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TETRAHEDRON: *ASYMMETRY*

Diastereoselective synthesis of enantiopure 5-[2-(alkoxyalkyl)-1-(hydroperoxypropyl)]-3-alkoxycarbonyl-2-alkyl furans

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Abstract

The diastereoselective approach to enantiomerically pure furyl hydroperoxides of general type **1** has been accomplished starting from (*S*)-(−)-ethyl lactate. In the first part of the synthesis the alkylating reagents **7a**,**b** were efficiently produced to be used in the second part for a 4-step known methodology to obtain furyl hydroperoxides. The most relevant transformation of the synthesis is the first reported diastereoselective iodoenoletherification of 2-acetyl-4-heptenoate esters **8a**,**b** possessing a ϕ-chiral center. Furthermore, the final radical oxidation performed on (*E*)-5-alkylidene-4,5-dihydrofurans **11a**,**b** led to formation of hydroperoxides (*S*,*S*)-**12a**,**b** in a diastereocontrolled manner due to 1,2-asymmetric induction.

1. Introduction

The most relevant employment of alkyl hydroperoxides in organic synthesis is in the Sharpless asymmetric epoxidation[1] of allylic alcohols and its further modification for asymmetric sulfoxidation[2] of prochiral sulfides. Ti(O^iPr)$_4$, *tert*-butylhydroperoxide (TBHP) and L- or D-tartrate esters as chiral ligands are combined in active complexes that induce high enantioselectivity in the processes. Studies on the sulfoxidation have shown how different experimental conditions involving ratios of reagents,[2] structure of the hydroperoxides,[2d] presence of water[2b,d] and chiral diols[3] can provide high asymmetric induction.

We have recently been focusing our attention on the synthesis[4] and the reactivity[5] of a new class of oxidants, furyl hydroperoxides, which are a valuable alternative to the commercial TBHP and cumyl hydroperoxide (CHP) in Sharpless modified oxidations. Furthermore, they have proved, under the same conditions, to be the most suitable oxidants for the kinetic resolution of racemic methyl aryl sulfoxides[6] and β-keto sulfoxides[7] (ee values 50–90% of unreacted sulfoxides). The results of this research confirmed

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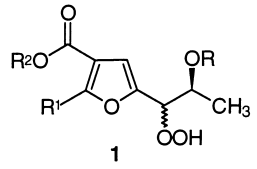

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Figure 1.

and expanded on the previous data reported by Sharpless[1] and Kagan[2] about the need of the well established stereoelectronic requirements of hydroperoxides to be used in order to ensure high levels of enantioselectivity.

Limited investigations have been conducted on asymmetric metal-mediated oxidations carried out with enantiomerically pure hydroperoxides[8] in the absence of chiral ligands. In this case the asymmetric induction is exclusively promoted by the oxidant. The enantioselectivity of these processes does not exceed 30% for epoxyalcohols and sulfoxides, however Adam et al. recently reported the best example of asymmetric sulfoxidation with an enantiomerically pure hydroperoxide[9] (ee up to 80%).

No general methodology and only limited examples exist for the synthesis of alkyl hydroperoxides in optically active form.[8a,10] The best results have been achieved by kinetic resolution of the racemic mixture of hydroperoxides mediated by enzymes such as horseradish peroxidase,[11] chloroperoxidase,[12] lipase,[13] etc. where one enantiomer of the starting oxidants is preferentially obtained at the expense of the consumption of the other. Herein, we report the diastereoselective synthesis of enantiomerically pure compounds of general type **1** (Fig. 1).

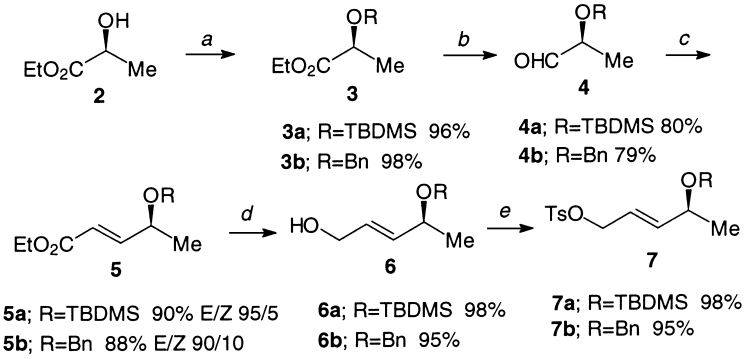
2. Results and discussion

Our strategy was to proceed from the commercially available and low cost (*S*)-(−)-ethyl lactate to introduce a stereodefined moiety next to the carbon bearing the hydroperoxide group. We followed a suitable modification of a known sequence[14] to obtain enantiomerically pure γ-alkoxy-α,β-unsaturated esters **5** (Scheme 1). After the quantitative protection of (*S*)-(−)-ethyl lactate **2** as *tert*-butyldimethylsilyl ether **3a** and as benzyl ether **3b**, compounds **3** were selectively reduced with DIBALH to afford aldehydes **4**, which without purification were transformed into α,β-unsaturated esters **5**. The Wadsworth–Horner–Emmons olefination of **4** conducted with triethylphosphonacetate and $LiOH \cdot H_2O$ in THF,[15] instead of the reported[14] triethylphosphonacetate and NaH in THF, furnished esters **5a**,**b** in good yield and with higher *E*/*Z* ratios. The (*E*)-esters **5**, separated by silica gel chromatography, were reduced with DIBALH to allylic alcohols **6**.

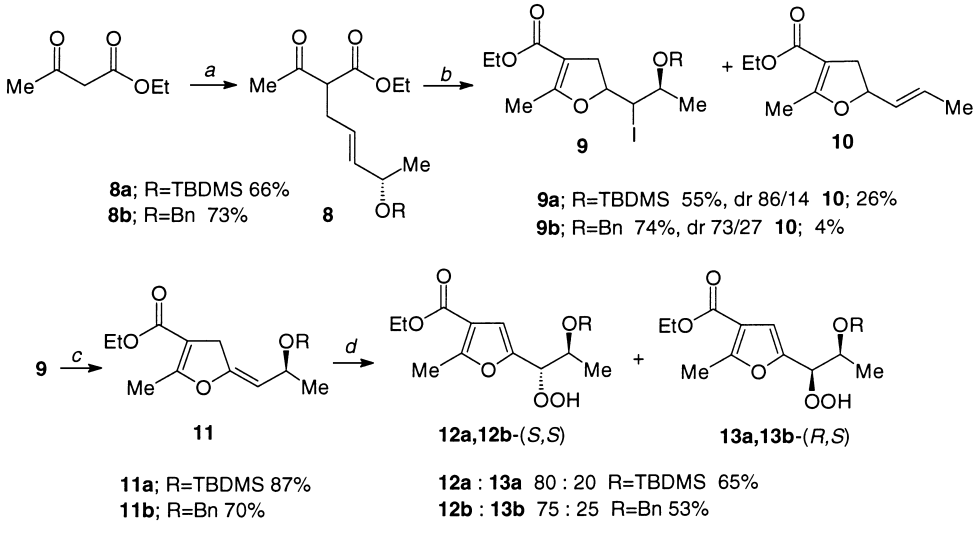
Finally, compounds **6** were treated with tosyl chloride and KOH under phase transfer catalysis[16] to give tosylates **7** quantitatively. This efficient route allowed us to prepare compounds **7a** and **7b** by simple transformations with ca. 60% overall yield starting from **2**.

