DOI: 10.1002/ejoc.200700439

Synthesis of 3-Fluorofuran-2(5*H*)-ones Based on *Z*/*E* Photoisomerisation and Cyclisation of 2-Fluoro-4-hydroxybut-2-enoates

Karel Pomeisl,*[a] Jan Čejka,[b] Jaroslav Kvíčala,[c] and Oldřich Paleta[c]

Keywords: Horner–Wadsworth–Emmons reaction / Phosphonates / Photolysis / Isomerization / Fluorofuranones

Mixtures of some (*E*)- and (*Z*)-2-fluoroalk-2-enoates prepared from the corresponding 2-hydroxycarbonyl compounds and ethyl 2-(diethoxyphosphoryl)-2-fluoroacetate have been transformed in high conversions into the target 3-fluorofuran-2(5*H*)-ones by an efficient *Z*/*E* photoisomerisation of noncyclisable *Z* isomers followed by acid-catalysed cyclisation. In contrast, the acid-catalysed deprotection of ethyl (*E*)- and (*Z*)-4-[*tert*-butyl(dimethyl)silyloxy]-2-fluoro-4-phenylbut-2-enoates resulted in the displacement of vinylic fluorine, affording ethyl (*E*)-2-oxo-4-phenylbut-3-enoate. 3-Fluoro-4-phenylfuran-2(5*H*)-one was transformed into 2-[*tert*-butyl(dimethyl)silyloxy]-3-fluoro-5-methylfuran as a novel fluorinated building block.

Introduction

The furan-2(5*H*)-one (but-2-en-4-olide) ring is a component of several classes of bioactive natural compounds. Some natural butenolides exhibit antitumour activity,[1] cytotoxic properties towards human tumour cells,[2] intestinal carcinogenicity inhibition,[3] significant activity against lymphotic leukemia systems[4] and also HIV-1 protease-inhibitor activity.[5] Some analogues of natural butenolides have also been proven to have antitumour[6] and antitumour-promoter activity.[7]

Furthermore, alkyl-substituted butenolides are appropriate building blocks in the synthesis of bioactive compounds. As an example, angelicalactone[8a,8b] has been utilised as a simple chiral butenolide precursor for the preparation of (+)-himbacine,[8c] known to be a significant inhibitor of M_2 receptors. The presence of several alkyl and aryl groups in one structure is also an essential feature of terpenoides that exhibit antifungal activity,[10] such as mintlactone[9] and derivatives of (–)-incrustoporine, or powerful pharmacophores, for example, in antitumour drugs Tamoxiphen and Droloxifene or in coronary vasodilator Amotriphene.

Our investigation into fluorine-containing butenolides was stimulated by the fact that the butenolide ring is a component of several classes of bioactive natural compounds and that fluoro substituents such as F, CF_3 or OCF_3 are generally powerful modifiers of the chemical and biological properties of organic compounds,[11,12] as evidenced by hundreds of pharmaceuticals and biocides. Some fluorinated analogues of tetronic and L-ascorbic acids have recently been prepared[13] for biochemical studies and 2-fluoro-4-hydroxy-3-styrylbut-2-en-4-olide was even found to exhibit a phospholipase inhibitory effect.[14]

In this present study, we directed our research efforts towards the synthesis of some alkyl- and phenyl-substituted 2-fluorobut-2-en-4-olides (**28** and **37**–**39**) as fluorinated derivatives of the above-mentioned angelicalactone or natural mintlactone and (–)-incrustoporine (Figure 1). The combination of a fluorine substituent with an alkyl- and phenyl-substituted butenolide ring could thus afford compounds with new and interesting properties. Therefore, our study focused on their rapid preparation.

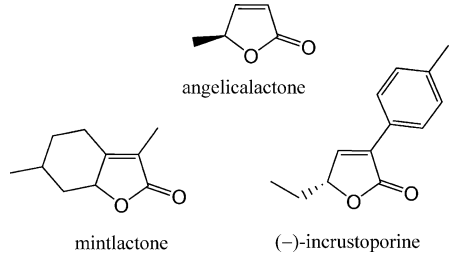


Figure 1. Alkyl and phenyl-substituted but-2-enolides as the bioactive compounds and building blocks.

The synthesis of 2-fluorobut-2-enolides has usually been accomplished by deprotection of 2-fluoro-4-hydroxyalk-2-enoates followed by the spontaneous closure of the lactone ring.[14,15] A simple synthetic pathway leading to these

[a] Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic,
Flemingovo nám. 2, 16610 Prague, Czech Republic
Fax: +420-220-183-560
E-mail: pomeisl@uochb.cas.cz
[b] Department of Solid State Chemistry, Prague Institute of Chemical Technology,
Technická 5, 16628 Prague 6, Czech Republic
[c] Department of Organic chemistry, Prague Institute of Chemical Technology,
Technická 5, 16628 Prague 6, Czech Republic

Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.

hydroxyalkenoates has appeared to be the Horner–Wadsworth–Emmons (HWE) synthesis involving the reaction of 2-(diethoxyphosphoryl)-2-fluoroacetate (**10**) with an appropriate α-hydroxycarbonyl compound.[14,15]

However, we have found that this method for the synthesis of 3-fluoro-4,5-diphenylfuran-2(5*H*)-one prepared from benzoin ethers[16] has its limitations as the intermediate 4-alkoxybutenoates are formed predominantly in a noncyclisable configuration. It seems the stereoselectivity of the HWE reaction depends on the structure of the starting α-hydroxycarbonyl compound. However, the structure of some α-hydroxycarbonyl compounds can be modified by including the *tert*-butyl(dimethyl)silyl protecting group, as documented in this paper. Secondly, the noncyclisable configuration of some 2-fluoroalkenoates can be transformed by using a suitable *Z*/*E* isomerisation method which has not so far been studied in detail by this process. Therefore, we decided to isomerise the α,β double bond of 2-fluoroalkenoates in the synthesis of target butenolides **28** and **37**–**39** by using UV irradiation followed by acid-catalysed cyclisation.

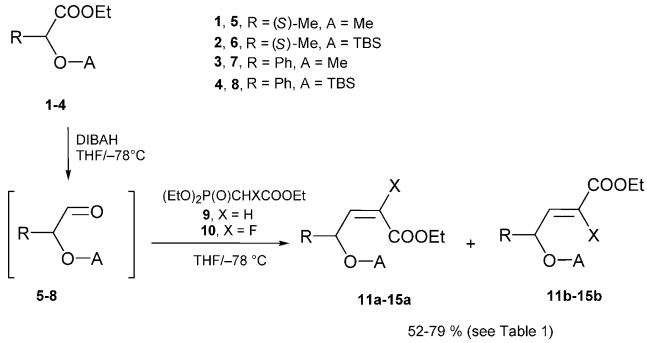
Results and Discussion

For the synthesis of the target but-2-enolide **28** we followed the above-described methodology, exploiting the HWE reaction synthetic sequence and then hydrolysing the resulting intermediates. Aldehydes **5**–**8**, prepared in situ by the selective reduction of easily available esters[17] **1**–**4** using diisobutylaluminium hydride at –78 °C, were selected as the starting carbonyl compounds. The precursor of the HWE reagent, ethyl 2-(diethoxyphosphoryl)-2-fluoroacetate (**10**), was prepared from chlorotrifluoroethene using our optimised synthetic protocol.[15d]

The reaction of derivatives **5**–**8** with the HWE reagent prepared in situ by the reaction of fluorophosphonate **10**[15d] with *n*-butyllithium at –78 °C afforded the corresponding products **11**–**15** as *E*–*Z* mixtures (Scheme 1, Table 1). Data show the stereoselective course of the HWE reaction; the desired cyclisable *E* isomers **12a**–**15a** were highly prevalent in the stereoisomeric mixtures, forming in amounts of 84–96%. In this case, the influence of aldehyde structures and their protecting groups is only marginal with respect to the stereoselectivity of the HWE reaction.

To compare some of the stereochemical results, we carried out an analogous HWE reaction of aldehyde **5** with a nonfluorinated HWE reagent prepared from ethyl 2-(diethoxyphosphoryl)acetate (**9**). The reaction afforded the noncyclisable *Z* isomer **11b** in a relative amount of 65% (monitoring of the reaction mixtures by ^{1}H NMR). In comparison with the content of the *E* and *Z* isomers in the mixture of fluoroalkenoate **12**, this result indicates that a fluorine atom in place of a hydrogen in the phosphonate agent could significantly influence the stereochemistry of the HWE reaction.

A similar procedure was chosen for the preparation of **22**–**26**, the intermediates leading to butenolides **37**–**39**



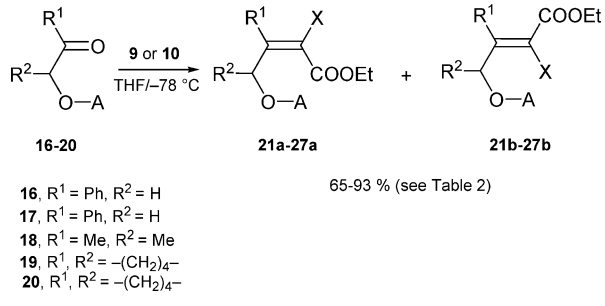
Scheme 1. HWE synthesis of 2-fluoroalkenoates from protected α-hydroxy aldehydes.

Table 1. Stereoselectivity of the reaction of aldehydes **1**–**4** with phosphonates **9** and **10**.

Starting esters			Products		Yields		
					a[a]	**b**[a]	**a**+**b**[b]
	R	A		X	(%, rel.)	(%, rel.)	(%)
1	(*S*)-Me	Me	**11**	H	35	65	54
1	(*S*)-Me	Me	**12**	F	96	4	52
2	(*S*)-Me	TBS	**13**	F	84	16	79
3	Ph	Me	**14**	F	91	9	69
4	Ph	TBS	**15**	F	85	15	52

[a] The relative content of the *E* and *Z* isomers was determined by ^{19}F NMR spectroscopic analysis of the reaction mixture. [b] Isolated yield.

