Isomerisation of (*E*)-2-Tetrahydrofurylidenealkanecarboxylic Esters and Amides into Their (*Z*) Isomers by Chelation Control with Metallated Bases or Lewis Acids

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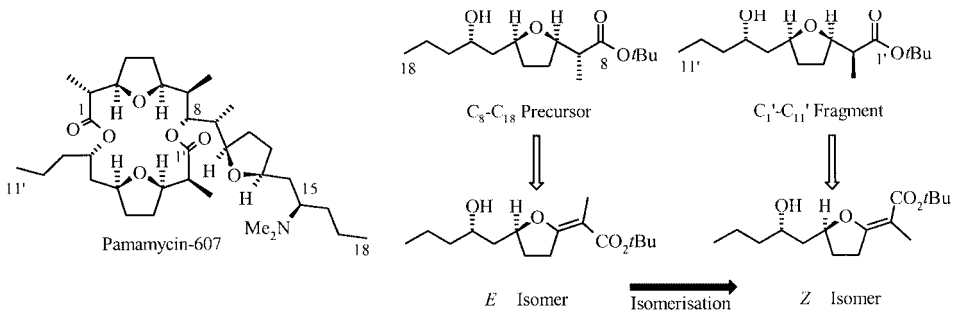
2-(2-Tetrahydrofurylidene)propionates, usually obtained only in the more stable (*E*) configuration **1**, were efficiently isomerised into their (*Z*) isomers **2** by use of Lewis acids or metallated bases. The (*E*)/(*Z*) isomerisation was governed by different factors (type of chelating agent, nature and steric demand of the α,β-unsaturated group). We demonstrated that judicious selection of the α,β-unsaturated group, in combination with the chelating agent, afforded yields of up to 95% with either LDA [R = $N(Me)_2$, *t*Bu] or $MgBr_2$ and ZnI_2 (R = OBn), and that the reaction was also influenced by 1,3-allylic strains.

Introduction

Considerable efforts have been devoted to the synthesis of structurally complex tetrahydrofurans, since they are important components of many natural products including several polyether ionophore antibiotics.[1]

During the course of our studies on the total synthesis of Pamamycin-607,[2] which contains three tetrahydrofuran rings, we used a diastereodivergent strategy to prepare two fragments (C_8-C_{18} and $C_{1'}-C_{11'}$) differing in the *syn* and *anti* configuration of one chiral centre α to the tetrahydrofuran ring (Scheme 1). The key step of this strategy was the (*E*)/(*Z*) isomerisation of the substituted vinyltetrahydrofuran intermediate, which was obtained only in the more stable (*E*) configuration.

Although several methods for the preparation of (*E*)-2-(2-tetrahydrofurylidene)propionates have been reported in the literature,[3] only a few gave direct access to the corresponding (*Z*) isomer.[4] Despite the simplicity of the idea, no (*E*)/(*Z*) isomerisation reaction of such substrates has been described so far. Only little attention has been given to the thermodynamically favoured (*Z*)/(*E*) isomerisation under either acidic or basic conditions.[4b,5,6] A few months ago, some interesting papers described the direct preparation of (*Z*)-2-alkylidene-5-(hydroxymethyl)tetrahydrofurans under kinetic reaction control in the Lewis acid mediated domino reaction between 1,3-dicarbonyl dianions and 1-bromo-2,3-epoxypropanes.[6] In these studies the Lewis acid, used in excess, was necessary both to activate the epoxide cleavage and to control the (*Z*) geometry of the nucleophile.



Scheme 1

We now wish to report the results of a preliminary study we performed on racemic models to obtain the thermodynamically less stable (*Z*)-2-(2-tetrahydrofurylidene)propionates **2** from their corresponding (*E*) isomers **1** by chelation control (Figure 1). We describe all the details of this reac-

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tion, with use either of a metallated base or of a Lewis acid, together with studies related to the preparative scope of the reaction.

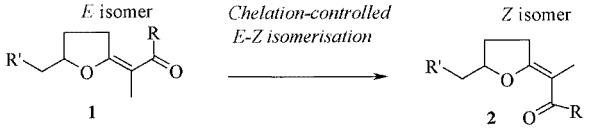
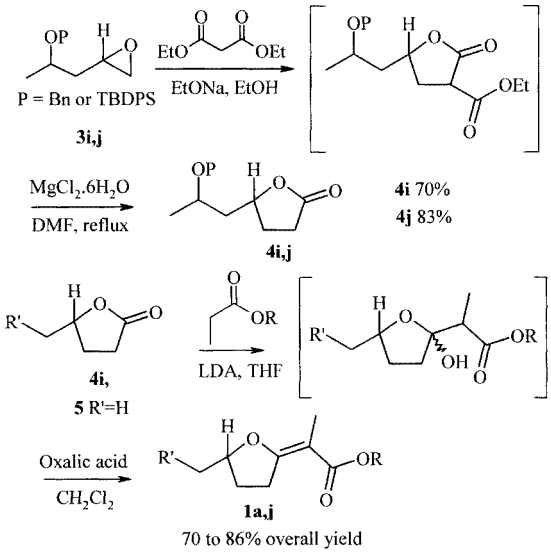


Figure 1. **a**: R′ = H, R = OMe; **b**: R′ = H, R = OBn; **c**: R′ = H, R = O*i*Pr; **d**: R′ = H, R = O*t*Bu; **e**: R′ = H, R = ODMP; **f**: R′ = H, R = ODBMP; **g**: R′ = H, R = OH; **h**: R′ = H, R = $N(Me)_2$; **i**: R′ = $CH_3CH(OBn)$, R = O*t*Bu; **j**: R′ = $CH_3CH(OTBDPS)$, R = O*t*Bu; DMP = 1,5-dimethylphenyl; DBMP = 1,5-di-*tert*-butyl-3-methylphenyl; Bn = benzyl; TBDPS = *tert*-butyldiphenylsilyl

Substrates **1a**−**h** were prepared as depicted in Scheme 2, from commercially available γ-valerolactone (**5**), and **1i** and **1j** from the corresponding epoxides of the protected homoallylic alcohols **3** by way of the butanolides **4**.[7]



Scheme 2

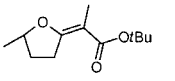
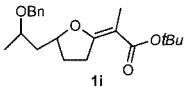
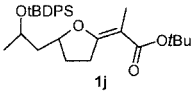
Results and Discussion

Isomerisation by Amides

Our first attempt to induce (*E*)/(*Z*) isomerisation of the *tert*-butyl ester **1d**, by use of 1 equiv. of LDA in THF at −78 °C, resulted in 75% conversion into the (*Z*) isomer **2d**, a very promising result. After optimisation and extension to substrates **1i** and **j** (Table 1), we found that yields of up to 90% were obtained when the reaction was carried out in ether at −78 °C with 2 equiv. of LDA in the presence of 3 equiv. of lithium chloride.

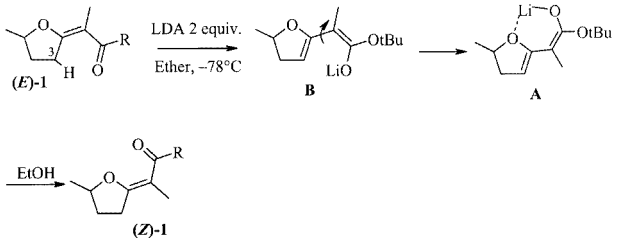
We speculated that the formation of the (*Z*) isomer could be explained by hydrogen abstraction at C-3 of the tetrahydrofuran ring, resulting in an intermediate **A** stabilised by chelation of the Li^+ ion (Scheme 3). The complexation between the lithium enolate and the lithium amide was plausible, and could explain the necessity to use 2 equiv. of LDA.

