J* = 14.1, 8.3 Hz, 1 H, CH), 2.64 (ABqd, *J* = 13.9, 7.8 Hz, 1 H, CH_2=CHCH_AH_B), 2.76 (ABqd, *J* = 13.9, 6.9 Hz, 1 H, CH_2=CHCH_AH_B), 2.81 (dd, *J* = 14.1, 8.0 Hz, 1 H, CH), 5.24 (t, *J* = 8.0 Hz, 1 H, CH), 5.31–5.33 (m, 1 H, CH_AH_B=CH), 5.36–5.38 (m, 1 H, CH_AH_B=CH), 5.88–6.02 (m, 1 H, CH_2=C*H*), 6.81–6.87 (m, 2 H, H_{Ar}), 6.91–6.98 (m, 2 H, H_{Ar}), 7.39–7.45 (m, 2 H, H_{Ar}), 7.47–7.53 (m, 1 H, H_{Ar}), 7.61–7.65 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.8, 41.2, 56.2, 77.0, 115.5, 121.0, 127.5, 129.4, 130.0, 130.1, 131.4, 135.1, 137.4, 162.4, 176.5.

MS (NSI$^+$): *m*/*z* (%) = 346 ([M + NH_4]$^+$, 100).

HRMS (NSI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{18}FO_2S$: 329.1006; found: 329.1005.

3-Benzyl-5-(4-fluorophenyl)-3-(phenylthio)dihydrofuran-2(3*H*)-one (16)

Following general procedure **B** using *n*-BuLi (5.42 mL, 13.5 mmol), *i*-Pr_2NH (1.90 mL, 13.5 mmol), THF (10 mL), lactone (±)-**10** (3.0 mg, 10.4 mmol) in THF (10 mL) and BnBr (1.36 mL, 11.5 mmol) in DMPU (7 mL) gave a mixture of both diastereomers of lactone (±)-**16** (98:2 ratio). Chromatographic purification (EtOAc–PE, 10:90) gave lactone (±)-**16** (2.45 g, 62%) as a white solid.

Major diastereomer

Mp 82–84 °C.

IR (KBr): 3066, 2923 (C–H), 1770 (C=O), 1607, 1509 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.16 (dd, *J* = 14.2, 8.9 Hz, 1 H, CH), 2.66 (dd, *J* = 14.2, 7.4 Hz, 1 H, CH), 2.88 (ABq, *J* = 13.2 Hz, 1 H, C*H*$_A$H$_B$), 3.35 (ABq, *J* = 13.2 Hz, 1 H, CH$_A$*H*$_B$), 3.86 (dd, *J* = 8.9, 7.4 Hz, 1 H, CH), 6.38–6.43 (m, 2 H, H_{Ar}), 6.65–6.71 (m, 2 H, H_{Ar}), 7.17–7.37 (m, 8 H, H_{Ar}), 7.48–7.51 (m, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.5, 43.3, 58.1, 77.1, 115.4, 127.4, 127.9, 129.0, 129.5, 130.0, 130.0, 130.2, 134.9, 135.2, 137.5, 162.6, 177.0.

MS (NSI$^+$): *m*/*z* (%) = 396 ([M + NH_4]$^+$, 100).

HRMS (NSI$^+$): *m*/*z* [M + NH_4]$^+$ calcd for $C_{23}H_{23}O_2NFS$: 396.1428; found: 396.1427.

3-Methyl-5-phenyl-3-(phenylthio)dihydrofuran-2(3*H*)-one (17)

Following general procedure B using 2.5 M *n*-BuLi in hexanes (3.8 mL, 9.60 mmol), *i*-Pr_2NH (1.4 mL, 9.60 mmol) in THF (15 mL), lactone **9** (2.00 g, 7.40 mmol) in THF (10 mL), and MeI (23.1 mmol, 2.7 mL) in DMPU (4.3 mL) gave crude product. NMR crude shows 14:1 mixture of diastereomers. Purification by chromatography (silica gel, CH_2Cl_2–PE, 50:50–100:0) gave the major diastereomer (1.41 g, 67%) as a white solid; mp 42–44 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.67 (s, 3 H, CH_3), 2.42 (ABX, J_{AB} = 13.8 Hz, J_{AX} = 9.2 Hz, 1 H, CH*H*), 2.61 (ABX, J_{BA} = 13.6 Hz, J_{BX} = 6.8 Hz, 1 H, CH*H*), 5.34 (ABX, J_{XA} = 9.2 Hz, J_{XB} = 6.8 Hz, 1 H, CH), 6.95–6.97 (m, 2 H, H_{Ar}), 7.25–7.30 (m, 3 H, H_{Ar}), 7.34–7.39 (m, 2 H, H_{Ar}), 7.41–7.46 (m, 1 H, H_{Ar}), 7.58–7.60 (m, 2 H, H_{Ar}).

3-Ethyl-5-phenyl-3-(phenylthio)dihydrofuran-2(3*H*)-one (18)

Following general procedure B using 2.5 M *n*-BuLi in hexanes (9.6 mL, 24.1 mmol), *i*-Pr_2NEt (3.4 mL, 24.1 mmol) in THF (40 mL), lactone **9** (5.00 g, 18.5 mmol) in THF (20 mL), and EtI (1.5 mL, 18.5 mmol) in DMPU (11 mL) gave crude product. NMR crude shows 84% conversion, 9:1 mixture of diastereomers. Purification by chromatography (silica gel, EtOAc–PE, 5:95) gave the major diastereomer (3.53 g, 64%) as a white solid; mp 84–86 °C.

IR (KBr disc): 2976 (C–H), 1772 (C=O), 1458, 1323, 1180 (C–O), 1025, 958, 755, 696.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19 (t, *J* = 7.4 Hz, 3 H, CH_3), 2.00 (qd, *J* = 7.4, 1.6 Hz, 2 H, CH_2), 2.37 (ABX, J_{AB} = 14.0 Hz, J_{AX} = 8.5 Hz, 1 H, CH*H*), 2.75 (ABX, J_{BA} = 14.0 Hz, J_{BX} = 7.5 Hz, 1 H, CH*H*), 5.28 (t, *J* = 8.0 Hz, 1 H, CH), 6.89 (dd, *J* = 7.5, 1.8 Hz, 2 H, H_{Ar}), 7.22–7.28 (m, 3 H, H_{Ar}), 7.36 (tt, *J* = 7.4, 1.6 Hz, 2 H, H_{Ar}), 7.42–7.46 (m, 1 H, H_{Ar}), 7.58 (dd, *J* = 8.2, 1.3 Hz, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.5, 29.8, 41.4, 57.7, 77.7, 125.7, 128.6, 128.7, 129.3, 129.9, 130.4, 137.3, 139.4, 177.0.

MS (ES+): *m*/*z* (%) = 316.1 (100, [M + NH_4]$^+$), 299.1 (37, [M + H]$^+$).

HRMS (ES+): *m*/*z* [M + NH_4]$^+$ calcd for $C_{18}H_{22}O_2NS$: 316.1366; found: 316.1367.

3-(4-Bromobenzyl)-5-phenyl-3-(phenylthio)dihydrofuran-2(3*H*)-one (19)

Following general procedure **B** using 2.5 M *n*-BuLi in hexanes (5.6 mL, 13.9 mmol), *i*-Pr_2NH (1.7 mL, 12.2 mmol) in THF (25 mL), lactone **9** (3.00 g, 11.1 mmol) in THF (5 mL), and 4-bromobenzyl bromide (2.78 g, 11.1 mmol) in DMPU (6.7 mL) gave crude product. NMR crude shows 15:1 mixture of diastereomers. Purification by chromatography (silica gel, Et_2O–PE, 25:75) gave the major diastereomer (3.00 g, 62%) as a white solid; mp 126–127 °C.

IR (KBr): 2977, 1769 (C=O), 1488, 1439, 1405, 1326, 1237, 1218, 1164 (C–O), 1072, 1043, 1027, 1012, 984, 752, 696 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (ABX, J_{BA} = 14.2 Hz, J_{BX} = 8.6, 1 H, CH*H*), 2.77 (ABX, J_{AB} = 14.2 Hz, J_{AX} = 7.6 Hz, 1 H, C*H*H), 2.99 (ABq, *J* = 13.4 Hz, 1 H, CH*H*), 3.39 (ABq, *J* = 13.4 Hz, 1 H, C*H*H), 4.26 (app t, *J* = 8.0 Hz, 1 H, CH), 6.66–6.69 (m, 2 H, H_{Ar}), 7.15–7.22 (m, 5 H, H_{Ar}), 7.37–7.41 (m, 2 H, H_{Ar}), 7.45–7.51 (m, 3 H, H_{Ar}), 7.59–7.62 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.4, 42.7, 57.5, 77.8, 125.6, 128.58, 128.62, 129.5, 130.0, 130.2, 131.9, 132.2, 134.3, 137.5, 139.0, 176.9.

MS (ESI+): *m*/*z* (%) = 458 (100, [^{81}BrM + NH_4]$^+$), 456 (97, [^{79}BrM + NH_4]$^+$).

HRMS (ESI+): *m*/*z* [^{79}BrM + NH_4]$^+$ calcd for $C_{23}H_{23}{}^{79}BrO_2NS$: 456.0627; found: 456.0627.

3-Allyl-5-phenyl-3-(phenylthio)dihydrofuran-2(3*H*)-one (20)

Following general procedure B using 2.5 M *n*-BuLi in hexanes (7.7 mL, 19.2 mmol), *i*-Pr_2NH (2.7 mL, 19.2 mmol) in THF (30 mL), lactone **9** (4.00 g, 14.8 mmol) in THF (15 mL), and allyl bromide (1.7 mL, 19.2 mmol) and NaI (0.450 g, 3.00 mmol) in DMPU (11 mL) gave crude product. NMR crude shows 8:1 mixture of diastereomers. Purification by chromatography (silica gel, EtOAc–PE, 10:90) gave the major diastereomer (3.44 g, 75%) as a colourless oil.