(Scheme 2). Methoxyacetophenone **16** and methoxycyclohexanone **19**, which are industrially available, were transformed as well as compounds **17**, **18** and **20** into the corresponding fluoroalkenoates **22**–**26** in good yields of 66–86% (Table 2). In most cases the desired cyclisable *E* isomers **22a** and **24a**–**26a** prevailed slightly in the stereoisomeric mixtures but only in amounts of 52–65%. Furthermore, the stereoselectivity can be decreased or reversed by replacement of the ether functionality with the sterically hindered *tert*-butyl(dimethyl)silyloxy protecting group (products **22**/**23** and **26**/**27**, Table 2) or influenced in different directions by using fluorophosphonate **10** instead of **9** (products **21**/**22** and **25**/**27**, Table 2).



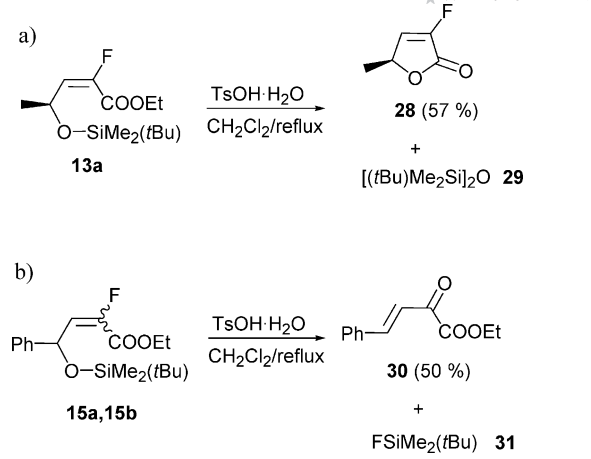
Scheme 2. HWE synthesis of 2-fluoroalkenoates from protected α-hydroxy ketones.

The transformation of 4-alkoxybut-2-enoates **12**, **14**, **22** and **27** into the corresponding intermediate 4-hydroxybut-2-enoates, which usually cyclise in acidic media to afford

Table 2. Stereoselectivity of the reaction of ketones **16**–**20** with phosphonates **9** and **10**.

Starting compounds				Products		Yields		
						a[a]	**b**[a]	**a**+**b**[b]
	R^1	R^2	A		X	(%, rel.)	(%, rel.)	(%)
16	Ph	H	Me	**21**	H	75	25	93
16	Ph	H	Me	**22**	F	59	41	77
17	Ph	H	TBS	**23**	F	10	90	80
18	Me	Me	TBS	**24**	F	52	48	78
19	$-(CH_2)_4-$		Me	**25**	H	65	35	66
20	$-(CH_2)_4-$		TBS	**26**	F	60	40	86
19	$-(CH_2)_4-$		Me	**27**[c]	F	82	18	65

[a] The content of *E* and *Z* isomers was determined by ^{19}F NMR spectroscopic analysis of the reaction mixture. [b] Isolated yield. [c] Analytical data for **27** and reaction details for the HWE reaction of **19** with ethyl 2-(diethoxyphosphoryl)-2-fluoroacetate (**10**) are reported in ref.[16].

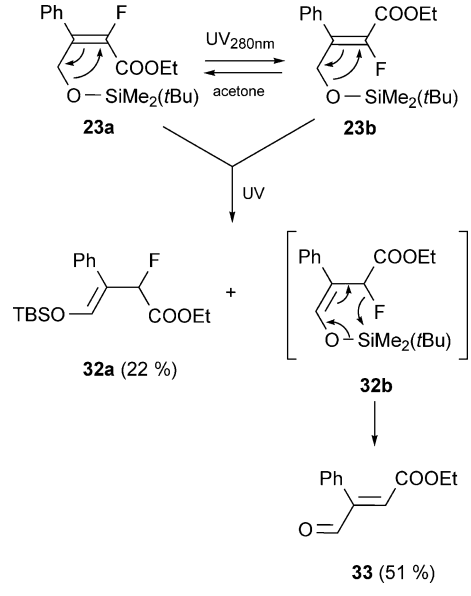


Scheme 3. The result of acid-catalysed deprotection of 4-alkyl(phenyl)-2-fluoroalkenoates with $TsOH·H_2O$: a) cyslisation; b) defluorination and allyl rearrangement of the π system.

the target butenolides, required the cleavage of the ether bond. Because the cleavage of the ether bond in 4-alkoxybutenoates using boron tribromide results in an increase in unfavoured products[16] we applied bromine-catalysed radical *Z*/*E* isomerisation followed by cleavage of the in-situ-formed hydrobromide, as reported in our previous paper.[16] Unfortunately, the selective closure of 2-fluoroalkenoates to the but-2-enolide ring did not proceed, probably owing to the absence of bulky substituents at positions C-3 and C-4 of the alkenoate moiety, as shown in the *Z*/*E* isomerisation of ethyl 2-alkoxy-2-fluoro-3,4-diphenylbut-2-enoates.[16] In this case, the steric effect of aryl groups could influence, for example, the efficient flexibility of the bond system during the cyclisation as an important reaction step of the *Z*/*E* isomerisation sequence. Instead, mixtures of unfavoured products were observed by ^{19}F NMR spectroscopy.

In contrast to the ether functionality, the *tert*-butyl(dimethyl)silyloxy group in compounds **13**, **15**, **23**, **24** and **26** was easily removed by acid-catalysed hydrolysis using *p*-toluenesulfonic acid. However, the hydrolysis of phenyl derivatives **15a** and **15b** resulted in an unexpected defluorination reaction although the deprotection of 2-fluoroalkenoate **13a** readily afforded the desired butenolide **28** and siloxane **29** (Scheme 3). The defluorination reaction is probably the result of an allyl rearrangement of **15** exclusively to (*E*)-4-phenyl-2-oxobut-3-enoate (**30**) in which the double bond system is more extensive due to the phenyl substituent at the C-4 position. The displacement of the vinylic fluorine is in accord with the monitoring of the reaction mixture content by ^{19}F NMR analysis in which *tert*-butyl(dimethyl)-fluorosilane (**31**) was found to be a single fluorinated product with a characteristic chemical shift (septet, –170.1 ppm),[18] while the signals of the starting phenyl derivatives **15a** and **15b** had completely disappeared.

In this study we found that the unfavourable *Z* configuration of the 2-fluoro-2-hydroxyalkenoates can be transformed into the *E* configuration, which is suitable for cyclisation, by an appropriate *Z*/*E* isomerisation reaction during which the ester group and the more bulky hydroxyalkyl group are placed in the *cis* position. Such *Z*-to-*E* isomerisation of some of the 2-fluoroalkenoates was carried out by several methods including by photochemical[19,20] and thermal[21,22] processes. In contrast, irradiation of the *E*–*Z* mixtures of the precursor **23** using unfiltered UV light from a medium-pressure mercury lamp led to a complex mixture of products **32a** and **32b** (Scheme 4). As shown in Scheme 4, the *Z* isomer **32b** further decomposed to oxo ester **33** due to defluorination of the alkenoate. This was probably caused by a selective interaction of the fluorine atom with the silyl group in the *cis* position of the alkenoate. Therefore, characterisation of the proposed intermediate isomer **32b** by analysis was not entirely successful.

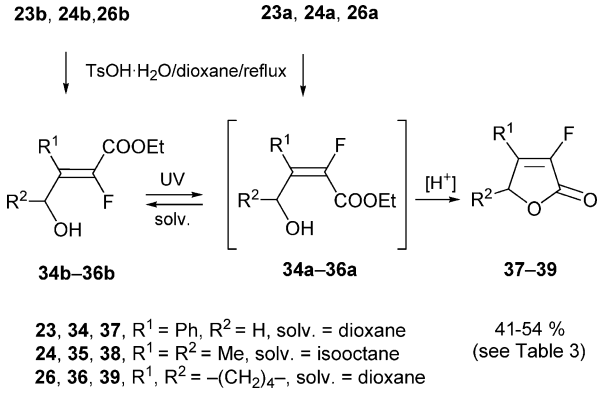


Scheme 4. Photoinduced isomerisation and defluorination of 3-phenyl-2-fluorobut-2-enoates.

However, the mild photosensitised *Z*/*E* isomerisation of our HWE precursor **23** using UV light with a wavelength above 280 nm (selected by a Simax® filter) in the presence

of acetone as a sensitiser was partly efficient, giving the desired *E* isomer **23a** in a maximum relative yield of only 20%. The results of these photoinduced isomerisaton reactions led us to focus our research on influencing the proportion of *Z* and *E* isomers that can be formed which has allowed us to obtain significant amounts of cyclisable 2-fluoroalkenoates (see below).

To date photochemical methods have been used only for the *Z*/*E* isomerisation of fluorinated cinnamates[15] and (*Z*)-2-fluoro-3-phenylprop-2-enoate.[20] As shown in Scheme 5, this method can be also used for the isomerisation of 4-hydroxy-2-fluoroalkenoates **34b**–**36b** which were obtained by deprotection of silyl derivatives **23**, **24** and **26** in the presence of *p*-toluenesulfonic acid. In this case, the relative amounts of *Z* and *E* isomers formed was influenced by spontaneous acid-catalysed cyclisation of the intermediates **34a**–**36a** during UV irradiation (see electronic supporting information). Thus the corresponding butenolides **37**–**39** were prepared with high conversion of the deprotected hydroxy derivatives, as verified by ^{19}F NMR analysis, but only in 41–54% preparative yields, probably due to losses caused by difficulties in purification (Table 3). From this point of view, only the unoptimised yields for the cyclisation reactions are presented.



