Tetrahedron Vol. 46, No. 4, pp. 1199-1210, 1990
Printed in Great Britain

0040-4020/90 $3.00+.00
Pergamon Press plc

NEW ASPECTS IN THE SYNTHESIS OF MONO- AND DIALKYLFURANS

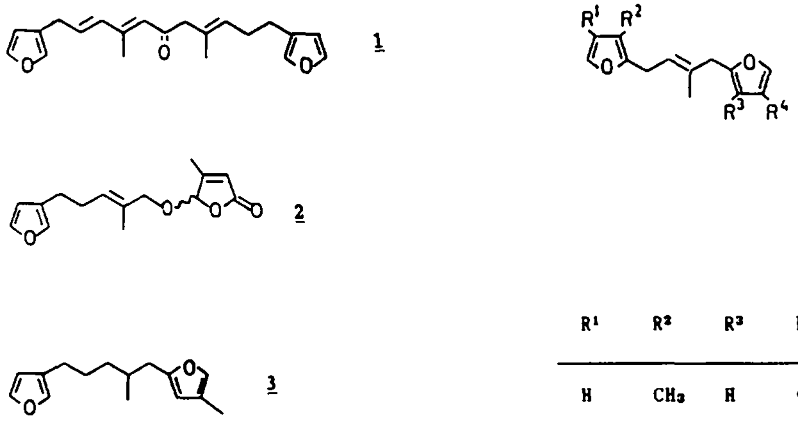
Inge Bock, Hans Bornowski*, Andreas Ranft and Heinz Theis
Institut für Organische Chemie der Technischen Universität Berlin
Straße des 17. Juni 135, D-1000 Berlin 12

(*Received in Germany* 2 *August* 1989)

Summary- 3-substituted furan systems can be obtained by alkylation of 3-lithium furans with various electrophiles in the presence of hexamethylphosphoric acid triamide in good yields. The 2- or 5-position of 3-methyl furan is blocked with high regioselectivity by silylation. After metalation and alkylation of the remaining free α-position and subsequent desilylation the 2,3- and 2,4-disubstituted furans are obtained. These methods are used to synthesize the naturally occuring compounds ursinanolide (2) and longifolin (4).

INTRODUCTION

Alkyl substituted furan systems, especially 3-alkyl furans, 2-alkyl-3- and 2-alkyl-4-methyl furans are part of some naturally occurring compounds such as furospongin-2 (1), ursinanolide (2), lasiosperman (3) and longifolin [1-4] (4) (Scheme 1).



R^1	R^2	R^3	R^4	
H	CH_3	H	CH_3	4
H	CH_3	CH_3	H	5
CH_3	H	H	CH_3	6
CH_3	H	CH_3	H	7

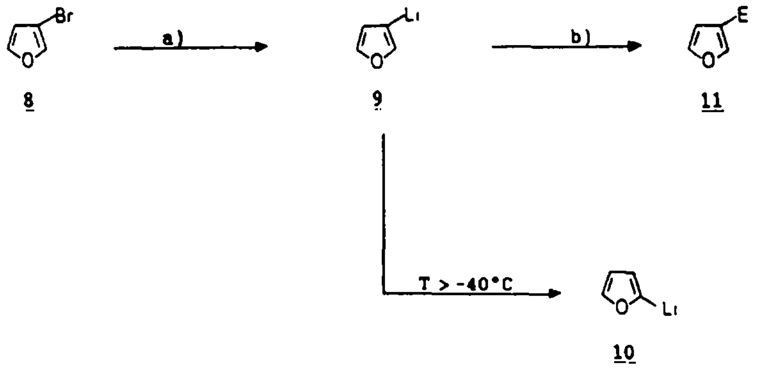
Scheme 1

Alkyl furans are of increasing interest in organic synthesis, since the furan system is an important intermediate [5,6] and easily can be converted into open chain or cyclic functionalized structures by means of oxidizing or dienophilic reagents. [7,8]

We herein report simple synthetic routes to 3-alkyl furans [9,10] and 2-alkyl-3- resp. 2-alkyl-4-methyl furans, exemplified by the syntheses of the natural occurring compounds ursinanolide (2), longifolin (4) and three isomers thereof 5 - 7 (see Scheme 1).

3-ALKYL FURANS

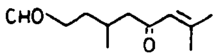
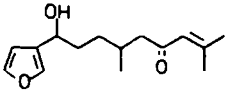
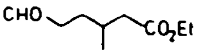
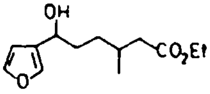
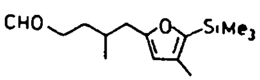
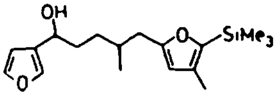
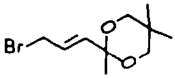
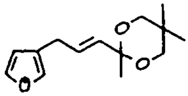
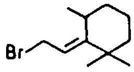
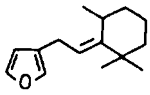
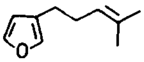
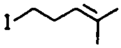
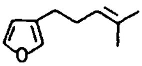
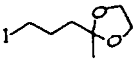
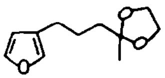
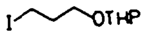
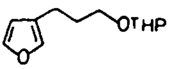
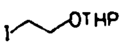
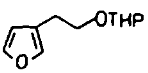
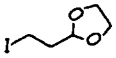
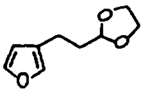
The synthetic scheme is based on the preparation of 3-lithium furan (9), which was obtained by lithiation of 3-bromo furan (8) [11] with n-butyl lithium (BuLi) in tetrahydrofuran (THF) at -78 °C.[12] Further alkylation with alkylhalides or aldehydes as electrophiles led to 3-alkyl furans. The alkylation of 3-lithium furan (9) is limited to very reactive electrophiles, such as aldehydes and allylic halides, if carried out in THF (Scheme 2). To achieve a regiospecific metalation it is important to work at temperatures below -40 °C, because at higher temperatures 2-lithium furan (10) is formed from 3-lithium furan (9) by transmetalation. However it was found, that in the presence of hexamethylphosphoric acid triamide (HMPA) as cation-complexing agent [13], primary alkyl halides also reacted in good yields (Table 1).