IR (thin film): 3062, 2933 (C–H), 1769 (C=O), 1439, 1325, 1172 (C–O), 1026, 995, 752, 695 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 (dd, *J* = 14.1, 8.4 Hz, 1 H, CHC*H*H), 2.48 (app. dd, *J* = 13.9, 7.8 Hz, 1 H, C*H*HCH=), 2.61 (app. dd, *J* = 13.8, 6.8 Hz, 1 H, C*H*HCH=), 2.68 (app. dd, *J* = 14.0, 7.6 Hz, 1 H, CHC*H*H), 5.11 (t, *J* = 8.0 Hz, 1 H, CH_2CH), 5.15–5.16 (m, 1 H, =CH*H*), 5.19–5.22 (m, 1 H, =CH*H*), 5.73–5.87 (m, 1 H, =CH), 6.71–6.74 (m, 2 H, H_{Ar}), 7.07–7.14 (m, 3 H, H_{Ar}), 7.21–7.27 (m, 2 H, H_{Ar}), 7.29–7.35 (m, 1 H, H_{Ar}), 7.44–7.48 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.9, 41.3, 56.3, 77.8, 121.0, 125.7, 128.6, 128.7, 129.4, 130.0, 130.2, 131.6, 137.4, 139.3, 176.7.

MS (ES+): *m*/*z* (%) = 328.1 (100, [M + NH_4]$^+$), 311.1 (48, [M + H]$^+$).

HRMS (ES+): *m*/*z* [M + NH_4]$^+$ calcd for $C_{19}H_{22}O_2NS$: 328.1366; found: 328.1368.

3-Benzyl-5-phenylfuran-2-yl Phenyl Carbonate (21)

Following general procedure C using *m*-CPBA (1.65 g, 5.55 mmol), lactone **11** (2.00 g, 5.55 mmol) in $CHCl_3$ (40 mL) gave the crude sulfoxide, which was heated in toluene (40 mL). NMR analysis of the crude reaction product indicates a 1:3.5 mixture of 3*H*/5*H* isomers. Purification by chromatography (silica gel, EtOAc–PE, 5:95–10:90) gave both butenolides 3-benzyl-5-phenylfuran-2-one **46** (ratio 5*H*/3*H* 4:1) (1.16 g, 83%) as a white solid.

Major (5*H*)-tautomer
^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.64–3.76 (m, 2 H, CH_2), 5.90 (q, *J* = 1.9 Hz, 1 H, PhC*H*), 6.94 (q, *J* = 1.9 Hz, 1 H, CH=C), 7.24–7.48 (m, 10 H, H_{Ar}).

Minor (3*H*)-tautomer
^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.20 (ddd, *J* = 17.5, 6.0, 3.0 Hz, 1 H, CH*H*), 3.72–3.77 (m, 1 H, C*H*H), 5.65 (dd, *J* = 8.3, 6.0 Hz, 1 H, CH=C), 7.24–7.55 (m, 10 H, H_{Ar}), 7.68 (t, *J* = 2.9 Hz, 1 H, PhC*H*).

Following general procedure F using Et_3N (0.89 mL, 6.40 mmol), butenolide **46** (0.800 g, 3.20 mmol), THF (15 mL) and phenyl chloroformate (0.84 mL, 6.40 mmol) gave, after purification by chromatography (silica gel, CH_2Cl_2–PE, 15:85), **21** (0.595 g, 50%) as a white solid; mp 94–96 °C.

IR (KBr): 3063 (C–H), 2924, 2858, 1796 (C=O), 1656 (ArH), 1648 (C=C), 1218 (C–O), 1194 (C–O), 1115, 1052, 760 cm^{-1} (furan CH).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.78 (s, 2 H, CH_2), 6.46 (s, 1 H, CH), 7.21–7.45 (m, 13 H, H_{Ar}), 7.56–7.59 (m, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.0, 107.8, 108.8, 120.8, 123.5, 126.6, 126.8, 127.6, 128.7, 128.8, 128.8, 129.8, 130.2, 139.2, 146.4, 147.6, 150.7, 151.0.

MS: *m*/*z* (%) = 371 (100, $[M + H]^+$).

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{19}O_4$: 371.1278; found: 371.1279.

3-Benzyl-5-phenylfuran-2-yl 2,2,2-Trichloroethyl Carbonate (22)
Following general procedure F using Et_3N (0.70 mL, 5.00 mmol), butenolide **46** (0.630 g, 2.50 mmol), THF (10 mL), and 2,2,2-trichloroethyl chloroformate (0.69 mL, 5.00 mmol) gave, after purification by chromatography (silica gel, CH_2Cl_2–PE, 15:85), **22** (0.490 g, 46%) as a white solid; mp 92–94 °C.

IR (KBr disc): 2965 (C–H), 1792 (C=O), 1655 (C=C), 1283 (C–O), 1208 (C–O), 758 (C–Cl), 712 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.73 (s, 2 H, CH_2Ph), 4.87 (s, 2 H, CH_2CCl_3), 6.45 (s, 1 H, CH), 7.21–7.38 (m, 8 H, H_{Ar}), 7.54–7.58 (m, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 29.9, 77.9, 93.8, 107.8, 108.8, 123.5, 126.6, 127.7, 128.7, 128.8, 130.1, 139.1, 146.1, 147.7, 151.4.

3-Benzyl-5-(4-fluorophenyl)furan-2-yl Phenyl Carbonate (23)
Following general procedure C using lactone (±)-**16** (2.30 g, 6.09 mmol), *m*-CPBA (1.50 g, 6.09 mmol), and $CHCl_3$ (150 mL) gave the crude sulfoxide. Subsequent heating at reflux in toluene (50 mL) overnight gave, after chromatographic purification (EtOAc–PE, 10:90), a mixture of both tautomers of butenolide 3-benzyl-5-(4-fluorophenyl)furan-2-one **51** (ratio 5*H*/3*H* 81:19) (1.28 g, 78%) as a yellow oil.

Major (5*H*)-tautomer
IR (thin film): 3501, 3064, 3030, 2917 (C–H), 1760 (C=O), 1655, 1606 (Ar C=C), 1512 cm^{-1} (C=C).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.71 (s, 2 H, CH_2Ph), 5.89–5.90 (m, 1 H, CH), 6.93 (q, *J* = 1.7 Hz, 1 H, H_{Ar}), 7.05–7.16 (m, 2 H, H_{Ar}), 7.20–7.42 (m, 6 H, H_{Ar}, CH), 7.44–7.55 (m, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.8, 81.7, 116.0, 127.0, 128.4, 128.9, 128.9, 130.8, 134.3, 137.2, 148.4, 163.1, 171.9.

MS (NSI^+): *m*/*z* (%) = 286 ($[M + NH_4]^+$, 100).

HRMS (NSI^+): *m*/*z* $[M + NH_4]^+$ calcd for $C_{17}H_{17}O_2NF$: 286.1238; found: 286.1241.

Following general procedure D using *i*-Pr_2NH (0.79 mL, 5.63 mmol) and *n*-BuLi (2.25 mL, 5.63 mmol) in THF (15 mL), butenolide (±)-**51** (1.16 g, 4.33 mmol) in THF (15 mL) and phenyl chloroformate (0.72 mL, 5.63 mmol) in THF (15 mL) gave, after chromatographic purification (EtOAc–PE, 2.5:97.5), carbonate **23** (320 mg, 19%) as a white solid; mp 100–102 °C.

IR (KBr): 3108 (C–H), 1795 (C=O), 1656, 1591, 1561 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.79 (s, 2 H, CH_2), 6.42 (s, 1 H, CH), 7.04–7.10 (m, 2 H, H_{Ar}), 7.25–7.38 (m, 8 H, H_{Ar}), 7.43–7.48 (m, 2 H, H_{Ar}), 7.53–7.59 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.9, 107.4, 108.8, 115.7, 120.7, 125.2, 126.4, 126.5, 126.7, 128.6, 128.7, 129.7, 139.0, 146.2, 146.7, 150.6, 150.8, 162.2.

MS (ES^+): *m*/*z* (%) = 411 ($[M + Na]^+$, 100).

HRMS (ES+): *m*/*z* $[M + Na]^+$ calcd for $C_{24}H_{17}O_4NaF$: 411.1009; found: 411.1008.

5-(4-Fluorophenyl)-3-methylfuran-2-yl Phenyl Carbonate (24)
Following general procedure C using lactone (±)-**12** (2.00 g, 6.62 mmol), *m*-CPBA (1.63 g, 6.62 mmol), and $CHCl_3$ (150 mL), gave the crude sulfoxide. Subsequent heating at reflux in toluene (50 mL) overnight gave, after chromatographic purification (EtOAc–PE, 15:85), a mixture of both tautomers of butenolide 5-(4-fluorophenyl)-3-methylfuran-2-one **52** (ratio 5*H*/3*H* 97:3) (1.06 g, 84%) as an orange solid.

Major (5*H*)-tautomer
Mp 30–32 °C.

IR (thin film): 2924 (C–H), 2852, 1760 (C=O), 1606 (Ar C=C), 1509 cm^{-1} (C=C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.03 (t, *J* = 1.8 Hz, 3 H, CH_3), 5.87 (app t, *J* = 1.8 Hz, 1 H, CH), 7.08–7.13 (m, 3 H, H_{Ar}, CH), 7.25–7.29 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.6, 81.5, 115.9, 128.5, 129.8, 131.0, 148.2, 163.0, 174.1.

MS (NSI^+): *m*/*z* (%) = 318 ($[M + H]^+$, 100).

HRMS (NSI^+): *m*/*z* $[M + H]^+$ calcd for $C_{11}H_{10}FO_2$: 193.0659; found: 193.0658.

