Monatshefte für Chemie 138, 121–129 (2007)
DOI 10.1007/s00706-006-0578-x
Printed in The Netherlands

Monatshefte für Chemie
Chemical Monthly

Radical Couplings as Key Steps for the Preparation of Derivatives of Nonactic Acid

François Loiseau, Jean-Mary Simone, David Carcache, Pavel Bobal, and **Reinhard Neier***

Institute of Chemistry, University of Neuchâtel, Neuchâtel, Switzerland

Received July 12, 2006; accepted (revised) July 21, 2006; published online January 19, 2007

Summary. Free radical couplings from furan, as cheap starting material, were studied in view of developing a rapid strategy *en route* to the synthesis of derivatives of nonactin. The chain containing the alcohol function was introduced in one or two steps in 86% yield. For the introduction of the second chain with the ester function two different coupling methods were tested. Starting from the advanced intermediates obtained nonactin derivatives can be prepared by catalytic hydrogenation of the furan ring.

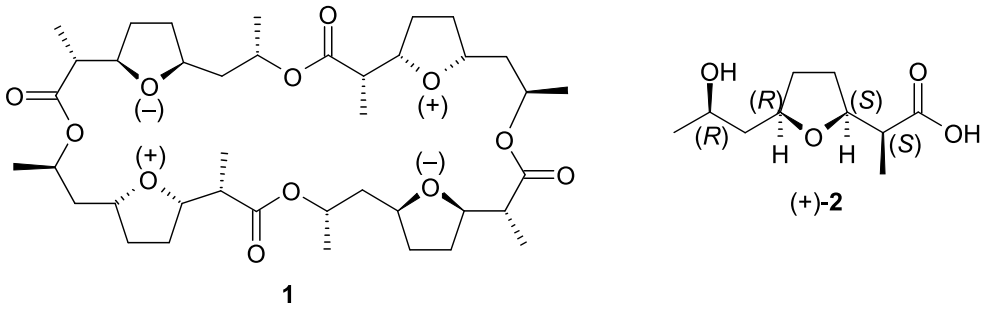
Keywords. Heterocycles; Radical couplings; Natural products; Nonactic acid.

Introduction

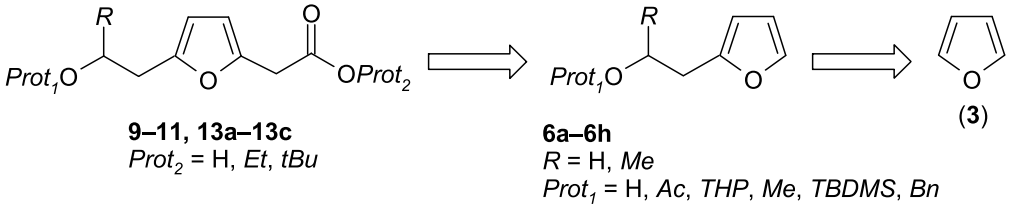
Furan and tetrahydrofuran rings are present as a significant structural element in many natural products. They have been used as essential building blocks in the construction of important synthetic targets. Furan (**3**) has attracted the interest of chemists for well over a century [1], reflecting the importance of this heterocycle in natural and synthetic substances [2]. The stereoselective substitution of furans has been extensively studied. Nonactin (**1**), an ionophore isolated from natural sources, has raised interest as well as in its use as antibiotic as in its use in ion selective electrodes. The capacity of **1** to mediate selectively ammonium and potassium transport is the predominant property of this macrotetralide [3]. First reported in 1955 [4], **1** is isolated from *Streptomyces* cultures and is the lowest homologue of the nactin family. Structurally, nonactin (**1**) consist of four nonactic acids (**2**) (Scheme 1) condensed in a (+)(−)(+)(−) atypical fashion which confers S_4 symmetry (*meso* compound). To our knowledge, around 30 syntheses of nonactate derivatives and their 8-epimers have been described so far [5]. These compounds represent good candidates to test the stereospecificity of modern synthesis methodology. In all the cases, delicate chromatographies are required in the latter stages of the syntheses. There are six total syntheses of **1** in literature [6]. Difficulties to produce enantiopure (+) and (−)-nonactic acids (**2**) separately and the problems associated with the assembly of the enantiomers have prevented syntheses to compete successfully with fermentation [7]. Consequently, **1** is expensive and not available in more than gram quantities.

Analysing the particular structure of nonactin the following question arises: Why did nature invests such efforts to create **1**, a 32-membered ring with 16 stereogenic centers if the result is an achiral molecule? As part of our ongoing studies on the macrocycle **1**, we plan to develop a new, short, and scalable route to generate 2,5-disubstituted furans (Scheme 2). These 2,5-disubstituted furans are precursors of nonactic acid derivatives through catalytic *cis*-hydrogenation of the furan rings.

* Corresponding author. E-mail: reinhard.neier@unine.ch



Scheme 1



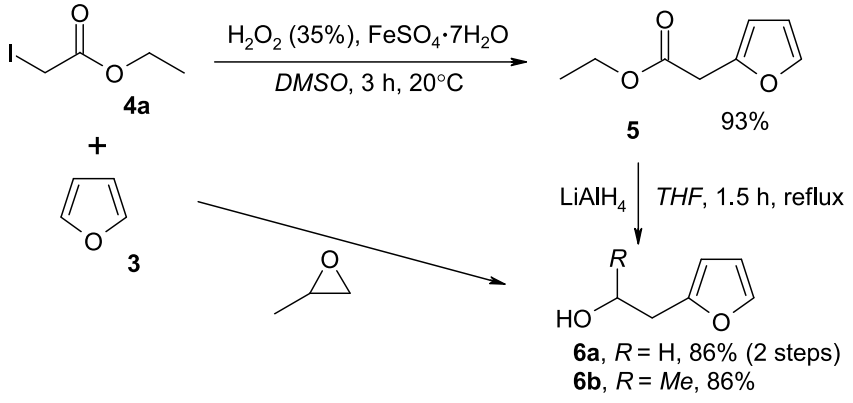
Scheme 2

Results and Discussion

Since our synthetic strategy has to be scalable and cheap, we chose furan (**3**) as starting material. We first introduced one lateral chain leading to alcohols **6a** and **6b** (Scheme 3). Heavy-metal-free radical coupling with an excess of **3** with ethyl 2-iodoethanoate (**4a**) according to *Baciocchi* conditions [8] led to ethyl 2-(furan-2-yl)acetate (**5**) in almost quantitative yield. Reduction of **5** gave 2-(furan-2-yl)ethanol (**6a**) in 93% yield without further purification. Reaction of 2-furyllithium with propylene oxide at 0°C is described in the literature to give 1-(furan-2-yl)propan-2-ol (**6b**) in good yield in *THF* [9] as solvent. However, we obtained low yields under these reported conditions but the reaction in diethyl ether [10] at 10°C gave **6b** in 86% yield (Table 1). Both radical and anionic couplings are regioselective in the 2-position of furan (**3**).