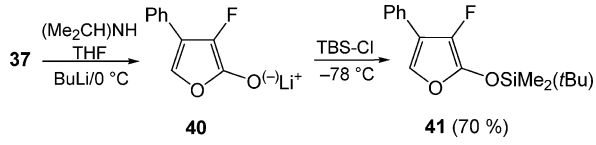
Scheme 5. Photoisomerisation and cyclisation of 2-fluoro-4-hydroxy-but-2-enoates.

Table 3. Results of the *E*–*Z* photoisomerisation of fluoroalkenoates **23**, **24** and **26**.

Starting compounds	**a**[a]	**b**[a]	Products	Content in reaction mixture[b]	Yield[c]
	(%, rel.)	(%, rel.)		(%, rel.)	(%)
23	7	93	**37**	95	42
24	52	48	**38**	89	41
26	62	38	**39**	77	54

[a] Content of *E* and *Z* isomers in isolated fluoroalkenoates. [b] The content of the butenolides was determined by ^{19}F NMR spectroscopic analysis of the resulting reaction mixture. [c] All products were isolated and characterised by NMR and MS spectroscopy; yields are unoptimised. In addition, the structure of **37** was determined by X-ray analysis. CCDC-646554 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Fluorinated furanone **37** was transformed into the corresponding silyloxyfuran **41** as a novel building block (Scheme 6). Nonfluorinated silyloxyfurans have been employed in electrophilic reactions[23] and pheromone synthesis.[23c] Among fluorinated analogues, only 4-chloro-3-fluoro-2-(trimethylsilyloxy)furan has been previously reported,[24] but it appeared to be unstable above about –30 °C. However, we recently reported that use of the *tert*-butyl(dimethyl)silyl protecting group could increase the stability of 3-fluoro-4,5-diphenyl-2-(trialkylsilyloxy)furan.[16] We carried out the transformation of furanone **37** into furan **41** by applying our improved protocol,[16] that is, low-temperature lithiation to enolate **40** and subsequent silylation, to obtain furan **41** in a yield of 70%. It was stable at 0–4 °C as was the reported 3-fluoro-4,5-diphenyl-2-(trialkylsilyloxy)furan (checked by ^{19}F NMR for 2 weeks). Based on both results, we assume that the effect of the higher conjugation of phenyl-substituted furans also increases their stability and this will be investigated in further research.



Scheme 6. Synthetic exploitation of 2-fluorobutenolides.

A series of synthesised 3-fluorobutenolides were investigated for their ability to possess various kinds of biochemical activities. We have found that the fluorinated mintlactone derivative **39** exhibits significant inhibitory activity on cyclin-dependent kinase[25] (CDK) (IC_{50} = 10 μM) in comparison with olomoucine (IC_{50} = 7 μM), but lower activity than that of roscovitine (IC_{50} = 0.1 μM) (see Figure 1).

On other hand, the antifungal effect of fluorobutenolide **37** was marginal[26] in comparison with that of known 3-aryl-substituted but-2-enolides[10,27] [e.g., (–)-incrustoporine as the lead structure, see Figure 1]. The lower antifungal activity could be caused, for example, by a different aryl substitution and is probably favoured by substitution at the C-3 position of the furan-2(5*H*)-one moiety as demonstrated in a series of incrustoporine derivatives.[10]

None of the presented compounds possess cytostatic activity in K-562 (chronic myeloid leukemia) and MCF7 (breast carcinoma) cells in contrast to olomoucine and roscovitine.

Conclusions

In summary, we have developed methods for the rapid preparation of alkyl- and phenyl-substituted 2-fluorobut-2-enolides synthesised either as derivatives of bioactive compounds (e.g., fluorinated mintlactone derivative **39**) or as fluorinated building blocks (see compound **28**, the fluorinated derivative of angelicalactone).

In some cases, we have found that the stereoselectivity of the HWE synthesis can be significantly influenced by steric hindrance of the substituents at C-1 and C-2 and/or the

protecting groups at C-2 of the starting carbonyl compound. In addition, some noncyclisable 2-fluoroalkenoates can undergo ring-closure to the but-2-enolide ring with high conversions by photochemical isomerisation in the presence of *p*-toluenesulfonic acid. From this point of view, *Z*/*E* photoisomerisation could be considered as a significant alternative tool for the preparation of alkyl- and aryl-substituted 2-fluorobut-2-enolides with regard to its simplicity and efficiency.

On the other hand, the reactions reported in this paper show that the annulation of the α-fluorobut-2-enolide ring by acid-catalysed deprotection of the silyl group in 4-phenyl-substituted HWE intermediates **15a**,**b** may completely fail due to allyl rearrangement of their double bond systems.

Experimental Section

General Remarks: Melting points were determined with a Kofler block and are uncorrected. Optical rotations were measured with an Opton PPP 0.005 polarimeter at 20 °C; $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. NMR spectra were measured with a Bruker 400 AM (FT, ^{19}F at 376.5 MHz) and a Gemini 300 (^{1}H at 300.1 MHz and ^{13}C at 75.5 MHz using ^{1}H decoupling) spectrometer in $CDCl_3$. Chemical shifts (δ, ppm) and coupling constants (*J*, Hz) obtained by first-order analysis of the spectra were measured relative to tetramethylsilane and fluorotrichloromethane. IR spectra were recorded with a FTIR Spec Nicolet 740 in $CHCl_3$. Mass spectra were scanned with an Autospec Ultima (Micromass) spectrometer using GC (HP 6890, ionisation with electron impact at 70 eV) and a ZAB-EQ (VG Analytical) spectrometer using FAB (Xe ionisation, accelerating voltage 8 kV, glycerol matrix). *E* and *Z* configurations were assigned on the basis of ^{19}F-{^{1}H} and ^{1}H-{^{1}H} NOE Dif. NMR experiments carried out with a Bruker Avance DRX 500.1 (at 470.4 MHz) apparatus on stereoisomeric mixtures. Irradiation was performed by using a polychromatic UV medium-pressure mercury lamp (TESLA, RVK 400 W, system S1) and the same lamp using a wavelength above 280 nm (selected by a Simax® filter, system S2). The distance between the UV lamp and the silicious cell was 40 mm (diameter 50 mm; thickness 10 mm) equipped with a magnetic stirrer and loaded with alkenoate **23**, **24** or **26** dissolved in solvent (see below).

The chemicals that were used are as follows. Ethyl 2-(diethoxyphosphoryl)acetate (**9**) was prepared according to ref.[28] and ethyl 2-(diethoxyphosphoryl)-2-fluoroacetate (**10**) was synthesised from trifluorochloroethene by our improved procedure.[15d] Compounds **2**, **4**, **17**, **18** and **20** were prepared by reaction of *tert*-butyl(dimethyl)silyl chloride with ethyl (*S*)-2-hydroxypropanoate,[29a] ethyl 2-hydroxy-2-phenylacetate,[29b] 2-hydroxyacetophenone,[29c] 3-hydroxy-2-butanone[29d] and 2-hydroxycyclohexanone (a similar procedure to that reported in ref.[29d]) purchased as well as 2-methoxy ketones **16** and **19** and standard chemicals from Sigma–Aldrich. Compounds **1** and **3** were prepared according to ref.[30]. Isooctane and dioxane as appropriate solvents used for the UV irradiation of **23**, **24** and **26** were obtained from Lachema. Tetrahydrofuran and dichloromethane were dried and purified according to standard procedures.

General Procedure for the HWE Synthesis of Alkenoates 11–15: A solution of diisobutylaluminium hydride (1.2 M, 24.9 mmol) in toluene was added through a septum to a solution of compound **1**–**4** (14.6 mmol) in THF (50 mL) cooled to around –75 °C under nitrogen. After 1–5 h of stirring, a solution of *n*-butyllithium (2.5 M, 21.9 mmol) in hexane was separately added through a septum to a solution of the phosphonate **9** or **10** (21.9 mmol) in THF (70 mL) cooled to around –75 °C under nitrogen. After 20 min of stirring, the mixture containing aldehyde **5**–**8** was added dropwise by syringe at the same temperature to the flask charged with a phosphonate salt. The resulting mixture was stirred for 1 h, then slowly allowed to warm to room temp. for 6 h and stirred for another 14 h. THF was removed on a rotary evaporator under reduced pressure, the residue was dissolved in dichloromethane and 1 N HCl was added to the mixture at 5 °C. The mixture was filtered through a Celite pad under pressure and concentrated on a rotary evaporator to a minimum volume. The residue was diluted with dichloromethane, a solution was dried with $MgSO_4$ and the solvent was removed on a rotary evaporator. The residue was purified by chromatography on a silica gel column or by microdistillation to afford the products **11**–**15** as mixtures of *E*/*Z* isomers (see below).

Ethyl (*S*)-4-Methoxypent-2-enoate (11): Yield 1.26 g (54.4%) of the mixture **11a/11b** (31:69). Column chromatography was performed on silica gel (benzene/ethyl acetate, 10:1); slightly yellow oil. $C_8H_{14}O_3$ (158.2): calcd. C 60.74, H 8.92; found C 60.57, H 8.81. MS (EI): *m*/*z* (%) = 158 (13) $[M]^+$. **11a** (*Z*): ^{1}H NMR ($CDCl_3$): δ = 1.31 (m, 6 H); 3.30 (d, *J* = 0.6 Hz, 3 H), 4.21 (q, *J* = 7.1 Hz, 2 H), 4.93 (pent, *J* = 7.1 Hz, 1 H), 5.84 (dd, *J* = 11.8, *J* = 1.2 Hz, 1 H), 6.13 (dd, *J* = 8.0, *J* = 1.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.5, 20.1, 56.6, 60.2, 73.2, 120.5, 152.0, 165.8 ppm. **11b** (*E*): ^{1}H NMR ($CDCl_3$): δ = 1.31 (m, 6 H), 3.33 (d, *J* = 0.6 Hz, 3 H), 3.90 (pent, *J* = 6.3 Hz, 1 H), 4.21 (q, *J* = 7.1 Hz, 2 H), 5.96 (d, *J* = 15.7 Hz, 1 H), 6.82 (dd, *J* = 15.7, *J* = 0.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.2, 20.3, 56.6, 60.4, 76.2, 121.3, 148.9, 166.3 ppm.