Following general procedure D using *i*-Pr_2NH (0.71 mL, 5.08 mmol) and *n*-BuLi (2.03 mL, 5.08 mmol) in THF (15 mL), butenolide (±)-**52** (750 mg, 3.91 mmol) in THF (15 mL), and phenyl chloroformate (0.65 mL, 5.08 mmol) in THF (15 mL) gave, after chromatographic purification (EtOAc–PE, 2.5:97.5), **24** (944 mg, 84%) as a white solid; mp 63–65 °C.

IR (KBr): 3059, 2935 (C–H), 1794 (C=O), 1659, 1597, 1561 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.04 (s, 3 H, CH_3), 6.48 (s, 1 H, CH), 7.06–7.11 (m, 2 H, H_{Ar}), 7.31–7.35 (m, 3 H, H_{Ar}), 7.45–7.49 (m, 2 H, H_{Ar}), 7.57–7.60 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.6, 104.9, 108.4, 115.7, 120.7, 125.1, 126.6, 126.7, 129.7, 146.2, 146.2, 150.6, 150.9, 162.1.

MS (ES^+): *m*/*z* (%) = 335 ($[M + Na]^+$, 64).

HRMS (ES+): *m*/*z* $[M + Na]^+$ calcd for $C_{18}H_{13}O_4NaF$: 335.0696; found: 335.0699.

5-(4-Fluorophenyl)-3-methylfuran-2-yl 2,2,2-Trichloroethyl Carbonate (25)
Following general procedure D using *i*-Pr_2NH (0.73 mL, 5.21 mmol) and *n*-BuLi (2.08 mL, 5.21 mmol) in THF (15 mL), butenolide **52** (770 mg, 4.01 mmol) in THF (15 mL), and trichloroethyl chloroformate (0.70 mL, 5.21 mmol) in THF (15 mL) gave, after chromatographic purification (EtOAc–PE, 2.5:97.5), **25** (476 mg, 33%) as a white solid; mp 42–44 °C.

IR (KBr): 3013, 2965 (C–H), 2929, 1795 (C=O), 1662, 1600, 1562 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.99 (s, 3 H, CH_3), 4.92 (s, 2 H, CH_2), 6.46 (s, 1 H, CH), 7.05–7.09 (m, 2 H, H_{Ar}), 7.54–7.57 (m, 2 H, H_{Ar}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 8.5, 77.7, 93.7, 104.9, 108.3, 115.7, 125.1, 126.5, 145.9, 146.3, 151.3, 162.2.

Anal. Calcd for $C_{14}H_{11}O_4Cl_3F$: C, 45.7; H, 2.7. Found: C, 45.9; H, 2.6.

3-Ethyl-5-phenylfuran-2-yl Phenyl Carbonate (26)

Following general procedure C using *m*-CPBA (1.65 g, 6.70 mmol) and lactone **18** (2.00 g, 6.70 mmol) in $CHCl_3$ (20 mL) gave the crude sulfoxide, which was heated in toluene (20 mL). NMR analysis of the crude reaction product indicates an 18:1 mixture of 5*H*/3*H* isomers. Purification by chromatography (silica gel, EtOAc–PE, 5:95–10:90) gave 3-ethyl-5-phenylfuran-2(5*H*)-one (**48**) (1.32 g, 64%) as a pinkish oil.

IR (thin film): 2972 (C–H), 1756 (C=O), 1456, 1327, 1146 (C–O), 1055, 965, 752, 698, 596 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.09 (t, *J* = 7.5 Hz, 3 H, CH_3), 2.25 (dt, *J* = 7.5, 1.9 Hz, 1 H, CH*H*), 2.29 (dt, *J* = 7.4, 1.9 Hz, 1 H, CH*H*), 5.77 (q, *J* = 1.9 Hz, 1 H, CH), 6.98 (q, *J* = 1.7 Hz, 1 H, =CH), 7.14–7.16 (m, 2 H, H_{Ar}), 7.24–7.30 (m, 3 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.9, 18.8, 82.4, 126.5, 129.0, 129.2, 135.4, 135.6, 147.0, 173.9.

MS (ES+): *m*/*z* (%) = 206.1 (35, $[M + NH_4]^+$), 189.1 (100, $[M + H]^+$).

HRMS (ES+): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{13}O_2$: 189.0910; found: 189.0907.

Following general procedure D using 2.5 M *n*-BuLi in hexanes (2.5 mL, 6.32 mmol) and *i*-Pr_2NH (2.5 mL, 6.32 mmol) in THF (20 mL), butenolide **48** (1.50 g, 4.86 mmol) in THF (20 mL), and phenyl chloroformate (0.79 mL, 6.32 mmol) in THF (20 mL) gave, after purification by chromatography (silica gel, CH_2Cl_2–PE, 25:75), **26** (0.730 g, 48%) as a yellow oil.

IR (thin film): 2972 (C–H), 1796 (C=O), 1492, 1195 (C–O), 760, 692 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.15 (t, *J* = 7.6 Hz, 3 H, CH_3), 2.36 (q, *J* = 7.6 Hz, 2 H, CH_2), 6.49 (s, 1 H, CH), 7.14–7.38 (m, 8 H, H_{Ar}), 7.53 (dd, *J* = 8.4, 1.2 Hz, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 17.0, 107.3, 111.2, 120.8, 123.5, 126.8, 127.4, 128.8, 129.8, 130.4, 145.6, 147.3, 150.9, 151.0.

MS (ES+): *m*/*z* (%) = 330.9 (100, [M + Na]), 302.9 (27, [M + Na – C_2H_5]).

HRMS (ES+): *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{16}O_4Na$: 331.0946; found: 331.0945.

3-Ethyl-5-(4-fluorophenyl)furan-2-yl Phenyl Carbonate (27)

Following general procedure C using lactone (±)-**13** (2.50 g, 7.91 mmol), *m*-CPBA (1.95 g, 7.91 mmol), and $CHCl_3$ (150 mL) gave the crude sulfoxide. Subsequent heating at reflux in toluene (100 mL) overnight gave, after chromatographic purification (EtOAc–PE, 10:90), a mixture of both tautomers of 3-ethyl-5-(4-fluorophenyl)furan-2-one **53** (ratio 5*H*/3*H* 99:1) (1.23 g, 75%) as a yellow solid.

Major (5*H*)-tautomer

Mp 24–26 °C.

IR (KBr): 3080, 2974 (C–H), 2939, 1759 (C=O), 1656, 1607 (Ar C=C), 1509 cm^{-1} (C=C).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.13 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 2.31 (qt, *J* = 7.5, 1.9 Hz, 2 H, CH_2CH_3), 5.79 (q, *J* = 1.9 Hz, 1 H, CH), 6.97–7.03 (m, 3 H, H_{Ar}, CH), 7.15–7.19 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.8, 18.7, 81.6, 115.9, 128.4, 131.1, 135.9, 146.6, 163.0, 173.6.

MS (NSI^+): *m*/*z* (%) = 207 ($[M + H]^+$, 100).

HRMS (NSI^+): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{12}FO_2$: 207.0816; found: 207.0812.

Following general procedure D using *i*-Pr_2NH (0.86 mL, 6.15 mmol) and *n*-BuLi (2.46 mL, 6.15 mmol) in THF (15 mL), butenolide (±)-**53** (975 mg, 4.73 mmol) in THF (15 mL), and phenyl chloroformate (0.79 mL, 6.15 mmol) in THF (15 mL) gave, after chromatographic purification (EtOAc–PE, 2:98), **27** (340 mg, 22%) as a white solid; mp 48–50 °C.

IR (KBr): 3080, 2935 (C–H), 2880, 1797 (C=O), 1655, 1594 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.6 Hz, 3 H, CH_3), 2.46 (q, *J* = 7.6 Hz, 2 H, CH_2CH_3), 6.53 (s, 1 H, CH), 7.07–7.11 (m, 2 H, H_{Ar}), 7.31–7.35 (m, 3 H, H_{Ar}), 7.45–7.49 (m, 2 H, H_{Ar}), 7.58–7.61 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 16.8, 106.9, 111.1, 115.7, 120.7, 125.1, 126.6, 126.7, 129.7, 145.5, 146.4, 150.8, 150.9, 162.1.

MS (ES+): *m*/*z* (%) = 349 ($[M + Na]^+$, 8).

HRMS (ES+): *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{15}O_4NaF$: 349.0852; found: 349.0848.

3-(4-Bromobenzyl)-5-phenylfuran-2-yl Phenyl Carbonate (28)

Following general procedure C using *m*-CPBA (1.44 g, 8.36 mmol) and lactone **19** (2.70 g, 6.15 mmol) in CH_2Cl_2 (8 mL) gave the crude sulfoxide, which was heated in toluene (10 mL). NMR analysis of the crude reaction product indicates a 4:1 mixture of 5*H*/3*H* isomers. Purification by chromatography (silica gel, Et_2O–PE, 15:85) gave both butenolides 3-(4-bromobenzyl)-5-phenylfuran-2-one **49** (1.46 g, 72% yield) as a yellow solid.

Major (5*H*) tautomer

^1H NMR (400 MHz, $CDCl_3$): δ = 3.60–3.72 (m, 2 H, CH_2), 5.91 (q, *J* = 1.7 Hz, 1 H, CH), 6.97 (q, *J* = 1.7 Hz, 1 H, =CH), 7.15–7.18 (m, 2 H, H_{Ar}), 7.23–7.25 (m, 2 H, H_{Ar}), 7.36–7.42 (m, 3 H, H_{Ar}), 7.46–7.49 (m, 2 H, H_{Ar}).

Following general procedure F using Et_3N (0.40 mL, 2.72 mmol), butenolide **46** (0.448 g, 1.36 mmol), THF (3 mL), and phenyl chloroformate (0.34 mL, 2.72 mmol) gave, after purification by chromatography (silica gel, CH_2Cl_2–PE, 5:95), **28** (0.354 g, 58%) as a white solid; mp 92 °C.