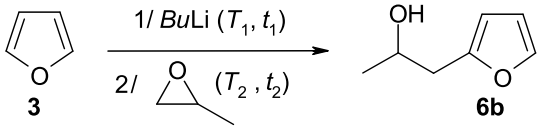
Before introducing the lateral chain in the fifth position of our 2-subtituted furans **6a** and **6b**, we have studied the protection of the alcohol function (Table 2). Different protecting groups were introduced, in 62–99% yields. The different protecting groups of **6c**–**6h** will give us a choice in order to adapt the intermediates and their stabilities according to the synthetic strategies used in the further steps of our syntheses.

For the introduction of the second chain, we were tempted to use the radical coupling with ethyl 2-iodoethanoate (**4a**) according to *Baciocchi* condi-



Scheme 3

Table 1. Optimized reaction of 2-furyllithium with propylene oxide



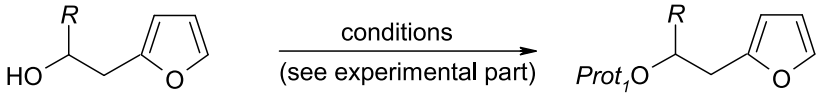
Solvent	T_1/°C	t_1/h	T_2/°C	t_2/h	Yield/%
THF	0	2.5	−5, 12	2	36
THF	−2	1.5	0, 12	1, 1	55
THF	0	1.25	0, 12	1, 1	26
THF	0, 20	1, 0.5	0, 12	1, 1	32
Et_2O	10, 20	1, 3	5–20	3	86

tions a second time. A large excess of 18 equivalents is necessary to avoid dialkylation in the transformation of **3** to **5**. The product **5** is isolated in almost quantitative yield, in the presence of traces of *DMSO*. Using sylvan (**7**) on 10 g scale, the yield in **8a** is 65% after filtration over silica gel with 19 equivalents of **7** as well as with 10 equivalents (Table 3). Using **7** on 100 g scale didn't decrease much the yield in **8a**, which was 59%. The reaction is also efficient with ethyl 2-iodopropanoate (**4b**), which is suitable to introduce a methyl group in α-position as in nonactic acid (**2**). We then started to decrease the excess of **7**. We could show that the excess of the heterocycle is necessary to ensure total conversion of the iodoester. Only 2 equivalents of **7** were required to obtain acceptable 53% yield on 2 g scale.

Less than 10% of unreacted iodoester **4a** or **4b** remained. To remove the unreacted iodoesters the following procedure was applied. The mixture of the furan derivatives and iodoester was refluxed in dry *n*-hexane in the presence of activated zinc. Under these conditions the *Reformatsky* enolate [11] of the iodoester was created. Subsequent acidic hydrolysis led to the volatile ethyl acetate or ethyl propionate, which could be removed by evaporation (Scheme 4). The heat-sensitivity of furans led to the loss of about 20% of the product when applying the conditions necessary for the formation of the *Reformatsky* enolate.

The *Baciocchi* reaction was then tried starting from our previously synthesized 2-substituted furans. To our delight, the radical coupling reaction works with 2 equivalents of the benzyl protected furan **6e**

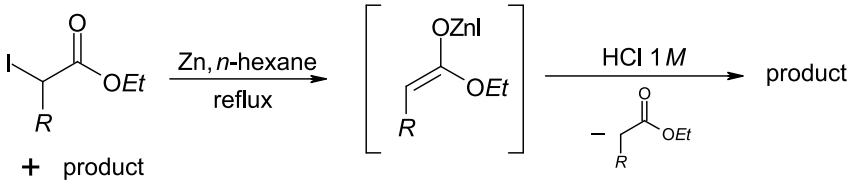
Table 2. Protection of alcohol function



6a, *R* = H
6b, *R* = *Me*

6c–6h
R = H, *Me*
$Prot_1$ = *Ac*, *THP*, *Me*, *TBDMS*, *Bn*

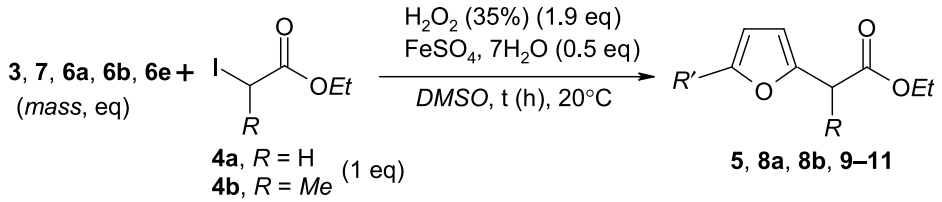
6	$Prot_1$	*R*	Yield/%
c	*Ac*	H	64
d	*THP*	H	89
e	*Bn*	H	82
f	*Bn*	*Me*	99
g	*Me*	H	94
h	*TBDMS*	H	62



+ product

Scheme 4

Table 3. Radical couplings under *Baciocchi* conditions



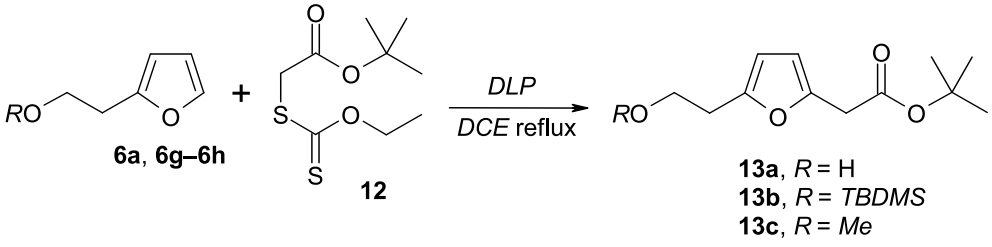
Reagent	*mass*/g; eq	*R*	*t*/h	Conversion[a] (Yield/%)[b]
3	20; 18	H	4	–(93)[c] **5**
7	10; 19	H	5	–(65)[d] **8a**
7	10; 10	H	6	–(65)[d] **8a**
7	100; 19	H	7	–(59)[d] **8a**
7	45; 10	*Me*	16	–(54)[d] **8b**
7	2; 2	H	19	–(53)[d] **8a**
6e	0.2; 2	H	30	–(53)[d] **9**
6e	0.1; 1	H	14	–(14)[d] **9**
6a	1.48; 2	H	21	50 (71)[e] **10**
6b	0.38; 2	H	22	50 (64)[d] **11**
6b	0.06; 1	H	2	100 (0)[f] –

[a] Conversion based on the starting aromatic heterocycle, according to ^{1}H NMR; [b] isolated yield, based on ICH*R*CO$_2$*Et*; [c] isolated without chromatography, with traces of *DMSO*; [d] isolated by chromatography; [e] isolated without chromatography, after distillation of the excess of **6a**; [f] the mixture was warmed to 70°C

and the free alcohols **6a** and **6b**. Using stoechiometric quantities of our 2-substituted furan **6e** we did not obtain complete conversion to the corresponding iodoesters. More dramatically the yield in **9** decreased to an unacceptable 14%. Attempts to push the reaction to completion by heating the reaction mixture to 70°C led to the degradation of the furan derivatives. We could show that the reaction works with free iodoacids using *DMSO* as a solvent. The isolation of the polar product was experimentally very difficult.