In the second part of the synthesis we applied the sequence reported in previous papers[4] to obtain furyl hydroperoxides (Scheme 2).

The alkylation of ethyl acetoacetate with the crude mixture[17] of **7** using $LiOH \cdot H_2O$ in THF at 50°C[18] furnished in good yields the α-mono-alkylated β-ketoesters **8**. Compounds **8** were reacted[4a] with iodine and Na_2CO_3 in dry dichloromethane under kinetic control, affording derivatives **9** coming from the expected stereospecific 5-*exo*-*tet* closure.[19,4a] Moreover, iododihydropyran derivatives coming from the equally favored[19a,b] 6-*endo*-*trig* closure were not detected. Iodocyclized compounds **9** were isolated as unseparable mixtures of diastereomers in ratio 86/14 for **9a** and 73/27 for **9b** as judged by ^1H NMR, whose absolute configurations were impossible to assign. This is the first example of iodine-



Scheme 1. Reagents and conditions: (*a*) **3a**: TBDMSCl, imidazole, CH_2Cl_2, 0°C; **3b**: NaH, BnBr, CH_2Cl_2, 0°C. (*b*) DIBALH, CH_2Cl_2, −78°C. (*c*) $LiOH \cdot H_2O$, THF, 15°C, $(EtO)_2POCH_2CO_2Et$. (*d*) DIBALH, CH_2Cl_2, 0°C. (*e*) TsCl, $(n\text{-}Bu)_4NHSO_4$, KOH, C_6H_6, rt



Scheme 2. Reagents and conditions: (*a*) **7**, $LiOH \cdot H_2O$, THF, 50°C. (*b*) **8a**: I_2, Na_2CO_3, CH_2Cl_2, −25°C; **8b** −5°C. (*c*) DBU, C_6H_6, 50°C. (*d*) AIBN, O_2, C_6H_6, 50°C

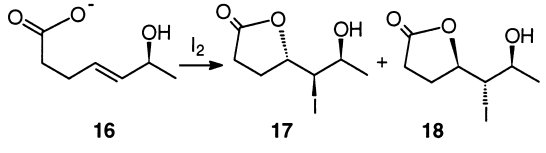


Figure 2.

induced enoletherification of 2-acetyl-4-heptenoate esters **8a**,**b** possessing a ϕ-chiral center. Closely related to this transformation, Chamberlain et al.[20] reported the kinetically controlled iodolactonization of compound **16** but they found nearly equal proportions of the two diastereomers **17** and **18** (Fig. 2).

Interestingly, in our case the stereogenic center with the protected alcoholic function forced the enol of **8** to attack preferentially one of the two diastereoisomeric iodonium intermediates to give high prevalence for one diastereomer of **9**. As a by-product of the iodoenoletherification we isolated compound **10** that could be derived from an intramolecular S_N2' displacement[21] of the protected hydroxyl group from the enol of **8**. The nature of the alcoholic protective group greatly affected the iodocyclization and, as a result, a substantially limited formation of the undesired product **10** occurred, changing from 26% to 4% yield,

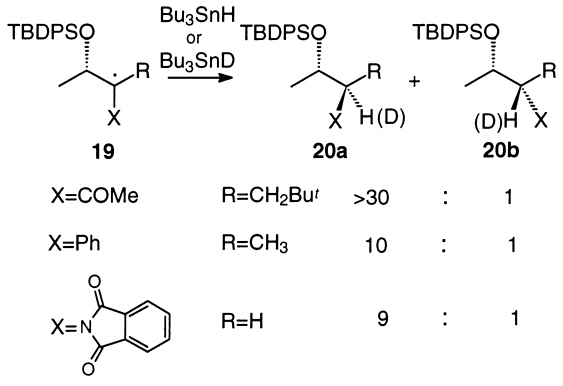


Figure 3.

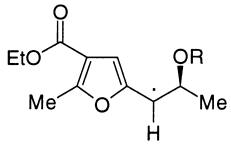


Figure 4.

respectively, in going from R=TBDMS to R=Bn. As previously mentioned, the absolute configuration of the stereogenic centers generated in the iodine-induced enoletherification could not be determined. However, the stereochemical outcome of the following reaction allowed us to define their configurations either as 5*R*,1*S* or 5*S*,1*R*. The elimination of HI conducted on iodoalkyl diastereoisomeric mixtures **9a** and **9b** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) took place stereospecifically, leading to satisfactory yields of (*E*)-5-alkylidene-4,5-dihydrofurans **11a** and **11b**. In fact, ^{1}H NMR spectra of **11a** and **11b** revealed the presence of the diagnostic olefinic proton of the (*E*)-isomer only, centered as a double triplet at 5.3 ppm.[4a,22]

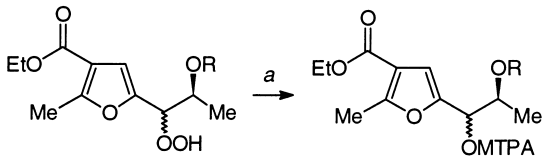
Finally, the radical oxidation carried out on **11a**,**b** with[4b] AIBN and bubbling O_2 at 50°C furnished chromatographically separable **12a**,**b** and **13a**,**b** in a diastereoselective manner. The authoritative work of Giese,[23] Curran,[24] Porter,[25] Guindon,[26] Renaud[27] and Liotta[28] about 1,2-asymmetric induction in radical reactions allows the establishment of the preferred conformation of the reactive radicals when X is a substituent planar and in conjugation with the singly occupied orbital,[29] on the basis of allylic strain effects[30] (Fig. 3).

Consequently, it is possible to predict with good confidence the direction of 1,2-stereoinduction in the products of trapped acyclic radicals although the degree of stereoselectivity depends upon the nature of the radical traps as well as of the substituents on the stereogenic center. In general, the direction of stereoselectivity for acyclic radicals leads to the prevalent formation of the **20a** diastereoisomer.[31] Applying these rules to the furyl radical (Fig. 4) involved in the oxidation,[4b] the absolute configuration of the major diastereoisomer **12a**,**b** must be *S*,*S* and *R*,*S* for the minor **13a**,**b**.