Table 1. Influence of the solvents and the counter-cations on the (*E*)/(*Z*) isomerisation of **1d**, **1i** and **1j**; all experiments were performed at −78 °C for 1 h and quenched with ethanol; a blank experiment with lithium ethoxide in ethanol on the (*Z*) isomer **2d** at −78 °C afforded starting materia1

Substrate	Entry	Reaction conditions			(*E*)/(*Z*)
		Base	Additive	Solvent	ratio
 **1d**	1	LDA 2 equiv.	no	THF	10:90
	2	LDA 2 equiv.	no	Ether	7:93
	3	**LDA 2 equiv.**	**LiCl 3 equiv.**	**Ether**	**3:97**
	4	LDA 2 equiv.	12-C-4 after (*E*)-**1d**	Ether	3:97
	5	LDA 2 equiv.	12-C-4 before (*E*)-**1d**	Ether	56:44
	6	LiHMDS 2 equiv[a]	no	Ether	30:70
	7	NaHMDS 2 equiv[b]	no	Ether	55:45
	8	KHMDS 2 equiv[c]	no	Ether	76:24
 **1i**	9	LDA 2 equiv.	no	THF	11:89
	10	LDA 2 equiv.	no	Ether	5:95
	11	**LDA 2 equiv.**	**LiCl 3 equiv.**	**Ether**	**4:96**
 **1j**	12	LDA 2 equiv.	no	THF	22:78
	13	LDA 2 equiv.	no	Ether	20:80
	14	**LDA 2 equiv.**	**LiCl 3 equiv.**	**Ether**	**7:93**

[a] 1 M in THF. [b]1 M in THF. [c] 0.5 M in toluene. These three experiments performed with bis(trimethylsilyl)amides resulted in the formation of unidentified products; after chromatography, the isomers mixtures were isolated in moderate yields (37−65%).

Quenching with ethanol resulted in decomplexation to give the free (*Z*)-configured 2-alkylidenetetrahydrofuran. Although these compounds underwent slow conversion into the more stable (*E*)-configured isomers,[6] they were sufficiently stable (several weeks at 0 °C) to be fully characterised and used in further transformations.[2b] We should point out that quenching under more acidic conditions (acetic acid for example) gave rise to spontaneous (*Z*)/(*E*) isomerisation.



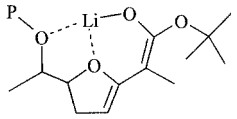
Scheme 3

The nature of the counter-cation was varied in order to examine the chelating effect of the lithium ion (Entries 6−8). Despite the moderate yields observed with the bis(trimethylsilyl)amides, due to the formation of degradation products, these experiments showed that lithium was the better counter-cation and provided evidence in favour of a six-membered chelate **A**. Furthermore, the addition of crown ether (12-C-4) to the medium before the introduction of the substrate resulted in a dramatic decrease in the conversion into the desired (*Z*) isomer (Entry 5).

If the crown ether was introduced after the formation of the enolate intermediate **A**, the level of conversion into the (*Z*) isomer was very high (Entry 4) and even better than that achieved without the crown ether (Entry 2). This

proved that the chelate with the lithium ion was strong enough to avoid exchange with the crown ether.

Experiments carried out on substrates **1i** and **1j** showed higher levels of conversion when the hydroxy group β to the ring was protected with a benzyl group (Entries 9−11) than with a *tert*-butyldiphenylsilyl moiety (Entries 12−14). This result confirmed our chelation hypothesis and was in agreement with the intermediate of type **C** proposed by P. Langer (Figure 2).[6]



C

Figure 2. Intermediate proposed for the (*E*) → (*Z*) isomerisation of β-benzyloxy-2-alkylidenetetrahydrofuran controlled by lithium amides

In order to study the influence of the steric demand of the R group on the isomerisation of substrates **1**, we varied the ester substituents (Table 2). We then completed the study with the dimethylamide **1h**.

Table 2. Influence of the steric demand of the R group (all experiments were performed in ether at −78 °C and quenched after 1 h with ethanol); R′ = H

R	**1a** OMe	**1b** OBn	**1c** O*i*Pr	**1d** O*t*Bu	**1e** ODMP	**1f** ODtBMP	**1h** $N(Me)_2$
Ratio (*E*)/(*Z*)	13:87	10:90	10:90	7:93	81:19	97:3	> 3:97

The results listed in Table 2 showed a correlation between the steric demand of the ester substituent on substrates **1a**−**d** and the levels of conversion into their corresponding (*Z*) isomers **2a**−**d**. In the more hindered cases, the level of conversion dropped drastically (**1e**), becoming totally unsuccessful for the more bulky substrate **1f**. These results could be explained by 1,3-allylic strain control, as depicted in Scheme 4. Such stereocontrol has already been mentioned in the literature for the preparation of (*E*)-2-(2-tetrahydrofurylidene)propionates bearing a methyl group at C-3 of the ring.[8]

From the (*E*) substrates **1**, the two vinylogous enolates **B** and **D** could be generated by use of LDA, but only one geometry (**B**) would allow the formation of the chelate **A**, resulting in the (*Z*) isomers **2** after ethanolysis. As 1,3-allylic strains became more important, the equilibrium between the two intermediate species would be in favour of the desired isomer and the (*Z*) selectivity would increase.

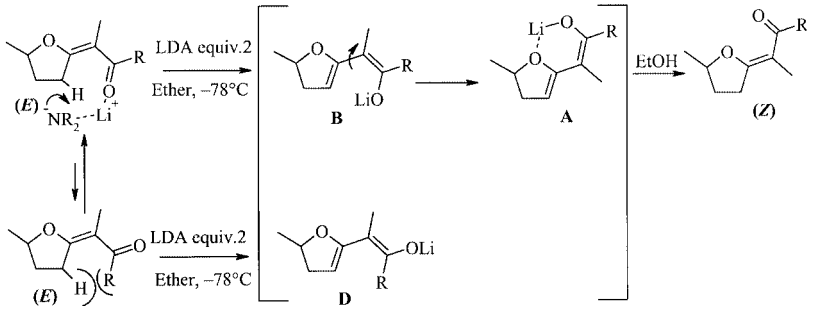
Since the amide **1h** was also prepared according to Scheme 2, the dehydration reaction afforded a 1:1 mixture of both stereoisomers. Isomerisation was carried out on the chromatographically isolated pure (*E*) isomer, using only LDA in ether at −78 °C, to afford the corresponding (*Z*) isomer **2h** quantitatively after ethanolysis.