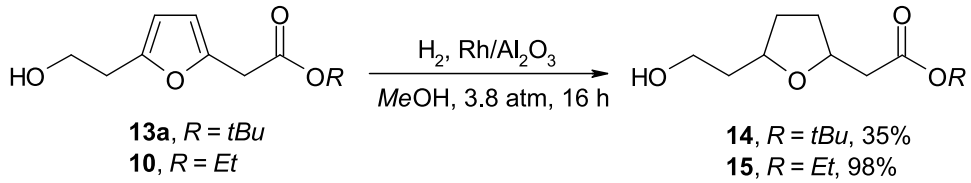
To obtain better conversions, we tested a tin-free radical coupling methodology developed few years ago by *Miranda* [13], following *Zard* xanthate (such as *tert*-butyl ethoxythiocarbonylsulfanylacetate (**12**)) based radical chemistry [14]. According

Table 4. Radical coupling with xanthate **12**



13	*R*	addition *t*/h	Recovered material Yield/%	Yield/%
a	H	1.25	**6a**, 50	18
a	H	4.5	**6a**, 10	32
a	H	5.5[a]	**6a**, 16	42
b	*TBDMS*	5.5	**6h**, 23	44
c	*Me*	6.5	–	61

[a] With only 0.87 equivalent of xanthate **12** and *DLP*



13a, *R* = *tBu*
10, *R* = *Et*

14, *R* = *tBu*, 35%
15, *R* = *Et*, 98%

Scheme 5

to the reaction mechanism, one equivalent of initiator dilauroyl peroxide (*DLP*) is necessary. In this case, **6e** is not suitable since the phenyl ring can compete with the furan. Attempts to completely remove *DLP* derivatives as their barium salts or by filtration using basic alumina failed. Chromatographic purification was required accompanied by a considerable loss of product. During chromatography the non polar xanthate derivatives (mainly dithiocarbonic acid *O*-ethyl-*S*-undecyl ester) are removed first. The polar *DLP* derivatives are eluted later. The use of the lighter benzoyl peroxide instead of *DLP* allowed easier purification, but it gave slightly lower conversions.

The percentage of conversion can be increased by slow portionwise addition of the peroxide while refluxing the reaction mixture using 1,2-dichloroethane (*DCE*) as solvent. The addition time reported is 12 hours. *Miranda* used 1.2 equivalents of the xanthate **12** and *DLP*. In our trials we used 1 equivalent of both reagents to obtain easier purification and we optimized the reaction time (see Table 4).

Following our proposed synthetic scheme, the furan ring has to be reduced by a stereoselective *cis* hydrogenation with 5% Rh over alumina [15] in order to obtain a single diastereomer of our analogues of nonactic acid (Scheme 5). In the case of substrate **14** prepared from xanthate **12**, traces of impurities poisoned the rhodium catalyst. Therefore the furan derivative **13a** had to be subjected to the conditions of the heterogenous reduction three times in order to obtain complete conversion. Probably the impurities had to be consumed first.

Conclusion

In conclusion, 2,5-disubstituted furans and tetrahydrofurans where prepared in few steps, with only one chromatographic separation. The yields obtained for the individual steps and the overall yield for the transformation of **3** to **14** and **15** are satisfactory and allowed us to continue our investigations.

Experimental

All moisture-sensitive reactions were carried out under Ar and N_2 using oven-dried glassware. All reagents were of commercial quality if not specifically mentioned. Solvents were freshly distilled prior to use. Flash chromatography (FC): Brunschwig silica gel 60, 0.032–0.063 mm, under positive pressure. TLC: Merck precoated silica gel thin-layer sheets 60 F 254, detection by UV and treatment with basic $KMnO_4$ sol. Mp: Gallenkamp MFB-595. IR spectra: Perkin Elmer Spectrum One FT-IR, in cm^{-1}. NMR spectra: Bruker Avance-400 (400 MHz (^{1}H) and 100 MHz (^{13}C)), at rt, chemical shifts δ in ppm rel. to $CDCl_3$ (^{1}H: 7.264 ppm, ^{13}C: 77.0 ppm) as internal reference, coupling constants *J* in Hz. ESI-MS: Finnigan LCQ. HR-ESI-MS analyses of novel compounds agreed favourably with calculated values.

1-(Furan-2-yl)propan-2-ol (**6b**, $C_7H_{10}O_2$)
Freshly distilled furan (**3**) (3.27 cm^3, 45 mmol) stirred in 50 cm^3 dry diethyl ether was reacted at 10°C with *Bu*Li (1.6 *M* in *n*-hexane, 32 cm^3, 51.2 mmol). After 1 h at 10°C, the solution was warmed at 20°C for 2 h and then cooled at 5°C, propylene oxide (4 cm^3, 57 mmol) was added other 15 min. The solution was warmed to rt and stirred for 3 h, washed with saturated $NaHCO_3$ solution and extracted 3 times with diethyl ether. The combined organic layers were washed with brine and dried over $MgSO_4$. Evaporation of the solvent *in vacuo* afforded **6b** (4.89 g, 38.8 mmol, 86%). Oil; $R_f = 0.26$ (*n*-hexane/*AcOEt* = 75/25); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.36$ (dd, $J = 1.9$, 0.8 Hz, H-6), 6.33 (dd, $J = 3.2$, 1.9 Hz, H-5), 6.12 (dq, $J = 3.2$, 0.8 Hz, H-4), 4.11 (dqd, $J = 7.6$, 6.2, 4.7 Hz, H-1), 2.81 (dd, $J = 14.9$, 4.7 Hz, H-2a), 2.76 (dd, $J = 14.9$, 7.6 Hz, H-2b), 2.06 (s, OH), 1.25 (d, $J = 6.2$ Hz, H-1^1) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 153.4$, 142.0, 110.7, 107.4, 67.2 (C-1), 38.2 (C-2), 23.2 (C-1^1) ppm; EI-MS: $m/z = 126$ (25, $[M]^+$), 109 (11, $[M - OH]^+$), 83 (12, $[M + H - CO_2]^+$), 82 (100, $[M - CO_2]^+$), 81 (95, $[M - 45]^+$), 54 (8, $[M + H - CO_2C_2H_5]^+$), 53 (16, $[M - CO_2C_2H_5]^+$).

