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A Straightforward Synthetic Approach to the Spiroketal-Enol Ethers Synthesis of Natural Antifeeding Compound Tonghaosu and Its Analogs*

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Abstract Tonghaosu **1**, a natural product discovered from several plants of tribe *Athemdeae*, is a [4.4]spiroketal with an enediyne side-chain and shows interesting insect antifeeding activity. In this paper a general and convenient synthetic methodology for the synthesis of **1**, **2** and its spiroketal-enol ether derivatives is described. Thus, 3-(2′-furyl)-propan-1-ol **7a** or 4-(2′-furyl)-butan-1-ol **7b** prepared from furaldehyde was treated with *n*-butyl lithium and unsaturated aldehyde to provide the diol **5**. Diol **5** could also be obtained from 5-(3-acetoxypropyl)-2-furaldehyde or 5-(4-acetoxybutyl)-2-furaldehyde and alkynyllithium. By careful treatment of **5** or **7** with acid, dehydration-cyclization occurred to give the desired spiroketal-enol ether in moderate to excellent yields.

Introduction

Tonghao (*Chrysanthemum segetum L.*) is a very common vegetable in southern China during spring and autumn. Some fractions of its essential oil show obvious insect antifeeding activity. In these fractions, besides several known aromatic compounds and monoterpenes, an interesting spiroketal compound **1** as a *Z/E* mixture was identified[1] and named as tonghaosu in our laboratory. This compound and its analogs **2**, **3**, and **4**, featuring a spiroketal-enol ether functionality, have been isolated from similar plant *Chrysanthemum coronarium l.* and other plants of tribe *Athemdeae*.[2] Tada has reported its antifeeding activity toward silkworm,[3a] and (*E*)-**1** has also been reported to exhibit spasmolytic and antiphlogistic properties.[3b, 3c]

Spiroketals are subunits of many naturally occurring substances of biological interest, such as insect pheromones, antifeedants and polyether antibiotics. A wide variety of synthetic strategies have been developed for this functionality.[4] Most of the existing methodologies, however, are not very suitable for spiroketal-enol ethers found in tonghaosu **1**. In the early 1960s, Bohlman reported a 5-step approach to tonghaosu. The overall yield of this route was quite low.[5] Recently Y.Q. Tu[6a] and H. Toshima[6b] have also

* In memory of the late professor Yu Wang

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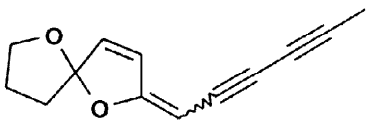
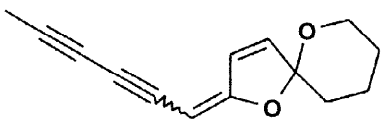
mentioned the synthesis of tonghaosu, but neither of them has reach the end product. In recent years, the need for synthetic methods, which could directly afford unsaturated spiroacetals, has been further stimulated by the isolation and characterization of simpler unsaturated spiroacetals (e.g., a 1,6-dioxaspiro[4.4]nona-3, 8-diene[7] and a 1,6-dioxaspiro[4.5]decene[8] from *Artemisia* species. Related unsaturated spiroacetals[9] have also been found in a culture broth). In order to develop efficient synthetic routes towards these compounds, a practical and high-yielding method for the synthesis of unsaturated spiroacetal is obviously desirable.



1
tonghaosu



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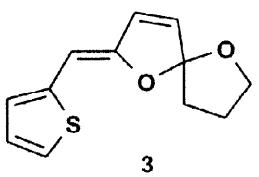

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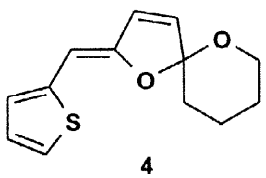
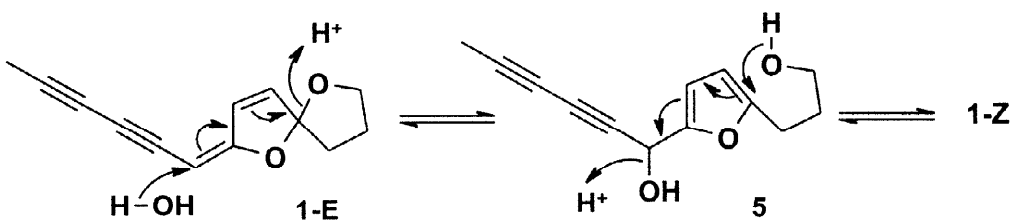