Scheme 2

a)BuLi/THF/-78 °C/2h; b) electrophile (see Table 1)

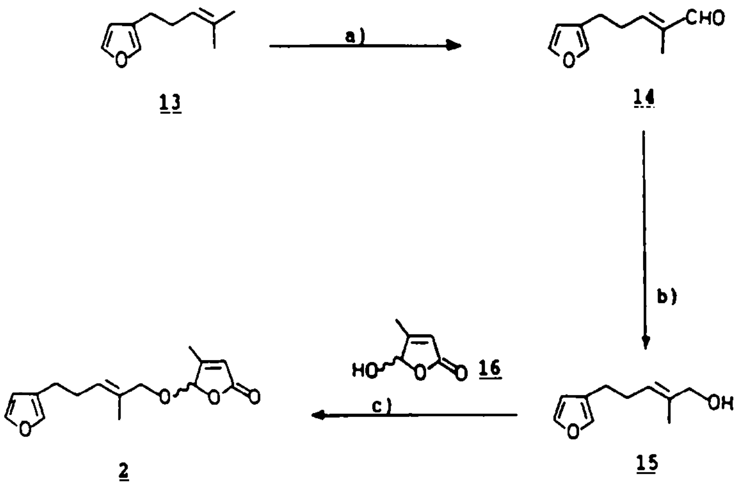
Table 1: Alkylation of 9 with various electrophiles

Reaction	Electrophile	3-Alkylfuran 11	Conditions	Yields
a			20h/-78°C/ THF	0% *
b			"	40% **
c			"	90% ***
d			20h/-78°C/ THF/HMPA	82%
e		 12	"	71%
f		 13	48h/-78°C/ THF/NaI/ HMPA	35%
g		 13	60h/-78°C-r.t./THF/ HMPA	26%
h			48h/-78°C/ THF/HMPA	74%
i			60h/-78°C-r.t./THF/ HMPA	79%
j			"	11%
k			48h/-78°C/ THF/HMPA	54%

* mainly bisadduct; ** mainly trisadduct; *** crude product

The poor results of reaction j (Table 1) can be explained by steric hindrance caused by the tetrahydropyranyl group in the α-position to the reaction center. Comparing saturated halides (h and i) with homoallylic halides (f and g), the latter give low results due to their higher tendency to elimination reactions.
Products like microcionin [14] (12) and perillene [15] (13) are naturally occurring compounds.

The natural aldehyde perillenal [16] (14) was obtained by oxidation of perillene (13) with selenium dioxide in the presence of t-butylhydroperoxide. [17] Reduction of 14 with lithium aluminiumhydride, followed by etherification with 4-hydroxy-3-methyl-2-butenolide (16)[18] and dicyclohexylcarbodiimide (DCC) as waterbinding agent, gave the naturally occuring compound ursinanolide [2] (2) (Scheme 3).

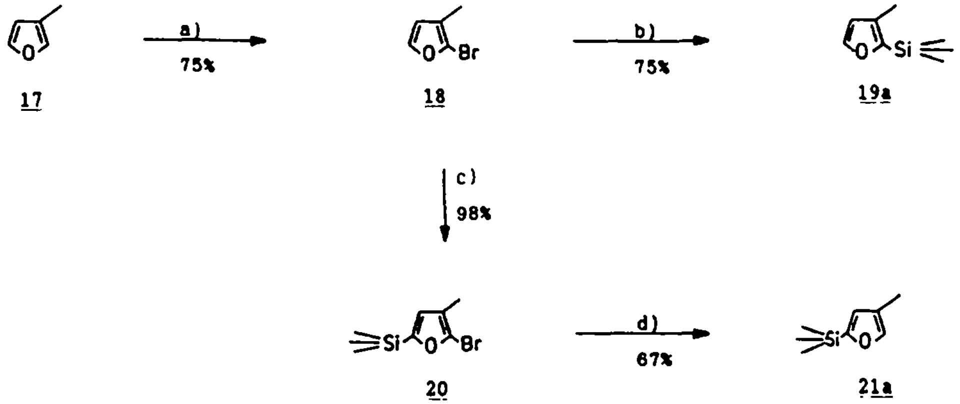


Scheme 3

a) SeO_2/t-BuOOH/ 58%; b) $LiAlH_4$/ether/92%; c) 16/CH_2Cl_2/DCC/ 27% of 2, 59% educt retained

2-ALKYL-3- AND 2-ALKYL-4-METHYL FURANS

Starting with the easily obtainable 3-methyl furan [19] (17), the furan building blocks 19a and 21a were prepared (Scheme 4).

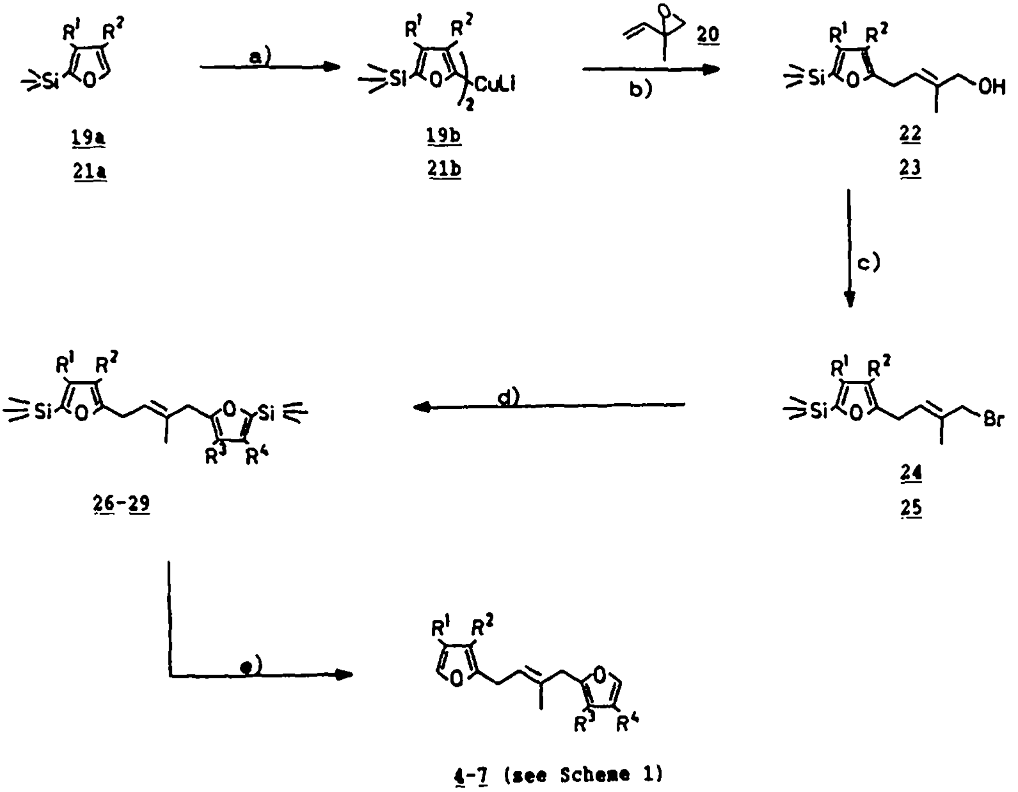


Scheme 4

a) NBS/AIBN/ether/reflux/1h; b) 1. n-BuLi/THF-ether/-78°C/1h; 2. $ClSiMe_3$/-78°C;
c) 1. LDA, 2. $ClSiMe_3$ (same cond. as in b)); d) 1. n-BuLi, 2. H_2O/THF/-78°C/1h

Bromination of 17 with N-bromosuccinimide (1 eq) gave 18 in high regioselectivity (^1H NMR, 90 MHz, in ether: d 7.4 (2 Hz)= α-furyl-H, d 6.3 (2 Hz) = β-furyl-H). After bromine-lithium exchange with n-butyllithium in ether/tetrahydrofuran and further reaction with chlorotrimethylsilane at -78°C, reagent 19a was obtained.
The reaction of 18 with lithium diisopropylamide under the same conditions exclusively led to α-deprotonation. [20] The silylated bromide 20 was too unstable for purification by means of distillation or chromatography, and therefore further reacted to give 21a.