2-(Furan-2-yl)ethanol (**6a**, $C_6H_8O_2$)
Ester **5** (4.18 g, 27.13 mmol) stirred in 160 cm^3 dry *THF* was reacted at 0°C with $LiAlH_4$ (2.08 g, 58.55 mmol) added by

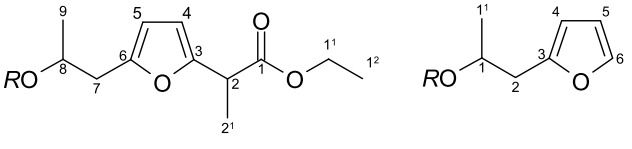


Fig. 1. Labeling used for NMR assignment

portions. The mixture was heated to reflux for 1.5 h, cooled, and hydrolysed with 90 cm^3 brine. The salts were filtered off and washed with *AcOEt*. The aqueous layer was extracted 3 times with 90 cm^3 *AcOEt* and the combined organic layers were washed with 90 cm^3 brine and dried over $MgSO_4$. Evaporation of the solvents *in vacuo* provided **6a** as a malodorous yellow oil (2.86 g, 25.56 mmol, 93%). Oil; $R_f = 0.28$ (*n*-hexane/*AcOEt* = 95/5); IR (film): $\bar{\nu} = 3368, 3118, 2956, 2928, 2079, 1736, 1598, 1507, 1469, 1422, 1374, 1341, 1241, 1210, 1146, 1079, 1047, 1002, 731\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.32$ (dd, $J = 1.9$, 0.8 Hz, H-6), 6.29 (ddt, $J = 3.1$, 1.9, 0.3 Hz, H-5), 6.08 (dq, $J = 3.1$, 0.8 Hz, H-4), 3.82 (t, $J = 6.5$ Hz, Hz, H-1), 2.86 (t, $J = 6.5$ Hz, H-2), 1.76 (s, OH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 153.4$ (C-3), 141.8 (C-6), 110.7 (C-5), 106.72 (C-4), 61.2 (C-1), 31.9 (C-2) ppm; APCI-MS: $m/z = 113$ (100, $[M + H]^+$), 95 (28, $[M + H - H_2O]^+$).

General Procedure for the Protection of the Alcohol Function [16]

A solution of **6a** (1 eq) in dry *THF* was added dropwise at 0°C to a stirred suspension of NaH (1.2–1.7 eq) in dry *THF*. After 30 min at 0°C, the electrophile (1–2 eq) was added slowly and the solution was warmed to rt for 6–16 h. The mixture was then slowly diluted with brine and extracted with diethyl ether. The organic layers were washed with brine and dried over $MgSO_4$, and the volatiles were removed by evaporation *in vacuo*.

2-(2-(Benzyloxy)ethyl)furan (**2e**, $C_{13}H_{14}O_2$)

General procedure with 9.18 g (82 mmol) **6a**, 3.31 g (138 mmol) NaH, and 9.87 cm^3 (83 mmol) benzyl bromide. Purification in reduced pressure yielded **2e** (13.5 g, 67 mmol, 82%). Oil; bp 60°C (3.10^{-2} atm), 72–75°C (5.10^{-2} atm) (Ref. [17] 100°C (4 mm Hg)); $R_f = 0.53$ (*n*-hexane/*AcOEt* = 95/5); IR (film): $\bar{\nu} = 3063, 3030, 2860, 2796, 1951, 1874, 1810, 1719, 1598, 1506, 1496, 1453, 1362, 1205, 1180, 1146, 1103, 1028, 1006, 734, 697\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.41$–7.33 (m, H-6, *Ph*), 6.34 (dd, $J = 3.1$, 1.9 Hz, H-5), 6.13 (ddt, $J = 3.1$, 1.7, 0.8 Hz, H-4), 4.59 (s, CH_2–*Ph*)); 3.77 (t, $J = 6.9$ Hz, H-1), 3.01 (t, $J = 6.9$ Hz, H-2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 153.5$ (C-3), 141.5 (C-6), 138.7, 128.8, 128.1 (*Ph*), 110.7 (C-5), 106.4 (C-4), 73.4 (CH_2–*Ph*), 68.7 (C-1), 29.3 (C-2) ppm; APCI-MS: $m/z = 203$ (100, $[M + H]^+$), 185 (85), 92 (3), 91 (55), 65 (19).

2-(2-(Benzyloxy)propyl)furan (**2f**, $C_{14}H_{16}O_2$)

General procedure with 1.33 g (10.5 mmol) **6b**, 0.87 g (18.1 mmol) NaH, and 1.3 cm^3 (10.9 mmol) benzyl bromide. Crude **2f** was obtained (2.27 g, 10.5 mmol, 99%). Oil; $R_f = 0.50$ (*n*-hexane/*AcOEt* = 75/25 + 1% *Me*OH).

2-(2-Methoxyethyl)furan (**2g**, $C_7H_{10}O_2$)

General procedure with 2.71 g (24.2 mmol) **6a**, 0.7 g (29.2 mmol) NaH, and 3 cm^3 (48.3 mmol) methyl iodide. Without further purification, **2g** (2.86 g, 22.7 mmol, 94%) was obtained. Oil; $R_f = 0.43$ (*n*-hexane/*AcOEt* = 95/5); IR (film): $\bar{\nu} = 2981, 2926, 2740, 1727, 1598, 1507, 1460, 1380, 1340, 1270, 1146, 1118, 1047, 1008, 732\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.33$ (dd, $J = 1.9$, 0.8 Hz, H-6), 6.31 (dd, $J = 3.2$, 1.9 Hz, H-5), 6.08 (dq, $J = 3.2$, 0.8 Hz, H-4), 3.66 (t, $J = 6.8$ Hz, H-1), 3.38 (s, OCH_3), 2.93 (dt, $J = 6.8$, 0.8 Hz, H-2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 153.5$ (C-3), 141.5 (C-6), 110.6 (C-5), 106.3 (C-4), 77.3 (C-1), 59.1 (OCH_3), 29.3 (C-2) ppm; APCI-MS: $m/z = 127$ (5, $[M + H]^+$), 126 (38, $[M]^+$), 95 (18, $[M - CH_3O]^+$), 94 (100), 81 (40), 53 (46).

tert-Butyl (2-(furan-2-yl)ethoxy)dimethylsilane (**2h**, $C_{12}H_{22}O_2Si$)

Following the procedure of Ref. [18]: 2-(Furan-2-yl)ethanol (**6a**) (4.5 g, 40 mmol), *DMAP* (489 mg, 4 cm^3), and *TEA* (8.35, 4 cm^3) stirred in 40 cm^3 dried CH_2Cl_2 were reacted at 5°C with a solution of *TBDMS*Cl (6.63 g, 44.0 mmol) added dropwise in 10 cm^3 of CH_2Cl_2. The solution was warmed to rt for 3 h and then diluted with CH_2Cl_2, and respectively washed with saturated $NaHCO_3$ solution and brine. The organic layer was dried over $MgSO_4$, and the CH_2Cl_2 was removed by evaporation *in vacuo*. Purification by chromatography on a silica gel column using *n*-hexane/*AcOEt* = 98/2 as an eluent afforded **2h** (5.6 g, 24.7 mmol, 62%). Oil; $R_f = 0.55$ (*n*-hexane/*AcOEt* = 98/2); IR (film): $\bar{\nu} = 2956, 2929, 2885, 2858, 1599, 1507, 1472, 1463, 1388, 1361, 1338, 1256, 1213, 1180, 1147, 1105, 1035, 1005, 969, 924, 904, 885, 837, 811, 776, 728, 680, 659, 599\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.33$ (dd, $J = 1.9$, 0.8 Hz, H-6), 6.30 (dd, $J = 3.1$, 1.9 Hz, H-5), 6.08 (dd, $J = 3.2$, 0.8 Hz, H-4), 3.88 (t, $J = 6.9$ Hz, H-1), 2.88 (t, $J = 6.9$ Hz, H-2), 0.90 (s, Si–C(CH_3)$_3$), 0.04 (s, Si–(CH_3)$_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 153.7$ (C-3), 141.3 (C-6), 110.6 (C-5), 106.5 (C-4), 62.1 (C-1), 32.3 (C-2), 26.3 (Si–C(CH_3)$_3$), 18.7 (Si–*C*(CH_3)), −5.0 (Si–(CH_3)$_2$) ppm.