4

During the isolation of tonghaosu (**1**), we noticed that in the presence of acid and trace amounts of water (or during silica gel chromatography or even in aged deuterated chloroform in an NMR tube) the *E*- and *Z*- isomers were in an equilibrium with each other, with the furandiol compound **5** as an intermediate. This phenomenon suggested that the desired spiroketal-enol ether functionality would be easily accessible if a proper furandiol was available. Since the furandiols are relatively simple compounds, if this concise synthetic protocol is executable, it would promise a good supply of a series of spiroketal-enol ethers and related derivatives. Such work would also be beneficial to future biological and pharmaceutical evaluation. In this paper, we wish to report our results on the successful realization of a general strategy that allows for synthesis of tonghaosu and its analogues in moderate to high yields. To the best of our knowledge, this type of conversion has not been reported before.

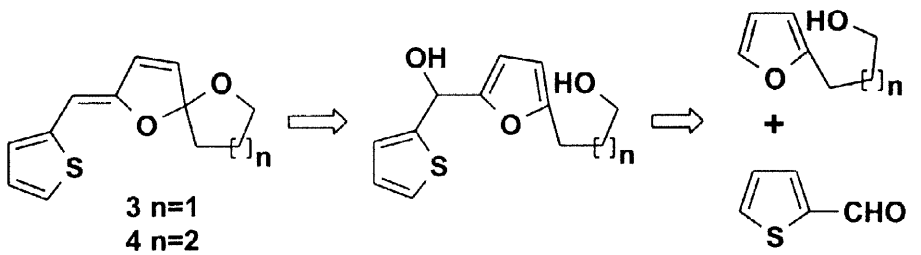


1-E 5 1-Z

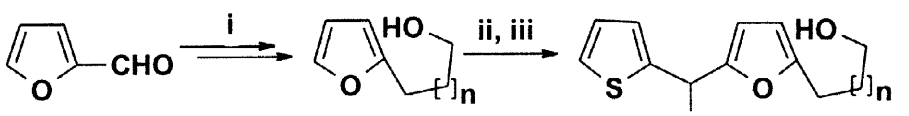
Equilibrium between Z- and E-isomer

Results and Discussion

Our synthetic effort was first directed towards the synthesis of natural compounds **3** and **4**, and the establishment of optimum conditions for the transformation of furandiol precursors to spiroketal-enol ethers. Based on the protocol mentioned above, we first disconnect the targets **3** and **4** by retrosynthetic analysis as shown in Scheme 1. This reveals that furyl-propanols and thiophenecarboxaldehyde would be excellent building blocks; the propanols are known compounds, whilst the thiophenecarboxaldehyde is a commercially available reagent.



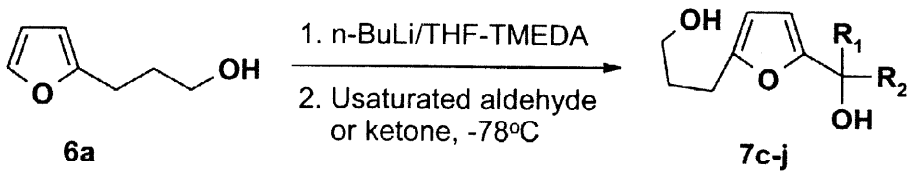
Scheme 1



Reagents and conditions: (i) reference 10; (ii) BuLi, THF, TMEDA, 0°C--r.t.; (iii) 2-thiophenecarboxaldehyde, -78°C--r.t.,77% for 7a, 71% for 7b.

Scheme 2

Thus, the known 3-(2'-furyl)-propan-1-ol **6a** and 4-(2'-furyl)-butan-1-ol **6b** were prepared from furaldehyde according to the procedure described in the literature.[10] Treatment of **6** with butyllithium and 2-thiophenecarboxaldehyde provided furandiol **7a** and **7b** in 77% and 71% yield, respectively (Scheme 2). Several other aromatic aldehydes or α,β-unsaturated aldehydes were also tested in place of thiophenecarboxaldyhyde. The yields were usually good except for **7g**, presumably due to the presence of the nitro group (Scheme 3). All these products were unstable; during the isolation and purification there were always some cyclization products formed, signalling the ease with which the spiroketalization took place.