Ethyl (*S*)-2-Fluoro-4-methoxypent-2-enoate (12): Yield 1.34 g (52.0%) of the mixture **12a/12b** (81:19). Microdistillation, b.p. 54 °C/2.0 kPa; colourless liquid. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2888 (w), 1729 (s), 1667 (w), 1375 (s), 1311 (m-s), 1151 (m), 1108 (m), 1078 (m) cm^{-1}. $C_8H_{13}FO_3$ (176.2): calcd. C 54.54, H 7.44; found C 54.25, H 7.60. **12a** (*E*): ^{1}H NMR ($CDCl_3$): δ = 1.31 (dd, *J* = 6.3, *J* = 1.1 Hz, 3 H), 1.37 (t, *J* = 7.1 Hz, 3 H), 3.30 (s, 3 H), 4.31 (q, *J* = 7.1 Hz, 2 H), 4.77 (dqd, *J* = 8.8, *J* = 6.3, *J* = 1.1 Hz, 1 H), 5.98 (dd, *J* = 20.8, *J* = 8.9 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.2, 21.0, 57.4, 61.8, 71.3 (*J* = 6 Hz), 125.4 (*J* = 5 Hz), 147.2 (*J* = 260 Hz), 160.2 (*J* = 37 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –120.1 (d, *J* = 20.4 Hz, 1 F) ppm. **12b** (*Z*): ^{1}H NMR ($CDCl_3$): δ = 1.31 (dd, *J* = 6.3, *J* = 1.1 Hz, 3 H), 1.37 (t, *J* = 7.1 Hz, 3 H), 3.30 (s, 3 H), 4.30 (q, *J* = 7.1 Hz, 2 H), 4.77 (dqd, *J* = 8.8, *J* = 6.3, *J* = 1.1 Hz, 1 H), 6.17 (dd, *J* = 33.2, *J* = 8.9 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.1, 20.6, 55.9, 61.0, 70.2 ppm; the signals of *C*=CF, CF and COO were not found due to their very low intensity. ^{19}F NMR ($CDCl_3$): δ = –127.2 (d, *J* = 33.4 Hz, 1 F) ppm.

Ethyl (*S*)-4-[*tert*-Butyl(dimethyl)silyloxy]-2-fluoropent-2-enoate (13): Yield 3.18 g (78.8%) of the mixture **13a/13b** (95:5). Column chromatography was performed on silica gel (benzene); slightly yellow oil. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3031 (w), 2982 (w), 2959 (m), 2931 (m), 2888 (w), 2859 (m-w), 1728 (s), 1668 (w), 1472 (m-w), 1446 (w), 1377 (m-w), 1318 (m), 1259 (s), 1145 (m), 1079 (s), 834 (s) cm^{-1}. $C_{13}H_{25}FO_3Si$ (276.4): calcd. C 56.49, H 9.12; found C 56.22, H 9.05. **13a** (*E*): ^{1}H NMR ($CDCl_3$): δ = 0.04, 0.06 (2 × s, 3 H), 0.88 (s, 9 H), 1.29 (dd, *J* = 6.1, *J* = 1.1 Hz, 3 H), 1.36 (t, *J* = 7.1 Hz, 3 H), 4.30 (q, *J* = 7.1 Hz, 2 H), 5.26 (dqd, *J* = 8, *J* = 6.3, *J* = 1.1 Hz, 1 H), 5.90 (dd, *J* = 20.9, *J* = 8.5 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –4.8, –4.6, 14.2, 18.2, 24.3 (*J* = 3 Hz), 25.8, 61.6, 63.7 (*J* = 6 Hz), 128.2 (*J* = 15 Hz), 144.8 (*J* = 257 Hz), 160.5

(J = 36 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –125.3 (d, J = 20.7 Hz, 1 F) ppm. **13b** (*Z*): ^{1}H NMR ($CDCl_3$): δ = 0.06, 0.08 (2 × s, 6 H), 0.88 (s, 9 H), 1.28 (dd, J = 6.1, J = 1.1 Hz, 3 H), 1.34 (t, J = 7.1 Hz, 3 H), 4.28 (q, J = 7.1 Hz, 2 H), 4.80 (dqd, J = 8.6, J = 6.3, J = 1.4 Hz, 1 H), 6.10 (dd, J = 33.6, J = 8.3 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): signals were not found due to their very low intensity. ^{19}F NMR ($CDCl_3$): δ = –129.2 (d, J = 33.7 Hz, 1 F) ppm.

Ethyl 2-Fluoro-4-methoxy-4-phenylbut-2-enoate (14): Yield 2.40 g (69.0%) of the mixture **14a/14b** (93:7). Column chromatography was performed on silica gel (benzene); slightly yellow oil. $C_{13}H_{10}FO_3$ (238.3): calcd. C 65.54, H 6.35; found C 65.61, H 6.54. MS (EI): *m/z* (%) = 238 (32) $[M]^+$. **14a** (*E*): ^{1}H NMR ($CDCl_3$): δ = 1.39 (t, J = 7.1 Hz, 3 H), 3.35 (s, 3 H), 4.35 (q, J = 7.1 Hz, 2 H), 5.78 (dd, J = 9.4, J = 1.4 Hz, 1 H), 6.02 (dd, J = 20.4, J = 9.6 Hz, 1 H), 7.28–7.43 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.2, 56.5, 61.9, 76.6, 123.4 (J = 17 Hz), 126.5, 128.1, 128.5, 140.0 (J = 3 Hz), 147.3 (J = 261 Hz), 160.5 (J = 35 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –119.4 (d, J = 20.8 Hz, 1 F) ppm. **14b** (*Z*): ^{1}H NMR ($CDCl_3$): δ = 1.32 (t, J = 7.1 Hz, 3 H), 3.37 (s, 3 H), 4.27 (qd, J = 7.1, J = 2.2 Hz, 2 H), 5.22 (dd, J = 8.2, J = 1.1 Hz, 1 H), 6.24 (dd, J = 32.2, J = 9.1 Hz, 1 H), 7.28–7.43 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): the signals were not found due to their very low intensity. ^{19}F NMR ($CDCl_3$): δ = –126.4 (d, J = 33.1 Hz, 1 F) ppm.

Ethyl 4-[*tert*-Butyl(dimethyl)silyloxy]-2-fluoro-4-phenylbut-2-enoate (15): Yield 2.49 g (52.2%) of the mixture **15a/15b** (93:7). Column chromatography was performed on silica gel (benzene); slightly yellow oil. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1728 (s), 1376 (s), 1063 (s), 840 (s) cm^{-1}. $C_{17}H_{27}FO_3Si$ (326.5): calcd. C 63.87, H 8.04; found C 63.61, H 7.91. **15a** (*E*): ^{1}H NMR ($CDCl_3$): δ = 0.04, 0.09 (2 × s, 6 H), 0.92 (s, 9 H), 1.41 (t, J = 7.1 Hz, 3 H), 4.38 (q, J = 7.1 Hz, 2 H), 5.96 (dd, J = 20.4, J = 9.4 Hz, 1 H), 6.35 (dd, J = 9.4, J = 1.7 Hz, 1 H), 7.22–7.47 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –4.8, –4.5, 14.3, 18.3, 25.9, 61.9, 68.1 (J = 9 Hz), 125.6, 126.2 (J = 16 Hz), 127.5, 128.3 (J = 1 Hz), 142.7 (J = 3 Hz), 145.4 (J = 259 Hz), 160.7 (J = 35 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –123.1 (d, J = 22.0 Hz, 1 F) ppm. **15b** (*Z*): ^{1}H NMR ($CDCl_3$): δ = 0.06, 0.10 (2 × s, 6 H), 0.92 (s, 9 H), 1.32 (t, J = 7.1 Hz, 3 H), 4.26 (q, J = 7.1 Hz, 2 H), 5.73 (d, J = 9.1 Hz, 1 H), 6.19 (dd, J = 32.8, J = 9.1 Hz, 1 H), 7.22–7.47 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): signals were not found due to their very low intensity. ^{19}F NMR ($CDCl_3$): δ = –123.1 (d, J = 22.0 Hz, 1 F) ppm.

General Procedure for the HWE Synthesis of Alkenoates 21–26: A solution of *n*-butyllithium (2.5 M, 6.25 mmol) in hexane was added through a septum to a solution of phosphonate **9** or **10** (6.16 mmol) in THF (70 mL) cooled to around –75 °C under nitrogen. The mixture was stirred for 20 min and then ketone **16**–**19** (4.75 mmol) in THF (20 mL) was added dropwise by syringe at the same temperature into the flask. The resulting mixture was stirred for 20 min, allowed to warm to room temp. for 2 h and then stirred overnight.

Separation of Compounds 21, 23, 25 and 26: The mixtures were filtered through neutral Al_2O_3 (dichloromethane) and the residues purified by chromatography on a silica gel column (benzene followed by benzene/ethyl acetate, 10:1) or purified by microdistillation to afford products as mixtures of *E*/*Z* isomers (see below).

Separation of Compounds 22 and 24: THF was removed on a rotary evaporator under reduced pressure, the residue was dissolved in dichloromethane and 1 N HCl was added to the mixture at 5 °C. The mixture was neutralised with a solution of $NaHCO_3$ and saturated with a solution of NaCl. The organic layer was dried with $MgSO_4$. The solvent was removed (rotary evaporator) and the residue purified by chromatography on a silica gel column to afford products as mixtures of *E*/*Z* isomers (see below).

Compounds **22**, **23** and **26** were then purified by microdistillation (see below).