IR (KBr): 3062 (ArH), 2924, 2858, 1797 (C=O), 1655 (ArH), 1648 (ArH), 1606 (ArH), 1594 (ArH), 1556 (ArH), 1488, 1405, 1216 (C–O), 1194 (C–O), 1114, 1072 (ArC–Br), 1053, 1011, 930, 760 cm^{-1} (furan CH).

^1H NMR (400 MHz, $CDCl_3$): δ = 3.71 (s, 2 H, CH_2), 6.42 (s, 1 H, CH), 7.14–7.16 (m, 2 H, H_{Ar}), 7.22–7.28 (m, 3 H, H_{Ar}), 7.28–7.32 (m, 1 H, H_{Ar}), 7.33–7.37 (m, 2 H, H_{Ar}), 7.41–7.45 (m, 4 H, H_{Ar}), 7.56–7.59 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.5, 107.5, 108.2, 120.4, 120.7, 123.5, 126.8, 127.7, 128.8, 129.8, 130.0, 130.6, 131.7, 138.1, 146.4, 147.7, 150.6, 150.8.

MS (ESI+): *m*/*z* (%) = 348 (100, $[^{81}BrM + NH_4 – PhOCO]^+$), 346 (97, $[^{79}BrM + NH_4 – PhOCO]^+$).

HRMS (ESI+): *m*/*z* $[^{81}BrM + NH_4 – PhOCO]^+$ calcd for $C_{17}H_{17}{}^{81}BrNO_2$:348.0417; found: 348.0416.

3-(4-Bromobenzyl)-5-(4-fluorophenyl)furan-2-yl Phenyl Carbonate (29)

Following general procedure C using lactone (±)-**14** (2.45 g, 5.35 mmol) and *m*-CPBA (1.32 g, 5.35 mmol) and $CHCl_3$ (100 mL) gave the crude sulfoxide. Subsequent heating at reflux in toluene (100 mL) overnight gave, after chromatographic purification (EtOAc–PE, 10:90), a 50:50 mixture of both tautomers of 3-(4-bromobenzyl)-5-(4-fluorophenyl)furan-2-one **54** (ratio 5*H*/3*H* 52:48) (1.45 g, 78%) as a light-yellow solid.

5*H*- and 3*H*-Tautomers

Mp 64–66 °C.

IR (KBr): 3086, 2932 (C–H), 1741 (C=O), 1649, 1607 (Ar C=C), 1509 cm^{-1} (C=C).

^1H NMR (400 MHz, $CDCl_3$): δ = 3.12 (ddd, *J* = 17.6, 6.0, 3.1 Hz, 1 H, C*H*$_A$H$_B$), 3.65–3.71 (m, 3 H, C*H*$_A$H$_B$, C*H*$_2$), 5.62 (dd, *J* = 8.1, 6.0 Hz, 1 H, CH), 5.88–5.89 (m, 1 H, CH), 6.94 (q, *J* = 1.6 Hz, 1 H, H$_{Ar}$), 7.06–7.23 (m, 8 H, H$_{Ar}$), 7.34–7.38 (m, 4 H, H$_{Ar}$), 7.46–7.50 (m, 2 H, H$_{Ar}$, CH), 7.57–7.60 (m, 3 H, H$_{Ar}$, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.3, 36.5, 77.6, 81.7, 115.9, 116.1, 120.9, 124.5, 124.6, 127.3, 128.4, 130.6, 130.6, 130.6, 131.4, 132.0, 132.3, 133.3, 133.7, 135.9, 136.1, 148.7, 162.8, 163.1, 171.5, 173.0.

MS (NSI$^+$): *m*/*z* (%) = 366 ([M + NH_4]$^+$, 100).

HRMS (NSI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{13}O_2{}^{79}BrF$:347.0077; found: 347.0086.

Following general procedure D using *i*-Pr_2NH (0.42 mL, 3.00 mmol) and *n*-BuLi (1.20 mL, 3.00 mmol) in THF (10 mL), butenolide **54** (800 mg, 2.31 mmol) in THF (10 mL), and phenyl chloroformate (0.38 mL, 3.00 mmol) in THF (10 mL) gave, after chromatographic purification (CH_2Cl_2–PE, 20:80), **29** (93 mg, 9%) as a white solid; mp 64–66 °C.

IR (KBr): 3098 (C–H), 3060, 2919, 1792 (C=O), 1651, 1599, 1561 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.62 (s, 2 H, C*H*$_2$), 6.27 (s, 1 H, CH), 6.94–6.98 (m, 2 H, H$_{Ar}$), 7.05–7.07 (m, 2 H, H$_{Ar}$), 7.14–7.17 (m, 2 H, H$_{Ar}$), 7.20–7.24 (m, 1 H, H$_{Ar}$), 7.33–7.37 (m, 4 H, H$_{Ar}$), 7.43–7.47 (m, 2 H, H$_{Ar}$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.4, 107.1, 108.2, 115.7, 120.4, 120.6, 125.2, 126.3, 126.8, 129.8, 130.5, 131.7, 138.0, 146.3, 146.8, 150.6, 150.8, 162.2.

MS (CI$^+$): *m*/*z* (%) = 467 ([M + H]$^+$, 100).

HRMS (CI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{17}O_4{}^{79}BrF$: 467.0294; found: 467.0294.

3-Allyl-5-phenylfuran-2-yl Phenyl Carbonate (30)

Following general procedure C using *m*-CPBA (2.38 g, 9.66 mmol) and lactone **20** (2.38 g, 9.66 mmol) in $CHCl_3$ (40 mL) gave the crude sulfoxide, which was heated in toluene (40 mL). NMR analysis of the crude reaction product indicates a 1:3.5 mixture of 3*H*/5*H* isomers. Purification by chromatography (silica gel, EtOAc–PE, 5:95–10:90) gave 3-allyl-5-phenylfuran-2(5*H*)-one (**50**) (1.52 g, 79%) as a yellow oil.

Major (5*H*)-tautomer

IR (thin film): 3082 (C–H), 1758 (C=O), 1455, 1296, 1186 (C–O), 1047, 921, 754, 699 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.08 (ddt, *J* = 6.7, 3.2, 1.6 Hz, 2 H, CH_2), 5.15 (dq, *J* = 2.6, 1.3 Hz, 1 H, =CH*H*), 5.16 (dq, *J* = 24.6, 1.4 Hz, 1 H, =CH*H*), 5.83–5.93 (m, 2 H, CH_2=C*H*, C*H*Ph), 7.10 (q, *J* = 1.7 Hz, 1 H, =CH), 7.22–7.24 (m, 2 H, H$_{Ar}$), 7.32–7.39 (m, 3 H, H$_{Ar}$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.7, 82.5, 118.1, 126.5, 129.1, 129.3, 132.5, 133.1, 135.1, 148.6, 173.6.

MS (ES+): *m*/*z* (%) = 218.1 (77, [M + NH_4]$^+$), 201.1 (100, [M + H]$^+$).

HRMS (ES+): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{13}O_2$: 201.0910; found: 201.0910.

Following general procedure F using Et_3N (0.99 mL, 7.12 mmol), butenolide **50** (0.710 g, 3.56 mmol), THF (15 mL), and phenyl chloroformate (0.89 mL, 7.12 mmol) gave, after purification by chromatography (silica gel, CH_2Cl_2–PE, 15:85), **30** (0.660 g, 58%) as a light-yellow solid; mp 44–46 °C.

IR (KBr disc): 2980 (C–H), 1794 (C=O), 1655 (C=C), 1492, 1196 (C–O), 990, 928, 760, 689 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.16 (dt, *J* = 6.4, 1.4 Hz, 2 H, CH_2), 5.10 (dq, *J* = 10.1, 1.5 Hz, 1 H, =CH*H*), 5.17 (dq, *J* = 17.1, 1.7 Hz, 1 H, =C*H*H), 5.93 (ddt, *J* = 17.9, 10.2, 6.6 Hz, 1 H, C*H*=CH_2), 6.52 (s, 1 H, =C*H*), 7.21–7.30 (m, 4 H, H$_{Ar}$), 7.33–7.36 (m, 2 H, H$_{Ar}$), 7.39–7.43 (m, 2 H, H$_{Ar}$), 7.57–7.60 (m, 2 H, H$_{Ar}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.2, 107.5, 107.8, 116.4, 120.8, 123.5, 126.8, 127.5, 128.8, 129.8, 130.2, 135.2, 146.2, 147.4, 150.7, 151.0.

MS (ES+): *m*/*z* (%) = 343.1 (100, [M + Na]).

HRMS (ES+): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{16}O_4Na$: 343.0946; found: 343.0952.

3-Allyl-5-(4-fluorophenyl)furan-2-yl Phenyl Carbonate (31)

Following general procedure C using lactone **15** (2.63 g, 8.38 mmol) and *m*-CPBA (2.07 g, 8.38 mmol) and $CHCl_3$ (150 mL) gave the crude sulfoxide. Subsequent heating at reflux in toluene (100 mL) overnight gave, after chromatographic purification (EtOAc–PE, 10:90), a mixture of both tautomers of 3-allyl-5-(4-fluorophenyl)furan-2-one **55** (ratio 5*H*/3*H* 62:38) (1.25 g, 68%) as a yellow solid.

Major (5*H*)-tautomer

IR (thin film): 3082, 3012, 2982 (C–H), 2913, 1761 (C=O), 1656, 1607 (Ar C=C), 1509 cm^{-1} (C=C).

^1H NMR (400 MHz, $CDCl_3$): δ = 3.12–3.15 (m, 2 H, C*H*$_2$CH=CH_2), 5.18–5.25 (m, 2 H, CH_2CH=C*H*$_2$), 5.88–5.98 (m, 2 H, CH, CH_2C*H*=CH_2), 7.07–7.14 (m, 3 H, H$_{Ar}$), 7.25–7.29 (m, 2 H, H$_{Ar}$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.6, 81.7, 116.0, 118.1, 128.4, 130.8, 132.8, 132.8, 148.1, 163.1, 173.2.

MS (NSI$^+$): *m*/*z* (%) = 219 ([M + H]$^+$, 100).