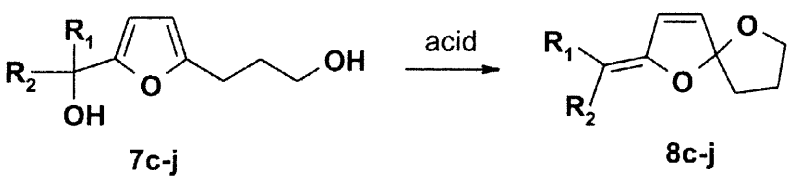


6a 7c-j

7c R_1=H, R_2=phenyl, 71%
7d R_1=H, R_2= *p*-chlorophenyl, 70%
7e R_1=R_2=phenyl, 59%
7f R_1=H, R_2= *p*-nitrophenyl, 40%
7g R_1=H, R_2=*p*-methoxyphenyl, 65%
7h R_1=H, R_2=3,4-methylene dioxyphenyl, 62%
7i R_1=H, R_2=*trans*-propenyl, 64%
7j R_1=H, R_2=*trans*-styryl, 71%

Scheme 3

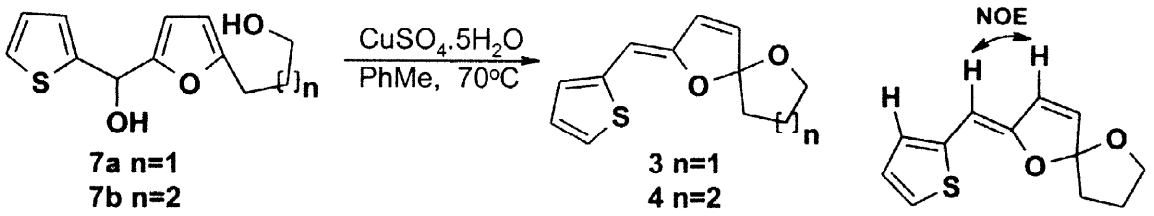
In the course of investigation of the dehydration-spiroketalization step, several acids and dehydration agents had been examined (Scheme 4 and Table 1). For those furandiols prepared from benzaldehyde, substituted benzaldehyde or α,β-unsaturated aldehydes, the reaction took place at room temperature in the presence of trace amounts of protonic acid, such as hydrochloric acid, toluenesulfonic acid. The yields were usually not very good because of the equilibrium (except for the *p*-nitrophenyl substituted furandiol, which gave a yield as high as 97%). Pyridinium *p*-toluenesulfonate could also promote the reaction, and slightly improve the yield. With thiophenyl substituted furandiol as substrate, the reaction became very complicated; even at temperatures as low as -78 °C, the desired product was formed only in negligible amounts, accompanied by a lot of unidentified side-products.



7c-j 8c-j

Scheme 4

The unsatisfactory results with protonic acids impelled us to turn our attention to Lewis acids. We found in the literature that $CuSO_4$ and its hydrates had been used as excellent dehydration agents, especially for α,β-unsaturated alcohols.[11] Our initial experiments using this reagent at refluxing temperature did not succeed, giving practically no desired products. The situation, however, changed dramatically when we lowered the reaction temperature to 70 °C. The optimum conditions were found with $CuSO_4 \cdot 5H_2O$ in dry toluene, under which natural product **3**, **4** and those aromatic analogues could be prepared in almost quantitative yields and only in the *Z*-form (Scheme 5).



Scheme 5

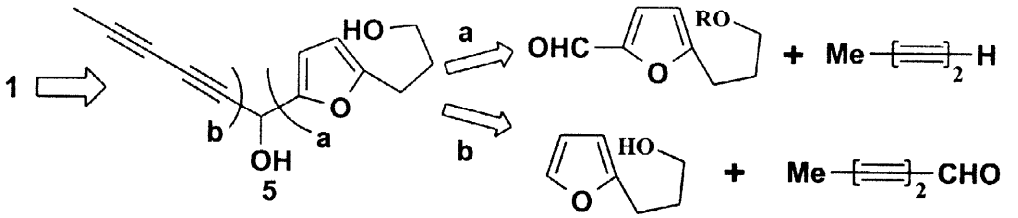
The stereochemistry of the products was unambiguously established by 2D NMR spectroscopy. All physical data of **3** and **4** were consistent with their structures and those reported in the literature.[12] For the furandiols substituted with a *trans*-propenyl or *trans*-styryl group (**7i** and **7j**), the reaction was a little more complicated; the yields were low and the product was formed as a *Z/E* mixture in a ratio of about 3 : 1, presumably due to their instability. Anhydrous $CuSO_4$ could also promote the cyclization reaction excellently, but higher temperatures were required. Some of the cyclization results are listed in Table 1.