The first step in the synthesis of 4 - 7 was the preparation of the E-allylic alcohols [21] 22 and 23 (Scheme 5). 19a and 21a were lithiated by action of n-butyllithium in tetrahydrofuran at 0°C, the solutions of the furanolithium reagents were dropped into a stirred suspension of copper(I)iodide in ether at -40°C and 1,2-isoprene oxide (20) was added. The E/Z ratio of 22 and 23 was 85 : 15 in both cases, indicated by ^1H NMR (400 MHz, $CDCl_3$; 4.02 ppm (E) and 4.23 ppm (Z), HO-CH_2-C=). Furthermore, pyridinium dichromate oxidation of 22 and 23 gave the corresponding E- and Z-aldehydes with the same E/Z ratio (^1H NMR, 90 MHZ, $CDCl_3$: 9.3 ppm (E) and 10.3 ppm (Z), OHC-).



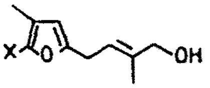
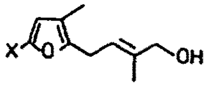
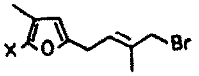
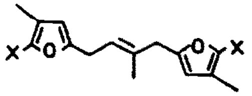
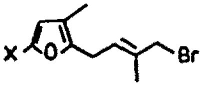
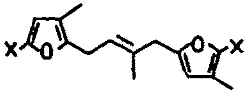
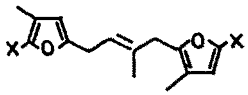
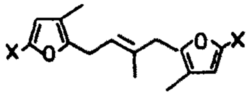
Scheme 5

a) 1.n-BuLi/THF/0°C/1h; 2. CuI/ether/-40°C/30 min.; b) -40°C/20h; c) Ph$_3$P/Br$_2$/ether/ -20°C - r.t./20h; d) 19b resp. 21b/ether-THF/-40°C/20h e) p-TsOH/MeOH/r.t./6h

The bromination of 22 and 23 gave only poor yields of the extremely unstable halides 24 and 25. The second furan system was introduced by coupling of 24 and 25 with the cuprates 19b and 21b (Scheme 5 and Table 2). After thin layer chromatography of the crude products only the E-isomers of the bisfuryls 26 - 29 were isolated.

The desilylation of 26 - 29 was performed under mild conditions by stirring in 5% methanolic solution of para-toluenesulfonic acid at room temperature for 6 hours.[22] Longifolin (4) and its isomers 5 - 7 were purified by thin layer chromatography in yields of 59% (4 from 26), 54% (5 from 27), 60% (6 from 28) and 65% (7 from 29).

Table 2: Alkylation of furans **19a** and **21a** (according to Scheme 5)

Furan	Electrophile		Product		Yield (%)
19a		**20**		**22**	63
21a		**20**		**23**	86
19a		**24**		**28**	53
19a		**25**		**26**	61
21a	**24**			**29**	73
21a	**25**			**27**	76

EXPERIMENTAL

^{1}H NMR spectra were obtained on Bruker WM 400, WH 270 and Varian EM 390 spectrometers (tetramethylsilane as internal standard). MS spectra were recorded on a Varian MAT 711 and 44S, (EI: operating with an ionization potential of 70 eV, CI: chemical ionization with isobutane, DI = direct inlet). IR spectra were measured on a Beckman IR 9 spectrometer. Tetrahydrofuran (THF) and ether were distilled from sodium benzophenon ketyl before use. All reaction vessels used in reactions with metalated compounds were dried in vacuo and filled with dry nitrogen. Thin layer chromatography was performed on silica gel or aluminium oxide plates (20x20 cm) with visualization by UV (254 nm), $KMnO_4$- or H_2SO_4-spray reagent. Column chromatography was performed with glass columns packed with silica gel 60 (150-300 and 32-63 µm) or aluminium oxide 60 (neutral, 63-200 µm, cont. 7% of water).

General procedure for the alkylation of 3-bromo furan (see Table 1)
3-bromo furan (<u>8</u>)(7.35 g, 50 mmol) was added to n-butyllithium (34 ml, 1.6 N solution in hexane) in dry THF (50 ml) during 15 min at -78°C under nitrogen atmosphere. After stirring for 2 h, a mixture of HMPA (55 mmol), alkyl halide (45 mmol) in dry THF (10 ml) was added. The reaction mixture was allowed to stir under the conditions given in Table 1. Ether (50 ml) was added, the solution was hydrolized with saturated ammonium chloride solution and the organic layer was separated. The aqueous phase was extracted with ether and the combined extracts were washed with water, dried over magnesium sulfate and evaporated. The crude product was purified by flash chromatography (silica gel, ether/petroleum ether , gradient eluation).

Spectral data
Ethyl (6-(3'-furyl)-6-hydroxy-3-methyl)hexanoate (<u>11b</u>) : ***^{1}H NMR*** (400 MHz, $CDCl_3$): δ= 7.36 (s_{br}, 2H, α-furyl-H); 6.38 (s_{br}, 1H, β-furyl-H); 4.36 (t, 1H, J= 6, $-C\underline{H}(OH)-$); 4.09 (q, 2H, J= 7, $-O-C\underline{H}_2-$); 2.24 - 2.32 (m, 1H, J= 15, 6.5, $-C\underline{H}_2-C=O$); 2.06-2.16 (m, 1H, J= 15, 7.5, $-C\underline{H}_2-C=O$); 2.07-2.17 (m, 2H, $-CH(OH)-C\underline{H}_2-$); 1.36-2.04 (m, 3H, $-C\underline{H}_2-C\underline{H}(CH_3)-$); 1.22 (t, 3H, J= 7, $C\underline{H}_3-CH_2-O-$); 0.92 (d, 3H, J= 7, $C\underline{H}_3-$).- ***MS*** (via GC): m/e= 222 (1%, $(M - H_2O)^+$); 195 (10%, $(M - OEt)^+$); 194 (36%, $(M - HOEt)^+$); 115 (92%, $C_6H_{11}O_2^+$); 97 (100%, furyl-$CH=OH^+$).- ***IR*** : ν = 3600, 3340 cm^{-1} (O-H); 1735 cm^{-1} (ester).