Ethyl 4-Methoxy-3-phenylbut-2-enoate (21): Yield 974 mg (93.1%) of the mixture **21a/21b** (77:23). Column chromatography was performed on silica gel (benzene/ethyl acetate, 10:1); slightly yellow oil. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2984 (w), 2902 (w), 2826 (w), 1710 (s), 1631 (w-m), 1577 (w), 1494 (w), 1448 (w), 1372 (w), 1339 (w), 1180 (s), 1099 (w), 1039 (w), 697 (w-m) cm^{-1}. MS (EI): *m/z* (%) = 220 (100) $[M]^+$. $C_{13}H_{16}O_3$ (220.3): calcd. C 70.89, H 7.32; found C 70.43, H 7.48. **21a** (*Z*): ^{1}H NMR ($CDCl_3$): δ = 1.07 (t, J = 6.9 Hz, 3 H), 3.43 (s, 3 H), 4.01 (q, J = 7.2 Hz, 2 H), 4.15 (d, J = 1.7 Hz, 2 H), 6.14 (t, J = 1.9 Hz, 1 H), 7.20 (m, 2 H), 7.36 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.0, 58.7, 59.9, 76.0, 116.5, 127.4, 128.0, 128.1, 137.0, 154.5, 165.9 ppm. **21b** (*E*): ^{1}H NMR ($CDCl_3$): δ = 1.32 (t, J = 7.1 Hz, 3 H), 3.32 (s, 3 H), 4.23 (q, J = 7.1 Hz, 2 H), 4.94 (s, 2 H), 6.20 (s, 1 H), 7.37 (m, 3 H), 7.51 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.2, 58.2, 60.3, 68.1, 120.1, 127.1, 128.4, 129.1, 154.6, 166.0 ppm.

Ethyl 2-Fluoro-4-methoxy-3-phenylbut-2-enoate (22): Yield 868 mg (76.7%) of the mixture **22a/22b** (60:40). Microdistillation, b.p. 120–122 °C/133 Pa; colourless liquid. Column chromatography was performed on silica gel (benzene/ethyl acetate, 10:1). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3014 (w), 2934 (w), 2828 (w), 1726 (s), 1651 (w), 1493 (w), 1465 (w), 1371 (m), 1276 (s) cm^{-1}. $C_{13}H_{15}FO_3$ (238.3): calcd. C 64.31, H 6.38; found C 64.15, H 5.98. **22a** (*E*): ^{1}H NMR ($CDCl_3$): δ = 1.03 (t, J = 6.9 Hz, 3 H), 3.32 (s, 3 H), 4.06 (q, J = 7.1 Hz, 2 H), 4.39 (d, J = 4.2 Hz, 2 H), 7.19–7.25, 7.30–7.47 (2 × m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.6, 58.3, 61.4, 69.5 (J = 7 Hz), 127.86, 127.92, 128.01, 128.05, 128.11, 128.31, 128.36, 128.46, 129.8, (J = 13 Hz), 134.8 (J = 5 Hz), 145.6 (J = 259 Hz), 160.2 (J = 37 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –120.80 (t, J = 3.7 Hz, 1 F) ppm. **22b** (*Z*): 1.40 (t, J = 7.1 Hz, 3 H), 3.34 (s, 3 H), 4.36 (q, J = 7.1 Hz, 2 H), 4.75 (d, J = 2.5 Hz, 2 H), 7.19–7.25, 7.30–7.47 (2 × m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.2, 58.1, 61.8, 69.0 (J = 5 Hz), 127.86, 127.92, 128.01, 128.05, 128.11, 128.31, 128.36, 128.46, 129.9 (J = 10 Hz), 134.1 (J = 1 Hz), 145.5 (J = 264 Hz), 160.9 (J = 35 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –119.61 (s, 1 F) ppm.

Ethyl 4-[*tert*-Butyl(dimethyl)silyloxy]-2-fluoro-3-phenylbut-2-enoate (23): Yield 1.29 g (80.3%) of the mixture **23a/23b** (7:93). Microdistillation, b.p. 136–138 °C/240 Pa; colourless liquid. Column chromatography was performed on silica gel (benzene). HRMS (EI): calcd. for $C_{14}H_{18}FO_3Si$ 281.1009; found 281.1015. MS (EI): *m/z* (%) = 281 (32) $[M - t\text{Bu}]^+$, 253 (96), 233 (14), 207 (5), 159 (9), 131 (11), 115 (12), 105 (9), 103 (24), 77 (75) $[C_6H_5]^+$, 73 (25) $[C_3H_5O_2]^+$, 57 (13) $[t\text{Bu}]^+$, 29 (21) $[C_2H_5]^+$. **23a** (*E*): ^{1}H NMR ($CDCl_3$): δ = –0.08 (s, 6 H), 0.77 (s, 9 H), 0.99 (t, J = 7.1 Hz, 3 H), 4.03 (q, J = 7.1 Hz, 2 H), 4.56 (d, J = 3.9 Hz, 2 H), 7.15–7.21, 7.29–7.39 (2 × m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –5.7, 13.5, 18.1, 25.6, 60.2, 60.5 (J = 9 Hz), 127.56, 127.61, 128.43, 128.47, 133.0, 134.9 (J = 4 Hz), 144.0 (J = 256 Hz), 160.5 (J = 37 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –124.32 (t, J = 3.7 Hz, 1 F) ppm. **23b** (*Z*): ^{1}H NMR ($CDCl_3$): δ = –0.04 (s, 3 H), 0.75 (s, 9 H), 1.37 (t, J = 7.1 Hz, 3 H), 4.34 (q, J = 7.1 Hz, 2 H), 4.96 (d, J = 2.8 Hz, 2 H), 7.15–7.21, 7.29–7.39 (2 × m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): signals were not found due to their very low intensity. ^{19}F NMR ($CDCl_3$): δ = –123.6 (s, 1 F) ppm.

Ethyl 4-[*tert*-Butyl(dimethyl)silyloxy]-2-fluoro-3-methylpent-2-enoate (24): Yield 1.1 g (77.8%) of the mixture **24a/24b** (52:48). Column chromatography was performed on silica gel (benzene); slightly yellow oil. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3030 (w), 2982 (w), 2958 (m), 2932 (m), 2859 (m-w), 1728 (s), 1660 (w), 1472 (w), 1446 (w), 1371 (m-w), 1297 (s), 1090 (s), 836 (s) cm^{-1}. HRMS (EI): calcd. for

$C_{14}H_{27}FO_3Si$ 290.1714; found 290.1719. MS (EI): *m*/*z* (%) = 290 (8) $[M]^+$. $C_{14}H_{27}FO_3Si$ (290.5): calcd. C 57.89, H 9.37; found C 57.53, H 9.28. **24a** (*E*): ^1H NMR ($CDCl_3$): δ = 0.01, 0.05 (2 × s, 6 H), 0.88 (s, 9 H), 1.24 (d, *J* = 6.3 Hz, 3 H), 1.35 (t, *J* = 7.1 Hz, 3 H), 1.86 (d, *J* = 4.7 Hz, 3 H), 4.28 (q, *J* = 7.1 Hz, 2 H), 5.56 (dq, *J* = 6.3, *J* = 1.9 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –4.95, –4.89, 9.7 (*J* = 8 Hz), 14.3, 18.2, 22.8, (*J* = 4 Hz), 25.82, 61.2, 64.7 (*J* = 5 Hz), 137.4 (*J* = 9 Hz), 142.0 (*J* = 251 Hz), 160.7 (*J* = 35 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –127.0 (s, 1 F) ppm. **24b** (*Z*): ^1H NMR ($CDCl_3$): δ = 0.03, 0.07 (2 × s, 6 H), 0.89 (s, 9 H), 1.22 (d, *J* = 6.3 Hz, 3 H), 1.36 (t, *J* = 7.1 Hz, 3 H), 2.05 (d, *J* = 3.0 Hz, 3 H), 4.28 (q, *J* = 7.1 Hz, 2 H), 4.98 (dq, *J* = 6.3, *J* = 1.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –5.01, –4.94, 10.2 (*J* = 2 Hz), 14.3, 18.2, 22.3 (*J* = 1.4 Hz); 25.81, 61.2, 64.5 (*J* = 11 Hz), 136.4 (*J* = 10 Hz), 141.3 (*J* = 247 Hz), 161.2 (*J* = 35 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –127.0 (s, 1 F) ppm.

Ethyl 2-(2-Methoxycyclohexylidene)acetate (25): Yield 618 mg (65.7%) of the mixture **25a**/**25b** (65:35). Column chromatography was performed on silica gel (benzene/ethyl acetate, 10:1); slightly yellow oil. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3025 (w), 2986 (w), 2941 (m), 1709 (s), 1653 (m-w), 1464 (w), 1447 (w), 1381 (w), 1198 (w), 1167 (s), 1143 (m), 1095 (m), 1036 (w) cm^{-1}. HRMS (EI): calcd. for $C_{11}H_{18}O_3$ 198.1256; found 198.1248. MS (EI): *m*/*z* (%) = 198 (34) $[M]^+$. **25a** (*Z*): ^1H NMR ($CDCl_3$): δ = 1.27 (t, *J* = 7.1 Hz, 3 H), 1.31–2.02 (m, 6 H), 2.54 (m, 1 H), 3.05 (m, 1 H), 3.29 (s, 3 H), 4.15 (q, *J* = 7.2 Hz, 2 H), 5.79 (dd, *J* = 11.0, *J* = 0.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.3, 22.7, 28.5, 32.9, 34.6, 55.7, 59.7, 82.5, 112.8, 166.0. 166.7 ppm. **25b** (*E*): ^1H NMR ($CDCl_3$): δ = 1.27 (t, *J* = 7.1 Hz, 3 H), 1.31–2.02 (m, 6 H), 2.54 (m, 1 H), 3.24 (s, 3 H), 3.56 (m, 1 H), 4.14 (q, *J* = 7.2 Hz, 2 H), 5.24 (t, *J* = 6.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.3, 20.1, 27.2, 27.7, 32.8, 56.6, 59.8, 72.5, 116.5, 160.9, 166.1 ppm.