Table 1. Synthesis of Spiroketal-Enol Ethers

	Substrate	Conditions	Product	yield (%)	Notes
1	7a	$CuSO_4 \cdot 5H_2O$, PhMe, 70 °C	3	97	
2	7b	$CuSO_4 \cdot 5H_2O$, PhMe, 70 °C	4	97	
3	7c	HCl, CH_2Cl_2, R.T.	8c	75	
		$CuSO_4 \cdot 5H_2O$, PhMe, 70 °C		97	
4	7d	HCl, CH_2Cl_2, -78 °C; K_2CO_3	8d	92	
		$CuSO_4 \cdot 5H_2O$, PhMe, 70 °C		92	
5	7e	$CuSO_4 \cdot 5H_2O$, PhMe, 70 °C	8e	97	
6	7f	HCl, $CHCl_3$, R.T.	8f	97	
		$CuSO_4 \cdot 5H_2O$, PhMe, 70 °C		95	
7	7g	TsOH, CH_2Cl_2, R.T.	8g	60	
		$CuSO_4 \cdot 5H_2O$, PhMe, 70 °C		96	
8	7h	PhMe, PPTs, R.T.	8h	85	
		$CuSO_4 \cdot 5H_2O$, PhMe, 70 °C		92	
9	7i	HCl, acetone, R.T.	8i	42	3:1 Z/E [a]
		$CuSO_4 \cdot 5H_2O$, PhMe, 70 °C		44	mixture
10	7j	HCl, acetone, R.T.	8j	36	3:1 Z/E [a]
		$CuSO_4 \cdot 5H_2O$, PhMe, 70 °C		90	mixture

[a] The ratio was determined based on the integration in ^1H NMR spectrum.

With the optimized dehydration-spiroketalization conditions in hand, we set out to synthesize tonghaosu **1** and natural product **2**. As shown by the retrosynthetic analysis, these molecules could be built up through two routes (Scheme 6).