1-(3'-Furyl)-5-(2'-(4'-methyl-5'-trimethylsilyl)furyl)-4-methylpentane-1-ol (<u>11c</u>) :
^{1}H NMR (400 MHz, $CDCl_3$): mixture of diastomers; δ= 7.38 (s_{br}, 1H, $furyl_A$-H); 7.37 (m,1H, $furyl_A$-H); 6.39 (s_{br}, 1H, $furyl_A$-H); 5.80 / 5.79 (s, 1H, $furyl_B$-H); 4.62 (t_{br}, 1H, J= 7, $furyl_A-C\underline{H}(OH)-$); 2.55 / 2.57 (dd, 1H, J= 15, 6, $furyl_B-C\underline{H}_2-CH(CH_3)-$); 2.43 / 2.45 (dd, 1H, J= 15, 7,5, $furyl_B-C\underline{H}_2-CH(CH_3)-$); 2.04 (s, 3H, $furyl_B-C\underline{H}_3$); 1.65-1.85 (m, 1H, $-C\underline{H}_2(CH_3)-$); 1.08-1.53 (m, 4H, $-C\underline{H}_2-C\underline{H}_2-$); 0.91 / 0.92 (d, 3H, J= 7, $-CH(C\underline{H}_3)-$); 0.26 (s, 9H, $C\underline{H}_3-Si$).- ***MS*** (CI): m/e= 321 (2%, $(M+H)^+$); 303 (30%, $((M+H) - H_2O)^+$); 231 (100%, $((M'+H) - H_2O)^+$, M': desilylated compound).- ***IR*** : ν = 3600 cm^{-1} (O-H); 1255, 880, 850 cm^{-1} (furan).
1-(3'-Furyl)-4,4-(2',2'-dimethyl-1',3'-propanedioxy)-2-pentene (<u>11d</u>) : ***^{1}H NMR*** (400 MHz, $CDCl_3$): δ= 7.37 (dd, 1H, J= 1.5, 1.5, α-furyl-H); 7.22 (s_{br}, 1H, α-furyl-H); 6.26 (d_{br}, 1H, J= 7, β-furyl-H); 5.90 (dt, 1H, J=16, 7, furyl-$CH_2-C\underline{H}=CH-$); 5.48 (dt, 1H, furyl-$CH_2-CH=C\underline{H}-$); 3.30 - 3.60 (m, 4H, $-O-C\underline{H}_2-_{quart}C-$); 3.22 ($d_{br}$, J= 7, furyl-$C\underline{H}_2$); 1.41 (s, 3H, $C\underline{H}_3-$); 1.17 / 0.72 (2x s, 2x 3H, $C\underline{H}_3-$).- ***MS*** : no molpeak, m/e= 221 (100%, $(M - CH_3)^+$); 135 (64%, furyl-$CH_2-CH=CH-C{\equiv}O^+$).- ***IR*** : ν = 1505, 1375, 1085, 880 cm^{-1} (furan).
Microcionin III (<u>11e</u>, resp. <u>12</u>) : ***^{1}H NMR*** (400 MHz, $CDCl_3$): δ= 7.35 (dd, 1H, J= 1.5, 1, α-furyl-H); 7.19 (s_{br}, 1H, α-furyl-H); 6.27 (s_{br}, 1H, β-furyl-H); 5.39 (t, 1H, J= 7, $-C\underline{H}=$); 3.11 / 3.22 (2x dd, 2x 1H, J= 17, 7, furyl-$C\underline{H}_2-CH=$); 2.97 (m, 1H, $-C\underline{H}(CH_3)-$); 1.52 / 1.59 (ddd / d_{br}, 2x 1H, J= 13, 5, 4 / 13, $-C\underline{H}_2-$, H_{axial} / $H_{equatorial}$); 1.40-1.48 (m,2H, $-C\underline{H}_2-C\underline{H}_2-$, 2x H_{eq}); 1.28 (ddd, 1H, $-C\underline{H}_2-$, H_{ax}); 1.18 (dddd, 1H, J= 13, 13, 4, 4, $-C\underline{H}_2-$, H_{ax}); 1.15 (d, 3H, J= 7,5, $C\underline{H}_3-$); 1.11 / 1.08 (2x s, 2x 3H, 2x $C\underline{H}_3$).- ***MS*** : m/e= 218.167007 (high resolution, $C_{15}H_{22}O$); 218 (80%, M^+); 203 (14%, $(M - CH_3)^+$); 147 (32%,$(203 - C_4H_8)^+$); 137 (33%, (M - furyl-$CH_2)^+$); 81 (100%, furyl-CH_2^+).- ***IR*** : ν = 1505, 1390, 1170, 1075, 1035, 890 cm^{-1} (furan); 3050 cm^{-1} (olefin).
5-(3'-Furyl)-2-methyl-2-pentene (perillene) (<u>11f</u>, resp. <u>13</u>) : ***^{1}H NMR*** (400 MHz, $CDCl_3$): δ= 7.35 (m, 1H, α-furyl-H); 7.22 (m, 1H, α-furyl-H); 6.28 (s_{br}, 1H, β-furyl-H); 5.16 (tq, 1H, J= 7, 1.5, $-C\underline{H}=$); 2.45 (t, 2H, furyl-$C\underline{H}_2-$); 2.24 (dt, 2H, $-C\underline{H}_2-$); 1.61 / 1.70 (2x s_{br}, 2x 3H, $(C\underline{H}_3)_2C=CH-$).- ***MS*** : m/e= 150 (28%, molpeak); 135 (9%, $(M - CH_3)^+$); 81 (52%, furyl-CH_2^+).- ***IR*** : ν = 1505, 1385, 1080, 1040, 890 cm^{-1} (furan).
2-(3'-(3''-Furyl)-propyl)oxy)tetrahydro-2H-pyran (<u>11i</u>) : ***^{1}H NMR*** (90 MHz, $CDCl_3$): 7.3 / 7.2 (2x s_{br}, 2x 1H, 2x α-furyl-H); 6.2 (s, 1H, β-furyl-H); 4.5 (s_{br}, 1H, $-O-C\underline{H}-O-$); 3.2 - 3.8 (m, 4-H, $-C\underline{H}_2-$); 2.5 (t, 2H, J= 7.5, furyl-$C\underline{H}_2-$); 2.1 (m, 2H, $-C\underline{H}_2-$); 1.6 (m, 6H, $-C\underline{H}_2-$).- ***MS*** : m/e= 210 (<1%, molpeak); 126 (18%, (M - pyranyl)$^+$); 85 (100%, pyranyl$^+$).