HRMS (NSI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{12}FO_2$: 219.0816; found: 219.0812.

Following general procedure D using *i*-Pr_2NH (0.90 mL, 6.39 mmol) and *n*-BuLi (2.56 mL, 6.39 mmol) in THF (15 mL), butenolide (±)-**55** (1.07 g, 4.92 mmol) in THF (15 mL), and phenyl chloroformate (0.81 mL, 6.39 mmol) in THF (15 mL) gave, after chromatographic purification (EtOAc–PE, 2.5:97.5), **31** (244 mg, 15%) as a white solid; mp 35–37 °C.

IR (KBr): 3102, 3061, 2974 (C–H), 1789 (C=O), 1641, 1597, 1561 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.09 (d, *J* = 6.3 Hz, 2 H, C*H*$_2$CH=CH_2), 5.05 (d, *J* = 10.0 Hz, 1 H, C*H*$_2$CH=C*H*H), 5.11 (d, *J* = 17.0 Hz, 1 H, C*H*$_2$CH=C*H*H), 5.82–5.90 (m, 1 H, CH_2C*H*=CH_2), 6.39 (s, 1 H, CH), 6.98 (t, *J* = 8.5 Hz, 2 H, H$_{Ar}$), 7.18–7.24 (m, 3 H, H$_{Ar}$), 7.36 (t, *J* = 7.7 Hz, 2 H, H$_{Ar}$), 7.47–7.50 (m, 2 H, H$_{Ar}$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.0, 107.4, 107.5, 115.7, 116.4, 120.7, 125.2, 126.5, 126.7, 129.7, 135.0, 146.1, 146.5, 150.6, 150.8, 162.2.

MS (ES+): *m*/*z* (%) = 361 ([M + Na]$^+$, 100).

HRMS (ES+): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{15}O_4NaF$:361.0852; found: 361.0841.

Phenyl (*S*)-3-Benzyl-2-oxo-5-phenyl-2,3-dihydrofuran-3-carboxylate [(*S*)-32]

Following general procedure E using carbonate **21** (37 mg, 0.10 mmol) and chiral isothiourea **1** (3.1 mg, 10 mol%) in Et_2O (0.4 mL) for 1 h gave, after chromatographic purification (CH_2Cl_2–PE, 50:50), the α-product **32** (26 mg, 70%) as a white solid; mp 110–112 °C; 83% ee; chiral HPLC (Chiralpak AS-H, 5% *i*-PrOH–hexane, flow rate 1 mL min^{-1}): t_R = 15.5 (*S*), 21.1 min (*R*).

$[\alpha]_D^{20}$ +124.3 (*c* 0.47, $CHCl_3$).

IR (thin film): 1803 (C=O), 1760 (C=O), 1653 (Ar C=C), 1493, 1449, 1280, 1209, 1187 (C–O), 1159, 1127, 1073, 696, 749, 688 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.49 (ABq, *J* = 13.6 Hz, 1 H, CH*H*), 3.64 (ABq, *J* = 13.6 Hz, 1 H, C*H*H), 5.96 (s, 1 H, =CH), 7.04–7.08 (m, 2 H, H_{Ar}), 7.22–7.27 (m, 6 H, H_{Ar}), 7.35–7.40 (m, 5 H, H_{Ar}), 7.53–7.57 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.9, 61.9, 101.8, 121.3, 125.4, 126.6, 127.6, 127.7, 128.6, 128.9, 129.7, 130.2, 130.5, 134.3, 150.5, 154.6, 166.4, 173.1.

MS (ESI+): *m*/*z* (%) = 388 (100, [M + NH_4]$^+$).

HRMS (ESI+): *m*/*z* [M + NH_4]$^+$ calcd for $C_{24}H_{22}NO_4$: 388.1543; found: 388.1543.

2,2,2-Trichloroethyl (*R*)-3-Benzyl-2-oxo-5-phenyl-2,3-dihydrofuran-3-carboxylate [(*R*)-33] and 2,2,2-Trichloroethyl 4-Benzyl-5-oxo-2-phenyl-2,5-dihydrofuran-2-carboxylate (34)

Following general procedure E using carbonate **22** (85.0 mg, 0.200 mmol), Et_2O (0.6 mL), and **1** (6.0 mg, 10 mol%) gave, after 1 h at r.t. and purification by chromatography (silica gel, CH_2Cl_2–PE, 50:50–100:0), the α-product **33** (37.3 mg, 44%) as a white solid and the γ-product **34** (32.8 mg, 39%) as a colourless oil which then solidified as a white solid.

Compound (*R*)-33

Mp 110–112 °C; 62% ee; chiral HPLC (Chiralcel OD-H, 2% *i*-PrOH–hexanes, flow rate 1.0 mL/min): t_R = 14.9 (*R*), 16.7 min (*S*).

$[\alpha]_D^{20}$ +74.5 (*c* 0.42, $CHCl_3$).

IR (KBr disc): 2967 (C–H), 1800 (C=O), 1766 (C=O), 1495 (C=C), 1449, 1281, 1213 (C–O), 1197 (C–O), 992, 807 (C–Cl), 757, 715 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.45 (ABq, J_{AB} = 13.6 Hz, 1 H, CH*H*), 3.56 (ABq, J_{BA} = 13.6 Hz, 1 H, CH*H*), 4.75 (ABq, J_{AB} = 11.9 Hz, 1 H, OCH*H*), 4.88 (ABq, J_{BA} = 11.9 Hz, 1 H, OCH*H*), 5.84 (s, 1 H, CH), 7.18–7.26 (m, 5 H, H_{Ar}), 7.35–7.39 (m, 3 H, H_{Ar}), 7.48–7.51 (m, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.4, 61.7, 74.8, 94.2, 101.3, 125.3, 127.4, 127.7, 128.6, 128.8, 130.1, 130.4, 133.9, 154.7, 166.2, 172.5.

Anal. Calcd for $C_{20}H_{15}Cl_3O_4$: C, 56.43; H, 3.55. Found: C, 56.44; H, 3.33.

Compound 34

Mp 94–96 °C; 26% ee; chiral HPLC (Chiralcel OD-H, 2% *i*-PrOH–hexanes, flow rate 1.0 mL/min): t_R = 27.2 (1), 30.1 min (2).

$[\alpha]_D^{20}$ +18.2 (*c* 0.57, $CHCl_3$).

IR (KBr disc): 3064 (C–H), 1762 (br, 2 C=O), 1192 (C–O), 1063, 1034, 710 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.62 (ABX, J_{AB} = 16.9 Hz, J_{AX} = 1.7 Hz, 1 H, CH*H*), 3.69 (ABX, J_{BA} = 16.9 Hz, J_{BX} = 1.6 Hz, 1 H, CH*H*), 4.71 (ABq, J_{AB} = 11.9 Hz, 1 H, OCH*H*), 4.82 (ABq, J_{BA} = 11.8 Hz, 1 H, OCH*H*), 7.22–7.24 (m, 2 H, H_{Ar}), 7.27–7.30 (m, 2 H, CH, H_{Ar}), 7.32–7.36 (m, 2 H, H_{Ar}), 7.39–7.41 (m, 3 H, H_{Ar}), 7.48–7.51 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.9, 74.7, 87.6, 94.1, 126.2, 127.2, 129.0, 129.0, 129.0, 129.7, 134.6, 135.7, 136.4, 146.4, 165.9, 170.9.

MS (ES+): *m*/*z* (%) = 442.0 (17, [M + NH_4]$^+$), 326.1 (100).

HRMS (ES+): *m*/*z* [M + NH_4]$^+$ calcd for $C_{20}H_{19}O_4NCl_3$: 442.0374; found: 442.0375.

Phenyl (*S*)-3-Benzyl-5-(4-fluorophenyl)-2-oxo-2,3-dihydrofuran-3-carboxylate [(*S*)-35]

Following general procedure E using carbonate **23** (38.8 mg, 0.10 mmol) and chiral isothiourea **1** (3.08 mg, 0.01 mmol) in Et_2O (0.4 mL) for 1 h gave, after chromatographic purification (CH_2Cl_2–PE, 50:50), the α-product **35** (25 mg, 64%) as a white solid; mp 108–110 °C; 83% ee; chiral HPLC (Chiralpak AS-H, 5% *i*-PrOH–hexane, flow rate 1 mL min^{-1}): t_R = 16.8 (*S*), 30.6 min (*R*).

$[\alpha]_D^{20}$ +95.0 (*c* 0.1, CH_2Cl_2).

IR (KBr): 3125, 2917 (C–H), 1804 (C=O), 1737 (C=O), 1652, 1591, 1508 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.41 (ABq, *J* = 13.6 Hz, 1 H, Ph-CH_AH$_B$), 3.55 (ABq, *J* = 13.6 Hz, 1 H, PhCH$_A$$H_B$), 5.82 (s, 1 H, CH), 6.98–7.02 (m, 4 H, H_{Ar}), 7.16–7.20 (m, 6 H, H_{Ar}), 7.28–7.32 (m, 2 H, H_{Ar}), 7.44–7.47 (m, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.2, 62.2, 101.7, 116.3, 121.6, 124.1, 126.9, 127.7, 128.0, 128.9, 130.0, 130.5, 134.5, 150.7, 153.9, 164.2, 166.6, 173.2.

MS (NSI$^+$): *m*/*z* (%) = 406 ([M + NH_4]$^+$, 100).

HRMS (NSI$^+$): *m*/*z* [M + NH_4]$^+$ calcd for $C_{24}H_{21}O_4NF$: 406.1449; found: 406.1448.