Ethyl 2-[2-*tert*-Butyl(dimethyl)silyloxycyclohexylidene]-2-fluoroacetate (26): Yield 883 mg (86.0%) of the mixture **26a**/**26b** (62:38). Microdistillation, b.p. 119–120 °C/240 Pa; colourless liquid. Column chromatography was performed on neutral Al_2O_3 (dichloromethane). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2938 (m), 2858 (m-w), 1720 (m), 1660 (m), 1463 (m), 1446 (w), 1370 (w), 1295 (s), 1254 (s), 1048 (s), 1018 (s) cm^{-1}. $C_{16}H_2FO_3Si$ (216.3): calcd. C 61.72, H 9.24; found C 60.98, H 9.43. **26a** (*E*): ^1H NMR ($CDCl_3$): δ = –0.02, 0.05 (2 × s, 6 H), 0.88 (s, 9 H), 1.33 (m, 2 H), 1.33 (t, *J* = 7.1 Hz, 3 H), 1.48 (dm, *J* = 12.6 Hz, 2 H), 1.87 (m, 2 H), 2.28 (m, 1 H), 2.68 (d, *J* = 12.9 Hz, 1 H), 4.28 (m, 2 H), 5.61 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –5.13, –4.90, 14.17, 17.95, 19.46, 22.6 (*J* = 8 Hz), 25.7, 27.1 (*J* = 2 Hz), 35.5 (*J* = 3 Hz), 61.2, 64.1 (*J* = 6 Hz), 137.7 (*J* = 11 Hz), 140.7 (*J* = 252 Hz), 161.2 (*J* = 36 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –131.4 (s, 1 F) ppm. **26b** (*Z*): ^1H NMR ($CDCl_3$): δ = 0.01, 0.06 (2 × s, 6 H), 0.88 (s, 9 H), 1.33 (m, 2 H), 1.33 (t, *J* = 7.1 Hz, 3 H), 1.48 (dm, *J* = 12.6 Hz, 2 H), 1.87 (m, 2 H), 2.28 (m, 1 H), 3.30 (d, *J* = 13.5 Hz, 1 H), 4.28 (m, 2 H), 4.93 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –5.23, –5.10, 14.11, 17.98, 19.53, 22.9 (*J* = 2 Hz), 25.7, 27.4 (*J* = 2 Hz), 35.2 (*J* = 2 Hz), 61.2, 63.3 (*J* = 11 Hz), 137.1 (*J* = 10 Hz), 140.0 (*J* = 249 Hz), 161.6 (*J* = 37 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –131.2 (d, *J* = 2.7 Hz, 1 F) ppm.

General Procedure for the Acid-Catalysed Cyclisation and the Rearrangement of Alkenoates 13 and 15: A mixture of alkenoate **13** or **15** (8.7 mmol) and *p*-toluenesulfonic acid (17.4 mmol) in dichloromethane (20 mL) was vigorously refluxed for 2–4 h until the conversion of the alkenoate to products was complete (checked by ^{19}F NMR). After cooling, the mixture was diluted with dichloromethane (20 mL) and washed with water (2 mL). The organic solution was dried with $MgSO_4$ and the solvent was removed to a minimum volume (rotary evaporator). The lower layer of **29** was separated from the residue containing butenolide **28** which was further purified by chromatography whereas the residue containing compound **30** on a silica gel column (see below).

3-Fluoro-5-methylfuran-2(5*H*)-one (28): Yield 605 mg (57%) of a colourless liquid obtained by microdistillation, b.p. 52–54 °C/80 Pa, $[\alpha]_D$ = +72.1 at 20 °C (*c* = 0.140 g/100 mL, $CHCl_3$). Column chromatography was performed on silica gel (benzene/ethyl acetate, 10:1). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1784 (s), 1682 (m) cm^{-1}. MS (EI): *m*/*z* (%) = 116 (11) $[M]^+$. $C_5H_5FO_2$ (116.1): calcd. C 51.73, H 4.34; found C 51.52, H 4.11. ^1H NMR ($CDCl_3$): δ = 1.51 (dd, *J* = 6.9, *J* = 1.1 Hz, 3 H), 5.26 (dqd, *J* = 6.6, *J* = 5.6, *J* = 1.9 Hz, 1 H), 6.71 (dd, *J* = 2.2, *J* = 1.9 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.5 (*J* = 3 Hz), 73.0 (*J* = 7 Hz), 126.7 (*J* = 5 Hz), 148.2 (*J* = 279 Hz), 164.4 (*J* = 32 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –141.5 (d, *J* = 4.9 Hz, 1 F) ppm.

Bis[*tert*-butyl(dimethyl)]siloxane (29): Yield 1.2 g (93.6%) of a colourless liquid. MS (EI): *m*/*z* (%) = 246 (1) $[M]^+$. ^1H NMR ($CDCl_3$): δ = 0.03 (s, 3 H), 0.87 (s, 9 H) ppm.

Ethyl (*E*)-2-Oxo-4-phenylbut-3-enoate (30):[31] Yield 884 mg (49.8%) of a slightly yellow oil. Column chromatography was performed on silica gel (benzene). The conversion of compound **15** to **30** was complete based on ^{19}F and ^1H NMR spectroscopy. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1730 (m), 1608 (s), 1083 (s) cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{21}O_3$ 204.0786; found 204.0780. MS (EI): *m*/*z* (%) = 204 (4) $[M]^+$. ^1H NMR ($CDCl_3$): δ = 1.42 (t, *J* = 7.1 Hz, 3 H), 4.40 (q, *J* = 7.1 Hz, 2 H), 7.36 (d, *J* = 16.0 Hz, 1 H), 7.43 (m, 3 H), 7.63 (m, 2 H), 7.86 (d, *J* = 16.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.2, 62.5, 120.4, 128.9, 131.5, 133.9, 148.3, 162.0, 182.6 ppm.

***tert*-Butyl(fluoro)dimethylsilane (31):**[18] The product was determined by ^{19}F and ^1H NMR analysis of the relevant reaction mixture. ^1H NMR ($CDCl_3$): δ = 0.18 (s, 3 H), 0.91 (s, 9 H) ppm. ^{19}F NMR ($CDCl_3$): δ = –170.1 (sept, *J* = 7.3 Hz, 1 F) ppm.

Photoinduced *Z*/*E* Isomerisation and Defluorination of Alkenoate 23: A mixture of alkenoate **23** (**23a**/**23b** = 97:3; 100 mg, 0.29 mmol) and acetone (110 mg, 1.89 mmol) in isooctane (8 mL) was vigorously stirred at room temp. in a silicious cell under UV irradiation (S1). After stirring for 1 h, the content of **23a**/**23b** was 80:20 and the ratio of *E*/*Z* isomers did not change further (checked by ^{19}F NMR of the reaction mixture). The mixture was irradiated by UV light (S2) for another 2 h leading to the complete decomposition of alkenoate **23** to **32**, formed in a ratio of **32a**/**32b** = 60:40 (checked by ^{19}F NMR of the reaction mixture). The mixture was allowed to stand for 2 days at room temperature during which time the decomposition of **32b** [^{19}F NMR ($CDCl_3$): δ = –169.13 ppm (dd, *J* = 48.8, *J* = 6.1 Hz, 1 F)] to oxo ester **33** was observed (conversion of **32b** checked by ^{19}F NMR of the reaction mixture). The solvent was removed (rotary evaporator) and the residue purified by chromatography on a silica gel column (benzene/ethyl acetate10:1) to afford products **32a** and **33**.

Ethyl (*E*)-4-[*tert*-Butyl(dimethyl)silyloxy]-2-fluoro-3-phenylbut-3-enoate (32a): Yield 22 mg (22.0%) of a slightly yellow oil. HRMS (FAB): calcd. for $C_{18}H_{27}FO_3Si$ 338.1710; found 338.1705. MS (FAB): *m*/*z* (%) = 338 (10) $[M + H]^+$. ^1H NMR ($CDCl_3$): δ = 0.22, 0.24 (2 × s, 6 H), 0.97 (s, 9 H), 1.07 (t, *J* = 7.1 Hz, 3 H), 4.12 (m, *J* = 7.1, *J* = 2.5 Hz, 2 H), 6.15 (d, *J* = 47.6 Hz, 1 H), 6.81 (d, *J* = 3.6 Hz, 1 H), 7.14–7.42 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –5.43, –5.32, 13.9, 18.3, 25.4, 61.2, 85.3 (*J* = 181 Hz), 117.0 (*J* = 16 Hz), 127.0, 127.6, 128.3, 135.7, 145.1 (*J* = 8 Hz), 169.2 (*J* = 28 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –181.37 (dd, *J* = 47.6, *J* = 3.7 Hz, 1 F) ppm.

Ethyl (*E*)-3-Phenyl-4-oxobut-2-enoate (33): Yield 30 mg (50.7%) of a slightly yellow oil. HRMS (EI): calcd. for $C_{12}H_{12}O_3$ 204.0786: found 204.0779. MS (EI): *m*/*z* (%) = 204 (34) $[M]^+$. ^1H NMR ($CDCl_3$): δ = 1.12 (t, *J* = 7.1 Hz, 3 H), 4.13 (q, *J* = 7.1 Hz, 2 H), 6.70 (s, 1 H), 7.20–7.26 (m, 3 H), 7.39–7.41 (m, 2 H), 9.77 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.8, 61.3, 128.0, 128.9, 129.0, 136.2, 149.5, 165.0, 192.8 ppm.