5-(3'-Furyl)-2-methyl-2-pentenal (perillenal) (14) : t-Butylhydroperoxide (1.5 ml, 90% solution) was dried over magnesium sulfate and diluted with dry methylenechloride to a volume of 5 ml. Selene dioxide (333 mg, 0.3 mmol) was added, the mixture was stirred for 30 min, cooled to 0°C and slowly treated with 13 (900 mg, 6 mmol). Stirring was continued for 20 h (TLC control) and saturated ammonium chloride solution (20 ml) was added. The organic layer was separated, the aqueous phase was extracted with ether (3 times), the combined organic solutions were dried over magnesium sulfate and evaporated. The residual crude product was purified by column chromatography (silica gel, ether/petroleum ether, eluation gradient) to obtain 578 mg (58%) of 14.
^{1}H NMR (400 MHz, CDCl$_3$): δ= 9.39 (s, 1H, -CHO); 7.36 / 7.24 (dd / s$_{br}$,2x 1H, J= 2, 1.5, α-furyl-H); 6.29 (s$_{br}$, 1H, β-furyl-H); 6.49 (t, 1H, J= 7, -CH=); 2.63 (m, 4H, -CH$_2$-CH$_2$-); 1.73 (s$_{br}$, 3H, CH$_3$-).- ***MS*** : m/e= 164 (10%, molpeak); 136 (4%, (M - CO)$^+$); 81 (100%, furyl-CH$_2$$^+$).- ***IR*** : v = 2700, 1695, 1645 cm^{-1} (conjugated -CHO); 730 cm^{-1} (E -C=C-).

5-(3'-Furyl)-2-methyl-2-pentene-1-ol (15) : To a stirred solution of lithium aluminium hydride (66 mg, 6 mmol) in dry ether (40 ml), 14 (578 mg, 3.5 mmol), dissolved in dry ether (10 ml),was added dropwise . The mixture was stirred at room temp. until the reaction was complete (TLC control). Saturated ammonium chloride solution was added carefully to destroy the excess of the hydride reagent. The precipitate of aluminium hydroxide was dissolved by treating it with 2 N hydrochloric acid. The organic layer was separated and the aqueous phase was extracted with ether (3 times). The combined organic phases were washed with saturated sodium hydrogen carbonate solution, water and brine, dried over sodium sulfate and evaporated under reduced pressure. The residue was purified by flash chromatography (silica gel, ether/petroleum ether, polarity gradient) giving 534 mg (92%) of 15.- ***^{1}H NMR*** (400 MHz, CDCl$_3$): δ= 7.34 / 7.21 (dd / s$_{br}$, 2x 1H, J= 2, 1.5, α-furyl-H); 6.28 (s$_{br}$, 1H, β-furyl-H); 5.44 (tq, 1H, J= 7, 1, -CH=); 3.99 (s$_{br}$, 2H, -CH$_2$-OH); 2.49 (t, 2H, J= 7.5, furyl-CH$_2$-); 2.31 (dt, 2H, J= 7, 7.5, furyl-CH$_2$-CH$_2$-); 1.65(s$_{br}$, 3H, CH$_3$-).- ***MS*** : m/e= 166 (2%, molpeak); 148 (5%, (M - H$_2$O)$^+$); 95 (10%, furyl-C$_2$H$_4$$^+$); 81 81 (100%, furyl-CH$_2$$^+$).- ***IR*** : v = 3610, 3400 cm^{-1}(OH); 1505, 1070, 1035, 880 cm^{-1} (furan).

Ursinanolide (2) : The solution of the butenolide 16 (367 mg, 3.2 mmol) in dry methylenechloride (35 ml) was treated with DCC (663 mg, 3.2 mmol), dissolved in dry methylenechloride (10 ml). After stirring for 30 min at room temp. the alcohol 15 (534 mg, 3.2 mmol), dissolved in dry methylenechloride (5 ml), was added. Stirring was continued for 3 days. The yellow precipitate was filtered off, the solvent was removed under reduced pressure and the residual crude product was purified by thin layer chromatography (silica gel, ether/petroleum ether 40:60). 226 mg (27%) of 2 were obtained.- ***^{1}H NMR*** (400 MHz, CDCl$_3$): δ= 7.34 (dd, 1H, J= 1.5, 1.5, α-furyl-H); 7.21 (dd, 1H, 1.5, 1,α-furyl-H); 6.27 (s$_{br}$, 1H, β-furyl-H); 5.87 (dq, 1H, J= 1.5, -C=CH-C=O); 5.61 (s, 1H, O-CH-O); 5.54 (t$_{br}$, 1H, J= 7, -CH=C(CH$_3$)-); 4.22 / 4.10 (2x d$_{br}$, 2x 1H, 2x J= 11, =C(CH$_3$)-CH$_2$-O-); 2.50 (td, 2H, J= 7, 1, furyl-CH$_2$-); 2.34 (td, 2H, J= 7, 7, -CH$_2$-CH$_2$-C=); 2.04 (d, 3H, J= 1.5, CH$_3$-lactone); 1.66 (s$_{br}$, 3H, CH$_3$-C=).- ***MS*** (DI) : m/e= 262.120510 (high resolution, C$_{15}$H$_{18}$O$_4$); 262 (0.3%, molpeak); 165 (12%, (M - methylbutenolide)$^+$); 149 (8%, C$_{10}$H$_{13}$O$^+$); 97 (78%, methylbutenolide$^+$); 81 (100%, pyrylium$^+$).- ***MS*** (CI) : 263 (19%, (M + H)$^+$); 245 (13%, (263 - H$_2$O)$^+$); 149 (100%, (263 - C$_5$H$_6$O$_3$)$^+$).- ***IR*** : v = 1810, 1780 cm^{-1}, (-lactone); 1080, 1020, 955, 855 cm^{-1} (furan); 855 cm^{-1} (C=C).

2-Bromo-3-methyl furan (18): 3-Methyl furan (17) (8.2 g, 0.1 mol), N-bromosuccinimide (17.3g, 0.1 mol) and azobis(isobutyronitrile) (100 mg) were refluxed in dry ether (100 ml) for 90 min. After cooling to room temp. the precipitate was filtered off and the filtrate was washed twice with sodium hydrogencarbonate solution (1%). Calcium carbonate and hydroquinone (100 mg of each) were added and the solution was dried with sodium sulfate for 3 days at +2°C and under exclusion of light. The product was too unstable to be isolated and had to be stored in diluted ethereal solution over molecular sieve at -20°C.- The yield (75 mmol) was determined by NMR from the original solution (comparision of the integrals with CH$_2$Cl$_2$ as reference).- ***^{1}H NMR*** (90 MHz, in ether): δ= 7.4 (d, 1H, J= 2, α-furyl-H); 6.3 (d, 1H, J= 2, β-furyl-H); 2.0 (s, 3H, CH$_3$-furyl).

