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Synthesis of New Homochiral Polyfunctionalized Furan-2(5*H*)-ones

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Abstract: The synthesis of enantio- and diastereomerically pure (5*S*)-4-bromo-5-(*l*-menthyloxy)furan-2(5*H*)-one (**2**) and a general method to obtain (5*S*)-4-alkylamino- and 4-alkylthio-5-(*l*-menthyloxy)furan-2(5*H*)-ones in very good yields are described.

5-Alkoxyfuran-2(5*H*)-ones are useful intermediates in organic synthesis, especially when they bear additional functional groups. The preparation of 5-methoxyfuran-2(5*H*)-one is readily achieved by photooxygenation of furan, furoic acid or furfural using methanol as solvent.[1] The application of this procedure to the synthesis of 3- or 4-substituted 5-methoxyfuran-2(5*H*)-ones is limited because of the difficult accessibility of the starting 3-substituted furans and the lack of regioselectivity of the process.[2] We have previously reported that halogen addition to 5-alkoxyfuran-2(5*H*)-ones followed by HX elimination under different experimental conditions, affords a regioselective synthesis of 3- and 4-halogenated alkoxyfuranones.[3] We have also described that nucleophilic halogen substitution on 4-bromofuranone **1** is a suitable method for the introduction of other functional groups, as alkylamino and alkylthio at C-4 of the furanone nucleus.[4]

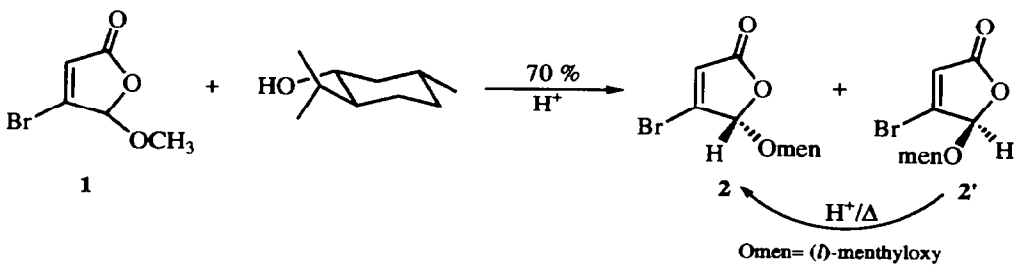
Optically active γ-substituted butenolides could be remarkably useful as chiral synthons for the synthesis of natural products.[5] Due to the high versatility of butenolides, there have been many reports on the preparation of optically active α,β-unsaturated γ-lactones.[6] They have been obtained both from natural sources and from synthetic compounds. Among the previously reported methods, most of them take multistep synthesis and it seems difficult to obtain large amounts of the material for practical use.

We considered the asymmetric transacetalization of 5-methoxy-4-substituted furan-2(5*H*)-ones with an enantiomerically pure auxiliary alcohol, such as menthol, as an attractive way to obtain large quantities of the enantio- and diastereomerically pure corresponding 5-menthyloxy-2(5*H*)-ones. However, all attempts to obtain the 5-(*l*-menthyloxy)-4-(pyrrolidin-1-yl)furan-2(5*H*)-one in moderate yield, by reaction of menthol with the 5-methoxy-4-(pyrrolidin-1-yl)furan-2(5*H*)-one, in the presence of boron trifluoride-diethyl ether or toluene-*p*-sulfonic acid failed, in contrast with the previous results reported by Pelter[5a], Feringa,[7] and us[8] on

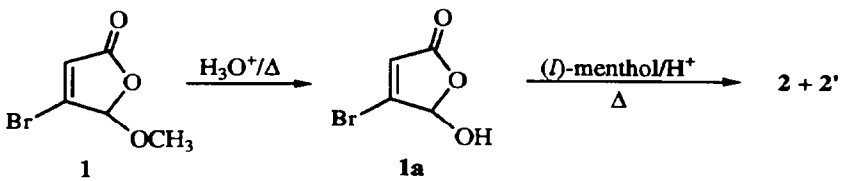
the substitution of 5-methoxy or 5-hydroxy groups by menthyloxy or ethylthio groups. In this paper we describe the synthesis of pure (5*S*)-furanone **2** and a general method to obtain 4-alkylamino- (tetronic acid derivatives) and 4-alkylthio-5-(*l*-menthyloxy)furan-2(5*H*)-ones by substitution of the bromine by primary and secondary amines and thiolates.