Isomerisation with Lewis Acids

Our first attempt to induce (*E*)/(*Z*) isomerisation reactions through the use of Lewis acids consisted of several series of experiments on substrate **1d** in order to select the Lewis acid and the appropriate solvents and temperature. This preliminary work is summarised in Table 3

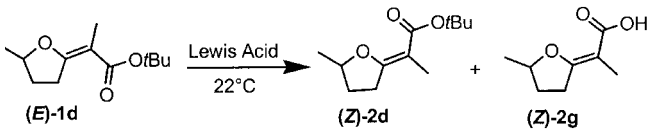
In two cases we observed high levels of conversion into the (*Z*) isomer **2d** (Entries 9 and 14): with zinc iodide (1.1 equiv. in dichloromethane) at room temperature and with magnesium bromide (2 equiv. in dichloromethane) at room temperature, with a better degree of conversion for the latter. The better conversion obtained with zinc iodide rather than zinc bromide can be attributed to its higher solubility in dichloromethane. In the case of zinc iodide, the use of an excess of Lewis acid did not improve the yields. The (*Z*)-acid **2g** resulted from cleavage of the *tert*-butyl ester under acidic conditions. The fact that no traces of the corresponding (*E*)-acid **1g** could be detected in all the reactions and that the acid **2g** appeared quite late during the reaction, showed that **2g** probably originated from the cleavage of the (*Z*)-*tert*-butyl ester **2d**. Another hypothesis might be the cleavage of the (*E*) isomer **1d** to the corresponding acid **1g**, followed by a quick and quantitative isomerisation to (*Z*)-**2g**. We tried to isomerise the (*E*)-acid **1g**, obtained by basic saponification of the corresponding methyl ester **1a**, with ZnI_2 but without any success. Only degradation products were obtained.

Since substrates **1** were obtained after dehydration of the hemiketal **6d** in acidic medium (Scheme 2), it should be possible to obtain the (*Z*) isomers **2** directly by using Lewis acids instead of oxalic acid (Scheme 5). The (*Z*) isomer was indeed the main product. Other relevant substrates studied



Scheme 4

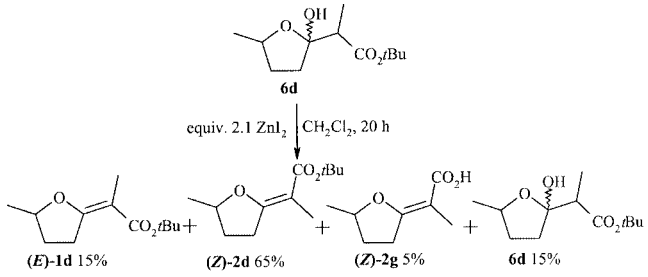
Table 3. Selection of the solvent, temperature and reaction time in the Lewis acid controlled isomerisation of substrate **1d** (all experiments were quenched with water); data in parentheses correspond to isolated yields after chromatography



Entry	Lewis acid	Solvent	**1d** (*E*)	**2d** (*Z*)	**2g** (*Z*)
1	LiI 1.1 equiv.	ether[a]	100		
2	$TiCl_4$ 1.1 equiv.	dichloromethane[b]	100		
3	$SnCl_4$ 1.1 equiv.	dichloromethane[b]	72	14	14
4	$Yb(OTf)_3$ 1.1 equiv.	dichloromethane[a]	degradation		
5	$ZnBr_2$ 1.1 equiv.	dichloromethane[c]	64	18	18
6	$ZnBr_2$ 1.1 equiv.	THF[a]	100		
7	$ZnBr_2$ 1.1 equiv.	dichloromethane[d]	degradation		
8	$ZnBr_2$ 1.1 equiv.	acetonitrile[a]	100		
9	**ZnI_2 1.1 equiv.**	**dichloromethane**[a]	**13 (9)**	**75 (70)**	**12 (5)**
10	ZnI_2 1.1 equiv.	dichloromethane[e]	75	25	
11	ZnI_2 2 equiv.	dichloromethane[a]			
12	$MgBr_2$ 1.1 equiv.	THF[a]	100		
13	$MgBr_2$ 1.1 equiv.	dichloromethane[a]	10	78	12
14	**$MgBr_2$ 2 equiv.**	**dichloromethane**[a]	**< 3**	**74 (70)**	**23 (15)**

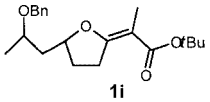
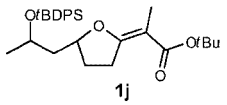
[a] 24 h, room temperature. [b] 6 h, −60 °C. [c] 48 h, room temperature. [d] 4 h, reflux. [e] 6 h, room temperature.

for isomerisation were the protected 5-(2-hydroxyalkyl)-2-tetrahydrofurylidene compounds **1i** and **1j** (Table 4).



Scheme 5

Table 4. Isomerisation of protected 5-(2-hydroxyalkyl)-2-tetrahydrofurylidene compounds **1i** and **1j**; the conversions given correspond to both (*Z*)-*tert*-butyl esters and the corresponding (*Z*)-acids

Substrates / Reaction conditions	 **1i**	 **1j**
ZnI_2 1.1 equiv./CH_2Cl_2	(*E*)/(*Z*) = 77:23	(*E*)/(*Z*) = 42:58
$MgBr_2$ 2 equiv./CH_2Cl_2	(*E*)/(*Z*) = 81:19	(*E*)/(*Z*) = 21:79

As can be seen in Table 4, the isomerisation of substrates **1i** and **1j** gave lower levels of conversion than that of substrate **1d**. This could be explained by competitive complexation of the Lewis acid by the ether oxygen atom at the β-position and the oxygen atom of the tetrahydrofuran ring and was supported by the lower level of conversion observed with the substrate **1i**, bearing the better Lewis base at the β-position.

Finally, we studied the influence of the steric demand of the R group on the isomerisation, as in the preceding paragraph. The results are collected in Table 5

These results showed the same correlation as observed with the amide-promoted reaction (see preceding paragraph) between the steric demand of the R group and the conversion rate of the isomerisation. In the more hindered cases, the level of conversion dropped dramatically, the (*E*) isomer being totally recovered for **1f**.

We found that the use of 2 equiv. of magnesium bromide in dichloromethane on the benzyl ester **1b** afforded the (*Z*) isomer **2b** in 90% isolated yield without formation of any acid **2g**.

Our working hypothesis to explain the reaction was based on the assumption that an "ate" complex **E** could be generated as intermediate, and that the **E/F** *transoid*/*cisoid* conformation equilibrium could be displaced to the stabilised **F** *cisoid* by chelation and provide the (*Z*) isomer after hydrolysis (Scheme 6). As for amide-promoted isomerisation, of the two possible conformers of the ester, only one would be able to react with the Lewis acid to give the intermediate that afforded the chelate. The other would give an "ate" complex unsuitable for chelation and disfavoured by 1,3-allylic strains.

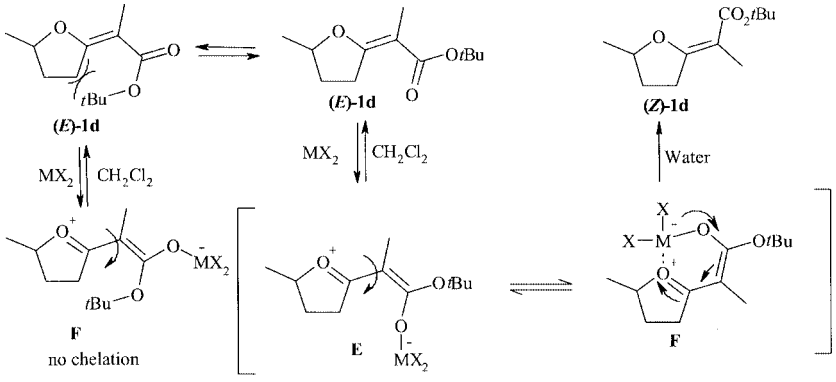
Isomerisation of the dimethylamide **1h** (Table 5) gave poor yields, probably because the mesomeric form of the conjugated amide disfavoured the stabilisation of the chelate **F**.