General Procedure for the Photoisomerisation and Cyclisation of Alkenoates 23, 24 and 26: Synthesis of 3-Fluorofuran-2(5*H*)-ones 37–39: A mixture of alkenoate **23**, **24** or **26** (4 mmol) and *p*-toluenesulfonic acid (4.8 mmol) in solvent (**23**/dioxane 8.4 mL, **24**/isooctane 8 mL, **26**/dioxane 3.5 mL) was vigorously refluxed for 1 h until the conversion of alkenoate to intermediates **34**, **35** or **36** was complete (checked by ^{19}F NMR). After cooling, the mixture was irradiated at room temperature in a silicious cell by UV light (S2) for 20–26.5 h until the complete isomerisation and cyclisation of **34**–**36** to **37**–**39** was observed (checked by ^{19}F NMR of the reaction mixture). The solvent was removed (rotary evaporator) and the residue was codistilled with hexane. The mixture was diluted with dichloromethane and neutralised with a solution of $NaHCO_3$. The organic solution was dried with $MgSO_4$ and the solvent was removed (rotary evaporator). The residue was purified by chromatography on a silica gel column (benzene/ethyl acetate, 10:1) to afford butenolides **37**–**39**.

Ethyl (*Z*)-2-Fluoro-4-hydroxy-3-phenylbut-2-enoate (34b): Yield 418 mg (50.2%) of a colourless oil obtained for analytical purposes by deprotection of alkenoate **23b** without further UV irradiation. Column chromatography was performed on silica gel (benzene/ethyl acetate, 10:1). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3608 (w), 1728 (s), 1465 (w), 1319 (m), 1260 (s), 1166 (m), 1019 (m) cm^{-1}. MS (EI): *m*/*z* (%) = 224 (29) $[M]^+$. $C_{12}H_{13}FO_3$ (224.2): calcd. C 64.28, H 5.86; found C 64.48, H 5.79. ^1H NMR ($CDCl_3$): δ = 1.01 (t, *J* = 7.1 Hz, 3 H), 1.62 (br. s, 1 H), 4.04 (q, *J* = 7.1 Hz, 2 H), 4.57 (d, *J* = 3.6 Hz, 2 H), 7.20–7.25 (m, 2 H), 7.34–7.40 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.5, 60.5 (*J* = 9 Hz), 61.4 (*J* = 0.8 Hz), 128.26, 128.27, 128.30, 128.34, 132.4 (*J* = 14 Hz), 134.1 (*J* = 5 Hz), 144.5 (*J* = 258 Hz), 160.4 (*J* = 36 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –123.5 (t, *J* = 3.7 Hz, 1 F) ppm.

Ethyl (*Z*)-2-Fluoro-4-hydroxy-3-methylpent-2-enoate (35b): Yield 251 mg (74.3%) of a colourless oil obtained for analytical purposes by deprotection of alkenoate **24b** without further UV irradiation. Column chromatography was performed on silica gel (benzene/ethyl acetate, 10:1). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3612 (w), 1721 (s), 1307 (s), 1230 (m), 1073 (m) cm^{-1}. HRMS (EI): calcd. for $C_8H_{13}FO_3$ 176.0849; found 176.0838. MS (EI): *m*/*z* (%) = 176 (1) $[M]^+$. ^1H NMR ($CDCl_3$): δ = 1.27 (d, *J* = 6.6 Hz, 3 H), 1.32 (t, *J* = 7.1 Hz, 3 H), 2.05 (d, *J* = 3.0 Hz, 3 H), 4.26 (q, *J* = 7.1 Hz, 2 H), 5.0 (q, *J* = 6.3 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 9.9 (*J* = 2 Hz), 14.0, 20.7 (*J* = 1 Hz), 61.2, 64.0 (*J* = 11 Hz), 135.1 (*J* = 10 Hz), 142.2 (*J* = 249 Hz), 161.2 (*J* = 35 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –128.4 (s, 1 F) ppm.

Ethyl (*Z*)-2-Fluoro-2-(2-hydroxycyclohexylidene)acetate (36b): Yield 32 mg (10.7%) of a colourless oil. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3609 (w), 2944 (m), 1723 (m), 1661 (w), 1301 (s), 1256 (m), 1219 (m), 1027 (m), 998 (w), 974 (w) cm^{-1}. HRMS (EI): calcd. for $C_{10}H_{15}FO_3$ 202.1005; found 202.1001. MS (EI): *m*/*z* (%) = 202 (12) $[M]^+$. ^1H NMR ($CDCl_3$): δ = 1.30 (m, 1 H), 1.30 (t, *J* = 7.1 Hz, 3 H), 1.50 (m, 2 H), 1.80 (m, 2 H), 1.95 (d, *J* = 12.0 Hz, 1 H), 2.20 (br. s, 1 H), 2.33 (m, 1 H), 3.28 (d, *J* = 15.0 Hz, 1 H), 4.24 (q, *J* = 7.1 Hz, 2 H), 4.95 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.0, 19.4, 22.8 (*J* = 1 Hz), 26.9 (*J* = 2 Hz), 33.6 (*J* = 2 Hz), 61.3, 62.9 (*J* = 11 Hz), 135.4 (*J* = 9 Hz), 141.2 (*J* = 251 Hz), 161.3 (*J* = 36 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –130.4 (s, 1 F) ppm.

3-Fluoro-4-phenylfuran-2(5*H*)-one (37): Yield 296 mg (41.5%) of a solid which was crystallised in hexane/acetone to afford white crystals, m.p. 127–129 °C. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1779 (s), 1684 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 178 (98) $[M]^+$. $C_{10}H_7FO_2$ (178.2): calcd. C 67.42, H 3.96, F 10.66; found C 67.43, H 3.91, F 10.52. ^1H NMR ($CDCl_3$): δ = 5.17 (d, *J* = 5.5 Hz, 2 H), 7.50 (m, 3 H), 7.58 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 66.3 (*J* = 7 Hz), 127.06, 127.14, 129.4, 131.3 (*J* = 2 Hz), 127.2, 133.6 (*J* = 3 Hz), 142.7 (*J* = 277 Hz), 165.4 (*J* = 32 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –144.5 (t, *J* = 4.9 Hz, 1 F) ppm.

3-Fluoro-4,5-dimethylfuran-2(5*H*)-one (38): Yield 215 mg (41.3%) of a colourless oil. $C_6H_7FO_2$ (130.1): calcd. C 55.38, H 5.42, F 14.60; found C 55.25, H 5.71, F 14.78. ^1H NMR ($CDCl_3$): δ = 1.47 (dd, *J* = 6.6, *J* = 1.4 Hz, 3 H), 1.98 (dd, *J* = 2.2, *J* = 0.9 Hz, 3 H), 4.86 (qd, *J* = 6.3, *J* = 1.1 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 8.9 (*J* = 2 Hz), 18.1 (*J* = 2 Hz), 76.1 (*J* = 7 Hz), 138.7 (*J* = 5 Hz), 143.9 (*J* = 271 Hz), 164.4 (*J* = 35 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –152.7 (s, 1 F) ppm.

3-Fluoro-5,6,7,7a-tetrahydro-1-benzofuran-2(4*H*)-one (39): Yield 338 mg (54.1%) of a colourless liquid. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1773 (s), 1719 (w) cm^{-1}. MS (FAB): *m*/*z* (%) = 157 (49) $[M + H]^+$. $C_8H_9FO_2$ (156.2): calcd. C 61.53, H 5.81, F 12.17; found C 61.25, H 5.67, F 12.16. ^1H NMR ($CDCl_3$): δ = 1.26 (m, 3 H), 1.88 (m, 2 H), 2.03 (m, 1 H), 2.45 (m, 1 H), 2.28 (m, 1 H), 2.87 (dm, *J* = 14.6 Hz, 1 H), 4.58 (2 × dd, *J* = 11.3, *J* = 5.5 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 23.0, 24.1 (*J* = 2 Hz), 26, 34.4 (*J* = 2 Hz), 77.0 (*J* = 7 Hz), 141.2 (*J* = 7 Hz), 141.5 (*J* = 271 Hz), 165.7 (*J* = 32 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –155.7 (d, *J* = 3.7 Hz, 1 F) ppm.

Synthesis of 2-[*tert*-Butyl(dimethyl)silyloxy]-3-fluoro-4-phenylfuran (41): A solution of *n*-butyllithium in hexane (2.5 M, 123 μL, 0.309 mmol) was added dropwise under nitrogen through a syringe into the flask charged with diisopropylamine (32 mg 0.309 mmol) and dry THF (5 mL) and cooled to 0 °C. The mixture was stirred for 20 min and then cooled to around –75 °C. Compound **37** (46 mg, 0.258 mmol) in THF (3 mL) was then added dropwise through a syringe while stirring. After 45 min, a solution of *tert*-butyl(dimethyl)silyl chloride (55 mg, 0.365 mmol) in THF (2 mL) was added through a syringe, the mixture was stirred for 20 min and then allowed to warm to room temp. The solvent was removed under reduced pressure at room temp. (rotary evaporator) and the residue purified by flash chromatography on neutral Al_2O_3 (light petroleum/dichloromethane, 1:1) to give 53 mg (70.2%) of **41** as a slightly yellow oil. No decomposition of the product was found during a week at 0–4 °C (checked by ^{19}F NMR). HRMS (FAB): calcd. for $C_{16}H_{21}FO_2Si$ 292.1295; found 292.1930. MS (EI): *m*/*z* (%) = 292 (20) $[M]^+$. ^1H NMR ($CDCl_3$): δ = 0.28 (s, 6 H), 1.00 (s, 9 H), 6.22 (*J* = 4.1 Hz), 7.29 (m, *J* = 6.3 Hz, 1 H), 7.36 (t, *J* = 7.4 Hz, 2 H), 7.52 (d, *J* = 7.4 Hz, ????) ppm. ^{13}C NMR ($CDCl_3$): δ = –4.7, 18.0, 25.3, 119.0 (*J* = 13 Hz), 124.9 (*J* = 7 Hz), 126.00, 126.04, 127.3, 128.7, 127.5, 130.3 (*J* = 4 Hz), 130.7 ppm. ^{19}F NMR ($CDCl_3$): δ = –189.73 (d, *J* = 3.4 Hz, 1 F) ppm.

Supporting Information (see also the footnote on the first page of this article): Further details of the monitoring by ^{19}F NMR spectroscopy of the *Z*/*E* isomerisation of **23b** to the butenolide **37**.