Synthesis of 4-bromo-5-(*l*-menthyloxy)furan-2(5*H*)-one

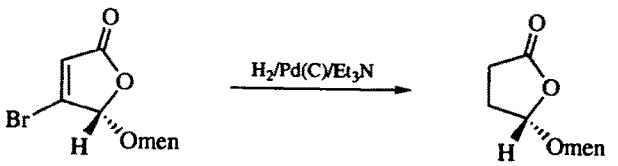
The synthesis of the title compound was carried out by heating 4-bromo-5-methoxyfuran-2(5*H*)-one (**1**) in chlorobenzene, at 80 °C for 72 h, in the presence of 1.5 equiv. of *l*-menthol and a catalytic amount of toluene *p*-sulfonic acid.[9] Pure (5*S*)-4-bromo-5-(*l*-menthyloxy)furan-2(5*H*)-one (**2**) was isolated as a white solid in 37% yield, by filtration after trituration of the crude reaction mixture with hexane. A mixture of **2** and **2'** (70% yield) was isolated by chromatography on silica gel, although all attempts to separate the epimers by this method were unsuccessful. Additional quantities of **2** can be obtained by re-equilibration of the mixture of **2** and **2'** (**2'** being the main product) by heating with toluene-*p*-sulfonic acid (0.3 mmol%) in toluene at reflux, followed by the above-mentioned workup. The open-chain esters **3a,b** and **4** were isolated in 11% combined yield.



The reaction of 4-bromo-5-hydroxyfuran-2(5*H*)-one (**1a**)[2,10] with 1.5 equiv. of *l*-menthol, with toluene *p*-sulfonic acid as a catalyst, after 24 h in refluxing chloroform, afforded a mixture of furanones **2** and **2'** in a yield similar to that obtained from methoxyfuranone **1**. However, since a more convenient method for the synthesis of hydroxyfuranone **1a** is the hydrolysis of **1**, the preparation of **2** starting from methoxyfuranone **1** was the one chosen by us.



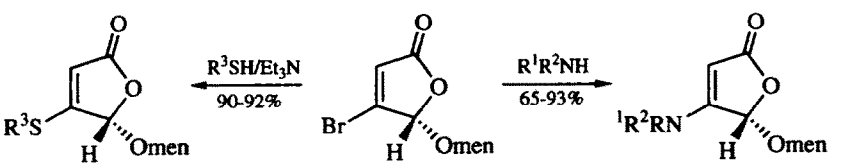
The absolute configuration at the acetal-type carbon of menthyloxyfuranone **2** was determined to be *S* by chemical correlation. Thus, treatment of bromofuranone **2** with hydrogen and 10% Pd/C gave only stereoisomer **5**, which was the epimer at C-5 of the (5*R*)-(*l*-menthyloxy)-3,4-dihydrofuran-2(5*H*)-one (**5'**) described by Feringa[7] and obtained by us,[11] together with **5**, starting from a 55:45 mixture of **2** and **2'**. The assignment was also based upon ^{13}C NMR data, since in the case of the stereoisomers with 5*R* configuration (**2'** and **5'**) the C-5 of furanone ring and C-1 of the menthyl group appear at lower δ value than those of the epimers 5*S* (**2** and **5**).



2 **5**

Synthesis of (5*S*)-4-alkylamino- and 4-alkylthio-5-(*l*-menthyloxy)furan-2(5*H*)-ones

Reactions of (5*S*)-bromofuranone **2** with 2.2 equiv. of benzylamine or a secondary amine (diethylamine, piperidine, and pyrrolidine) have been carried out in tetrahydrofuran at room temperature. Under these conditions the substitution products were obtained, in quantitative yields, except in the case of **6d**, which was isolated in a 65% yield. In all cases only one stereoisomer was achieved. Good yields of thioethers **7a,b** were also attained starting from menthyloxyfuranone **2** and the corresponding thiol using trietylamine as a base.[12]



7a: R^3= Ph
7b: R^3= Et

2

6a: R^1 R^2= $(CH_2)_4$
6b: R^1 R^2= $(CH_2)_5$
6c: R^1= H, R^2= Bn
6d: R^1= Et, R^2= Et