3-Methyl-2-trimethylsilyl furan (19a): A stirred solution of 18 (21 g, 0.129 mol) in dry ether (230 ml), cooled down to -78°C in a dry ice/acetone bath, was treated with n-butyllithium (81 ml, 1.6 N solution in hexane). After stirring for 30 min, chlorotrimethylsilane (20.1 g, 0.129 mol) was dropped into the mixture. Stirring was continued for 3 hours; after 1 hour the cooling bath was removed. Ether (500 ml) was added and the solution was washed neutral with water. The organic layer was dried with sodium sulfate, the solvent was removed under reduced pressure, the residue was dissolved in petrol ether and filtered through a short column, filled with aluminium oxide (neutral, containing 7 % water). Further purification by distillation in vacuo led to 14, 3 g (75%) of 19a; Kp: 58 - 62°C / 26 Torr.- ***^{1}H NMR*** (400 MHz, $CDCl_3$): δ= 7.45 (d, 1H, J= 1.5, α-furyl-H); 6.26 (d, 1H, J= 1.5, β-furyl-H); 2.15 (s, 3H, $C\underline{H}_3$-furyl); 0.32 (s, 9H, $C\underline{H}_3$-Si).- ***MS*** (DI): m/e= 154 (32%, molpeak); 139 (100%, $(M-CH_3)^+$); 111 (65%, $C_5H_7OSi^+$).

4-Methyl-2-trimethylsilyl furan (21a)

a) 2-Bromo-3-methyl-5-trimethylsilyl furan (20): n-Butyllithium (81.5 ml, 1.6 N solution in hexane) was dropped into a stirred solution of diisopropylamine (13.1 g, 0.13 mol) in dry THF (150 ml) at -5°C. The mixture was stirred at room temp. for 15 min, cooled down to -78°C and a solution of 18 (0.13 mol) in 200 ml of dry ether was added slowly.
After 2 h of stirring, chlorotrimethylsilane (14.0 g, 0.13 mol) was added. The mixture was stirred for 2 h (after 1 h the cooling bath was removed), diluted with petroleum ether (1.2 l) and washed neutral with water. Drying over magnesium sulfate and removing of the solvent under reduced pressure gave 26 g (100%) of crude 20.- ***^{1}H NMR*** (90 MHz, $CDCl_3$): δ= 6.5 (s, 1H, α-furyl-H); 1.9 (s,3H, $C\underline{H}_3$-furyl); 0.2 (s,9H, $C\underline{H}_3$Si).

b) 4-Methyl-2-trimethylsilyl furan (21a) : A stirred solution of crude 20 (26 g, ca. 0.13 mol) in dry ether (100 ml), cooled down to -78°C (dry ice/acetone), was treated with n-butyllithium (82 ml, 1.6 N solution in hexane). Stirring was continued for 1 h, 100 ml of brine were added slowly and the mixture was allowed to warm up to room temperature. Dilution with petroleum ether (400 ml), further work-up as described in the synthesis of 19a and subsequent distillation of the crude product gave 10.7 g (62%) of 21a (Kp: 65 - 67°C /34-38 Torr).- ***^{1}H NMR*** (270 MHz, $CDCl_3$): δ= 7.42 (m, 1H, α-furyl-H); 6.51 (s_{br}, 1H, β-furyl-H); 2.06 (d, 1H, J= 0.5, $C\underline{H}_3$-furyl); 0.30 (s, 9H, $C\underline{H}_3$-Si).- ***MS*** (DI): m/e = 154 (33%, molpeak); 139 (100%, $(M - CH_3)^+$); 111 (50%, $C_5H_7OSi^+$).

4-(2'-(4'-Methyl-5'-trimethylsilyl)furyl)-2-methyl-2-butene-1-ol (22) : A stirred solution of 3-methyl-2-trimethylsilyl furan (19a) (3.75 g, 23.2 mmol) in dry THF (23 ml) was cooled to 0°C and treated with n-butyllithium (9.2 ml, 2.5 N solution in hexane). After stirring for 1 h at room temp. the solution of the lithiated furan was dropped into a stirred and cooled (-40°C) suspension of copper(I)iodide (1.9 g, 10 mmol) in dry ether (12 ml) under nitrogen atmosphere and exclusion of light. The mixture was stirred for 30 min and 1,2-isoprene oxide (20) (0.84 g, 10 mmol), dissolved in dry ether (10 ml), was added during 1 h. Stirring was continued for 20 hours, and saturated ammonium chloride solution (15 ml) was added. After warming up to room temperature, the mixture was filtered through a vacuum funnel, the organic layer of the filtrate was separated and the aqueous phase was extracted with ether (3 times). The combined organic phases were washed neutral with brine, dried with magnesium sulfate and the solvent was removed under reduced pressure. The residue was purified by column chromatography (aluminium oxide neutral, containing 7% water; eluation at first with petrol ether, and than with petrol ether/ether = 1:1). 1.5 g (63%) of pure 22, with an E/Z ratio of 85:15, were obtained.- ***^{1}H NMR*** (400 MHz, $CDCl_3$): E-22: δ= 5.83 (s_{br}, 1H, β-furyl-H); 5.60 (tq, 1H, J= 7, 1.5, -C$\underline{H}$=C-); 4.03 (s_{br}, 2H, -$C\underline{H}_2$-OH); 3.36 (d, 2H, J= 7, furyl-$C\underline{H}_2$-CH=); 2.05 (s, 3H, $C\underline{H}_3$-furyl); 1.73 (s_{br}, 3H, =CH-$C\underline{H}_3$); 0.25 (s, 9H, $C\underline{H}_3$-Si).- Z-22: δ= 5.46 (tq, 1H, J= 7, 1.5, -C$\underline{H}$=C-); 4.18 (s_{br}, 2H, -$C\underline{H}_2$-OH); 3.37 (d_{br}, 2H, J= 7, furyl-$C\underline{H}_2$-CH=); 1.84 (s, 3H, $C\underline{H}_3$-furyl).- ***MS*** (DI): m/e= 238 (12%, molpeak); 220 (2%, $(M - H_2O)^+$); 207 (15%, $(M - CH_2OH)^+$).- ***IR*** : ν = 3610 cm^{-1} (O-H); 985 cm^{-1} (furan); 850 cm^{-1} (C=C).