In summary, we report a convenient (*E*)/(*Z*) isomerisation of 2-(2-tetrahydrofurlidene)propionates, which are versatile building blocks for the synthesis of biologically important natural products. Judicious selection of the propionate substituents, combined with the right chelating agent, has re-

Table 5. Influence of the steric demand of the R group; R′ = H

R	**1a** OMe	**1b**[a] OBn	**1c** O*i*Pr	**1d**[b] O*t*Bu	**1h** $N(Me)_2$	**1e** ODMP	**1f** ODBMP
ZnI_2 1.1 equiv./CH_2Cl_2 Ratio (*E*)/(*Z*)	40:60	32:68	30:70	13:87	87:13	85:15	97:3
$MgBr_2$ 2 equiv./CH_2Cl_2 Ratio (*E*)/(*Z*)	20:80	5:95	11:89	3:97	degradation	35:65	95:5

[a] The (*Z*) isomer **2b** was isolated in 90% yield after chromatography. [b] The conversion given corresponds to both (*Z*)-ester and (*Z*)-acid **4′**.



Scheme 6

sulted in yields of the (*Z*) isomer of up to 90% with either LDA [R = $N(Me)_2$ or *t*Bu] or magnesium bromide (R = benzyl). The usefulness of this isomerisation has been demonstrated with the preparation of the $C_{1'}$–$C_{11'}$ fragment of Pamamycin-607 (Scheme 1).[2b]

Experimental Section

General: All reactions were carried out under dry argon. Standard syringe and cannula techniques were employed for transfer of dry solvents and air- or moisture-sensitive reagents. Tetrahydrofuran (THF) was distilled under argon from sodium/benzophenone, diethyl ether from lithium aluminium hydride, dichloromethane from phosphorus pentoxide, and diisopropylamine from KOH. *n*-Butyllithium was purchased as a 1.5 M solution in hexane. Starting materials not mentioned below were commercially available. The following compounds were prepared according to published procedures: 2,6-Di-*tert*-butyl-4-methylphenyl propionate and 2,6-dimethylphenyl propionate,[9] isopropyl propionate.[10] Reactions were monitored by thin layer chromatography on silica gel plates (Merck $60F_{254}$), and viewed by use of *p*-anisaldehyde. Merck silica gel 60H was used for column chromatography. NMR spectra were obtained at 400 MHz (^1H) or 100 MHz (^{13}C) with Bruker Avance 400 or at 200 MHz (^1H) or 50 MHz (^{13}C) with Bruker AC 200 instruments, with deuteriochloroform as solvent. Chemical shifts (δ) are given in ppm relative to tetramethylsilane (δ = 0 ppm) or to residual protons in the solvent as internal standard. IR spectra were recorded with a Perkin–Elmer Spectrum One, and absorption bands are given in cm^{-1}. Microanalyses were performed by the Microanalyses Service of the Strasbourg Faculty of Chemistry.

General Procedure for the Synthesis of 2-(2-Tetrahydrofurylidene)-propionates 1 Demonstrated with the Synthesis of 1d. *tert*-Butyl (*E*)-2-[5-Methyldihydrofuran-2(3*H*)-ylidene]propanoate (1d): A solution of BuLi (1.5 M in hexane, 3.7 ml, 5.5 mmol, 2.2 equiv.) was added under argon to a stirred and cooled (−78 °C) solution of diisopropylamine (0.77 ml, 5.5 mmol, 2.2 equiv.) in dry THF (9 mL). The mixture was stirred at −78 °C for 1 h, and *tert*-butyl propionate (0.79 ml, 5.24 mmol; 2.1 equiv.) was then added dropwise. After the mixture had been stirred for 40 min at −78 °C, a solution of γ-valerolactone (250 mg; 2.5 mmol; 1 equiv.) in 5 mL of dry THF was added and the mixture was stirred for 1.5 h at −78 °C and 1.5 h at room temperature. The reaction mixture was then quenched with a saturated solution of NH_4Cl and extracted with ethyl acetate. The organic phase was dried ($MgSO_4$), and the solvents were evaporated to dryness under reduced pressure. The resulting pale yellow oil was suspended in 15 mL of CH_2Cl_2, and oxalic acid (23 mg, 0.25 mmol, 0.1 equiv.) was added. The resulting solution was heated under reflux for 5 h. The reaction was quenched by addition of a saturated $NaHCO_3$ solution, and the residue was extracted with ethyl acetate. The organic phase was dried ($MgSO_4$) and the solvent was evaporated. Chromatography on silica gel with hexane/EtOAc (2:1) as eluent yielded the product **1d** (0.480 g, 90%) as a yellow oil. R_f = 0.76 (hexane/ethyl acetate, 2:1). ^1H NMR (200 MHz; $CDCl_3$): δ = 1.32 (d, *J* = 6.5 Hz, 3 H), 1.46 (s, 9 H), 1.55–1.71 (m, 1 H), 1.77 (t, *J* = 1.5 Hz, 3 H), 2.08–2.24 (m, 1 H), 2.78–2.99 (m, 1 H), 3.12–3.28 (m, 1 H), 4.37–4.53 (m, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.5, 20.5, 28.3, 31.3, 31.7, 78.9, 79.0, 98.5, 168.9, 169.0 ppm. IR (film): $\tilde{\nu}$ = 1105, 1199, 1631, 1718 cm^{-1}. $C_{12}H_{20}O_3$ (212.29): calcd. C 67.39, H 9.50; found C 67.89, H 9.43.

Methyl (*E*)-2-[5-Methyldihydrofuran-2(3*H*)-ylidene]propanoate (1a): Compound **1a** was isolated as a yellow oil (1.24 g, 73%) from methyl propionate (1.85 g, 21 mmol, 2.1 equiv.) and γ-valerolactone (1 g, 10 mmol); R_f = 0.69 (hexane/ethyl acetate, 2:1). ^1H NMR (200 MHz; $CDCl_3$): δ = 1.32 (d, *J* = 6.2 Hz, 3 H), 1.50–1.69 (m, 1 H), 1.77 (t, *J* = 1.5 Hz, 3 H), 2.08–2.24 (m, 1 H), 2.79–2.99 (m,

1 H), 3.14−3.32 (m, 1 H), 3.65 (s, 3 H), 4.37−4.54 (m, 1 H) ppm. ^{13}C NMR (50 MHz; $CDCl_3$): δ = 11.3, 20.6, 31.5, 31.8, 50.9, 79.7, 96.9, 170.0, 170.6 ppm. $C_9H_{14}O_3$ (170.21): calcd. C 63.51, H 8.29; found C 63.26, H 8.51.

Benzyl (*E*)-2-[5-Methyldihydrofuran-2(3*H*)-ylidene]propanoate (1b): Compound **1b** was isolated as a pale yellow oil (1.68 g, 77%) from benzyl propionate (3 g, 18.3 mmol, 2.1 equiv.) and γ-valerolactone (870 mg; 10 mmol), R_f = 0.71 (hexane/ethyl acetate, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (d, *J* = 6.4 Hz, 3 H), 1.52−1.72 (m, 1 H), 1.84 (t, *J* = 1.4 Hz, 3 H), 2.16−2.28 (m, 1 H), 2.83−3.06 (m, 1 H), 3.19−3.37 (m, 1 H), 4.42−4.59 (m, 1 H), 5.18 (s, 2 H), 7.3−7.42 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.8, 21, 31.9, 32.1, 65.7, 80.0, 97.3, 128−129, 137.5, 169.5, 171.3 ppm. $C_{15}H_{18}O_3$ (246.3): calcd. C 73.15, H 7.37; found C 73.06, H 7.57.