The *S* configuration at C-5 of both enamines and thioethers is based on the 5*S* configuration of the starting substrate. According to the proposed configurational assignment, the chemical shifts of C-5 of furanone and C-1 of cyclohexane ring in **6a**, obtained together with **6a'** from a mixture of **2'** and **2**, appear at higher δ than those of **6a'**, as occurs on bromo- and dihydrofuran-2(5*H*)-ones **2** and **5**. Additionally, the ratio 5*S*/5*R* obtained in the reaction of the pyrrolidine with a mixture of **2** and **2'**, was identical to that of the starting bromofuranones.

According to Feringa's reported results[6c], epimerization at C-5 of the furanone ring was not observed in the presence of amines. However, these results, as well as ours, contrast with the base-catalyzed epimerization of furan-2(5*H*)-ones described in the literature, but the latter substrates do not bear an alkoxy group at C-5.[6c]

EXPERIMENTAL

Column chromatography was performed on 230-400 mesh silica gel (Merck) and analytical TLC on Merck DC-Alufolien with F_{254} silica gel 60. Melting points were determined on a Gallenkamp apparatus in open capillaries and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Bruker-200-SY instrument in $CDCl_3$. J values are given in Hz. Multiplicities in the ^{13}C spectra were determined by DEPT experiments. IR spectra were recorded on a Perkin-Elmer model 681 spectrophotometer, ν values in cm^{-1}. Mass spectra were recorded on a VG 12-250 spectrometer using electron impact at 70 eV. Optical rotations were measured with a Perkin-Elmer 241 polarimeter, concentrations are given in g/100 ml. Microanalyses were performed with a Heraus analyser.

Reaction of l-menthol with 4-bromo-5-methoxyfuran-2(5H)-furanone

a) To a solution of 4-bromo-5-methoxyfuran-2-(5*H*)-one (**1**) (27.02 g, 140 mmol) in chlorobenzene (140 ml) was added *l*-menthol (32.76 g, 210 mmol) and a catalytic amount of toluene-*p*-sulfonic acid monohydrate. The reaction mixture was heated at 80 °C for 72 hours. The evolution of reaction was followed by t.l.c. After evaporation of the solvent, the residue was dissolved in dichloromethane and then washed with saturated aqueous sodium bicarbonate. The aqueous layer was extracted several times with dichloromethane. The combined organic layers were dried and the solvent evaporated to dryness. The signals corresponding to four new products (**2**, **2'**, **3**, **4**) and those of the starting material were observed by ^1H NMR. The products were separated and purified by flash column chromatography (dichloromethane/hexane 3:2) to afford, in decreasing order of Rf, compounds **4**, **3**, **2+2'** and **1** in 5, 6, 70 and 7 % yield respectively. The mixture **2+2'** was washed with hexane and the resulting solid was filtered to yield pure isomer **2**.

b) When the above-mentioned crude mixture was washed with hexane, after filtration pure isomer **2** was obtained (16.4 g, 51.8 mmol) as a white solid in a 37% yield.

(5*S*)-4-Bromo-5-(*l*-menthyloxy)furan-2-(5*H*)-one (2)

White solid. m.p. 137-8 °C. $[\alpha]_D$= + 30.7 (c=1.0, $CHCl_3$). ^1H NMR: 6.38 (d, 1H, H_3, $J_{3,5}$=0.9), 5.79 (d, 1H, H_5, J=0.9), 3.56 (dt., 1H ment., J=10.7, J=4.4), 2.5-0.8 (18 H ment.). ^{13}C NMR: 168.1 (s), 145.9 (s), 124.2 (d), 104.9 (d), 84.2 (d), 48.1 (d), 42.1 (t), 34.0 (t), 31.6 (d), 25.2 (d), 22.9 (t), 22.1 (q), 20.9 (q), 15.9 (q). IR(KBr): 1800, 1760, 1610. MS, m/z (relative intensity): 180-178 (2), 163-161 (35),138 (49), 123 (30), 95 (78), 81 (100), 69 (57), 57 (40), 55 (59). Analysis Calcd. for $C_{14}H_{21}O_3Br$: C, 53.00; H, 6.62; Br, 25.24. Found: C, 52.75; H, 6.75; Br, 25.54.