Phenyl (*S*)-5-(4-Fluorophenyl)-3-methyl-2-oxo-2,3-dihydrofuran-3-carboxylate [(*S*)-36]

Following general procedure E using carbonate **24** (31.2 mg, 0.1 mmol) and chiral isothiourea **1** (3.08 mg, 0.01 mmol) in Et_2O (0.3 mL) for 1 h gave, after chromatographic purification (CH_2Cl_2–PE, 50:50), the α-product **36** (20 mg, 64%) as a white solid; mp 42–44 °C; 81% ee; chiral HPLC (Chiralpak AS-H, 5% *i*-PrOH–hexane, flow rate 1 mL min^{-1}): t_R = 12.6 (*S*), 17.0 min (*R*).

$[\alpha]_D^{20}$ +130.0 (*c* 0.1, CH_2Cl_2).

IR (KBr): 3119, 3073, 2925 (C–H), 2854, 1805 (C=O), 1769, 1741 (C=O), 1653, 1601, 1510 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.71 (s, 3 H, CH_3), 5.86 (s, 1 H, CH), 7.00–7.09 (m, 4 H, H_{Ar}), 7.14–7.18 (m, 1 H, H_{Ar}), 7.27–7.31 (m, 2 H, H_{Ar}), 7.57–7.61 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.4, 56.0, 103.4, 116.1, 121.1, 123.8, 126.5, 127.4, 129.5, 150.4, 153.8, 163.9, 166.9, 174.2.

MS (NSI$^+$): *m*/*z* (%) = 330 ([M + NH_4]$^+$, 100).

HRMS (NSI$^+$): *m*/*z* [M + NH_4]$^+$ calcd for $C_{18}H_{17}O_4NF$: 330.1136; found: 330.1139.

2,2,2-Trichloroethyl (*R*)-5-(4-Fluorophenyl)-3-methyl-2-oxo-2,3-dihydrofuran-3-carboxylate [(*R*)-37] and 2,2,2-Trichloroethyl 2-(4-Fluorophenyl)-4-methyl-5-oxo-2,5 dihydrofuran-2-carboxylate (38)

Following general procedure E using carbonate **25** (36.8 mg, 0.1 mmol) and chiral isothiourea **1** (3.08 mg, 0.01 mmol) in Et_2O (0.4 mL) for 1 h gave, after chromatographic purification (CH_2Cl_2–PE, 50:50) the α-product **37** (18 mg, 49%) as a white solid and the γ-product **38** (10 mg, 27%) as a white solid.

Compound (*R*)-37

71% ee; chiral HPLC (Chiralpak AS-H, 5% *i*-PrOH–hexane, flow rate 1 mL min^{-1}): t_R = 10.3 (*R*), 13.0 min (*S*).

$[\alpha]_D^{20}$ +94.0 (*c* 0.1, CH_2Cl_2).

IR (thin film): 3112, 2962, 2938 (C–H), 2876, 1814 (C=O), 1761 (C=O), 1652, 1603, 1509 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.69 (s, 3 H, CH_3), 4.67 (ABq, *J* = 11.9 Hz, 1 H, $CH_AH_BCCl_3$), 4.80 (ABq, *J* = 11.9 Hz, 1 H, $CH_AH_BCCl_3$), 5.77 (s, 1 H, CH), 7.04–7.08 (m, 2 H, H_{Ar}), 7.54–7.57 (m, 2 H, H_{Ar}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.2, 55.7, 74.6, 94.2, 103.1, 116.1, 123.7, 127.4, 153.8, 163.9, 166.8, 173.7.

MS (NSI$^+$): *m*/*z* (%) = 384 ([M + NH_4]$^+$, 17).

HRMS (NSI$^+$): *m*/*z* [^{35}ClM + NH_4]$^+$ calcd for $C_{14}H_{14}O_4NF^{35}Cl_3$: 383.9967; found: 383.9972.

Compound 38

Mp 84–86 °C; racemic; chiral HPLC (Chiralpak AS-H, 5% *i*-PrOH–hexane, flow rate 1 mL min^{-1}): t_R = 20.8 (*R*), 24.7 min (*S*).

IR (KBr): 3530, 3097, 2979 (C–H), 2929, 1777 (C=O), 1765 (C=O), 1660, 1603, 1509 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.94 (d, *J* = 1.5 Hz, 3 H, CH_3), 4.69–4.74 (m, 2 H, CH_2), 7.02–7.05 (m, 2 H, H_{Ar}), 7.43–7.44 (m, 1 H, CH), 7.46–7.49 (m, 2 H, H_{Ar}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 10.8, 74.7, 86.6, 94.0, 116.0, 128.2, 130.6, 131.5, 145.5, 163.2, 165.8, 171.5.

MS (NSI$^+$): *m*/*z* (%) = 384 ([M + NH_4]$^+$, 35).

HRMS (NSI$^+$): *m*/*z* [^{35}ClM + NH_4]$^+$ calcd for $C_{14}H_{14}O_4NF^{35}Cl_3$: 383.9967; found: 383.9970.

Phenyl (*S*)-3-Ethyl-2oxo-5-phenyl-2,3-dihydrofuran-3-carboxylate [(*S*)-39]

Following general procedure E using carbonate **26** (61.7 mg, 0.200 mmol), Et_2O (0.6 mL), and **1** (6.0 mg, 10 mol%) gave, after 1 h at r.t. and purification by chromatography (silica gel, CH_2Cl_2–PE, 50:50), the α-product **39** (24.0 mg, 39%) as a sticky white solid; 83% ee; chiral HPLC (Chiralcel OD-H, 5% *i*-PrOH–hexanes, flow rate 1.0 mL min^{-1}): t_R = 10.1 (*S*), 13.6 min (*R*).

$[\alpha]_D^{20}$ +86.6 (*c* 0.81, $CHCl_3$).

IR (thin film): 2974 (C–H), 1794 (C=O), 1747 (C=O), 1492 (C=C), 1226, 1192 (C–O), 1096, 1076, 1012, 947, 759, 688 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05 (t, *J* = 7.5 Hz, 3 H, CH_3), 2.30 (q, *J* = 7.5 Hz, 2 H, CH_2), 5.96 (s, 1 H, CH), 7.09 (dd, *J* = 8.6, 1.1 Hz, 2 H, H_{Ar}), 7.22–7.26 (m, 1 H, H_{Ar}), 7.37 (t, *J* = 7.9 Hz, 2 H, H_{Ar}), 7.44–7.47 (m, 3 H, H_{Ar}), 7.68–7.71 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.0, 28.1, 61.2, 101.8, 121.3, 125.4, 126.5, 127.7, 129.0, 129.6, 130.5, 150.5, 155.0, 166.8, 173.7.

MS (ES+): *m*/*z* (%) = 326.1 (100, [M + NH_4]$^+$), 309.1 (25, [M + H]$^+$).

HRMS (ES+): *m*/*z* [M + NH_4]$^+$ calcd for $C_{19}H_{20}O_4N$: 326.1387; found: 326.1389.

Phenyl (*S*)-3-Ethyl-5-(4-fluorophenyl)-2-oxo-2,3-dihydrofuran-3-carboxylate [(*S*)-40]

Following general procedure E using carbonate **27** (32.6 mg, 0.10 mmol) and chiral isothiourea **1** (3.08 mg, 0.01 mmol) in Et_2O (0.3 mL) for 1 h gave, after chromatographic purification (CH_2Cl_2–PE, 50:50), the α-product **40** (18 mg, 55%) as a white solid; mp 62–64 °C; 81% ee; chiral HPLC (Chiralpak AS-H, 5% *i*-PrOH–hexane, flow rate 1 mL min^{-1}): t_R = 11.9 (*S*), 13.7 min (*R*).

$[\alpha]_D^{20}$ +138.0 (*c* 0.1, CH_2Cl_2).

IR (KBr): 3112, 3079, 2974 (C–H), 2938, 1809 (C=O), 1757 (C=O), 1653, 1602, 1509 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (t, *J* = 7.5 Hz, 3 H, CH_3), 2.22 (q, *J* = 7.5 Hz, 2 H, CH_2CH_3), 5.82 (s, 1 H, CH), 7.01–7.10 (m, 4 H, H_{Ar}), 7.15–7.19 (m, 1 H, H_{Ar}), 7.28–7.33 (m, 2 H, H_{Ar}), 7.59–7.63 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.8, 28.1, 61.2, 101.3, 116.0, 121.2, 123.8, 126.4, 127.3, 129.5, 150.3, 153.9, 163.8, 166.5, 173.3.

MS (NSI$^+$): *m*/*z* (%) = 344 ([M + NH_4]$^+$, 100).

HRMS (NSI$^+$): *m*/*z* [M + NH_4]$^+$ calcd for $C_{19}H_{19}O_4NF$: 344.1293; found: 344.1295.

Phenyl (*S*)-3-(4-Bromobenzyl)-2oxo-5-phenyl-2,3-dihydrofuran-3-carboxylate [(*S*)-41]

Following general procedure E using carbonate **28** (67.5 mg, 0.200 mmol), Et_2O (0.7 mL), and **1** (6.0 mg, 10 mol%) gave, after 1 h at r.t. and purification by chromatography (silica gel, CH_2Cl_2–PE, 50:50), the α-product **41** (38.3 mg, 57%) as a white solid; mp 150–152 °C; 82% ee; chiral HPLC (Chiralpak AS-H, 5% *i*-PrOH–hexanes, flow rate 1.0 mL min^{-1}): t_R = 19.8 (*S*), 29.2 min (*R*).

$[\alpha]_D^{20}$ +100.9 (*c* 0.53, $CHCl_3$).

IR (KBr): 3090, 1778 (C=O), 1757 (C=O), 1591 (C=C), 1489, 1421, 1405, 1209, 1188 (C–O), 1056, 1024, 1013, 963, 913, 798, 738, 689 cm^{-1} (C–Br).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.46 (ABq, *J* = 13.7 Hz, 1 H, CH*H*), 3.58 (ABq, *J* = 13.7 Hz, 1 H, C*H*H), 5.94 (s, 1 H, CH), 7.06–7.09 (m, 2 H, H_{Ar}), 7.12–7.16 (m, 2 H, H_{Ar}), 7.26–7.29 (m, 1 H, H_{Ar}), 7.37–7.43 (m, 7 H, H_{Ar}), 7.56–7.59 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 39.9, 61.7, 101.3, 121.3, 122.0, 125.5, 126.7, 127.4, 129.0, 129.8, 130.7, 131.8, 132.0, 133.3, 150.5, 155.1, 166.3, 172.9.