Isopropyl (*E*)-2-[5-Methyldihydrofuran-2(3*H*)-ylidene]propanoate (1c): Compound **1c** was isolated as a colourless oil (1.8 g, 89%) from isopropyl propionate (2.4 g, 21 mmol, 2.1 equiv.) and γ-valerolactone (1 g; 10 mmol), R_f = 0.66 (hexane/ethyl acetate, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (d, *J* = 7.0 Hz, 6 H), 1.38 (d, *J* = 5.6 Hz, 3 H) 1.52−1.74 (m, 1 H), 1.80 (t, *J* = 1.1 Hz, 3 H), 2.09−2.28 (m, 1 H), 2.82−3.12 (m, 1 H), 3.15−3.33 (m, 1 H), 4.39−4.56 (m, 1 H); 4.92−5.32 (h, *J* = 7.0 Hz, 1 H) ppm. ^{13}C NMR (50 MHz; $CDCl_3$): δ = 11.3, 20.6, 31.5, 31.8, 50.9, 79.7, 96.9, 170.0, 170.6 ppm. IR (film): ṽ = 1105, 1196, 1631, 1719 cm^{-1}.

2,6-Dimethylphenyl (*E*)-2-[5-Methyldihydrofuran-2(3*H*)ylidene]propanoate (1e): Compound **1e** was isolated as a pale yellow oil (1.08 g, 62%) from 2,6-dimethylphenyl propionate (2.5 g, 14 mmol, 2.2 equiv.) and γ-valerolactone (0.67 g, 0.67 mmol), R_f = 0.61 (hexane/ethyl acetate, 2:1), bp 150 °C/10 mm. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.41 (d, *J* = 6.0 Hz, 3 H), 1.58−1.84 (m, 1 H), 2.01 (t, *J* = 1.2 Hz, 3 H), 2.18 (s, 6 H), 2.15−2.33 (m, 1 H), 2.89−3.15 (m, 1 H), 3.33−3.45 (m, 1 H); 4.5−4.58 (m, 1 H), 6.93−7.1 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.9, 16.9, 21.1, 32.1, 32.2, 80.5, 96.6, 125.6, 128.7, 130.9, 149.1, 167.4, 172.8 ppm. $C_{16}H_{20}O_3$ (260.3): calcd. C 73.82, H 7.74; found C 73.59, H 7.81.

2,6-Di-*tert*-butyl-4-methylphenyl (*E*)-2-[5-Methyldihydrofuran-2(3*H*)-ylidene]propanoate (1f): Compound **1f** was isolated as white crystals (1.4 g, 58%) from 2,6-di-*tert*-butyl-4-methylphenyl propionate (4 g, 14.5 mmol, 2.2 equiv.), and γ-valerolactone (0.66 g, 6.6 mmol), m.p. 103−105 °C, R_f = 0.7 (hexane/ethyl acetate, 2:1), ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.31 (s, 9 H), 1.43 (d, *J* = 5.9 Hz, 3 H), 1.52−1.74 (m, 1 H), 2.08 (t, *J* = 0.9 Hz, 3 H), 2.11−2.32 (m, 1 H), 2.41 (s, 3 H), 2.83−3.05 (m, 1 H), 3.21−3.42 (m, 1 H), 4.46−4.53 (m, 1 H), 7.1 (s, 2 H) ppm. ^{13}C NMR (50 MHz; $CDCl_3$): δ = 11.5, 20.8, 21.6, 31.5, 31.6, 31.8, 35.8, 80.2, 96.8, 126.8, 127.1, 133.9, 142.4, 170.0, 173.2 ppm. IR (neat): ṽ = 1042, 1187, 1628, 1714 cm^{-1}. $C_{23}H_{34}O_3$ (358.5): calcd. C 77.05, H 9.56; found C 76.81, H 9.42.

(*E*)-2-[5-Methyldihydrofuran-2(3*H*)-ylidene]propanoic Acid: Saponification of methyl ester **1a** under standard conditions (KOH/THF/water) afforded, after chromatography (hexane/ethyl acetate, gradient 1:1 to 0:1), pure acid **1g** as white crystals. R_f = 0.24 (hexane/ethyl acetate, 2:1), m.p. 131 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.38 (d, *J* = 6.3 Hz, 3 H), 1.51−1.75 (m, 1 H), 1.82 (t, *J* = 0.4 Hz, 3 H), 2.1−2.28 (m, 1 H), 2.84−3.07 (m, 1 H), 3.19−3.38 (m, 1 H), 4.42−4.58 (m, 1 H), 12.1 (br, 2 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.2, 20.6, 31.6, 32.0, 80.1, 96.6, 172.9, 175.9. IR (neat): ṽ = 1112, 1307, 1591, 1674, 2800−3260 cm^{-1}. $C_8H_{12}O_3$ (156.2): calcd. C 61.52, H 7.74; found C 61.26, H 7.57.

***N*,*N*-Dimethyl-2-[5-methyldihydrofuran-2(3*H*)-ylidene]-propionamides 1h and 2h:** A 1:1 mixture of (*E*)/(*Z*) isomers **1h** and **2h** (1.6 g, 87%) was obtained as a pale yellow oil from *N*,*N*-dimethylpropionamide (2.2 g, 22 mmol, 2.1 equiv.) and γ-valerolactone (1 g, 10 mmol). Isomers **1h** and **2h** were separated by chromatography, with hexane/ethyl acetate (gradient 4:1 to 1:1) as eluent. R_f = 0.59 (hexane/ethyl acetate, 2:1). $C_{10}H_{17}NO_2$ (183.2): calcd. C 65.54, H 9.35; found C 65.81, H 9.2.

Isomer (*E*)-1h: ^{1}H NMR (200 MHz; $CDCl_3$): δ = 1.29 (d, *J* = 3.0 Hz, 3 H), 1.44−1.68 (m, 1 H), 1.75 (t, *J* = 0.8 Hz, 3 H), 1.9−2.22 (m, 1 H), 2.45−2.68 (m, 1 H), 2.96 (s, 6 H), 4.28−4.45 (m, 1 H) ppm. ^{13}C NMR (50 MHz; $CDCl_3$): δ = 13.2, 20.8, 28.5, 32.3, 36.0, 37.7, 78.7, 99.0, 156.9, 173.3 ppm.

Isomer (*Z*)-2h: ^{1}H NMR (200 MHz; $CDCl_3$): δ = 1.27 (d, *J* = 3.0 Hz, 3 H), 1.48−1.65 (m, 1 H), 1.73 (t, *J* = 0.5 Hz, 3 H), 1.98−2.20 (m, 1 H), 2.45−2.68 (m, 1 H), 2.96 (s, 6 H), 4.39−4.47 (m, 1 H) ppm. ^{13}C NMR (50 MHz; $CDCl_3$): δ = 15.5, 21.2, 28.1, 31.9, 34.9, 38.3, 79.3, 97.7, 154.0, 172.0 ppm.