Attempts to synthesize the corresponding furyl hydroperoxides **12a**,**b** and **13a**,**b** through the ene reaction with singlet oxygen[32] on **11a**,**b** failed and only complex reaction mixtures were obtained.

Confirmation of the stereochemistry of the newly formed stereogenic carbon as *S* for the major diastereoisomers **12a**,**b** and *R* for the minor **13a**,**b** was accomplished on the corresponding furyl alcohols of **14a** and **15a** (Scheme 3) obtained after the reduction of **12a** and **13a**, respectively, using the Mosher ester method for the determination of the absolute configuration.[33]

Furthermore, we confirmed that no racemization of the stereogenic carbon derived from (*S*)-lactate



12,13a **14,15a**

Scheme 3. Reagents and conditions: (*a*) (i) **12**, **13a**, $(Ph)_3P$, CH_2Cl_2, rt, (ii) (*R*) or (*S*)-MTPA-Cl, CH_2Cl_2, Et_3N, DMAP, rt

occurred during the synthesis. In fact, no isomer was detected in ^1H NMR spectra of (*R*)- and (*S*)-Mosher esters of furyl alcohols **14a** and **15a**.

3. Conclusion

The general diastereoselective approach to enantiomerically pure furyl hydroperoxides of type **1** has been established representing one of the few reported chemical routes to enantiomerically pure hydroperoxides. Consequently, furyl hydroperoxide analogues can be synthesized with a similar effort in a predictable way choosing appropriate starting materials (1,3-dicarbonyl compound and protected lactate). In addition, this synthetic sequence offers the approach to interesting enantiomerically pure intermediates such as (*E*)-5-alkylidene-4,5-dihydrofurans and functionalized furyl 1,2-diols.

4. Experimental

4.1. General

Unless otherwise noted, all reagents were obtained from commercial suppliers and were used without further purification. All solvents were distilled under nitrogen immediately before use: THF from sodium/benzophenone, dichloromethane and benzene from calcium hydride. All reactions requiring anhydrous conditions were conducted under an argon atmosphere in flame dried glassware. Reactions were monitored by thin layer chromatography (TLC) on Merck silica gel plates and visualized using UV light followed by charring with 10% sulfuric acid–ethanol spray or 0.5% phosphomolybdic acid in 95% ethanol. Unless otherwise stated, standard workup refers to the combination of organic extracts, washing with brine and drying over anhydrous Na_2SO_4. Flash column chromatography was performed using Kieselgel 60 (Merck, 230–400 mesh). ^1H NMR and ^{13}C NMR spectra were recorded at 400 and 100.6 MHz, respectively, with a Bruker DRX 400 MHz spectrometer. The chemical shifts were measured on the δ scale relative to the residual signal of $CDCl_3$ (7.26 and 77 ppm) and C_6D_6 (7.16 and 128.39 ppm). Optical rotations were measured with a JASCO Dip-1000 digital polarimeter at λ=589 nm. Mass spectra were determined at an ionizing voltage of 70 eV.

*4.2. Synthesis of ethyl (2*E*,4*S*)-4-[(*tert*-butyldimethylsilyl)oxy]-2-pentenoate **5a***

To a CH_2Cl_2 solution (50 mL) of (*S*)-ethyl lactate (5.7 mL, 50 mmol) at 0°C were added imidazole (4.1 g, 60 mmol) and TBDMSCl (8.3 g, 55 mmol) and the mixture was stirred for about 5 h at room temperature. Water (50 mL) was added and the mixture was extracted with CH_2Cl_2, followed by standard workup and the solvent was removed in vacuo. The residue was dissolved in dry CH_2Cl_2 (50 mL) and a 1 M CH_2Cl_2 solution of DIBALH (50 mL, 50 mmol) was added dropwise in 45 min at −78°C under

an argon atmosphere. The mixture was stirred for 1.5 h and 50 mL of saturated solution of potassium tartrate was added dropwise at −78°C and stirred overnight till room temperature. The resulting mixture was extracted with ethyl acetate (2×50 mL), standard workup yielded an oil. The residue was used for further manipulation without purification. To a solution of triethyl phosphonoacetate (7.9 mL, 40 mmol) in dry THF (30 mL) were added activated (4 Å) molecular sieves (10 g) and $LiOH \cdot H_2O$ (1.68 g, 40 mmol) and they were stirred under an argon atmosphere for 20 min at 40°C. Then the mixture was cooled at 0°C and the residue containing the aldehyde was added (38 mmol) with 8 mL of THF. The mixture was stirred for 1 h at 0°C and 10 h at room temperature. The reaction progress was monitored by TLC. Addition of 100 mL of H_2O, extraction with diethyl ether (2×50 mL), standard workup followed by flash chromatography of ethyl esters (*E*:*Z*=95:5) gave **5a** (8.7 g, 68% from (*S*)-ethyl lactate). $[\alpha]_D^{19}$=+7.3 (*c* 2.76, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 6.94 (dd, *J*=15.6, 4.3 Hz, 1H), 5.97 (dd, *J*=15.6, 1.5 Hz, 1H), 4.45 (ddq, *J*=6.4, 4.3, 1.5 Hz, 1H), 4.20 (q, *J*=7.0 Hz, 2H), 1.29 (t, *J*=7.0 Hz, 3H), 1.25 (d, *J*=6.4 Hz, 3H), 0.91 (s, 9H), 0.07 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 165.2, 151.8, 118.9, 68.4, 60.6, 25.7, 21.2, 18.2, 14.1, −4.9, −5.3. EIMS *m/z* (rel. intensity): 258 (M^+, 24), 212 (100), 201 (55), 173 (11), 127 (15). Anal. calcd for $C_{13}H_{26}O_3Si$: C, 60.42; H, 10.14. Found: C, 60.14; H, 10.31.