2-Furan-2-ylethylacetate (**2c**, $C_8H_{10}O_3$)

Following the procedure of Ref. [16]: 2-(Furan-2-yl)ethanol (**6a**) (1 g, 9 mmol) stirred in 40 cm^3 dried CH_2Cl_2, was reacted at 0°C with pyridine (0.81 cm^3, 10 mmol) and acetyl chloride (0.71 cm^3, 10 mmol). After 1 h at 0°C, the solution was warmed to rt for 6 h, then diluted with CH_2Cl_2, and washed two times with 1 *M* HCl and with saturated $NaHCO_3$ solution. The organic layer was dried over $MgSO_4$, and the CH_2Cl_2 was removed by evaporation *in vacuo*. Purification by chromatography on a silica gel column using *n*-hexane/*AcOEt* increasing the *AcOEt* ratio afforded **2c** (0.889 mg, 5.76 mmol, 64%). Oil; $R_f = 0.50$ (*n*-hexane/*AcOEt* = 75/25); IR (film): $\bar{\nu} = 2964, 2908, 1742, 1599, 1508, 1430, 1381, 1366, 1239, 1183, 1147, 1086, 1038, 1010, 737, 601\ 599\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.32$ (dd, $J = 1.9$, 0.9 Hz, H-6), 6.29 (ddt, $J = 3.1$, 1.9, 0.4 Hz, H-5), 6.08 (dq, $J = 3.1$, 0.9 Hz, H-4), 4.31 (t, $J = 6.8$ Hz, H-1), 2.97 (td, $J = 6.9$, 0.9 Hz, H-2), 2.04 (s, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.9$ (*C*=O), 151.8 (C-3), 141.4 (C-6), 110.2 (C-5), 106.3 (C-4), 62.3 (C-1), 27.7 (C-2), 20.9 (*C*H_3) ppm.

2-(2-(Furan-2-yl)ethoxy)tetrahydro-2H-pyran (**2d**, $C_{11}H_{16}O_3$)

Following the procedure of Ref. [19]: A solution of **6a** (300 mg, 2.7 mmol) and dihydropyrane (338 mg, 4.0 mmol)

stirred in 50 cm^3 dried CH_2Cl_2 was reacted at rt with *PPTS* (67 mg, 0.3 mmol) in 20 cm^3 dried CH_2Cl_2 for 12 h. The solution was diluted with diethyl ether and washed with brine/H_2O = 1/1. The organic layer was dried over $MgSO_4$, and the CH_2Cl_2 removed by evaporation *in vacuo*. Purification by chromatography on a silica gel column using CH_2Cl_2/diethyl ether = 75/25 as an eluent afforded **2d** (469 mg, 2.39 mmol, 89%). Oil; R_f = 0.20 (CH_2Cl_2); IR (film): $\bar{\nu}$ = 2943, 2872, 1598, 1507, 1466, 1455, 1441, 1385, 1353, 1261, 1201, 1184, 1136, 1121, 1075, 1033, 1005, 973, 730, 492 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (dd, J = 1.9, 0.9 Hz, H-6), 6.28 (dd, J = 3.2, 1.9 Hz, H-5), 6.07 (dq, J = 3.2, 0.9 Hz, H-4), 4.61 (t, J = 3.5 Hz, OC*H*–O), 3.97 (dt, J = 9.7, 7.1 Hz, H-1a), 3.80 (m, 1H), 3.66 (dt, J = 9.7, 7.1 Hz, H-1b), 3.48 (m, 1H), 2.94 (t, J = 7.1 Hz, H-2), 1.85–1.46 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.2 (C-3), 140.9 (C-6), 110.2 (C-5), 105.1 (C-4), 98.7 (O*C*H–O), 65.4 (C-1), 62.1 (*C*H_2O), 30.6, 28.8, 25.4, 19.4 ppm; DCI-MS: m/z = 214 (38, $[M + H_2O]^+$), 197 (30, $[M + H]^+$), 102 (100, $[M + H_2O -$ CH_2-furyl$]^+$), 94 (30), 85 (47).

Ethyl 2-iodopropanoate (**4b**, $C_5H_9IO_2$)
A solution of NaI (15.48 g, 103.3 mmol.) and ethyl 2-bromopropanoate (17 g, 93.9 mmol) stirred in 300 cm^3 acetone was refluxed for 3 h. The mixture was cooled to rt, filtered, and acetone was removed by evaporation *in vacuo*. 100 cm^3 *n*-hexane and 100 cm^3 H_2O were added and the product was extracted with 3 × 100 cm^3 *n*-hexane. The combined organic layers were washed with 100 cm^3 brine, dried over Na_2SO_4, and the volatiles were removed by evaporation *in vacuo* to afford **4b** (20.2 g (86 mmol, 94%). Oil; R_f = 0.06 (*n*-hexane/*AcOEt* = 95/5); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.49 (q, J = 7.0 Hz, H-2), 4.26 (dq, J = 11.5, 7.1 Hz, H-1^{1a}), 4.22 (dq, J = 11.5, 7.1 Hz, H-1^{1b}), 1.98 (d, J = 7.0 Hz, H-3), 1.31 (t, J = 7.1 Hz, H-1^2).

General Procedure for the Radical Coupling in Baciocchi Conditions
To a stirred mixture of the aromatic heterocycle (1–20 eq, see Table 3, commercials furan (**3**) and sylvan (**7**) were freshly distilled), the alkyl iodide (1 eq), and $FeSO_4 \cdot 7H_2O$ (0.5 eq) in *DMSO*, 1.9 eq H_2O_2 (35% in H_2O) were added dropwise, while the solution was kept at rt with a H_2O bath. The mixture was then slowly diluted with brine and extracted with diethyl ether. The organic layers were washed with brine, dried over $MgSO_4$, and the volatiles were removed by evaporation *in vacuo*. If necessary, the residue was purified by chromatography on a silica gel column using *n*-hexane/*AcOEt* or CH_2Cl_2 as an eluent.

Ethyl 2-(furan-2-yl)acetate (**5**, $C_8H_{10}O_3$)
Oil; R_f = 0.41 (CH_2Cl_2); IR (film): $\bar{\nu}$ = 2984, 2940, 2908, 1741, 1603, 1507, 1478, 1466, 1448, 1392, 1369, 1338, 1301, 1272, 1229, 1185, 1157, 1097, 1075, 1031, 1013, 951, 737, 601 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (dd, J = 1.8, 0.9 Hz, H-6), 6.35 (dd, J = 3.2, 1.8 Hz, H-5), 6.23 (dq, J = 3.2, 0.8 Hz, H-4), 4.20 (q, J = 7.1 Hz, H-1^1), 3.69 (s, H-2), 1.28 (t, J = 7.2 Hz, H-1^2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.4 (C-1), 147.7 (C-3), 142.0 (C-6), 110.5 (C-5), 107.9 (C-4), 61.1 (C-1^1), 34.1 (C-2)), 14.1 (C-1^2) ppm; EI-MS: m/z = 154 (44, $[M]^+$), 153 (95), 125 (27, $[M - C_2H_5]^+$), 97 (61), 86 (30), 84 (55), 83 (61), 82 (28), 81 (100, $[M - CO_2Et]^+$), 69 (32), 55 (30), 49 (57).