2-(Benzyloxy)pent-4-ene Oxide (3i):[11] Pent-4-en-2-ol (1.2 ml, 11.6 mmol, 1 equiv.) was added under Ar at 0 °C to a THF suspension (35 mL) of NaH (310 mg, 12.8 mmol, 1.1 equiv.). After the mixture had been stirred for 75 min at 20 °C, benzyl bromide (1.45 ml, 12 mmol, 1.05 equiv.) was added. After the solution had been stirred for 22 h, a saturated aqueous NH_4Cl solution (50 mL) was added. The aqueous layer was extracted with ether, the combined organic fractions were dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo. The resulting yellow oil was dissolved in 30 mL of CH_2Cl_2 and cooled to 0 °C. To this solution, *m*CPBA (3.2 g, 18.5 mmol, 1.6 equiv., 60% active oxygen) was added portionwise. After 2 h at 0 °C, the solution was allowed to warm to room temperature and was stirred for 12 h. The resulting mixture was treated with saturated aq. $NaHCO_3$ and $Na_2S_2O_3$ (75 mL) and extracted with ether. The organic phase was washed with brine and dried, and the solvents were evaporated to afford a yellow liquid. Chromatography on silica gel with hexane/ethyl acetate (25:3) as eluent yielded **3i** (1.76 g, 88%) as a mixture of two diastereomers (*syn*/*anti*: 60:40). R_f = 0.57 (hexane/ethyl acetate, 2:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.27 (d, 1.8 H, *J* = 6.2 Hz, major isomer), 1.29 (d, 1.2 H, H-5, *J* = 6.2 Hz, minor isomer), 1.43−1.96 (m, 2 H), 2.45−2.53 (m, 1 H), 2.72−2.82 (m, 1 H), 3.01−3.15 (m, 1 H), 3.67−3.88 (m, 1 H), 4.54 (ABq, 6.8 H, *J* = 1 2.0 Hz, Δν = 50 Hz, minor isomer), 4.57 (ABq, 1.2 H, *J* = 11.6 Hz, Δν = 85 Hz, major isomer), 7.26−7.38 (m, 5 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.8, 20.1, 39.4, 40.3, 46.9, 47.5, 49.7, 49.9, 70.4, 70.8, 72.7, 73.0, 127.6, 127.7, 128.5, 138.8. ppm.

Ethyl 5-[2-(Benzyloxy)propyl]-2-oxotetrahydrofuran-3-carboxylate (4i):[12] Diethyl malonate (1.72 mL, 11.4 mmol) was added to a solution of EtONa [prepared from Na (0.26 g, 11.4 mmol) in EtOH (11 mL)], followed by the epoxide **3i** (0.5 g, 2.84 mmol) in EtOH (5.5 mL). After having been heated under reflux for 3 h, the mixture was poured into a saturated aqueous solution of NH_4Cl and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated in vacuo. The resulting yellow oil was suspended in 20 mL of DMF, and $MgCl_2{\cdot}6H_20$ (2.90 g) was added. The mixture was heated under reflux for 3 h with stirring. After cooling, a saturated aqueous solution of NH_4Cl was added. The combined organic layers were washed with brine, dried ($MgSO_4$) and filtered, and the solvent was evaporated off. Flash chromatography (hexane/ethyl acetate, 5:1) afforded **4i** as a yellow oil (0.405 g, 70%) and as a diastereomeric mixture (*syn*/*anti*: 60:40). R_f = 0.67 (hexane/ethyl acetate, 2:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.25 (d, 1.8 H, *J* = 6.2 Hz, major isomer), 1.28 (d, 1.2 H, *J* = 6.2 Hz, minor isomer), 1.62−1.95 (m,

3 H), 2.06−2.43 (m, 1 H), 2.45−2.58 (m, 2 H), 3.62−3.90 (m, 2 H), 4.49 (ABq, 0.8 H, J = 11.3 Hz, Δν = 83 Hz, minor isomer), 4.52 (ABq, 1.2 H, J = 11.3 Hz, Δν = 79 Hz, major isomer), 4.56−4.84 (m, 1 H), 7.22−7.39 (m, 5 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.5, 20.1, 28.3, 28.5, 28.9, 29.0, 42.2, 43.9, 70.4, 71.2, 71.3, 72.2, 78.2, 127.8, 128.3, 138.6, 177.3 ppm. IR (film): ν̃ = 1140, 1765 cm^{-1}.

***tert*-Butyl (*E*)-2-{5-[2-(Benzyloxy)propyl]dihydrofuran-2(3*H*)-ylidene}-jypropanoate (1i):**[11] Compound **1i** (0.304 g, 71%) was isolated as a yellow oil from the starting material **4i** (0.290 g, 1.24 mmol), by the method described for **1d**. R_f = 0.67 (hexane/ethyl acetate, 2:1). Two isomers (*syn*/*anti*: 60:40) were observed. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.24 (d, 1.2 H, J = 6.2 Hz, minor isomer), 1.28 (d, 1.8 H, J = 6.2 Hz, major isomer), 1.48 (s, 9 H), 1.75 (s, 3 H), 1.53−1.89 (m, 3 H), 1.99−2.24 (m, 1 H), 2.75−2.98 (m, 1 H), 3.08−3.26 (m, 1 H), 3.62−3.86 (m, 1 H), 4.52 (ABq, 1.2 H, J = 11.8 Hz, Δν = 70 Hz, major isomer), 4.58 (ABq, 0.8 H, J = 11.4 Hz, Δν = 66 Hz, minor isomer), 4.51−4.66 (m, 1 H), 7.29−7.36 (m, 5 H) ppm. ^{13}C NMR (50 MHz; $CDCl_3$): δ = 11.9, 19.7, 20.2, 28.6, 30.4, 30.6, 31.2, 41.9, 43.2, 70.4, 71.0, 72.0, 72.2, 79.1, 79.8, 80.1, 98.9, 127.7, 127.8, 128.5, 138.8, 168.4, 169.0 ppm. IR (film): ν̃= 1101, 1136, 1628, 1716.

2-(*tert*-Butyldiphenylsilyloxy)pent-4-ene Oxide (3j):[13] Imidazole (4.1 g, 60 mmol, 4 equiv.) and *tert*-butyldiphenylsilyl chloride (7.8 mL, 30 mmol, 2 equiv.) were added under argon at room temperature to a pent-4-en-2-ol (1.29 g, 15 mmol, 1 equiv.) solution in DMF (40 mL). After stirring for 15 h, the solution was treated with a saturated aqueous NH_4Cl solution (50 mL). The aqueous layer was extracted with ether, the combined organic fractions were dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo. The resulting yellow oil was dissolved in 50 mL of CH_2Cl_2 and cooled to 0 °C. To this solution, *m*CPBA (4.2 g, 24.3 mmol, 1.6 equiv., 60% active oxygen) was added portionwise. After 2 h at 0 °C, the solution was allowed to warm to room temperature and was stirred for 12 h. The resulting mixture was treated with saturated aq. $NaHCO_3$ and $Na_2S_2O_3$ (75 mL) and extracted with ether. The organic phase was washed with brine and dried, and the solvents were evaporated to afford a yellow liquid. Chromatography on silica gel with hexane/ethyl acetate (100:1) as eluent yielded **3j** (3.54 g, 70%) as a diastereomeric mixture (*syn*/*anti*: 60:40). R_f = 0.54 (hexane/ethyl acetate, 4:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.05 (s, 9 H), 1.14 (d, 1.8 H, J = 6.2 Hz, major isomer), 1.18 (d, 1.2 H, H-5, J = 6.5 Hz, minor isomer), 1.55−1.80 (m, 2 H), 2.31−2.42 (m, 1 H), 2.62−2.75 (m, 1 H), 2.89−3.16 (m, 1 H), 4.00−4.18 (m, 1 H), 7.31−7.47 (m, 6 H), 7.62−7.73 (m, 4 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.3, 19.4, 23.5, 24.0, 27.1, 42.1, 42.8, 46.8, 47.6, 49.5, 49.8, 67.7, 68.0, 127.6, 127.7, 129.7, 129.8, 134.1, 134.2, 134.5, 134.6, 136.0 ppm.