MS (ESI+): *m*/*z* (%) = 466 (100, [^{79}BrM + NH_4]$^+$), 468 (98, [^{81}BrM + H]$^+$).

HRMS (ESI+): *m*/*z* [^{79}BrM + NH_4]$^+$ calcd for $C_{24}H_{21}{}^{79}BrNO_4$: 466.0648; found: 466.0641.

Phenyl (*S*)-3-(4-Bromobenzyl)-5-(4-fluorophenyl)-2-oxo-2,3-dihydrofuran-3-carboxylate [(*S*)-42]

Following general procedure E using carbonate **29** (46.7 mg, 0.10 mmol) and chiral isothiourea **1** (3.08 mg, 0.01 mmol) in Et_2O (0.4 mL) for 1 h gave, after chromatographic purification (CH_2Cl_2–PE, 50:50), the α-product **42** (31 mg, 66%) as a white solid; mp 110–112 °C; 81% ee; chiral HPLC (Chiralpak AS-H, 5% *i*-PrOH–hexane, flow rate 1 mL min^{-1}): t_R = 20.5 (*S*), 39.7 min (*R*).

$[\alpha]_D^{20}$ +87.3 (*c* 0.15, CH_2Cl_2).

IR (KBr): 3127, 2925 (C–H), 1801 (C=O), 1759 (C=O), 1660, 1591, 1508 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.37 (ABq, *J* = 13.7 Hz, 1 H, CH_AH_B), 3.49 (ABq, *J* = 13.7 Hz, 1 H, CH_AH_B), 5.78 (s, 1 H, CH), 6.98–7.06 (m, 6 H, H_{Ar}), 7.15–7.21 (m, 1 H, H_{Ar}), 7.27–7.356 (m, 4 H, H_{Ar}), 7.44–7.50 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 39.8, 61.6, 100.7, 116.1, 121.1, 121.1, 123.5, 126.6, 127.4, 129.6, 131.7, 131.8, 133.1, 150.2, 154.0, 163.9, 166.0, 172.6.

MS (NSI$^+$): *m*/*z* (%) = 486 ([M + NH_4]$^+$, 100).

HRMS (NSI$^+$): *m*/*z* [^{79}BrM + NH_4]$^+$ calcd for $C_{24}H_{20}O_4{}^{79}BrNF$: 484.0554; found: 484.0551.

Phenyl (*S*)-3-Allyl-2-oxo-5-phenyl-2,3-dihydrofuran-3-carboxylate [(*S*)-43] and Phenyl 4-Allyl-5-oxo-2-phenyl-2,5-dihydrofuran-2-carboxylate (44)

Following general procedure E using carbonate **30** (64.0 mg, 0.200 mmol), Et_2O (0.6 mL), and **1** (6.0 mg, 10 mol%) gave, after 1 h at r.t. (NMR of the crude shows a mixture α/γ 72:28) and purification by chromatography (silica gel, CH_2Cl_2–PE, 50:50–100:0), the desired α-product (*S*)-**43** (35.6 mg, 56%) as a colourless oil and the γ-product **44** (10.0 mg, 16%) as a colourless oil.

Compound (*S*)-43

81% ee; chiral HPLC (Chiralpak AD-H, 5% *i*-PrOH–hexanes, flow rate 1.0 mL min^{-1}): t_R = 12.3 (*R*), 16.3 min (*S*).

$[\alpha]_D{}^{20}$ +125.8 (*c* 0.41, $CHCl_3$).

IR (thin film): 3084 (C–H), 1807 (C=O), 1768 (C=O), 1492 (C=C), 1278, 1188 (C–O), 980, 759, 688 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.92 (ABX, J_{AB} = 13.9 Hz, J_{AX} = 7.9 Hz, 1 H, CH*H*), 3.05 (ABX, J_{BA} = 13.9 Hz, J_{BX} = 6.8 Hz, 1 H, CH*H*), 5.20–5.22 (m, 1 H, =CH*H*), 5.28 (app. dd, *J* = 17.0, 1.4 Hz, 1 H, =CH*H*), 5.75–5.85 (m, 1 H, C*H*=CH_2), 5.98 (s, 1 H, CH), 7.08–7.10 (m, 2 H, H_{Ar}), 7.22–7.26 (m, 1 H, H_{Ar}), 7.35–7.39 (m, 2 H, H_{Ar}), 7.43–7.46 (m, 3 H, H_{Ar}), 7.67–7.69 (m, 2 H, $H2_{Ph}$, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 38.9, 60.5, 101.7, 121.0, 121.2, 125.4, 126.5, 127.6, 128.9, 129.6, 130.5, 130.6, 150.4, 154.8, 166.3, 173.0.

MS (ES+): *m*/*z* (%) = 338.1 (100, [M + NH_4]$^+$).

HRMS (ES+): *m*/*z* [M + NH_4]$^+$ calcd for $C_{20}H_{20}O_4N$: 338.1387; found: 338.1391.

Compound 44

16% ee; chiral HPLC (Chiralpak AD-H, 5% *i*-PrOH–hexanes, flow rate 1.0 mL min^{-1}): t_R = 18.7 (1), 25.0 min (2).

$[\alpha]_D{}^{20}$ +4.8 (*c* 0.48, $CHCl_3$).

IR (thin film): 2977 (C–H), 1778 (C=O br), 1492 (C=C), 1213 (C–O), 1185 (C–O), 1032, 734 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.08–3.19 (m, 2 H, CH_2), 5.21 (t, *J* = 1.3 Hz, 1 H, =CH*H*), 5.23–5.25 (m, 1 H, =C*H*H), 5.85–5.98 (m, 1 H, C*H*=CH_2), 7.02–7.04 (m, 2 H, H_{Ar}), 7.22–7.26 (m, 1 H, H_{Ar}), 7.34–7.38 (m, 2 H, H_{Ar}), 7.43–7.48 (m, 3 H, H_{Ar}), 7.58 (t, *J* = 1.7 Hz, 1 H, CH), 7.59–7.62 (m, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 29.7, 87.9, 118.7, 121.0, 125.9, 126.6, 129.2, 129.7, 129.7, 132.3, 133.8, 135.2, 146.8, 150.3, 166.0, 171.3.

MS (ES+): *m*/*z* (%) = 338.1 (100, [M + NH_4]$^+$), 321.1 (16, [M + H]$^+$), 276.1 (77, [M – CO_2]$^+$).

HRMS (ES+): *m*/*z* [M + NH_4]$^+$ calcd for $C_{20}H_{20}O_4N$: 338.1387; found: 338.1386.

Phenyl (*S*)-3-Allyl-5-(4-fluorophenyl)-2-oxo-2,3-dihydrofuran-3-carboxylate [(*S*)-45]

Following general procedure E using carbonate **31** (33.8 mg, 0.10 mmol) and chiral isothiourea **1** (3.08 mg, 0.01 mmol) in Et_2O (0.3 mL) for 1 h gave, after chromatographic purification (CH_2Cl_2–PE, 50:50), **45** (21 mg, 62%) as a white solid; mp 26–28 °C; 76% ee; chiral HPLC (Chiralpak AS-H; 5% *i*-PrOH–hexane, flow rate 1 mL min^{-1}): t_R = 11.7 (*S*), 14.0 min (*R*).

$[\alpha]_D{}^{20}$ +88.5 (*c* 0.2, CH_2Cl_2).

IR (KBr): 3081, 2923 (C–H), 1809 (C=O), 1756 (C=O), 1652, 1593, 1509 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.85 (ABqd, *J* = 13.9, 7.9 Hz, 1 H, C*H*HCH=CH_2), 2.97 (ABqd, *J* = 13.9, 6.8 Hz, 1 H, CH*H*CH=CH_2), 5.14 (d, *J* = 10.0 Hz, 1 H, CH_2CH=C*H*H), 5.19–5.23 (m, 1 H, CH_2CH=CH*H*), 5.67–5.75 (m, 1 H, CH_2C*H*=CH_2), 5.84 (s, 1 H, CH), 7.00–7.09 (m, 4 H, H_{Ar}), 7.16–7.20 (m, 1 H, H_{Ar}), 7.28–7.32 (m, 2 H, H_{Ar}), 7.58–7.61 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 38.9, 60.4, 101.2, 116.1, 121.0, 121.2, 123.8, 126.5, 127.4, 129.6, 130.4, 150.3, 153.8, 163.8, 166.1, 172.7.

MS (NSI$^+$): *m*/*z* (%) = 356 ([M + NH_4]$^+$, 100).

HRMS (NSI$^+$): *m*/*z* [M + NH_4]$^+$ calcd for $C_{20}H_{19}O_4NF$: 356.1293; found: 356.1296.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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References and Notes

(1) For representative examples, see: (a) Figadére, B. *Acc. Chem. Res.* **1995**, *28*, 359. (b) Tu, L.; Zhao, Y.; Yu, Z.; Cong, Y.; Xu, G.; Peng, L.; Zhang, P.; Cheng, X.; Zhao, Q. *Helv. Chim. Acta* **2008**, *91*, 1578. (c) de Guzman, F. S.; Schmitz, F. J. *J. Nat. Prod.* **1990**, *53*, 926. (d) Evidente, A.; Sparapano, L. *J. Nat. Prod.* **1994**, *57*, 1720. (e) Dogné, J.; Supuran, C. T.; Pratico, D. *J. Med. Chem.* **2005**, *48*, 2251. (f) Braña, M. F.; García, M. L.; Lòpez, B.; de Pascual-Teresa, B.; Ramos, A.; Pozuelo, J. M.; Domínguez, M. T. *Org. Biomol. Chem.* **2004**, *2*, 1864.