Ethyl 2-(5-methylfuran-2-yl)acetate (**8a**, $C_9H_{12}O_3$)
Oil; R_f = 0.28 (*n*-hexane/*AcOEt* = 95/5); IR (film): $\bar{\nu}$ = 2984, 2925, 1742, 1620, 1603, 1570, 1448, 1335, 1310, 1266, 1220, 1180, 1142, 1032, 1022, 998, 972, 956, 939, 913, 785, 700, 646, 573 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.10 (m, J = 3.1 Hz, H-4), 5.91 (m, J = 3.1 Hz, H-5), 4.17 (q, J = 7.1 Hz, H-1^1), 3.61 (*s*, H-2), 2.22 (*s*, H-7), 1.26 (*t*, J = 7.1 Hz, H-1^2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.1 (C-1), 152.0 , 146.0 (C-3, C-6), 109.0 (C-5), 107.7 (C-4), 61.5 (C-1^1), 34.6 (C-2), 14.5 (C-1^2), 13.9 (C-7) ppm; ESI-MS: m/z = 191 (100, $[M + Na]^+$).

Ethyl 2-(5-methylfuran-2-yl)propanoate (**8b**, $C_{10}H_{14}O_3$)
Reaction with freshly prepared or freshly distilled ethyl 2-iodopropanoate (**4b**). Oil; R_f = 0.21 (*n*-hexane/*AcOEt* = 95/5); IR (film): $\bar{\nu}$ = 3108, 2985, 2941, 1739, 1614, 1566, 1455, 1377, 1322, 1250, 1202, 1160, 1073, 1023, 955, 940, 861, 784, 712 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.07 (dd, J = 3.1, 0.3 Hz, H-4), 5.91 (dq, J = 3.1, 1.0 Hz, H-5), 4.19 (q, J = 7.1 Hz, H-1^1), 3.77 (q, J = 7.3 Hz, H-2), 2.28 (d, J = 1.0 Hz; H-7), 1.24 (d, J = 7.3 Hz, H-2^1), 1.28 (t, J = 7.1 Hz, H-1^2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.3 (C-1), 152.0 , 151.7 (C-3, C-6), 106.9 (C-4), 106.5 (C-5), 61.4 (C-1^1), 39.9 (C-2), 16.2 (C-2^1), 14.5 (C-1^2), 13.9 (C-7) ppm; ESI-MS: m/z = 205 (100, $[M + Na]^+$), 101 [M-82 (sylvan)]$^+$).

Ethyl 2-(5-(2-hydroxypropyl)furan-2-yl)acetate (**11**, $C_{11}H_{16}O_4$)
Oil; R_f = 0.13 (*n*-hexane/*AcOEt* = 75/25); IR (film): $\bar{\nu}$ = 3444, 2977, 2932, 1739*s*, 1644, 1615, 1565, 1448, 1401, 1371, 1301, 1268, 1233, 1183, 1030, 1015, 975, 940, 878, 844, 788, 686, 624, 577, 471 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.15 (d, J = 3.1 Hz, H-4), 6.07 (d, J = 3.1 Hz, H-5) 4.19 (q, J = 7.2 Hz, H-1^1), 4.17 (dqd, J = 7.6, 6.2 Hz, 4.7 Hz, H-8), 3.66 (s, H-2), 2.98 (dd, J = 14.9, 4.7 Hz, H-7a), 2.71 (dd, J = 14.9, 7.6 Hz, H-7b), 1.86 (br, OH), 1.29 (t, J = 7.2 Hz, H-1^2), 1.25 (d, J = 6.2 Hz, H-9) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.9 (C-1), 157.2 (C-3), 152.8 (C-6), 109.0 (C-4), 108.4 (C-5), 67.2 (C-8), 61.6 (C-1^1), 38.3 (C-7), 34.6 (C-2), 23.0 (C-9), 14.6 (C-1^2) ppm; ESI-MS: m/z = 235 (52, $[M + Na]^+$), 152 (32, $[M + Na\text{-}83]^+$), 150 (100, $[M + Na\text{-}85]^+$).

Ethyl 2-(5-(2-(benzyloxy)ethyl)furan-2-yl)acetate (**9**, $C_{17}H_{20}O_4$)
Oil; R_f = 0.20 (*n*-hexane/*AcOEt* = 90/10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 – 7.28 (m, *Ph*), 6.15 (d, J = 3.1 Hz, H-4), 6.04 (d, J = 3.1 Hz, H-5), 4.56 (s, CH_2-*Ph*), 4.20 (q, J = 7.1 Hz, H-1^1), 3.74 (t, J = 6.9 Hz, H-8), 3.65 (s, H-2), 2.96 (t, J = 6.9 Hz, H-7), 1.29 (t, J = 7.1 Hz, H-1^2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.0 (*C*=O), 153.0 (C-3), 146.6 (C-6), 138.7 (1C, *Ph*), 128.8, 128.1, 128.0, (5C,

Ph), 109.0 (C-4), 107.4 (C-5), 73.4 (*C*H$_2$-*Ph*), 68.7 (C-8), 61.5 (C-1^1), 34.7 (C-2), 29.3 (C-7), 14.6 (C-1^2) ppm.

Ethyl 2-(5-(2-hydroxyethyl)furan-2-yl)acetate (**10**, $C_{10}H_{14}O_4$)

Oil; $R_f = 0.21$ (*n*-hexane/*AcOEt* = 75/25); IR (film): $\bar{\nu}$ = 3457, 2960, 2983, 2934, 1738, 1640, 1615, 1566, 1466, 1447, 1370, 1323, 1268, 1226, 1184, 1162, 1030, 971, 915, 855, 791, 686 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.14$ (d, $J = 3.1$ Hz, H-4), 6.06 (d, $J = 3.1$ Hz, H-5) 4.19 (q, $J = 7.1$ Hz, H-1^1), 3.86 (t, $J = 6.2$ Hz, H-8), 3.65 (s, H-2), 2.88 (t, $J = 6.2$ Hz, H-7), 1.83 (br, OH), 1.28 (t, $J = 7.1$ Hz, H-1^2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.0$ (C-1), 152.8 (C-3), 147.1 (C-6), 109.1 (C-4), 107.9 (C-5), 61.6 (C-1^1), 61.5 (C-8), 34.6 (C-2), 32.0 (C-7), 14.5 (C-1^2) ppm; ESI-MS: $m/z = 221$ (100, $[M + Na]^+$).