5-[2-(*tert*-Butyldiphenylsilyloxy)propyl]tetrahydro-2-furanone (4j): Compound **4j** (3.27 g, 83%) was isolated as a yellow oil from the starting material **3j** (3.50 g, 10.3 mmol), by the method described for **4i**. R_f = 0.58 (hexane/ethyl acetate, 2:1). Two isomers (*syn*/*anti*: 60:40) were observed. ^{1}H NMR (200 MHz; $CDCl_3$): δ = 1.07 (s, 9 H), 1.08 (d, 1.8 H, J = 6.2 Hz, major isomer), 1.19 (d, 1.2 H, J = 6.2 Hz, minor isomer), 1.58−1.81 (m, 2 H), 1.92−2.32 (m, 2 H), 2.37−2.51 (m, 2 H), 3.97−4.19 (m, 1 H), 4.55−4.71 (m, 1 H), 7.32−7.49 (m, 6 H), 7.63−7.75 (m, 4 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.3, 19.5, 23.4, 24.3, 27.1, 28.4, 28.5, 28.7, 28.9, 44.7, 46.0, 66.5, 67.0, 78.0, 78.1, 127.6, 127.7, 127.8, 129.6, 129.7, 129.8, 129.9, 133.9, 134.0, 134.3, 134.6, 135.8, 135.9, 177.2, 177.3 ppm. $C_{23}H_{30}O_3Si$ (382.5): calcd. C 72.21, H 7.90; found C 71.98, H 7.96.

***tert*-Butyl (*E*)-2-{5-[2-(*tert*-Butyldiphenylsilyloxy)propyl]dihydrofuran-2(3*H*)-ylidene}propanoate (1j):** Compound **1j** (1.250 g, 70%) was isolated as a yellow oil from the starting material **4j** (1.38 g, 3.61 mmol), by the method described for **1d**. R_f = 0.70 (hexane/ethyl acetate, 4:1). Two isomers (*syn*/*anti*: 60:40) were observed. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.07 (d, 1.8 H, J = 6.2 Hz, major isomer), 1.08 (s, 9 H), 1.18 (d, 1.2 H, J = 6.2 Hz, minor isomer), 1.50 (s, 9 H), 1.69 (t, 1.2 H, J = 1.1 Hz, minor isomer), 1.73 (t, 1.8 H, J = 1.1 Hz, major isomer), 1.41−2.22 (m, 4 H), 1.71−2.96 (m, 1 H), 2.97−3.21 (m, 1 H), 3.94−4.19 (m, 1 H), 4.38−4.61 (m, 1 H), 7.32−7.49 (m, 6 H), 7.63−7.75 (m, 4 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.8, 19.3, 19.5, 23.4, 24.4, 27.1, 28.6, 30.5, 31.1, 31.2, 44.6, 45.6, 67.1, 67.3, 79.1, 79.7, 79.9, 98.8, 127.5, 127.7, 129.7, 129.8, 134.0, 134.1, 134.5, 134.8, 136.0, 169.1. ppm

Isomerisation with ZnI_2. General Procedure Demonstrated by the Preparation of *tert*-Butyl (*Z*)-2-[5-Methyldihydrofuran-2(3*H*)-ylidene]propanoate (2d): A solution of **1d** (50 mg, 0.23 mmol, 1 equiv.) in 0.5 mL of CH_2Cl_2 was added under argon to a stirred suspension of ZnI_2 (83 mg, 0.25 mmol, 1.1 equiv.), previously dried by heating, in 0.5 mL of dried CH_2Cl_2. The resulting suspension was stirred at room temperature for 19 h. The reaction was quenched by addition of 2 mL H_2O, and the resulting mixture was extracted with CH_2Cl_2. The organic phase was washed with brine and dried ($MgSO_4$), and the solvents were evaporated to dryness. A mixture of **1d**, **2d** and **2g** (12:75:12) was obtained, giving, after flash chromatography (hexane/ethyl acetate, 5:1), 0.035 g of **2d** (70%), 0.004 g of **1d** (9%) and 0.002 g of **2g** (5%).

Isomerisation with $MgBr_2$. General Procedure Demonstrated by the Preparation of *tert*-Butyl (*Z*)-2-[5-Methyldihydrofuran-2(3*H*)-ylidene]propanoate (2d): A solution of **1d** (50 mg, 0.23 mmol, 1 equiv.) in 0.5 mL of CH_2Cl_2 was added under argon to a stirred suspension of dried $MgBr_2$ (92 mg, 0.5 mmol, 2 equiv.), freshly prepared from magnesium and dibromoethane in ether, in 0.5 mL of dried CH_2Cl_2. The resulting suspension was stirred at room temperature for 20 h. The reaction was quenched by addition of 2 mL H_2O, and the resulting mixture was extracted with CH_2Cl_2. The organic phase was washed with brine and dried ($MgSO_4$), and the solvents were evaporated to dryness. A mixture of **1d**, **2d** and **2g** (3:74:23) was obtained, giving after flash chromatography (hexane/ethyl acetate, 5:1), 0.034 g of **2d** (70%) and 0.005 g of **2g** (15%).

Isomerisation with LDA. General Procedure Demonstrated by the Preparation of *tert*-Butyl (*Z*)-2-[5-Methyldihydrofuran-2(3*H*)-ylidene]propanoate (2d): A solution of BuLi in hexane (1.55 M, 1.44 ml, 2.2 mmol, 2 equiv.) was added dropwise under argon to a stirred and cooled (−78 °C) solution of diisopropylamine (0.31 ml, 2.2 mmol, 2 equiv.) in dry ether (4 mL). The resulting solution was maintained at −78 °C for 1 h, and a solution of **1d** (226 mg, 1.07 mmol, 1 equiv.) in ether (2.5 mL) was then added dropwise. After 1 h of stirring at −78 °C, LiCl (136 mg, 3.2 mmol; 3 equiv.) was added. After 45 min, the solution was quenched with ethanol (5 mL) and allowed to warm to room temperature. Water was added to the suspension, and the resulting mixture was then extracted with ethyl acetate. The organic phase was dried ($MgSO_4$), and the solvents were evaporated to leave a yellow oil. Chromatography on silica gel with hexane/ethyl acetate (25:3) as eluent yielded **2d** (0.206, 91%), with 0.005 g of **1d** (5%) also being obtained as a pale yellow oil. R_f = 0.56 (hexane/ethyl acetate, 2:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.40 (d, J = 6.5 Hz, 3 H), 1.48 (s, 9 H), 1.72 (t, J = 1.1 Hz, 3 H), 1.58−1.76 (m, 1 H), 2.04−2.20 (m, 1 H), 2.52−2.83 (m, 2 H), 4.52−4.68 (m, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.5, 20.6, 28.3, 30.4, 31.2, 78.9, 81.4, 96.2, 166.5, 166.9 ppm.