4.3. *Synthesis of ethyl (2*E*,4*S*)-4-[(benzyl)oxy]-2-pentenoate **5b***

To a suspension of NaH (2.75 g, 55 mmol, 60% in mineral oil) in dry CH_2Cl_2 (90 mL) at 0°C under an argon atmosphere was added dropwise a solution of (*S*)-ethyl lactate (5.7 mL, 50 mmol) in 10 mL of CH_2Cl_2; after 10 min benzyl bromide (6.3 mL, 53 mmol) was added. The mixture was stirred for 5 h and monitored by TLC. Addition of 100 mL of H_2O and extraction with CH_2Cl_2 (3×50 mL) was followed by standard workup. Then **5b** was prepared as described above for **5a**. Purification of ethyl esters (*E*:*Z*=90:10 flash silica gel) gave **5b** (7.1 g, 61% from (*S*)-ethyl lactate). Colorless oil. $[\alpha]_D^{22}$=−46.5 (*c* 2.48, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.27 (m, 5H), 6.82 (dd, *J*=15.8, 6.3 Hz, 1H), 5.95 (dd, *J*=15.8, 1.1 Hz, 1H), 4.49 (AB, *J*=11.8 Hz, 1H), 4.36 (AB, *J*=11.8 Hz, 1H), 4.14 (q, *J*=7.0 Hz, 2H), 4.04 (ddq, *J*=6.4, 6.3, 1.1 Hz, 1H), 1.25 (d, *J*=6.4 Hz, 3H), 1.23 (t, *J*=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 166.2, 149.1, 138.1, 128.5, 127.6, 127.5, 121.2, 73.7, 70.6, 60.3, 20.5, 14.1. EIMS *m/z* (rel. intensity): 234 (M^+, 11), 188 (100), 171 (25), 127 (16), 91 (10). Anal. calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.96; H, 7.50.

4.4. *General procedure for the preparation of compounds **6a**,**b***

To a cold solution (0°C) of **5a**,**b** (30 mmol) in dry CH_2Cl_2 (60 mL) was added dropwise a 1 M CH_2Cl_2 solution of DIBALH (60 mL, 60 mmol) under an argon atmosphere. The mixture was stirred for 1 h and 60 mL of a saturated solution of potassium tartrate was added dropwise and then stirred for 3 h at room temperature. The resulting mixture was neutralized and extracted with ethyl acetate (2×60 mL) followed by standard workup.

4.5. *(2*E*,4*S*)-4-[(*tert*-Butyldimethylsilyl)oxy]-2-pentenol **6a***

After flash chromatography of the residue, alcohol **6a** was obtained as a colorless oil (6.3 g, 98% yield). $[\alpha]_D^{19}$=+3.7 (*c* 2.86, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.73 (m, 2H), 4.30 (m, 1H), 4.11 (d, *J*=4.9 Hz, 2H), 1.70 (br, 1H), 1.20 (d, *J*=6.3 Hz, 3H), 0.88 (s, 9H), 0.051 (s, 3H), 0.043 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 136.2, 127.2, 68.4, 63.0, 25.8, 24.2, 18.2, −4.6, −4.7. EIMS *m/z* (rel. intensity): 215 (M^+−1, 2), 199 (100), 159 (4), 142 (7). Anal. calcd for $C_{11}H_{24}O_2Si$: C, 61.06; H, 11.18. Found: C, 60.75; H, 10.91.

4.6. (2E,4S)-4-[(Benzyl)oxy]-2-pentenol **6b**

After flash chromatography of the residue, alcohol **6b** was obtained as a colorless oil (5.4 g, 95% yield). $[\alpha]_D^{21}=-27.1$ (*c* 2.85, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.29 (m, 5H), 5.82 (dt *J*=15.5, 5.3 Hz, 1H), 5.68 (ddt, *J*=15.5, 7.4, 1.2 Hz, 1H), 4.55 (AB, *J*=11.9 Hz, 1H), 4.42 (AB, *J*=11.9 Hz, 1H), 4.17 (d, *J*=4.7 Hz, 2H), 3.97 (quint, *J*=6.5 Hz, 1H), 1.82 (br, 1H), 1.29 (d, *J*=6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 138.7, 133.2, 130.9, 128.3, 127.6, 127.4, 75.1, 70.0, 62.8, 21.3. EIMS *m/z* (rel. intensity): 193 (M^++1, 100), 192 (22), 176 (20), 130 (37), 91 (6), 84 (95). Anal. calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.24; H, 8.60.

4.7. General procedure for the preparation of compounds **7a**,**b**

To a benzene (30 mL) solution of **6a**,**b** (10 mmol), at room temperature, were successively added KOH solution (30%, 30 mL), $(Bu)_4NHSO_4$ (2 mmol) and finally tosyl chloride (12 mmol). The mixture was vigorously stirred and monitored by TLC. Water was added and extraction with diethyl ether (3×50 mL) was followed by standard workup. The crude reaction mixture of **7a**,**b** was used for further manipulation without purification.

4.8. (2E,4S)-4-[(tert-Butyldimethylsilyl)oxy]-2-penten-1-yl p-toluensulfonate **7a**

The conversion (98%) was estimated by ^{1}H NMR. ^{1}H NMR ($CDCl_3$) δ 7.80 (m, 2H) 7.31 (m, 2H), 5.74 (dd, *J*=15.6, 4.5 Hz, 1H), 5.60 (dt, *J*=15.6, 6.4 Hz, 1H), 4.52 (d, *J*=6.4 Hz, 2H), 4.25 (m, 1H), 2.44 (s, 3H), 1.14 (d, *J*=6.4 Hz, 3H), 0.86 (s, 9H), 0.01 (s, 3H), −0.002 (s, 3H).

4.9. (2E,4S)-4-[(Benzyl)oxy]-2-penten-1-yl p-toluensulfonate **7b**

The conversion (95%) was estimated by ^{1}H NMR. ^{1}H NMR ($CDCl_3$) δ 7.80 (m, 2H), 7.34–7.26 (m, 7H), 5.69 (m, 2H), 4.55 (d, *J*=5.0 Hz, 2H), 4.47 (AB, *J*=11.8 Hz, 1H), 4.33 (AB, *J*=11.8 Hz, 1H), 3.91 (m, 1H), 2.43 (s, 3H), 1.21 (d, *J*=6.6 Hz, 3H).

4.10. General procedure for the alkylation of ethyl acetoacetate with **7a**,**b**

To a dry THF solution (4 mL) of ethyl acetoacetate (1.27 ml, 10 mmol) under an argon atmosphere, was added $LiOH\cdot H_2O$ (420 mg, 10 mmol) and the mixture was stirred at 50°C for 15 min. Then the crude mixture of **7a**,**b** (~10 mmol) dissolved in 2 mL of dry THF was added and stirring was prolonged for about 24 h. The reaction solution was concentrated in vacuo to give crude **8a**,**b** extracted with diethyl ether (40 mL) followed by standard workup.