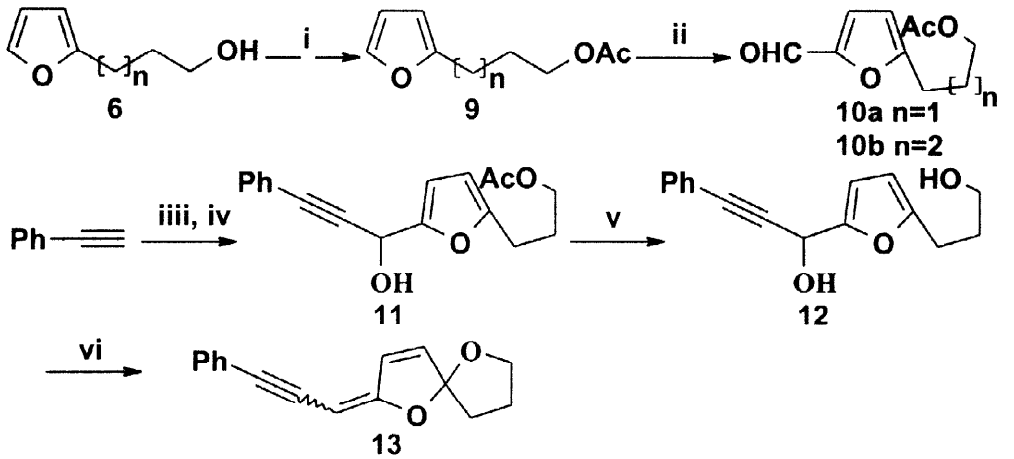


Scheme 6

We examined route **b** first, because it seemed to be straightforward. Unfortunately, it soon turned out that the 2,4-diyne-hexaldehyde (one of the two moieties in this route) was unstable under the strongly basic (coupling) conditions.[13] This made us turn to alternative route **a**. This time we first used commercially available phenylacetylene (in place of penta-1,3-diyne) as a model reagent to examine the feasibility of this route. Having noticed that compound **1**, **2** and **5** were sensitive to acids, we decided to choose acetyl group instead of THP to mask the hydroxyl in the furanaldehyde moiety so that deprotection at a later stage could be achieved under basic conditions. Thus, acetylation of compound **6** followed by Vilsmeier-Haack formylation of the furan nucleus furnished aldehyde **10** in high yield.[14] Addition of lithium phenylacetylenide (derived from phenylacetylene and butyl lithium in dry THF at -78 °C) to aldehyde **10a** in THF led to compound **11** as anticipated in 82% yield. Deprotection of **11** in $KHCO_3$-CH_3OH-H_2O mixture proceeded smoothly at 40°C, providing the required furandiol **12** in 95% yield (together with a small amount of cyclized product, which was formed during the chromatographic separation). Finally, treatment of **12** with 1 equivalent of $CuSO_4$¡¤$5H_2O$ in dry toluene yielded the desired spiroketal-enol ether **13** in 94% yield as a 1 : 1 *Z/E* mixture (Scheme 7). The two isomers of **13** could be separated by flash chromatography on silica gel. However, when each purified isomer was exposed to air at room temperature for prolonged time, a *Z/E* mixture was formed again. The same phenomenon was also observed during the isolation of tonghaosu.

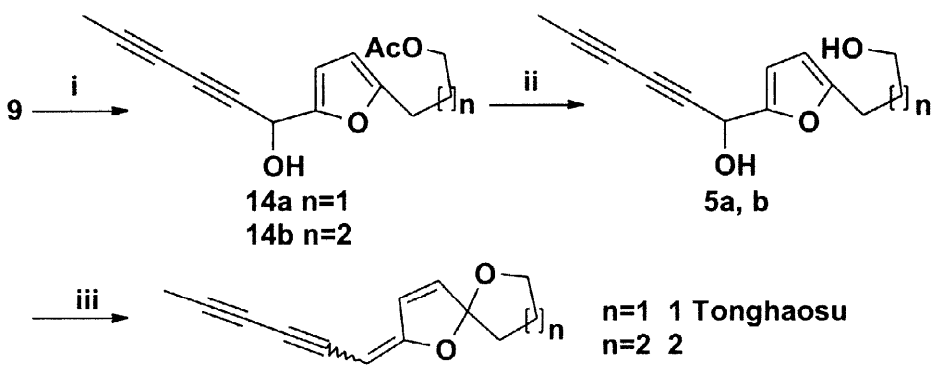
The successful synthesis of compound **13** unequivocally proved the high feasibility of our synthetic protocol (with compound **5** as the convenient precursor to tonghaosu **1**). Now our remaining task was to synthesize tonghaosu **1** and another natural product **2**. The synthetic strategy was the same as for the model compound **13**, except that penta-1,3-diyne was used in place of phenylacetylene. The pentadiyne, prepared according to the literature,[15] was treated with BuLi in dry THF at -78 °C to give the corresponding lithium salt, which in turn, after warming to room temperature, was added to the solution of aldehyde **10a** or **10b** in THF to furnish compound **14a** or **14b** in 75% or 69% yield, respectively. Deacetylation of **14** provided compound **5**, which was treated with $CuSO_4$·$5H_2O$ in dry toluene to finish tonghaosu **1** as a 1.5 : 1 *Z/E* mixture in high yield. Similarly, the other natural spiroketal-enol ether **2** was obtained as a 2 : 1 *Z/E* mixture (Scheme

8). In these cases due to their rapid interconversion, the *Z*- and *E*- isomers couldn't be separated by normal chromatography. Both **1** and **2** have a pleasant odor.



Reagents and conditions: (i) Ac_2O, Pyr., DMAP, 91%; (ii) DMF, $POCl_3$, CH_2Cl_2, 91%; (iii) BuLi, THF, TMEDA, -78°C--r.t.; (iv) **10a**, 0°C--r.t.; 82%; (v) $KHCO_3$, MeOH-H_2O, 95%; (vi) $CuSO_4.5H_2O$, PhMe, 70°C, 94%.