(*Z*)-2-[5-Methyldihydrofuran-2(3*H*)-ylidene]propanoic Acid (2g): R_f = 0.18 (hexane/ethyl acetate, 2:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.46 (d, *J* = 6.5 Hz, 3 H), 1.80 (t, *J* = 0.1 Hz, 3 H), 1.70−1.84 (m, 1 H), 2.20−2.34 (m, 1 H), 2.67−2.93 (m, 2 H), 4.66−4.82 (m, 1 H), 10.0 (1 H, large) ppm.

Methyl (*Z*)-2-[5-Methyldihydrofuran-2(3*H*)-ylidene]propanoate (2a): R_f = 0.32 (hexane/ethyl acetate, 2:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.42 (d, *J* = 6.2 Hz, 3 H), 1.52−1.72 (m, 1 H), 1.78 (t, *J* = 0.1 Hz, 3 H), 2.09−2.22 (m 1 H), 2.57−2.89 (m, 2 H), 3.71 (s, 3 H), 4.58−4.72 (m, 1 H) ppm. ^{13}C NMR (50 MHz; $CDCl_3$): δ = 14.5, 20.7, 30.5, 31.4, 51.1, 81.9, 94.6, 167.4, 167.9 ppm.

Benzyl (*Z*)-2-[5-Methyldihydrofuran-2(3*H*)-ylidene)propanoate (2b): R_f = 0.42 (hexane/ethyl acetate, 2:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.42 (d, *J* = 6.3 Hz, 3 H), 1.52−1.72 (m, 1 H), 1.81 (t, *J* = 0.3 Hz, 3 H), 2.09−2.23 (m 1 H), 2.59−2.9 (m, 2 H), 3.71 (s, 3 H), 4.53−4.71 (m, 1 H), 5.19 (ABq, 2 H, *J* = 1 2.0 Hz, Δν = 15 Hz), 7.3−7.5 (m,5 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.7, 21.0, 30.8, 31.7, 65.6, 82.2, 94.9, 127.8, 127.9, 128.7, 137.6, 167.5, 168.2 ppm.

Isopropyl (*Z*)-2-[5-Methyldihydrofuran-2(3*H*)-ylidene]propanoate (2c): R_f = 0.40 (hexane/ethyl acetate, 2:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.24 (d, *J* = 7.0 Hz, 6 H), 1.40 (d, *J* = 7.1 Hz, 3 H), 1.5−1.69 (m, 1 H), 1.72 (t, *J* = 0.4 Hz, 3 H), 2.06−2.21 (m 1 H), 2.52−2.87 (m, 2 H), 4.52−4.71 (m, 1 H), 4.95−5.23 (h, *J* = 7.0 Hz, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.7, 21.0, 30.8, 31.7, 65.6, 82.2, 94.9, 127.8, 127.9, 128.7, 137.6, 167.5, 168.2 ppm.

2,6-Dimethylphenyl (*Z*)-2-[5-Methyldihydrofuran-2(3*H*)-ylidene]propanoate (2e): R_f = 0.39 (hexane/ethyl acetate, 2:1). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 1.40 (d, *J* = 6.0 Hz, 3 H), 1.57−1.82 (m, 1 H), 1.89 (t, *J* = 0.2 Hz, 3 H), 2.18 (s, 6 H), 2.15−2.3 (m, 1 H), 2.62−2.81 (m, 2 H), 4.58−4.78 (m, 1 H), 6.98−7.17 (m, 3 H) ppm.

***tert*-Butyl (*Z*)-2-{5-[2-(Benzyloxy)propyl]dihydrofuran-2(3*H*)-ylidene}propanoate (2i):** This was obtained from the (*E*) isomer **1i** (0.080 g, 0.23 mmol, 1 equiv.) and 2 equiv. of LDA in 1.2 mL of dried ether. The crude product was purified by flash chromatography with hexane/ethyl acetate (9:1) as eluent. Isomer **2i** (0.070 g, 87%) was obtained as a diastereomeric mixture (*syn*/*anti*: 60:40). R_f = 0.51 for the *anti* isomer and 0.44 for the *syn* isomer (hexane/ethyl acetate, 4:1).^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.25 (d, 1.2 H, *J* = 6.2 Hz, minor isomer), 1.29 (d, 1.8 H, *J* = 6.2 Hz, major isomer), 1.48 and 1.50 (2s, 9 H, two isomers), 1.72 (s, 3 H), 1.58−2.24 (m, 4 H), 2.50−2.81 (m, 2 H), 3.69−3.92 (m, 1 H), 4.51 (ABq, 1.2 H, *J* = 11.8 Hz, Δν = 63 Hz, major isomer), 4.54 (ABq, 0.8 H, *J* = 11.1 Hz, Δν = 71 Hz, minor isomer), 4.52−4.73 (m, 1 H), 7.24−7.38 (m, 5 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) for the *anti* isomer, isolated by chromatography: δ = 14.8, 20.3, 28.6, 29.4, 31.2, 43.3, 71.0, 72.9, 79.1, 82.5, 96.4, 127.6, 127.8, 128.5, 138.9, 165.7, 167.2 ppm.

***tert*-Butyl (*Z*)-2-{5-[2-(*tert*-Butyldiphenylsilyloxy)propyl]dihydrofuran-2(3*H*)-ylidene}propanoate (2j):** A solution of BuLi in hexane (1.28 M, 0.32 ml, 0.4 mmol, 2 equiv.) was added dropwise under argon to a stirred and cooled (−78 °C) solution of diisopropylamine (0.057 ml, 0.40 mmol, 2 equiv.) in dry ether (1.5 mL). The resulting solution was maintained at −78 °C for 1 h, and a solution of **1j** (100 mg; 0.2 mmol; 1 equiv.) in ether (1.7 mL) was then added dropwise. After the mixture had been stirred for 1 h at −78 °C, LiCl (26 mg, 0.6 mmol, 3 equiv.) was added. After 45 min, the solution was quenched with ethanol (2 mL) and allowed to warm to room temperature. Water was added to the suspension, and the resulting mixture was then extracted with ethyl acetate. The organic phase was dried, and the solvents were evaporated to afford a yellow oil. The crude product was purified by preparative silica gel chromatography (hexane/ethyl acetate, 5:1), and **2j** was obtained as a yellow oil (0.086 g, 86%) in a diastereomeric mixture (*syn*/*anti*: 60:40). R_f = 0.54 for the *syn* isomer and 0.58 for the *anti* isomer (hexane/ethyl acetate, 9:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.04 (s, 9 H), 1.10 (d, *J* = 6.5 Hz, 3 H), 1.46 (s, 9 H), 1.70 (s, 3 H), 1.71−2.04 (m, 4 H), 2.40−2.72 (m, 2 H), 4.02−4.18 (m 1 H), 4.37−4.51 (m, 1 H), 7.39−7.47 (m, 6 H), 7.62−7.73 (m, 4 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) for the *anti* isomer isolated from chromatography: δ = 13.7, 18.5, 24.9, 25.8, 26.9, 28.2, 31.6, 42.8, 71.1, 77.0, 80.5, 98.5, 128.6, 129.5, 132.5, 165.5, 168.1 ppm.

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