(5*R*)-4-Bromo-5-(*l*-menthyloxy)furan-2-(5*H*)-one (2')

^{1}H NMR: 6.38 (d, 1H, H_3, $J_{3,5}$=0.8), 5.87 (d, 1H, H_5, J=0.8), 3.65 (dt., 1H ment., J=10.6, J=4.4), 2.5-0.8 (18H ment.). ^{13}C NMR: 168.1 (s), 146.0 (s), 124.0 (d), 101.6 (d), 80.4 (d), 47.4 (d), 40.2 (t), 33.9 (t), 31.3 (d), 25.2 (d), 22.8 (t), 22.0 (q), 20.9 (q), 15.6 (q). IR(2+2')(Nujol): 1800, 1760, 1610.

***l*-Menthyl 3-bromo-4-oxobut-2-enoates (3)**

All attempts to separate aldehydes **3a** and **3b** by column chromatography on silica gel were unsuccessful. ^{1}H NMR: 10.28 and 9.30 (2s, 1H(**a**) and 1H(**b**), CHO), 7.30 and 7.28 (2s, 1H(**b**) and 1H(**a**), HC=), 4.90 (dt, 1H ment., J=10.8, J=4.4), 2.2-0.7 (18H ment.).

***(E)*-*l*-Menthyl 3-Bromo-4,4-di(*l*-menthyloxy)but-2-enoate (4)**

Colourless oil. ^{1}H NMR: 6.42 and 6.28 (2s, 1H, H_2 and 1H, H_4), 4.74 (dt, 1H ment., J=10.8, J=4.4), 3.47 (dt, 1H ment., J=10.7, J=4.2), 3.18 (dt, 1H ment., J=10.4, J=4.1), 2.4-0.6 (54H ment.). ^{13}C NMR: 163.5 (s), 147.7 (s), 124.3 (d), 92.0 (d), 76.2 (d), 76.1 (d), 75.0 (d), 48.0 (d), 47.0 (d), 41.4 (t), 40.9 (t), 40.8 (t), 34.4 (t), 34.2 (t), 31.6 (d), 31.4 (d), 26.2 (d), 25.1 (d), 25.0 (d), 23.4 (t), 23.1 (t), 22.9 (t), 22.3 (q), 22.0 (q), 21.2 (q), 21.0 (q), 20.7 (q), 16.3 (q), 15.9 (q). IR($CHCl_3$): 1700, 1620. MS, m/z (relative intensity): 613-611 (M^++1, 2), 475-473 (5), 457-455 (5), 337-335 (10), 319-317 (18), 139 (100), 83-81 (41), 69 (59), 57 (49), 55 (54).

(5*S*)-5-(*l*-Menthyloxy)-3,4-dihydrofuran-2(5*H*)-one (5)

A solution of bromofuranone **2** (250 mg, 0.79 mmol) and triethylamine (0.45 ml, 3.16 mmol) in ethyl acetate (5 ml) containing 10% Pd/C (25 mg) was hydrogenated under atmospheric pressure at room temperature. After 2 hours the suspension was filtered through celite and the solvent was removed in vacuo. The residue analyzed by ^{1}H NMR contains **5** as a sole product, which was purified by flash chromatography (hexane/acetone 10:1) to afford **5** in a yield of 90%. White solid m.p. 35-6 °C. $[\alpha]_D$= + 28.3 (c=1.0, $CHCl_3$). ^{1}H NMR: 5.59 (dd, 1H, H_5, J=5.5, J=2.6), 3.40 (dt, 1H ment., J=10.6, J=4.4), 2.8-0.8 ($2H_3$, $2H_4$, 18 H ment.). ^{13}C NMR: 176.5 (s), 105.6 (d), 81.7 (d), 48.2 (d), 42.6 (t), 34.1 (t), 31.5 (d), 29.1 (t), 27.0 (t), 25.7 (d), 23.1 (t), 22.0 (q), 20.9 (q), 16.2 (q). IR(Film): 1785. MS, m/z (relative intensity): 241 (M^++1, 2), 155 (7), 139 (43), 138 (50), 123 (21), 95 (42), 85 (100), 69 (29), 57 (36), 55 (45). Analysis Calcd. for $C_{14}H_{24}O_3$: C, 69.96; H, 10.06. Found: C, 69.78; H, 10.30.