4.11. Ethyl 2-acetyl-(4E,6S)-6-[(tert-butyldimethylsilyl)oxy]-4-heptenoate **8a**

After flash chromatography of the residue, **8a** was obtained as a colorless oil (2.17 g, 66% yield). $[\alpha]_D^{26}=-3.9$ (*c* 1.20, $CHCl_3$). Ketone:enol, 10:1. Ketonic form: ^{1}H NMR ($CDCl_3$) δ 5.50 (m, 2H), 4.21 (quint, *J*=6.2 Hz, 1H), 4.19 (q, *J*=7.0 Hz, 2H), 3.46 (dt, *J*=6.8, 2.4 Hz, 1H), 2.53 (bt, *J*=6.8 Hz, 2H), 2.20 (s, 3H), 1.25 (t, *J*=7.0 Hz, 3H), 1.14 (d, *J*=6.3 Hz, 3H), 0.86 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 202.3, 169.2, 137.9, 124.0, 68.8, 61.3, 59.7, 30.6, 29.0, 25.8, 24.4, 18.2, 14.1, −4.6,

−4.8. EIMS *m/z* (rel. intensity): 271 (13), 227 (23), 197 (34), 159 (46), 75 (51), 43 (100). Anal. calcd for $C_{17}H_{32}O_4Si$: C, 62.15; H, 9.82. Found: C, 62.44; H, 10.21.

*4.12. Ethyl 2-acetyl-(4*E*,6*S*)-6-[(benzyl)oxy]-4-heptenoate **8b***

After flash chromatography of the residue, **8b** was obtained as a colorless oil (3.14 g, 73% yield). $[\alpha]_D^{21}$=−3.3 (*c* 3.00, $CHCl_3$). Ketone:enol, 10:1. Ketonic form: ^{1}H NMR ($CDCl_3$) δ 7.31 (m, 5H), 5.54 (m, 2H), 4.49 (AB, *J*=12.0 Hz, 1H), 4.32 (AB, *J*=12.0 Hz, 1H), 4.18 (q, *J*=6.3 Hz, 2H), 3.86 (quint, *J*=7.0 Hz, 1H), 3.50 (dt, *J*=7.0, 2.6 Hz, 1H), 2.60 (m, 2H), 2.23 (s, 3H), 1.27 (t, *J*=7.0 Hz, 3H), 1.24 (d, *J*=6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 202.1, 169.1, 138.7, 135.1, 128.3, 127.9, 127.5, 127.3, 75.2, 69.7, 61.3, 59.5, 30.6, 28.9, 21.5, 14.1. EIMS *m/z* (rel. intensity): 175 (3), 126 (11), 91 (100), 65 (5), 43 (79). Anal. calcd for $C_{18}H_{24}O_4$: C, 71.03; H, 7.95. Found: C, 71.29; H, 8.20.

*4.13. General procedure of iodoenoletherification of compounds **8a**,**b***

To a dry CH_2Cl_2 (5 mL) solution of **8a**,**b** (2 mmol), under an argon atmosphere (at −25°C for **8a** and −5°C for **8b**), were added anhydrous Na_2CO_3 (0.42 g, 4 mmol) and dropwise in 45 min a solution of I_2 (1.0 g, 4 mmol) dissolved in dry CH_2Cl_2 (45 mL). The mixture was stirred for 15 h (**8a**) and 2 days (**8b**). Then 0.1N $Na_2S_2O_3$ solution (10 mL) was added and the resulting mixture was stirred until decoloration of the organic phase. Then the mixture was diluted with water (30 mL) and extracted with CH_2Cl_2 (3×40 mL) followed by standard workup.

*4.14. 5-[(2*S*)-2-(*tert*-Butyldimethylsilyl)oxy-1-iodopropyl]-2-methyl-3-ethoxycarbonyl-4,5-dihydrofuran (5*R*,1*S*,2*S*/5*S*,1*R*,2*S*) **9a***

After flash chromatography of the residue, **9a** was obtained as a pale yellow oil of an unseparable mixture of diastereoisomers (dr 86/14), (0.5 g, 55% yield). Major diastereoisomer: ^{1}H NMR ($CDCl_3$) δ 4.79 (ddd, *J*=10.8, 9.6, 8.0 Hz, 1H), 4.16 (q, *J*=7.1 Hz, 2H), 4.03 (dd, *J*=9.6, 2.0 Hz, 1H), 3.46 (dq, *J*=6.2, 2.0 Hz, 1H), 3.09 (ddq, *J*=14.8, 10.8, 1.6 Hz, 1H), 2.79 (ddq, *J*=14.8, 8.0, 1.6 Hz, 1H), 2.15 (t, *J*=1.6 Hz, 3H), 1.27 (t, *J*=7.1 Hz, 3H), 1.18 (d, *J*=6.2 Hz, 3H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 167.0, 165.8, 101.7, 81.9, 65.6, 59.5, 50.2, 37.3, 25.7, 25.0, 22.4, 18.0, 14.4, −4.0, −5.0. EIMS *m/z* (rel. intensity): 397 (43), 270 (10), 215 (75), 195 (67), 127 (20), 73 (53), 43 (100). Minor diastereoisomer: ^{1}H NMR ($CDCl_3$) δ 4.58 (ddd, *J*=10.8, 8.0, 7.6 Hz, 1H), 4.26 (dd, *J*=7.6, 5.7 Hz, 1H), 4.15 (q, *J*=7.1 Hz, 2H), 3.67 (quint, *J*=5.7 Hz, 1H), 3.02 (ddq, *J*=14.8, 10.8, 1.6 Hz, 1H), 2.79 (ddq, overlap), 2.16 (t, *J*=1.6 Hz, 3H), 1.27 (t, *J*=7.1 Hz, 3H), 1.20 (d, *J*=6.0 Hz, 3H), 0.89 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 166.9, 165.7, 101.9, 81.6, 68.2, 59.4, 49.0, 36.6, 25.8, 25.0, 22.6, 19.7, 14.1, −4.2, −4.8. EIMS *m/z* (rel. intensity): 397 (10), 215 (17), 195 (56), 155 (100), 127 (35), 75 (74), 43 (54). Anal. calcd for $C_{17}H_{31}O_4SiI$: C, 44.92; H, 6.88. Found: C, 45.23; H, 7.09.