4-(2'-(3'-Methyl-5'-trimethylsilyl)furyl)-2-methyl-2-butene-1-ol (23) : Reaction of 4-methyl-2-trimethylsilyl furan (21a) (4.0 g, 26 mmol) with n-butyllithium (11.4 ml, 2,5 N solution in hexane), copper(I)iodide (2.5 g,13 mmol) and 1,2-isoprene oxi-de (20) (1.09 g, 13 mmol), similar to the synthesis of 22 gave 2.67g (86%) of pure 23; E/Z ratio was 85:15. ***^{1}H NMR*** (400 MHz, $CDCl_3$): E-23: δ= 6.41 (s, 1H, β-furyl-H); 5.57 (tq, 1H, J= 7, 1.3, -C$\underline{H}$=C-); 4.02 (s_{br}, 2H, -$C\underline{H}_2$-OH); 3.36 (d_{br}, 2H, J= 7, furyl-$C\underline{H}_2$-CH=); 1.96 (s, 3H, $C\underline{H}_3$-furyl); 1.79 (s_{br}, 3H, =C-$C\underline{H}_3$); 0.27 (s, 9H, $C\underline{H}_3$-Si).- Z-23: δ= 5.44 (tq, 1H, J= 7, 1.8, -C$\underline{H}$=C-); 4.23 (s_{br}, 2H, -$C\underline{H}_2$-OH); 3.37 (d_{br}, 2H, J= 7, furyl-$C\underline{H}_2$-CH=); 1.97 (s, 3H, $C\underline{H}_3$-furyl).- ***MS*** (DI): m/e= 238 (26%, molpeak); 220 (4%, $(M - H_2O)^+$); 207 (41%, $(M - CH_2OH)^+$); 85 (14%, $C_5H_9O^+$).- ***IR*** : ν = 3600 cm^{-1} (O-H); 950 cm^{-1} (furan); 850 cm^{-1} (C=C).

1-Bromo-4-(2'-(4'-methyl-5'-trimethylsilyl)furyl)-2-methyl-2-butene (24): Bromine (0.4 ml, 7.5 mmol), dissolved in hexane (6 ml) was dropped into a solution of triphenylphosphin (8 mmol) and pyridine (0.12 ml, 1.5 mmol) in dry ether (100 ml) at (2.1 g, -20°C. The mixture was stirred for 30 min and treated with 22 (360 mg, 1.5 mmol) and pyridine (1.5 ml, 16 mmol), dissolved in dry ether (8 ml). Stirring was continued for 20 h, during this time the mixture was allowed to warm up to room temp. The mixture was poured into hexane (250 ml) and filtered through a vacuum funnel, filled with celite ® or magnesium sulfate. The filtrate was treated with dimethyl formamide (20 ml), the ether was removed under reduced pressure and the residual DMF solution was extracted with hexane (7x 20 ml). The combined extracts were washed with water, dried over magnesium sulfate, filtered through aluminium oxide (neutral, cont. 7% water; 1g) and reduced to a definite volume of 5 ml. From this solution 0.5 ml were taken off, carefully evaporated, quickly dissolved in deutero benzene and the yield determined by NMR (methylenechloride as reference, ratio of integrals). The remaining solution of 24 was diluted with dry benzene, very carefully evaporated to a volume of 1-2 ml (2 times) and the product was stored in dry THF (5 ml) over molecular sieve (4 Angstroms) at -20°C. Yield determined was 0.3 mmol (20%).-***^{1}H NMR*** (400 MHz,C_6D_6): E-24 : δ= 5.82 (s_{br}, 1H, β-furyl-H); 5.53 (tq, 1H,J= 7, 1.2, -C$\underline{H}$=); 3.59 (s, 2H, -$C\underline{H}_2$-Br); 3.17 (d_{br}, 2H, J= 7, furyl-$C\underline{H}_2$-); 2.04 (s, 3H, $C\underline{H}_3$-furyl); 1,58 (d, 3H, J= 1.2, -$C\underline{H}_3$-C=); 0.34 (s, 9H, $C\underline{H}_3$-Si).- ***MS, IR*** : because of the high instability of 24 no data obtained.

1-Bromo-4-(2'-(3'-methyl-5'-trimethylsilyl)furyl)-2-methyl-2-butene (25) : The alcohol 23 (480 mg, 2 mmol) was brominated as described above. Yield determined: 0.6 mmol (30%). ***^{1}H NMR*** (400 MHz, $CDCl_3$): E-25: δ= 6.24 (s, 4H, β-furyl-H); 5.75 (t_{br}, 1H,J= 7, -C$\underline{H}$=); 3.99 (s, 2H, -$C\underline{H}_2$-Br); 3.35 (d_{br}, 2H, J= 7, furyl-$C\underline{H}_2$-); 1.96 (s, 3H, $C\underline{H}_3$-furyl); 1,88 (s_{br}, 3H, $C\underline{H}_3$-C=); 0.23 (s, 9H, $C\underline{H}_3$-Si).- ***MS, IR*** : because of the high instability of 25 no data obtained.

1-(2'-(4'-Methyl-5'-trimethylsilyl)furyl)-4-(2'-(3'-methyl-5'-trimethylsilyl)furyl)-2-methyl-2-butene (26), also 27 - 29 : 3-Methyl-2-trimethylsilyl furan (19a) (1.11 g, 7.2 mmol) was alkylated with the allylic halide 25 (0.9 mmol) by action of n-butyllithium (3.2 ml, 2.5 N solution in hexane) and copper(I)iodide (690 mg, 3.6 mmol) similar to the procedure described in the synthesis of the alcohol 22. 1 h after addition of the electrophile, HMPT (3ml, dissolved in 3 ml dry THF) was dropped into the mixture during 30 min. The crude product was purified by filtration on aluminium oxide neutral (cont. 7% water, petroleum ether as eluent) and subsequent thin layer chromatography (aluminium oxide neutral, petroleum ether). The compounds 27 - 29 were synthesized in the similar way. Starting materials and yields see Table 2.- **Spectral data of 26** : ***^{1}H NMR*** (400 MHz, $CDCl_3$): δ= 6.41 (s, 1H, β-$furyl_A$-H); 5.84 (s, 1H, β-$furyl_B$-H); 5.40 (tq, 1H, J= 7, 1.5, -C$\underline{H}$=); 3.35 (d,2H, J=7, $furyl_A$-$C\underline{H}_2$-); 3.29 (s_{br}, 2H, -$C\underline{H}_2$-$furyl_B$); 2.04 (s, 3H, $C\underline{H}_3$-$furyl_B$); 1.95 (s, 3H, $C\underline{H}_3$-$furyl_A$); 1.74 (d, 3H, J= 1.5, -$C\underline{H}_3$); 0.23 / 0.26 (2x s, 18H, $C\underline{H}_3$-Si).- ***MS*** (DI): m/e= 374 (22%, molpeak); 359 (4%, $(M - CH_3)^+$); 167 (22%, Me_3Si-furyl-CH_2^+); 73 (100%, Me_3Si^+).- ***IR*** : ν = 3090, 1505, 1260, 1120, 990, 960 cm^{-1} (furan); 1610, 860 cm^{-1} (C=C).- **Spectral data of 29** : ***^{1}H NMR*** (400 MHz, $CDCl_3$): δ= 6.43 (s, 1H, β-$furyl_B$-H); 5.83 (s, 1H, β-$furyl_A$-H); 5.35 (tq, 1H, J= 7, 1.5, -C$\underline{H}$=); 3.33 (d, 2H, J= 7, $furyl_A$-$C\underline{H}_2$-); 3.32 (s_{br}, 2H, -$C\underline{H}_2$-$furyl_B$); 2.05 (s, 3H, CH_3-$furyl_A$); 1.96 (s, 3H, $C\underline{H}_3$-$furyl_B$); 1.66 (d, 3H, -CH_3); 0.23 / 0.26 (2x s, 18H, $C\underline{H}_3$-Si).- ***MS and IR*** : similar to 26.