*General Procedure for the Radical Coupling with Xanthate **12***

A solution of xanthate **12** (1 eq) and the heteroatomic compound (1 eq) in dry *DCE* (2 cm^3 · mmol^{-1}) was heated at reflux, and a solution of *DLP* (1 eq) in *DCE* (0.5 cm^3 · mmol^{-1}) was added dropwise over a period of several hours. After filtration, the solvent was removed by evaporation *in vacuo* and the crude residue was purified by chromatography on a silica gel column using *n*-hexane/*AcOEt* as an eluent.

tert-Butyl 2-(5-(2-hydroxyethyl)furan-2-yl)acetate (**13a**, $C_{12}H_{18}O_4$)

General procedure with 0.5 g (4.5 mmol) **6a** over a 4.5 h period. Unreacted **6a** (0.34 mmol, 8%) was recovered, and **13a** (357 mg, 1.43 mmol, 32%) was yielded. Oil; $R_f = 0.18$ (*n*-hexane/*AcOEt* = 75/25); IR (film): $\bar{\nu}$ = 3446, 3108, 2981, 2979, 2930, 1736, 1642, 1565, 1477, 1456, 1393, 1369, 1244, 1147, 1048, 1011, 733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.12$ (d, $J = 3.1$ Hz, CH), 6.06 (d, $J = 3.1$ Hz, CH), 3.86 (t, $J = 6.4$ Hz, H-8), 3.57 (s, H-2), 2.88 (t, $J = 6.4$ Hz, H-7), 2.37 (s, OH), 1.48 (s, C(C*H*$_3$)$_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 169.3$ (C-1), 152.6 (C-3), 147.7 (C-6), 108.8 (C-4), 107.8 (C-5), 81.8 (*C*(CH$_3$)$_3$), 61.5 (C-8), 35.8 (C-2), 28.4 (C-7), 27.9 (C(*C*H$_3$)$_3$) ppm; ESI-MS: $m/z = 227$ (30, $[M + H]^+$), 226 (90, $[M]^+$), 196 (59), 140 (50), 125 (49), 108 (100), 95 (60); ESI-HR-MS: m/z $[M + Na]^+$ = calcd 249.1097, found 249.1093.

tert-Butyl 2-(5-(2-methoxyethyl)furan-2-yl)acetate (**13c**, $C_{13}H_{20}O_4$)

General procedure with 0.5 g (4.5 mmol) **6g** over a 5.5 h period. Product **13c** was yielded (568 mg, 2.36 mmol, 61%). Oil; $R_f = 0.81$ (*n*-hexane/*AcOEt* = 90/10); IR (film): $\bar{\nu}$ = 2979, 2927, 2856, 2738, 1737, 1614, 1566, 1478, 1456, 1392, 1368, 1278, 1146, 1119, 1044, 1014, 733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.10$ (d, $J = 3.1$ Hz, CH), 6.01 (d, $J = 3.1$ Hz, CH), 3.64 (t, $J = 6.9$ Hz, H-8), 3.56 (s, H-2), 3.37 (s, OC*H*$_3$), 2.89 (t, $J = 6.9$ Hz, H-7), 1.47 (s, C(C*H*$_3$)$_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 169.3$ (C-1), 152.7 (C-3), 147.3 (C-6), 108.7 (C-4), 107.2 (C-5), 81.6 (*C*(CH$_3$)$_3$), 71.1 (C-8), 59.1 (O*C*H$_3$), 35.8 (C-2), 29.2 (C-7), 28.4 (C(*C*H$_3$)$_3$) ppm; ESI-MS: $m/z = 264$ (23, $[M + Na + H]^+$), 263 (100, $[M + Na]^+$).

tert-Butyl 2-(5-(2-(tert-butyldimethylsilyloxy)ethyl)furan-2-yl)acetate (**13b**, $C_{18}H_{32}O_4Si$)

General procedure with 5.5 g (24.3 mmol) **6h** over a 6.5 h period. 1.26 g (5.58 mmol, 23%) unreacted **6h** were recovered, and **13b** was yielded (3.85 g, 10.7 mmol, 44%). Oil; $R_f = 0.56$ (*n*-hexane/*AcOEt* = 95/5); IR (film): $\bar{\nu}$ = 2957, 2930, 2858, 1714, 1651, 1473, 1463, 1367, 1258, 1198, 1134, 1096, 1035, 874, 836, 809, 775, 746, 662 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.08$ (d, $J = 3.1$ Hz, CH), 5.98 (d, $J = 3.1$ Hz, CH), 3.83 (t, $J = 7.0$ Hz, H-8), 3.53 (s, H-2), 2.81 (t, J = 7.0 Hz, H-7), 1.46 (s, C(C*H*$_3$)$_3$), 0.88 (s, Si-C(C*H*$_3$)$_3$), 0.02 (s, 6H, Si-(C*H*$_3$)$_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 169.3$ (C-1), 152.5 (C-3), 146.7 (C-6), 108.2 (C-4), 107.0 (C-5), 81.1 (*C*(CH$_3$)$_3$), 61.7 (C-8), 35.4 (C-2), 31.9 (C-7), 28.0 (C(*C*H$_3$)$_3$), 25.9 (Si–C(*C*H$_3$)$_3$), 18.3 (Si–*C*(CH$_3$)$_3$), −5.4 (Si–(*C*H$_3$)$_2$) ppm.

tert-Butyl 2-(5-(2-hydroxyethyl)tetrahydrofuran-2-yl)acetate (**14**, $C_{12}H_{22}O_4$)

The furan **13a** (358 mg, 1.58 mmol) and 5% Rh over alumina (170 mg, 0.082 mmol) in 30 cm^3 *Me*OH were placed in a 3.8 atm pressure of hydrogen in a *Parr* apparatus. After 16 h, the mixture was filtered through a celite/silica = 2/1 mixture. The procedure was repeated 2 more times to complete the reaction. **14** (130 mg, 0.56 mmol, 35%) was yielded in presence of traces of *tert*-butyl 2-(5-(2-hydroxyethyl)dihydrofuran-2(*3H*)-ylidene)acetate. According to NMR, *cis*/*trans* ratio of **14** is 85/15. Oil; $R_f = 0.08$ (*n*-hexane/*AcOEt* = 75/25); IR (film): $\bar{\nu}$ = 3437, 2974, 2935, 2930, 2876, 1729, 1458, 1393, 1368, 1300, 1257, 1155, 1071, 950, 843 cm^1; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.32$ (≈dq, $J = 7.4$, 6.0 Hz, H-3 *trans*), 4.21 (≈quint, J≈6.6 Hz, H-3 *cis*), 4.08-4.02 (m, H-6 *trans*, H-6 *cis*), 3.76-3.73 (m, H-8 *trans*), 3.75 (≈dd, J≈6.5, 4.5 Hz, H-8 *cis*), 2.73 (br, OH *cis*, OH *trans*), 2.52 (dd, $J = 14.7$, 7.2 Hz, H-2a *cis*), 2.48 (dd, $J = 14.9$, 7.4 Hz, H-2a *trans*), 2.39 (dd, $J = 14.7$, 6.2 Hz, H-2b *cis*), 2.37 (dd, $J = 14.9$, 6.0 Hz, H-2b *trans*), 2.17–1.99 (m, H-5a *cis*, H-5a *trans*, H-4a *cis*, H-4a *trans*), 1.83–1.69 (m, H-7 *cis*, H-7 *trans*), 1.65–1.57 (m, H-5b *cis*, H-5b *trans*, H-4b *cis*, H-4b *trans*), 1.43 (s, C(C*H*$_3$)$_3$ *cis*, C(C*H*$_3$)$_3$ *trans*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.5$ (*C*=O *cis*), 170.4 (*C*=O *trans*), 80.7 (*C*(CH$_3$)$_3$ *cis*), 80.6 (*C*(CH$_3$)$_3$ *trans*), 79.7 (C-6 *cis*), 79.1 (C-6 *trans*), 76.1 (C-3 *cis*), 75.2 (C-3 *trans*), 61.7 (C-8 *cis*), 61.4 (C-8 *trans*), 42.4 (C-2 *cis*), 42.0 (C-2 *trans*), 37.8 (C-7 *cis*), 37.3 (C-7 *trans*), 32.4, 31.4 (C-4 *trans*, C-5 *trans*), 31.1, 30.6 (C-4 *cis*, C-5 *cis*), 30.0 (C(*C*H$_3$)$_3$ *cis*, *trans*) ppm; APCI-MS: $m/z = 253$ (22, $[M + Na]^+$), 231 (28, $[M + H]^+$), 175 (100, $[M + 2H - C(CH_3)_3]^+$).