*4.15. 5-[(2*S*)-2-(Benzyl)oxy-1-iodopropyl]-2-methyl-3-ethoxycarbonyl-4,5-dihydrofuran (5*R*,1*S*,2*S*/5*S*,1*R*,2*S*) **9b***

After flash chromatography of the residue, **9b** was obtained as a pale yellow oil of an unseparable mixture of diastereoisomers (dr 73/27), (0.63 g, 74% yield). Major diastereoisomer: ^{1}H NMR ($CDCl_3$) δ 4.87 (ddd, *J*=10.2, 9.1, 7.9 Hz, 1H), 4.69 (AB, *J*=12.0 Hz, 1H), 4.55 (AB, *J*=12.0 Hz, 1H), 4.15 (q, *J*=7.1 Hz, 2H), 4.12 (dd, *J*=9.1, 2.4 Hz, 1H), 3.32 (dq, *J*=6.1, 2.4 Hz, 1H), 3.09 (ddq, *J*=14.9, 10.2, 1.3

Hz, 1H), 2.82 (ddq, *J*=14.9, 7.9, 1.3 Hz, 1H), 2.12 (t, *J*=1.3 Hz, 3H), 1.29 (d, *J*=6.1 Hz, 3H), 1.26 (t, *J*=7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 167.0, 165.9, 137.9, 128.3, 127.8, 127.7, 101.9, 81.9, 72.0, 70.7, 59.5, 46.4, 36.6, 20.6, 14.5, 14.1. EIMS *m/z* (rel. intensity): 385 (4), 197 (41), 167 (18), 149 (20), 107 (12), 91 (100), 65 (17), 43 (63). Minor diastereoisomer: ^{1}H NMR ($CDCl_3$) δ 4.67 (AB, *J*=12.0 Hz, 1H), 4.65 (ddd, *J*=10.4, 8.4, 7.4 Hz, 1H), 4.50 (AB, *J*=12.0 Hz, 1H), 4.44 (dd, *J*=7.4, 5.8 Hz, 1H), 4.15 (q, *J*=7.1 Hz, 2H), 3.40 (quint, *J*=5.8 Hz, 1H), 3.00 (ddq, *J*=15.1, 10.4, 1.3 Hz, 1H), 2.77 (ddq, overlap), 2.14 (t, *J*=1.3 Hz, 3H), 1.35 (d, *J*=6.1 Hz, 3H), 1.27 (t, *J*=7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 166.9, 165.8, 138.3, 128.4, 127.8, 127.6, 102.0, 81.7, 73.9, 65.3, 59.5, 44.9, 37.3, 18.7, 14.5, 14.0. EIMS *m/z* (rel. intensity): 431 (M^++1, 2), 197 (28), 167 (21), 149 (39), 107 (11), 91 (100), 77 (13), 43 (66). Anal. calcd for $C_{18}H_{23}O_4I$: C, 50.25; H, 5.39. Found: C, 50.47; H, 5.61.

*4.16. (±)-2-Methyl-5-(*E*)-propenyl-3-ethoxycarbonyl-4,5-dihydrofuran **10***

After flash chromatography of the residue of iodoenoletherification, (±)-**10** was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 5.75 (dq, *J*=15.6, 6.4 Hz, 1H), 5.56 (ddq, *J*=15.6, 8.0, 1.3 Hz, 1H), 4.96 (ddd, *J*=10.2, 8.5, 8.00 Hz, 1H), 4.14 (q, *J*=7.1 Hz, 2H), 3.00 (ddq, *J*=14.7, 10.2, 1.4 Hz, 1H), 2.62 (ddq, *J*=14.7, 8.5, 1.4 Hz, 1H), 2.16 (t, *J*=1.4 Hz, 3H), 1.71 (dd, *J*=6.4, 1.3 Hz, 3H), 1.25 (t, *J*=7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 167.4, 166.1, 130.0, 129.5, 101.7, 82.8, 59.3, 35.7, 17.5, 14.4, 14.0. EIMS *m/z* (rel. intensity): 197 (M^++1, 100), 196 (54), 151 (16), 135 (7), 107 (5). Anal. calcd for $C_{11}H_{16}O_3$: C, 67.31; H, 8.22. Found: C, 67.59; H, 8.50.

*4.17. General procedure for elimination of HI with DBU on **9a**,**b***

To a benzene solution (8 mL) of a diastereoisomeric mixture of **9a**,**b** (1 mmol) was added dropwise (0.46 mL, 3 mmol) DBU. The reaction was stirred at 60°C for 2 days. The reaction solution was diluted with diethyl ether (70 mL), water was added then extraction was followed by standard workup.

*4.18. 5-[(2*S*,3*E*)-2-(*tert*-Butyldimethylsilyl)oxypropylidene]-2-methyl-3-ethoxycarbonyl-4,5-dihydrofuran **11a***

After flash chromatography of the residue, **11a** was obtained as a colorless oil (284 mg, 87% yield). $[\alpha]_D^{23}$=+74.9 (*c* 0.98, $CHCl_3$); ^{1}H NMR (C_6D_6) δ 5.30 (dt, *J*=8.6, 3.1 Hz, 1H), 4.21 (dq, *J*=8.6, 6.3 Hz, 1H), 4.01 (q, *J*=7.1 Hz, 2H), 3.60 (ABX_3, *J*=20.8, 3.1 Hz, 1H), 3.41 (ABX_3, *J*=20.8, 3.1 Hz, 1H), 2.07 (t, *J*=1.7 Hz, 3H), 1.18 (d, *J*=6.3 Hz, 3H), 1.01 (t, *J*=7.1 Hz, 3H), 0.95 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (C_6D_6) δ 166.1, 164.5, 153.6, 108.4, 104.4, 66.8, 60.0, 32.5, 26.4, 25.3, 18.6, 14.8, 13.8, −3.8, −4.2. EIMS *m/z* (rel. intensity): 283 (100), 220 (65), 191 (61), 159 (10), 105 (10). Anal. calcd for $C_{17}H_{30}O_4Si$: C, 62.54; H, 9.26. Found: C, 62.21; H, 9.03.

*4.19. 5-[(2*S*,3*E*)-2-(Benzyl)oxypropylidene]-2-methyl-3-ethoxycarbonyl-4,5-dihydrofuran **11b***

After flash chromatography of the residue, **11b** was obtained as a colorless oil (212 mg, 70% yield). $[\alpha]_D^{19}$=+83.4 (*c* 1.06, $CHCl_3$); ^{1}H NMR (C_6D_6) δ 7.31–7.07 (m, 5H), 5.16 (dt, *J*=9.4, 2.9 Hz, 1H), 4.49 (AB, *J*=11.9 Hz, 1H), 4.17 (AB, *J*=11.9 Hz, 1H), 4.03 (q, *J*=7.2 Hz, 2H), 3.77 (dq, *J*=9.4, 6.2 Hz, 1H), 3.40 (ABX_3, *J*=20.9, 2.8 Hz, 1H), 3.27 (ABX_3, *J*=20.9, 2.8 Hz, 1H), 2.11 (t, *J*=1.9 Hz, 3H), 1.22 (d, *J*=6.2 Hz, 3H), 1.01 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (C_6D_6) δ 165.9, 164.4, 156.2, 139.9, 128.8, 128.1, 127.8, 105.1, 104.5, 72.2, 70.1, 60.0, 32.6, 22.2, 14.8, 13.7. EIMS *m/z* (rel. intensity): 194 (100), 165

(50), 123 (18), 108 (19), 91 (77), 79 (34), 57 (32). Anal. calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.23; H, 7.05.