1-(2'-(4'-Methyl)furyl)-4-(2'-(3'-methyl)furyl)-2-methyl-2-butene (longifolin) (4), also 5 - 7 : 26 (61 mg, 0.2 mmol) and para-toluene sulfonic acid (30 mg) were dissolved in methanol/ ether/water (3/0.6/0.3 ml) and stirred at room temp. for 6 h. The mixture was diluted with ether (100 ml), treated with powdered calcium chloride (5 g) and stirred for 10 min. After filtration through a vacuum funnel the filtrate was evaporated and the residual crude product was purified by thin layer chromatography (silica gel, petroleum ether). Same procedure for the synthesis of 5 - 7. Yields see text according to Scheme 5.- **Spectral data of 4 :** ***^1H NMR*** (400 MHz, $CDCl_3$): δ= 7.21 (d, 1H, J= 1.8, α-furyl$_A$-H); 7.06 (s$_{br}$, 1H, α-furyl$_B$-H); 6.15 (d, 1H, J= 1.8, β-furyl$_A$-H); 5.88 (s, 1H, β-furyl$_B$-H); 5.39 (tq, 1H, J= 7, 1.5, -C$\underline{H}$=); 3.32 (d, 2H, J= 7, furyl$_A$-C$\underline{H}_2$-); 2.27 (s$_{br}$, 2H, furyl$_B$-C$\underline{H}_2$-); 1.98 (d, 3H, J= 1.5, C$\underline{H}_3$-furyl); 1.95 (s, 3H, C$\underline{H}_3$-furyl); 1.71 (d, 3H, J= 1.5, C$\underline{H}_3$-C=).- ***MS*** (DI) : m/e= 230.1307 (high resolution, $C_{15}H_{18}O_2$); 230 (20%, molpeak); 135 (100%, $C_9H_{11}O^+$); 95 (40%, CH_3-furyl-CH_2^+).- ***IR*** : v = 3090, 1505, 1080, 950, 890 cm^{-1} (furan); 1610, 845 cm^{-1} (C=C).- **Spectral data of 7 :** ***^1H NMR*** (400 MHz, $CDCL_3$): δ= 7.23 (d, 1H, J= 1.8, α-furyl$_A$-H); 7.06 (s, 1H, α-furyl$_A$-H); 6.18 (d, 1H, J= 1.8, β-furyl$_B$-H); 5.83 (s, 1H, β-furyl$_A$-H); 5.37 (tq, 1H, J= 7, 1.5, -C$\underline{H}$=); 3.31 (d, 2H, J= 7, furyl$_A$-C$\underline{H}_2$-); 3.29 (s$_{br}$, 2H, furyl$_B$-C$\underline{H}_2$-); 1.98 (s, 3H, C$\underline{H}_3$-furyl); 1.97 (s, 3H, C$\underline{H}_3$-furyl); 1.64 (d, 3H, J= 1.5, C$\underline{H}_3$-C=).- ***MS*** (DI): m/e= 230 (45%, molpeak); 135 (100%); 95 (25%).- ***IR*** : v = 1505, 1220, 1100, 955, 910 cm^{-1} (furan).

Acknowledgement- Financial support of this study by the Fonds der Chemischen Industrie is gratefully acknowledged.

REFERENCES

1. a) R. Katzlauskas, P. T.Murphy, R. J. Quinn and R. J. Wells, *Tetrahedron Lett.* 17 (1976), 1331; b) ibid. *Tetrahedron Lett.* 17 (1976), 1333.
2. F. Bohlmann and R. Gupta, *Phytochem.* 21 (1982), 1309.
3. H. Bornowski, *Tetrahedron* 27 (1971), 4101.
4. N. Hayashi, S. Eguchi, M. Nakayama, S. Hayashi and T. Sakao, *Chem.& Ind.* 1972, 572.
5. F. M. Dean, *Adv. in Heterocycl. Chem.* 30 (1982), 167.
6. F. M. Dean, *ibid.* 31 (1982), 237.
7. a) M. Mortimore, G. S. Cockerill, P. Kocienski and R. Treadgold, *Tetrahedron Lett.* 28 (1987), 3747; b) S. Pikul, J. Raczko, K. Ankner and J. Jurkzak, *J. Am. Chem. Soc.* 109 (1987), 3981.
8. D. Craig, *Chem. Soc. Rev.* 16 (1987), 187.
9. R. Okazaki, Y. Negishi and N. Inamoto, *J. Org. Chem.* 49 (1984), 3819.
10. K. Kondo and M. Matsumoto, *Tetrahedron Lett.* 17 (1976), 4363.
11. a) A. Jerome, A. Berson and P. Swidler, *J. Am. Chem. Soc.* 75 (1953), 1721;
    b) J. Srogl, M. Janda and J. Stibor, *Coll. Czech. Chem. Comm.* 35 (1970), 3478.
12. L. Mangoni, M. Adinolfi, R. Laonigro and R. Caputo, *Tetrahedron* 28 (1972), 611.
13. C. Reichardt, "Lösungsmitteleffekte in der organischen Chemie", Verlag Chemie, Weinheim 1969.
14. G. Cimino, S. De Stefano, A. Guernero and L. Minale, *Tetrahedron Lett.* 20 (1979), 3723.
15. H. Kondo and H. Suzuki, *Chem. Ber.* 69 (1936), 2459.
16. All compounds were characterized by NMR-, MS- and IR-data.
17. M.A. Umbreit and B.K. Sharpless, *J. Am. Chem. Soc.* 99 (1977), 5526.
18. G. Pattenden and B.C.L. Weedon, *J. Chem. Soc.* (C) 1986, 1984.
19. a) M.D. Burness, *Org. Synth.* 39 (1959), 49; b) M.D. Burness, *ibid.* , 46.
20. M. Schlosser and N.D. Ly, *Helv. Chim. Acta* 60 (1977), 2085.
21. B.R. Baker, I.G. Junga and E.J. Reist, *J. Org. Chem.* 25 (1960), 1673.
22. W. Ebert, Dissertation 1980, Technische Universität Berlin, D 83.