(5S)-4-Alkylamino-5-(l-menthyloxy)furan-2-(5H)-ones (6a-d). General procedure:

a) To a stirred solution of 4-bromofuranone **2** (507 mg, 1.6 mmol) in dry tetrahydrofuran (6.4 ml), the corresponding amine (4 mmol) was added at room temperature. Disappearance of the halogenated substrate was monitored by TLC. After evaporation of the solvent the residue was dissolved in dichloromethane and then washed with water to remove the salts. The organic layer was dried ($MgSO_4$) and the solvent was removed under reduced pressure. The purity of the crude compounds (monitored by ^{1}H NMR) was, in all cases, suitable for preparative purposes. Analytical samples were obtained by flash

chromatography. Reaction times, eluents and yields of pure compounds are shown in each case.

b) Following the procedure outlined above, starting from a mixture of the bromofuranones **2** and **2'**, the reaction with pyrrolidine afforded the epimeric enamines **6a** and **6a'** (the ratios **6a**:**6a'** and **2a**:**2a'** were the same).

(5*S*)-5-(*l*-Menthyloxy)-4-(pyrrolidin-1-yl)furan-2-(5*H*)-one (6a)

Reaction time 17 hours, eluent ethyl acetate/hexane (22:15). White solid recrystallized from cyclohexane m.p. 114-5 °C. 90 % yield. $[\alpha]_D$= + 82.2 (c=1.0, $CHCl_3$). ^1H NMR: 5.79 (s, 1H, H_5), 4.49 (s, 1H, H_3), 3.58 (dt, 1H ment., J=10.5, J=4.3), 3.6 (m, 1H, CH_2N), 3.4-3.1 (m, 3H, CH_2N), 2.3-0.8 (18 H ment., 4H pyrro.). ^{13}C NMR: 172.5 (s), 163.8 (s), 98.2 (d), 81.7 (d), 80.1 (d), 49.5 (t), 48.2 (d), 47.8 (t), 42.3 (t), 33.9 (t), 31.6 (d), 25.8 (t), 25.0 (d), 24.5 (t), 22.6 (t), 22.1 (q), 21.1 (q), 15.6 (q). IR(KBr): 1790, 1735, 1630. MS, m/z (relative intensity): 308 (M^++1, 24), 307 (M^+, 7), 170 (55), 169 (75), 153 (43), 152 (84), 141 (100), 124 (56), 123 (29), 95 (60), 83 (37), 70 (40), 69 (40), 57 (21), 55 (54). Analysis Calcd. for $C_{18}H_{29}O_3N$: C, 70.35; H, 9.45; N, 4.56. Found: C, 70.45; H, 9.70; N, 4.60.

(5*R*)-5-(*l*-Menthyloxy)-4-(pyrrolidin-1-yl)furan-2-(5*H*)-one (6a')

^1H NMR: 5.85 (s, 1H, H_5), 4.47 (s, 1H, H_3), 3.8-3.1 (m, 1H ment., 4H pyrro.), 2.4-0.8 (18 H ment., 4H pyrro.). ^{13}C NMR: 172.7 (s), 163.6 (s), 94.8 (d), 82.0 (d), 77.9 (d), 49.5 (t), 48.2 (d), 47.6 (t), 39.7 (t), 34.2 (t), 31.4 (d), 25.8 (t), 25.1 (d), 24.5 (t), 23.0 (t), 22.1 (q), 20.9 (q), 15.7 (q). IR(**6a+6a'**),(Nujol): 1780, 1740, 1640.

(5*S*)-5-(*l*-Menthyloxy)-4-piperidinylfuran-2-(5*H*)-one (6b)

Reaction time 2 hours, eluent hexane/ethyl acetate 3:2. White solid of m.p. 133-5 °C. 85% yield. $[\alpha]_D$= - 32.0 (c=1.0, $CHCl_3$). ^1H NMR: 5.78 (s, 1H, H_5), 4.60 (s, 1H, H_3), 3.54 (dt, 1H ment., J=10.6, J=4.4), 3.2 (m, 4H, CH_2N), 2.4-0.7 (18 H ment. and 6H pipe.). ^{13}C NMR: 172.4 (s), 166.0 (s), 98.2 (d), 82.3 (d), 80.7 (d), 48.6 (t), 48.0 (d), 42.4 (t), 33.9 (t), 31.5 (d), 25.0 (t), 24.8 (d), 23.5 (t), 22.6 (t), 22.1 (q), 21.0 (q), 15.5 (q). IR(Nujol): 1730, 1610. Analysis Calcd. for $C_{19}H_{31}O_3N$: C, 71.03; H, 9.66; N, 4.36. Found: C, 71.33; H, 10.00; N, 4.49.