*4.20. General procedure of radical oxidation of **11a**,**b***

To a benzene solution (18 mL) of **11a**,**b** (0.5 mmol) was added AIBN portionwise (16 mg, 0.1 mmol). The mixture was stirred under O_2 bubbling at 50°C for about 36 h for **11b** and 2 days for **11a**. Then removal of solvent in vacuo afforded the crude residue.

*4.21. 5-[(2*S*,1*S*)-2-(*tert*-Butyldimethylsilyl)oxy-1-hydroperoxypropyl]-2-methyl-3-ethoxycarbonyl furan **12a***

After flash chromatography of the residue, **12a** was obtained as an amorphous solid (93 mg, 52% yield). $[\alpha]_D^{15}$=−2.8 (*c* 0.93, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.30 (br, 1H), 6.68 (s, 1H), 4.69 (d *J*=5.7 Hz, 1H), 4.27 (q *J*=7.1 Hz, 2H), 4.23 (m, overlap, 1H), 2.56 (s, 3H), 1.33 (t, *J*=7.1 Hz, 3H), 1.24 (d, *J*=6.2 Hz, 3H), 0.81 (s, 9H), 0.04 (s, 3H), −0.06 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 163.9, 159.0, 148.8, 114.2, 111.2, 85.1, 67.7, 60.1, 25.5, 20.5, 17.8, 14.2, 13.7, −4.6, −5.2. EIMS *m/z* (rel. intensity): 341 (18), 325 (100), 282 (70), 166 (32), 106 (43), 77 (47). Anal. calcd for $C_{17}H_{30}O_6Si$: C, 56.95; H, 8.43. Found: C, 57.20; H, 8.16.

*4.22. 5-[(2*S*,1*R*)-2-(*tert*-Butyldimethylsilyl)oxy-1-hydroperoxypropyl]-2-methyl-3-ethoxycarbonyl furan **13a***

After flash chromatography of the residue, **13a** was obtained as a colorless oil (23 mg, 13% yield). $[\alpha]_D^{18}$=+41.1 (*c* 0.39, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.99 (br, 1H), 6.63 (s, 1H), 4.73 (d, *J*=7.9 Hz, 1H), 4.27 (q, *J*=7.1 Hz, 2H), 4.23 (m, overlap, 1H), 2.56 (s, 3H), 1.33 (t, *J*=7.1 Hz, 3H), 1.08 (d, *J*=6.4 Hz, 3H), 0.91 (s, 9H), 0.15 (s, 3H), 0.12 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 163.8, 159.4, 148.5, 114.3, 110.7, 85.4, 69.2, 60.2, 25.7, 20.5, 18.0, 14.3, 13.8, −4.7, −5.2. EIMS *m/z* (rel. intensity): 358 (M^+, 65), 364 (28), 204 (100), 95 (44), 80 (21). Anal. calcd for $C_{17}H_{30}O_6Si$: C, 56.95; H, 8.43. Found: C, 57.26; H, 8.18.

*4.23. 5-[(2*S*,1*S*)-2-(Benzyl)oxy-1-hydroperoxypropyl]-2-methyl-3-ethoxycarbonyl furan **12b***

After flash chromatography of the residue, **12b** was obtained as a colorless oil (66 mg, 40% yield). $[\alpha]_D^{17}$=−2.5 (*c* 0.40, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.31 (br, 1H), 7.31 (m, 5H), 6.72 (s, 1H), 4.86 (d, *J*=5.3 Hz, 1H), 4.61 (AB, *J*=11.9 Hz, 1H), 4.52 (AB, *J*=11.9 Hz, 1H), 4.29 (q, *J*=7.1 Hz, 2H), 4.01 (quint, *J*=6.1 Hz, 3H), 2.56 (s, 3H), 1.34 (t, *J*=7.1 Hz, 3H), 1.29 (d, *J*=6.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 163.8, 159.2, 148.3, 138.1, 128.4, 128.3, 127.7, 114.4, 111.2, 83.8, 73.8, 71.5, 60.1, 16.5, 14.3, 13.8. EIMS *m/z* (rel. intensity): 287 (2), 261 (5), 183 (100), 153 (19), 137 (82), 79 (9), 53 (13). Anal. calcd for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63. Found: C, 64.30; H, 6.37.

*4.24. 5-[(2*S*,1*R*)-2-(Benzyl)oxy-1-hydroperoxypropyl]-2-methyl-3-ethoxycarbonyl furan **13b***

After flash chromatography of the residue, **13b** was obtained as a colorless oil (22 mg, 13% yield). $[\alpha]_D^{15}$=+35.0 (*c* 0.45, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 9.22 (br, 1H), 7.32 (m, 5H), 6.65 (s, 1H), 4.89 (d, *J*=8.4 Hz, 1H), 4.71 (AB, *J*=12.4 Hz, 1H), 4.65 (AB, *J*=12.4 Hz, 1H), 4.28 (q, *J*=7.1 Hz, 2H), 4.08 (dq, *J*=8.4, 6.2 Hz, 1H), 2.56 (s, 3H), 1.34 (t, *J*=7.1 Hz, 3H), 1.14 (d, *J*=6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$)

δ 163.7, 159.5, 148.0, 137.8, 128.5, 127.8, 127.7, 114.4, 111.1, 84.4, 75.7, 72.0, 60.2, 16.8, 14.3, 13.8. EIMS *m/z* (rel. intensity): 220 (86), 205 (100), 177 (19), 133 (16), 105 (30), 91 (33), 77 (10), 57 (79). Anal. calcd for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63. Found: C, 64.39; H, 6.42.

4.25. General procedure of reduction of furyl hydroperoxides

To a CH_2Cl_2 solution (4 mL) of **12** (**13**) (20 mg, 0.058 mmol) was added $(Ph)_3P$ (15 mg, 0.059 mmol) at room temperature. At the end of the reaction, monitored by TLC, removal of the solvent in vacuo afforded the crude residue.

*4.26. 5-[(2*S*,1*S*)-2-(*tert*-Butyldimethylsilyl)oxy-1-hydroxypropyl]-2-methyl-3-ethoxycarbonyl furan **14a***

After flash chromatography of the residue, **14a** was obtained as a colorless oil (17 mg, 89% yield). $[\alpha]_D^{18}$=+6.7 (*c* 0.57, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 6.53 (s, 1H), 4.49 (t, *J*=4.5 Hz, 1H), 4.27 (q, *J*=7.1 Hz, 2H), 4.09 (dq, *J*=6.2, 4.5 Hz, 1H), 2.55 (s, 3H), 1.57 (br, 1H), 1.33 (t, *J*=7.1 Hz, 3H), 1.12 (d, *J*=6.2 Hz, 3H), 0.87 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 164.1, 158.4, 151.7, 114.0, 108.1, 72.0, 70.5, 60.0, 25.7, 18.5, 17.9, 14.3, 13.7, −4.5, −5.0. EIMS *m/z* (rel. intensity): 325 (M^+−OH, 51), 297 (19), 165 (68), 103 (67), 73 (100). Anal. calcd for $C_{17}H_{30}O_5Si$: C, 59.62; H, 8.83. Found: C, 59.37; H, 8.62.