Acknowledgments

This study was performed as a part of a research project of the Institute of Organic Chemistry and Biochemistry (project

#Z 40550506). The research was supported by the Ministry of Education of the Czech Republic (project MSM 6046137301) and the Institute of Chemical Technology, Prague. Elemental analyses and measurements of some NMR spectra were carried out in the Central Laboratories of the Prague Institute of Chemical Technology. The authors thank Prof. Dr. Miroslav Strnad (Palacký University & Institute of Experimental Botany AS CR, Olomouc, Czech Republic) and Dr. Milan Pour (Faculty of Pharmacy, Charles University, Heyrovského, Hradec Králové, Czech Republic) for a biochemical assay of the synthesised 2-fluorobut-2-enolides. The authors also thank Dr. Hana Dvořáková (Institute of Chemical Technology, Prague, Czech Republic) for measurement of NOE Dif. NMR experiments.

[1] P. L. Triozze, J. Ailabouni, J. J. Rinehart, D. T. Witiak, *Int. J. Pharmacol.* **1993**, *15*, 47–54.
[2] X. P. Fang, J. E. Anderson, D. L. Smith, J. L. McLaughlin, K. V. Wood, *J. Nat. Prod.* **1992**, *55*, 1655–1663.
[3] H. Mori, N. Yoshimi, S. Sugie, T. Tanaka, Y. Morishita, G. Jinlong, Y. Tamai, M. Torihara, J. Yamahara, *Cancer Lett. (Shannon, Irel.)* **1992**, *66*, 93–98.
[4] a) X.-P. Fang, J. E. Anderson, C.-J. Chang, J. L. McLaughlin, *Tetrahedron* **1991**, *47*, 9751–9758; b) J. K. Ruprecht, Y. H. Hui, J. L. McLaughlin, *J. Nat. Prod.* **1990**, *53*, 237–278.
[5] a) B. E. Roggo, P. Hug, S. Moss, F. Raschorf, H. H. Peter, *J. Antibiot.* **1994**, *47*, 143–147; b) B. E. Roggo, F. Petersen, R. Delmendo, H. B. Jenny, H. H. Peter, J. J. Roesel, *J. Antibiot.* **1994**, *47*, 136–142.
[6] M. Ito, *Pure Appl. Chem.* **1991**, *63*, 13–22.
[7] H. Nishino, Y. Satomi, H. Tokuda, A. Nishino, A. Iwashima, Y. Tanaka, Y. Zamano, Y. Shibata, M. Torihara, *Kyoto-furitsu Ika Daigaku Zasshi* **1991**, *100*, 831–835.
[8] a) S. Tsuboi, J.-i. Sakamoto, T. Kawano, M. Utaka, A. Takeda, *J. Org. Chem.* **1991**, *56*, 7177–7179; b) R. Bloch, L. Gilbert, *J. Org. Chem.* **1987**, *52*, 4603–4605; c) M. Takadoi, T. Katoh, A. Ishiwata, S. Terashima, *Tetrahedron Lett.* **1999**, *40*, 3399–3402.
[9] D. W. Knight, *Contemp. Org. Synth.* **1994**, *1*, 287–315.
[10] M. Pour, M. Špulák, V. Buchta, P. Kubanová, M. Vopršálová, V. Wsól, H. Fáková, P. Koudelka, H. Pourová, R. Schiller, *J. Med. Chem.* **2001**, *44*, 2701–2706.
[11] a) I. Ojima, J. R. McCarthy, J. T. Welch (Eds.), *Proceedings of the ACS Symposium on Biomedical Frontiers of Fluorine Chemistry, Series 639*, American Chemical Society, Washington, DC, **1996**; b) J. T. Welch, *Tetrahedron* **1987**, *43*, 3123–3197 (*Tetrahedron* Rep. No. 221).
[12] R. Filler, Z. Kobayashi, L. M. Yagupolskii (Eds.), *Organo-fluorine Compounds in Medicinal Chemistry and Biomedical Applications*, Elsevier, Amsterdam, **1993**; R. E. Banks, K. C. Lowe (Eds.), *Fluorine in Medicine in the 21st Century* (Conference Papers), UMIST, Manchester, **1994**.
[13] a) P. Ge, K. L. Kirk, *J. Fluorine Chem.* **1997**, *84*, 45–47; b) P. Ge, K. L. Kirk, *J. Org. Chem.* **1997**, *62*, 3340–3343.
[14] a) Y. Komatsu, T. Kitazume, *J. Fluorine Chem.* **1998**, *87*, 101–104; b) Y. Komatsu, T. Kitazume, *J. Fluorine Chem.* **2000**, *102*, 61–68.
[15] a) T. Morikawa, J. Uchida, Y. Hasegawa, T. Taguchi, *Chem. Pharm. Bull.* **1991**, *39*, 2462–2464; b) K. Lee, Y. Choi, E. Gulden, S. Schlueter-Wirtz, R. F. Schinazi, Y. Cheby, C. K. Chu, *J. Med. Chem.* **1999**, *42*, 1320–1328; c) J. Kvíčala, R. Vlasáková, J. Plocar, O. Paleta, A. Pelter, *Synlett* **1997**, 986; d) J. Kvíčala, R. Vlasáková, J. Plocar, O. Paleta, A. Pelter, *Collect. Czech. Chem. Commun.* **2000**, *96*, 772–788.
[16] K. Pomeisl, J. Kvíčala, O. Paleta, *J. Fluorine Chem.* **2006**, *127*, 1390–1397.
[17] a) Y. Yamamoto, Y. Chounan, S. Nishii, T. Ibuka, H. Kitahura, *J. Am. Chem. Soc.* **1992**, *114*, 7652–7660; b) A. Patrizia, C. Gianfranco, P. Mauro, B. Elisa, M. Giorgio, S. Giuseppe, *J. Org. Chem.* **1991**, *56*, 5984–5990.
[18] T. J. Hairston, D. H. O'Brien, *J. Organomet. Chem.* **1971**, *29*, 79.
[19] a) F. D. Lewis, J. D. Oxman, *J. Am. Chem. Soc.* **1981**, *103*, 7345–7347; b) F. D. Lewis, J. D. Oxman, L. L. Gibson, H. L. Hampsch, S. Z. Quillen, *J. Am. Chem. Soc.* **1986**, *108*, 3005–3015; c) A. Guarino, E. Possagno, R. Bassanelli, *Bull. Soc. Chim. Fr.* **1988**, 253–257; d) A. Guarino, E. Possagno, R. Bassanelli, *Tetrahedron* **1987**, *43*, 1541–1549; e) F. D. Lewis, S. Z. Quillen, P. D. Hale, J. D. Oxman, *J. Am. Chem. Soc.* **1988**, *110*, 1261–1267; f) A. C. Weedon, D. F. Wong, *J. Photochem.* **1987**, *38*, 289–299.
[20] M. C. Pirrung, J. Chen, E. G. Rowley, A. T. McPhail, *J. Am. Chem. Soc.* **1993**, *115*, 7103–7110.
[21] a) R. E. Lutz, G. W. Scott, *J. Org. Chem.* **1948**, *13*, 284–296; b) F. Kuhn, K. Fischer, *Chem. Ber.* **1961**, *94*, 3060–3071.
[22] F. M. Lewis, F. R. Mayo, *J. Am. Chem. Soc.* **1948**, *70*, 1533–1536.
[23] a) Ch. Mukai, S. Hirai, I. J. Kim, M. Kido, M. Hanaoka, *Tetrahedron* **1996**, *52*, 6547–6560; b) K. Kawada, O. Kitagawa, T. Taguchi, Y. Hanzawa, Y. Kobayashi, Y. Iitaka, *Chem. Pharm. Bull.* **1985**, *33*, 4216–4222; c) C. W. Jefford, A. W. Sledeski, J. Boukouvalas, *Tetrahedron Lett.* **1987**, *28*, 949–950.
[24] O. Paleta, A. Volkov, J. Hetflejš, *J. Fluorine Chem.* **2000**, *102*, 147–157.
[25] E. A. Monaco III, C. M. Beaman-Hall, A. Mathur, M. Lou Vallano, *Biochem. Pharmacol.* **2004**, *67*, 1947–1964.
[26] M. Pour, K. Pomeisl, unpublished results.
[27] S. Zapf, T. Anke, O. Sterner, *Acta Chem. Scand.* **1995**, *49*, 233–234.
[28] a) G. W. K. Cavill, A. Robertson, W. B. Whalley, *J. Chem. Soc.* **1949**, 1567–1570; b) T. T. X-Upadhya, A. Sudalai, *Tetrahedron: Asymmetry* **1997**, *8*, 3685–3689.
[29] a) Y. Yamamoto, Y. Chounan, S. Nishii, T. Ibuka, H. Kitahura, *J. Am. Chem. Soc.* **1992**, *114*, 7652–7660; b) P. Andreoli, G. Cainelli, J. M. Panunzio, J. E. Bandini, G. Martelli, J. G. Spunta, *J. Org. Chem.* **1991**, *56*, 5984–5990; c) B. T. Cho, Y. S. Chun, *J. Org. Chem.* **1998**, *63*, 5280–5282; d) M. E. Jung, A. van den Heuvel, A. G. Leach, K. N. Houk, *Org. Lett.* **2003**, *5*, 3375–3378.
[30] a) A. G. M. Barret, D. Ch. Braddock, P. W. N. Christian, D. Pilipauskas, A. J. P. White, D. J. Williams, *J. Org. Chem.* **1998**, *63*, 5818–5823; b) W. J. Brouillette, G. L. Grunewald, *J. Med. Chem.* **1984**, *27*, 202–206.
[31] A. R. Katritzky, D. Feng, M. Qi, *J. Org. Chem.* **1998**, *63*, 1473–1477.

Received: May 16, 2007
Published Online: October 5, 2007