(5*S*)-4-(N-Benzylamino)-5-(*l*-menthyloxy)furan-2-(5*H*)-one (6c)

Reaction time 24 hours, eluent hexane/ethyl acetate 4:1. White solid of m.p. 133-4 °C. 80% yield. $[\alpha]_D$= + 61.7 (c=1.0, $CHCl_3$). ^1H NMR: 7.5-7.3 (m, 5H arom.) 5.69 (s, 1H, H_5), 4.86 (t, 1H, $CH_2N\underline{H}$, J=5.5), 4.73 (s, 1H, H_3), 4.31 (d, 2H, $C\underline{H}_2NH$, J=5.5), 3.53 (dt, 1H ment., J=10.6, J=4.4), 2.4-0.7 (18 H ment.). ^{13}C NMR: 172.3 (s), 165.2 (s), 136.1 (s), 128.8 (d), 127.9 (d), 127.2 (d), 99.7 (d), 83.1 (d), 82.1 (d), 49.0 (t), 48.0 (d), 42.4 (t), 33.9 (t), 31.5 (d), 25.7 (d), 22.9 (t), 22.0 (q), 20.9 (q), 15.9 (q). IR(Nujol): 3280, 3240, 1730, 1620. MS, m/z (relative intensity): 344 (M^++1, 1), 205 (11), 188 (33), 177 (43), 160 (7), 131 (5), 95 (12), 91 (100), 83 (38), 69 (27), 57 (23), 55 (48). Analysis Calcd. for $C_{21}H_{29}O_3N$: C, 73.47; H, 8.45; N, 4.08. Found: C, 73.55; H, 8.70; N, 4.01.

(5*S*)-4-(N,N-Diethylamino)-5-(*l*-menthyloxy)furan-2-(5*H*)-one (6d)

Reaction time 24 hours, eluent hexane/ethyl acetate 4:1. White solid of m.p. 73-5 °C. 65% yield. $[\alpha]_D$= + 18.4 (c=1.0, $CHCl_3$). ^1H NMR: 5.81 (s, 1H, H_5), 4.56 (s, 1H, H_3), 3.58 (dt, 1H ment., J=10.6, J=4.5), 3.2 (m, 4H, $CH_3C\underline{H}_2N$), 2.3-0.7 (18 H ment.), 1.20 (t, 6H, $C\underline{H}_3CH_2N$, J=7.1). ^{13}C NMR: 172.2 (s), 165.4 (s), 97.6 (d), 81.3 (d), 79.4 (d), 48.0 (d), 44.4 (t), 42.3 (t), 33.8 (t), 31.4 (d), 25.0 (d), 22.5 (t), 21.9 (q), 20.9 (q), 15.5 (q). IR(Nujol): 1730, 1620. MS, m/z (relative intensity): 310 (M^++1, 3), 171 (47), 155 (20), 154 (49), 143 (78), 126 (43), 97 (97), 95 (18), 83 (42), 82 (53), 70 (89), 69 (55), 57 (25), 55 (77), 41 (100). Analysis Calcd. for $C_{18}H_{31}O_3N$: C, 69.90; H, 10.03; N, 4.53. Found: C, 70.10; H, 10.21; N, 4.63.