*4.27. 5-[(2*S*,1*R*)-2-(*tert*-Butyldimethylsilyl)oxy-1-hydroxypropyl]-2-methyl-3-ethoxycarbonyl furan **15a***

After flash chromatography of the residue, **15a** was obtained as a colorless oil (16 mg, 79% yield). $[\alpha]_D^{16}$=+38.5 (*c* 0.42, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 6.53 (s, 1H), 4.32 (t, *J*=5.4 Hz, 1H), 4.27 (q, *J*=7.1 Hz, 2H), 4.07 (quint, *J*=6.0 Hz, 3H), 2.55 (s, 3H), 1.51 (s, br), 1.33 (t, *J*=7.1 Hz, 3H), 1.15 (d, *J*=6.0 Hz, 3H), 0.88 (s, 9H), 0.07 (s, 3H), 0.00_5 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 164.0, 158.6, 152.1, 114.1, 108.3, 72.2, 70.5, 60.0, 25.7, 20.1, 17.9, 14.3, 13.7, −4.3, −5.0. EIMS *m/z* (rel. intensity): 325 (M^+−OH, 65), 297 (17), 165 (77), 103 (64), 73 (100), 57 (25). Anal. calcd for $C_{17}H_{30}O_5Si$: C, 59.62; H, 8.83. Found: C, 59.80; H, 8.99.

4.28. General procedure for preparation of MTPA esters

To a dry pyridine solution (35 μL) of **14** and **15a** (3.5 mg, 0.01 mmol) was added MTPA-Cl (5.8 μL, 0.03 mmol) and DMAP (2.3 μL, 0.02 mmol). The reaction mixture was stirred for 20 min at room temperature during which time it was monitored by TLC. The solvent was removed in vacuo and flash chromatography with benzene as eluent furnished MTPA ester.

*4.29. (*R*)-MTPA ester of 5-[(2*S*,1*S*)-2-(*tert*-butyldimethylsilyl)oxy-1-hydroxypropyl]-2-methyl-3-ethoxycarbonyl furan **14a***

Colorless oil (4.7 mg, 89% yield); ^{1}H NMR ($CDCl_3$) δ 7.45–7.30 (m, 5H), 6.48 (s, 1H), 5.80 (d, *J*=5.4 Hz, 1H), 4.27 (q, *J*=7.1 Hz, 2H), 4.26 (overlap, 1H), 3.56 (s, 3H), 2.49 (s, 3H), 1.34 (t, *J*=7.1 Hz, 3H), 1.22 (d, *J*=6.1 Hz, 3H), 0.81 (s, 9H), 0.04 (s, 3H), −0.07 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.6, 163.7, 159.0, 147.4, 132.2, 129.5, 128.2, 127.3, 114.1, 110.6, 74.6, 68.3, 60.1, 55.6, 25.5, 19.3, 17.8, 14.3, 13.6, −4.7, −5.3.

*4.30. (S)-MTPA ester of 5-[(2S,1S)-2-(*tert*-butyldimethylsilyl)oxy-1-hydroxypropyl]-2-methyl-3-ethoxycarbonyl furan* ***14a***

Colorless oil (3.9 mg, 73% yield); ^{1}H NMR ($CDCl_3$) δ 7.46–7.30 (m, 5H), 6.67 (s, 1H), 5.71 (d, *J*=6.3 Hz, 1H), 4.27 (q, *J*=7.1 Hz, 2H), 4.19 (quint, *J*=6.1 Hz, 1H), 3.45 (s, 3H), 2.55 (s, 3H), 1.34 (t, *J*=7.1 Hz, 3H), 1.08 (d, *J*=6.1 Hz, 3H), 0.77 (s, 9H), −0.02 (s, 3H), −0.17 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.5, 163.7, 159.0, 147.6, 132.2, 129.8, 128.2, 127.3, 114.3, 111.6, 74.3, 68.1, 60.2, 55.4, 25.4, 19.9, 17.7, 14.2, 13.6, −4.7, −5.5.

*4.31. (R)-MTPA ester of 5-[(2S,1R)-2-(*tert*-butyldimethylsilyl)oxy-1-hydroxypropyl]-2-methyl-3-ethoxycarbonyl furan* ***15a***

Colorless oil (5.0 mg, 94% yield); ^{1}H NMR ($CDCl_3$) δ 7.50–7.31 (m, 5H), 6.61 (s, 1H), 5.72 (d, *J*=6.2 Hz, 1H), 4.26 (q, *J*=7.1 Hz, 2H), 4.22 (quint, *J*=6.2 Hz, 1H), 3.50 (s, 3H), 2.55 (s, 3H), 1.34 (t, *J*=7.1 Hz, 2H), 1.04 (d, *J*=6.2 Hz, 3H), 0.79 (s, 9H), 0.01 (s, 3H), −0.13 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.9, 163.7, 159.1, 147.4, 132.1, 129.5, 128.3, 127.3, 114.3, 111.1, 74.9, 67.8, 60.2, 55.4, 25.6, 19.5, 17.8, 14.3, 13.7, −4.7, −5.1.

*4.32. (S)-MTPA ester of 5-[(2S,1R)-2-(*tert*-butyldimethylsilyl)oxy-1-hydroxypropyl]-2-methyl-3-ethoxycarbonyl furan* ***15a***

Colorless oil (3.5 mg, 66% yield); ^{1}H NMR ($CDCl_3$) δ 7.45–7.25 (m, 5H), 6.51 (s, 1H), 5.71 (d, *J*=6.2 Hz, 1H), 4.27 (q, *J*=7.1 Hz, 2H), 4.23 (m, overlap), 3.51 (s, 3H), 2.50 (s, 3H), 1.34 (t, *J*=7.1 Hz, 3H), 1.09 (d, *J*=6.2 Hz, 3H), 0.85 (s, 9H), 0.04 (s, 3H), −0.01 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.9, 163.7, 159.0, 147.4, 131.8, 129.5, 128.2, 127.5, 114.1, 110.7, 75.2, 68.0, 60.1, 55.5, 25.6, 19.8, 17.9, 14.3, 13.6, −4.6, −4.9.

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