Ethyl 2-(5-(2-hydroxyethyl)tetrahydrofuran-2-yl)acetate (**15**, $C_{10}H_{18}O_4$)

Freshly purified by chromatography **10** (300 mg, 1.51 mmol) and 5% Rh over alumina (144 mg, 0.07 mmol) in 20 cm^3 *Me*OH were placed in a 3.8 atm pressure of hydrogen in a

Parr apparatus. After 16 h, the mixture was filtered on a celite/silica = 2/1 mixture. **15** (300 mg, 1.48 mmol, 98%) was yielded in presence of traces of ethyl 2-(5-(2-hydroxyethyl)dihydrofuran-2(*3H*)-ylidene)acetate. According to NMR, *cis*/*trans* ratio of **15** is about 80/20. Oil; $R_f = 0.05$ (*n*-hexane/*AcOEt* = 75/25); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.43$–4.02 (m, H3, H-6, H-1^1 *cis*, *trans*), 3.78–3.75 (m, H-8 *cis*, *trans*), 2.66 (br, OH *cis*, OH *trans*), 2.59 (dd, $J = 14.9$, 7.2 Hz, H-2a *cis*), 2.48 (dd, $J = 14.9$, 6.2 Hz, H-2b *cis*), 2.60–2.44 (m, H-2 *trans*), 2.17–1.99 (m, H-4 *trans*, H-5 *trans*, H-4^a *cis*, H-5^a *cis*), 1.86–1.59 (m, H-7 *cis*, H-7 *trans*), 1.68–1.29 (m, H-4^b *cis*, H-5^b *cis*), 1.26 (t, $J = 7.1$ Hz, H-1^2 *cis*, H-1^2 *trans*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.5$ (*C*=O *cis*), 170.5 (*C*=O *trans*), 80.1 (C-6 *cis*), 79.5 (C-6 *trans*), 76.3 (C-3 *cis*), 75.4 (C-3 *trans*), 62.0 (C-8 *trans*), 61.8 (C-8 *cis*), 60.9 (C-1^1 *cis*, C-1^1 *trans*), 41.6 (C-2 *cis*), 41.2 (C-2 *trans*), 38.2 (C-7 *cis*), 37.8 (C-7 *trans*), 32.5, 31.9 (C-4 *trans*, C-5 *trans*), 31.6, 31.1 (C-4 *cis*, C-5 *cis*), 14.6 (C-1^2 *cis*, C-1^2 *trans*) ppm.

Acknowledgements

NMR Spectra (400 MHz) were measured by *Heinz Bursian* and Dr. *Claude Saturnin*, mass spectra by Dr. *Nicolas Mottier* and Dr. *Bernard Jean-Denis*, HR-MS analyses were made in the Ecole d'ingénieurs et d'architectes de Fribourg. We thank the University of Neuchâtel and the Swiss National Science Foundation for financial support.

References

[1] Hou XL, Cheung HY, Hon TY, Kwan PL, Lo TH, Tong SY, Wong HNC (1998) Tetrahedron **54**: 1955
[2] Brown RCD (2005) Angew Chem Intl Ed **44**: 850
[3] Buhlmann P, Pretsch E, Bakker E (1998) Chem Rev **98**: 1593
[4] Corbaz R, Ettinger L, Gaumann E, Keller-Schlierlein W, Kradolfer F, Kyburz E, Neipp L, Prelog V, Zahner H (1955) Helv Chim Acta **38**: 1445
[5] Takatori K, Tanaka K, Matsuoka K, Morishita K, Kajiwara M (1997) Synlett **2**: 159
[6] a) Gerlach H, Oertle K, Thalmann A, Servi S (1975) Helv Chim Acta **58**: 2036; b) Schmidt U, Gombos J, Haslinger E, Zak H (1976) Chem Ber **109**: 2628; c) Bartlett PA, Meadows JD, Ottow E (1984) J Am Chem Soc **106**: 5304; d) Kim BH, Lee JY (1996) Tetrahedron **52**: 571; e) Fleming I, Ghosh SK (1998) J Chem Soc, Perkin Trans 1 2733; f) Wu Y, Sun Y-P (2006) Org Lett **8**: 2831
[7] Nikodinovic J, Dinges JM, Bergmeier SC, McMills MC, Wright DL, Priestley ND (2006) Org Lett **8**: 443
[8] Baciocchi E, Muraglia E, Sleiter G (1992) J Org Chem **57**: 6817
[9] Fogagnolo M, Giovannini PP, Guerrini A, Medici A, Pedrini P, Colombi N (1998) Tet Asym **9**: 2317
[10] Jones TH, Highet RJ, Warwick Don A, Blum MS (1986) J Org Chem **51**: 2712
[11] a) Reformatsky S (1887) Chem Ber **20**: 1210; b) Picotin G, Miginiac P (1987) J Org Chem **52**: 4796
[12] Schloemer GC, Greenhouse R, Muchowski JM (1994) J Org Chem **59**: 5230
[13] Osornio YM, Cruz-Almanza R, Jimenez-Montano V, Miranda LD (2003) Chem Commun: 2316
[14] a) Cordero Vargas A, Quiclet-Sire B, Zard SZ (2003) Org Lett **5**: 3717; b) Zard SZ (1997) Angew Chem Intl Ed **36**: 673
[15] Schmidt U, Werner J (1986) Synthesis 986
[16] Annunziata R, Benaglia M, Cinquini M, Cozzi F, Raimondi L (1995) J Org Chem **60**: 4697
[17] Kraus GA, Hagen MD (1985) J Org Chem **50**: 3252
[18] Bergmeier SC, Seth PP (1999) J Org Chem **64**: 3237
[19] Miyashita N, Yoshikoshi A, Grieco PA, (1977) J Org Chem **42**: 3772