(5*S*)-4-Phenylthio-5-(*l*-menthyloxy)furan-2-(5*H*)-one (7a)

To a stirred solution of the bromofuranone **2** (500 mg, 1.6 mmol) and triethylamine (0.245 ml, 1.8 mmol) in dry tetrahydrofuran (6.4 ml) was added thiophenol (0.181 ml, 1.8 mmol) at room temperature for 2 hours. Disappearance of furanone **2** was followed by TLC. Tetrahydrofuran was evaporated under reduced pressure and the residue was dissolved in dichloromethane and washed with water. The aqueous layer was extracted several times with dichloromethane. The combined organic layers were dried over anhydrous magnesium sulfate and the solvent removed *in vacuo*. The crude residue was purified by column chromatography (hexane/ethyl acetate 8:1). White solid of m.p. 139-40 °C. 92 % yield. $[\alpha]_D$= + 1.3 (c=1.0, $CHCl_3$). ^1H NMR: 7.6-7.4 (m, 5H arom.), 5.88 (d, 1H, H_3, J=0.8), 5.29 (d, 1H, H_5, J=0.8), 3.57 (dt, 1H ment., J=10.7, J=4.4), 2.4-0.8 (18 H ment.). ^{13}C NMR: 168.6 (s), 168.2 (s), 134.1 (d), 130.2 (d), 130.0 (d), 127.8 (s), 112.4 (d), 103.3 (d), 83.8 (d), 47.9 (d), 42.2 (t), 33.9 (t), 31.5 (d), 25.2 (d), 22.8 (t), 22.0 (q), 20.8 (q), 15.7 (q). IR(Nujol): 1810, 1750, 1585, 1580. MS m/z (relative intensity): 348 (M^+, 8), 209 (11), 192 (54), 191 (100), 163 (11), 137 (12), 134 (55), 109 (12), 95 (11), 77 (6), 69 (15), 57 (7), 55 (18). Analysis Calcd. for $C_{20}H_{26}O_3S$: C, 69.36; H, 7.51; S, 9.25. Found: C, 69.63; H, 7.25; S, 9.23.

(5*S*)-4-Ethylthio-5-(*l*-menthyloxy)furan-2-(5*H*)-one (7b)

The procedure used was the same as the above-mentioned for the synthesis of **7a**, starting from **2** (500 mg, 1.6 mmol), triethylamine (0.446 ml, 3.2 mmol) and ethanethiol (0.355 ml, 4.8 mmol). The reaction, after 9 days, gave the thioether **7b** as a white solid of m.p. 115-6 °C. Yield 90%. Eluent hexane/ethyl acetate 6:1. $[\alpha]_D$= + 23.5 (c=1.0, $CHCl_3$). ^1H NMR: 5.76, 5.70 (2s, 2H, H_3, H_5), 3.52 (dt, 1H ment., J=10.6, J=4.5), 2.94 (q, 2H, $CH_3C\underline{H}_2S$, J=7.5), 2.4-0.8 (18 H ment.), 1.42 (t, 3H, $C\underline{H}_3CH_2S$, J= 7.5). ^{13}C NMR: 169.2 (s), 167.2 (s), 110.8 (d), 103.8 (d), 83.8 (d), 48.0 (d), 42.3 (t), 34.0 (t), 31.6 (d), 26.9 (t), 25.2 (d), 22.8 (t), 22.0 (q), 20.8 (q), 15.8 (q), 12.9 (q). IR(Nujol): 1810, 1755, 1575. MS m/z (relative intensity): 298 (M^+, 4), 161 (22), 144 (67), 143 (100), 138 (16), 115 (23), 95 (16), 86 (72), 69 (15), 57 (7), 55 (11). Analysis Calcd. for $C_{16}H_{26}O_3S$: C, 64.93; H, 8.72; S, 10.74. Found: C, 65.15; H, 8.90; S, 10.76.

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9. In the absence of acid catalyst only traces of **2** and **2'** were formed.
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11. NMR data of **5'**; ^{1}H: 5.72 (dd, 1H, C_5, J=5.3 and 1.7), 3.52 (dt, 1H, C_{1ment}, J=10.7 and 4.3), 2.8-0.8 ($2H_2$, $2H_4$, and 18 H ment.); ^{13}C: 176.3 (s), 100.3 (d), 76.4 (d), 39.7 (t), 34.1 (t), 31.2 (d), 29.0 (t), 26.9 (t), 25.3 (d), 23.0 (t), 22.0 (q), 20.9 (q), 15.5 (q).
12. When the sodium thiolate was generated with sodium in methanol and there remained sodium methoxyde and/or methanol, it underwent substitution of menthyloxy by methoxy group and **7b** in the crude reaction mixture was a minor product.

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