(2) Singh, R. P.; Foxman, B. M.; Deng, L. *J. Am. Chem. Soc.* **2010**, *132*, 9558.

(3) Brown, S. P.; Goodwin, N. C.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2003**, *125*, 1192.

(4) Shaw, S. A.; Aleman, P.; Christy, J.; Kampf, J. W.; Va, P.; Vedejs, E. *J. Am. Chem. Soc.* **2006**, *128*, 925–934.

(5) For an excellent recent review of Lewis base mediated reaction processes, see: Denmark, S. E.; Beutner, G. L. *Angew. Chem. Int. Ed.* **2008**, *47*, 1560.

(6) For examples of our previous research programme concerned with applications of NHCs in organocatalysis, see: (a) Thomson, J. E.; Rix, K.; Smith, A. D. *Org. Lett.* **2006**, *8*, 3785. (b) Thomson, J. E.; Campbell, C. D.; Concellón, C.; Duguet, N.; Rix, K.; Slawin, A. M. Z.; Smith, A. D. *J. Org. Chem.* **2008**, *73*, 2784. (c) Campbell, C. D.; Duguet, N.; Gallagher, K. A.; Thomson, J. E.; Lindsay, A. G.; O'Donoghue, A.; Smith, A. D. *Chem. Commun.* **2008**, 3528. (d) Duguet, N.; Campbell, C. D.; Slawin, A. M. Z.; Smith, A. D. *Org. Biomol. Chem.* **2008**, *6*, 1108. (e) Thomson, J. E.; Kyle, A. F.; Concellón, C.; Gallagher, K. A.; Lenden, P.; Morrill, L. C.; Miller, A. J.; Joannesse, C.; Slawin, A. M. Z.; Smith, A. D. *Synthesis* **2008**, 2805. (f) Concellón, C.; Duguet, N.; Smith, A. D. *Adv. Synth.*

Catal. **2009**, *351*, 3001. (g) Duguet, N.; Donaldson, A.; Leckie, S. M.; Douglas, J.; Shapland, P.; Churchill, G.; Slawin, A. M. Z.; Smith, A. D. *Tetrahedron: Asymmetry* **2010**, *21*, 582. (h) Duguet, N.; Donaldson, A.; Leckie, S. M.; Shapland, P.; Slawin, A. M. Z.; Smith, A. D. *Tetrahedron: Asymmetry* **2010**, *21*, 601. (i) Douglas, J.; Ling, K. B.; Concellón, C.; Churchill, G.; Slawin, A. M. Z.; Smith, A. D. *Eur. J. Org. Chem.* **2010**, 5863. (j) Ling, K. B.; Smith, A. D. *Chem. Commun.* **2011**, *47*, 373. (k) Campbell, C. D.; Collett, C. J.; Thomson, J. E.; Slawin, A. M. Z.; Smith, A. D. *Org. Biomol. Chem.* **2011**, *9*, 4205.

(7) For examples of our previous research programme concerned with applications of isothioureas in organocatalysis, see: (a) Joannesse, C.; Simal, C.; Concellón, C.; Thomson, J. E.; Campbell, C. D.; Slawin, A. M. Z.; Smith, A. D. *Org. Biomol. Chem.* **2008**, *6*, 2900. (b) Woods, P. A.; Morrill, L. C.; Lebl, T.; Slawin, A. M. Z.; Bragg, R. A.; Smith, A. D. *Org. Lett.* **2010**, *12*, 2660. (c) Belmessieri, D.; Joannesse, C.; Woods, P. A.; MacGregor, C.; Jones, C.; Campbell, C. D.; Johnston, C. P.; Duguet, N.; Concellón, C.; Bragg, R. A.; Smith, A. D. *Org. Biomol. Chem.* **2011**, *9*, 559. (d) Belmessieri, B.; Morrill, L. C.; Simal, C.; Slawin, A. M. Z.; Smith, A. D. *J. Am. Chem. Soc.* **2011**, *133*, 2714.

(8) For initial work, see: (a) Steglich, W.; Höfle, G. *Tetrahedron Lett.* **1970**, *11*, 4727. For asymmetric Steglich rearrangements of oxazolyl carbonates, see: (b) Ruble, J. C.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 11532. (c) Shaw, S. A.; Aleman, P.; Vedejs, E. *J. Am. Chem. Soc.* **2003**, *125*, 13368. (d) Nguyen, H. V.; Butler, D. C. D.; Richards, C. J. *Org. Lett.* **2006**, *8*, 769. (e) Busto, E.; Gotor-Fernández, V.; Gotor, V. *Adv. Synth. Catal.* **2006**, *348*, 2626. (f) Seitzberg, J. G.; Dissing, C.; Søtofte, I.; Norrby, P.-O.; Johannsen, M. *J. Org. Chem.* **2005**, *70*, 8332. (g) Dietz, F. R.; Gröger, H. *Synlett* **2008**, 663. (h) Dietz, F. R.; Gröger, H. *Synthesis* **2009**, 4208. (i) Uraguchi, D.; Koshimoto, K.; Miyake, S.; Ooi, T. *Angew. Chem. Int. Ed.* **2010**, *49*, 5567. (j) Zhang, Z.; Xie, F.; Jia, J.; Zhang, W. *J. Am. Chem. Soc.* **2010**, *132*, 15939.

(9) Joannesse, C.; Johnston, C. P.; Concellón, C.; Simal, C.; Philp, D.; Smith, A. D. *Angew. Chem. Int. Ed.* **2009**, *48*, 8914.

(10) Selected alternative applications of chiral isothioureas in asymmetric catalysis are listed herein. For kinetic resolutions using anhydrides as acylating agents, see: (a) Birman, V. B.; Jiang, H.; Li, X.; Geo, V.; Uffman, E. W. *J. Am. Chem. Soc.* **2006**, *128*, 6536. (b) Birman, V. B.; Li, X. *Org. Lett.* **2006**, *8*, 1351. (c) Birman, V. B.; Geo, L. *Org. Lett.* **2006**, *8*, 4859. (d) Birman, V. B.; Jiang, H.; Li, X. *Org. Lett.* **2007**, *9*, 3237. (e) Birman, V. B.; Li, X. *Org. Lett.* **2008**, *10*, 1115. (f) Yang, X.; Birman, V. B. *Adv. Synth. Catal.* **2009**, *351*, 2525. (g) Xu, Q.; Zhou, H.; Geng, X.; Chen, P. *Tetrahedron* **2009**, *65*, 2232. (h) Belmessieri, D.; Joannesse, C.; Woods, P. A.; MacGregor, C.; Jones, C.; Campbell, C. D.; Johnston, C. P.; Duguet, N.; Concellón, C.; Bragg, R. A.; Smith, A. D. *Org. Biomol. Chem.* **2011**, *9*, 559. For kinetic resolutions using carboxylic acids as acylating agents utilising in situ formation of a reactive mixed anhydride, see: (i) Shiina, I.; Nakata, K. *Tetrahedron Lett.* **2007**, *48*, 8314. (j) Shiina, I.; Nakata, K.; Sugimoto, M.; Onda, Y.; Iizumi, T.; Ono, K. *Heterocycles* **2009**, *77*, 801. (k) Yang, X.; Birman, V. B. *Adv. Synth. Catal.* **2009**, *351*, 2301. (l) Shiina, I.; Nakata, K. *Heterocycles* **2010**, *80*, 169. (m) Shiina, I.; Nakata, K.; Onda, Y. *Eur. J. Org. Chem.* **2008**, 5887. (n) Shiina, I.; Nakata, K.; Ono, K.; Sugimoto, M.; Sekiguchi, A. *Chem. Eur. J.* **2010**, *16*, 167. (o) Nakata, K.; Onda, Y.; Ono, K.; Shiina, I. *Tetrahedron Lett.* **2010**, *51*, 5666. (p) Shiina, I.; Ono, K.; Nakata, K. *Chem. Lett.* **2011**, *40*, 147.

(11) **2** was readily prepared on a multigram scale by alkylation of the dianion of phenylacetic acid with 2-methyloxirane; see experimental section for synthesis.

(12) The selenation/elimination sequence was based upon literature precedent in these systems: Pour, M.; Spulák, M.; Balsánek, V.; Kunes, J.; Kubanová, P.; Buchta, V. *Bioorg. Med. Chem.* **2003**, *11*, 2843.

(13) (a) White, J. D.; Somers, T. C.; Reddy, G. N. *J. Org. Chem.* **1992**, *57*, 4991. (b) Donohoe, T. J.; Harris, R. M.; Burrows, J.; Parker, J. *J. Am. Chem. Soc.* **2006**, *128*, 13704.

(14) Reaction in toluene and Et_2O at –20 °C gave <10% conversion to *C*-carboxy products, that was assumed to be due to low solubility of **1** at these temperatures.

(15) (*R*)-TADMAP was kindly donated by Prof. Edwin Vedejs. Consistent with the literature, rearrangement of furanyl carbonate **5** with (*R*)-TADMAP gave a 60:40 mixture of α/γ regioisomers, with purification giving the major α-regioisomer **8** in 49% yield and 85% ee.

(16) For representative examples that demonstrate the preference of substituents adjacent to an *N*-acyl group in heterocyclic compounds to adopt a pseudoaxial position, see: (a) Sinclair, P. J.; Zhai, D.; Reibenspies, J.; Williams, R. M. J. *J. Am. Chem. Soc.* **1986**, *108*, 1103. (b) Dellaria, J. F.; Santarsiero, B. D. *J. Org. Chem.* **1989**, *54*, 3916. (c) Drew, M. G. B.; Harwood, L. M.; Park, G.; Price, D. W.; Tyler, S. N. G.; Park, C. R.; Cho, S. G. *Tetrahedron* **2001**, *57*, 5641.

(17) Anderson, R. J.; Adams, K. G.; Chinn, H. R.; Henrick, C. A. *J. Org. Chem.* **1980**, *45*, 2229.