Scheme 7

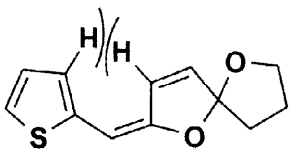


Reagents and conditions: (i) 1,3-Pentadiyne, BuLi, THF, -78°C--r.t., 75% for **14a**, 69% for **14b**; (ii) $KHCO_3$, MeOH-H_2O, 92% for **5a**, 90% for **5b**; (vi) $CuSO_4.5H_2O$, PhMe, 70°C, 94% for **1**, 92% for **2**.

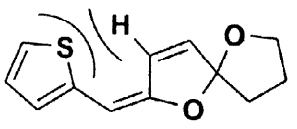
Scheme 8

In order to explain the selectivity difference observed with **1** and **3** (*Z*/*E*= 1.5 : 1 and only the *Z*-isomer, respectively), some calculations were carried out (with HF/3-21G work system). The result shows that the energy difference between the *Z*- and *E*-isomer of tonghaosu **1** is very small (ΔE = 0.5 kcal/mol), with the *Z*-**1** being of lower energy. The *Z*/*E* ratio calculated from ΔE is ca. 2.3 : 1, rather close to the experimental value (*Z*/*E* =1.5 : 1). For compound **3**, the energy for the *E*-isomer is much higher then that for the *Z*-isomer (ΔE = 3.4 kcal/mol). This is probably caused by the severe H-H and H-S repulsion as shown in the following

structures. The *Z/E* ratio calculated from ΔE for **3** is ca. 310 : 1, that explains why we can only get the *Z*-isomer. All the calculation results are consistent with the experimental ones.



3-E'



3-E"

In conclusion, we have developed a new and convenient synthetic approach to the spiroketal-enol ethers. Tonghaosu **1** and its three natural analogues **2**, **3**, **4**, together with several other unnatural analogues have been prepared in moderate to excellent yields. All the spiroketal-enol ether compounds show significant antifeeding activity in biological tests and the results will be reported in due time.

Experimental

Melting points were uncorrected. IR spectra were taken on a film (for oil) or a potassium bromide pellets (for solid samples) on a Bio-Rad FTS-20E or FTS-185 spectrometer. ^{1}H-NMR spectra were recorded on a Bruker AM-300 or AMX-600 spectrometer, with the coupling constants given in Hz. Mass spectra were obtained on a Finnigan 4021 or HP5989A spectrometer. Flash column chromatography was performed on silica gel H (10 - 40 um) or aluminum oxide (neutral, 200 - 300 mesh), with petroleum ether- ethyl acetate system as eluent.

Typical procedure I *α-(2-thienyl)-5-(3-hydroxypropyl)-2-furanmethanol* **7a**: A solution of *n*-butyllitium (9.6 mL of 2.4 M, 23 mmol) was added slowly to a solution of 3-(2'-furyl)-propan-1-ol (**7a**, 1.26 g, 10 mmol) and TMEDA (2.67 g, 23 mmol) in dry THF (20 mL) stirred at 0 °C under a nitrogen atmosphere. The reaction mixture was then stirred at room temperature for 2h, before being re-cooled to -78 °C. Freshly distilled 2-thiophenecarboxaldehyde (2.24 g, 20 mL) in THF (20 mL) was added dropwise. When the addition was completed, the reaction mixture was stirred at -78 °C for 4 h, and then was allowed to warm to room temperature and stirred overnight. Saturated aqueous NH_4Cl (15 mL) was added and the layers were separated. The aqueous layer was extracted with ether (20 mL × 3), and the combined organic layers were dried over $MgSO_4$, before being concentrated *in vacuo*. Purification by flash chromatography (silica; 2 : 1 petroleum ether/ethyl acetate containing 0.5% v/v triethylamine) afforded 1.83 g (77%) of **7a**: mp: 68.5-69.5 °C; IR (KBr, cm^{-1}): 3396, 3216, 2928, 1606, 1557, 1438; ^{1}H NMR (300 MHz, CD_3COCD_3): δ 7.29 (1H, dd, J = 1.2 Hz, 5.1 Hz), 6.93 (1H, ddd, J = 1.0 Hz, 1.2 Hz, 3.5 Hz), 6.90 (1H, dd, J = 3.5 Hz, 5.1 Hz), 6.08 (1H, dd, J = 0.3 Hz, 2.8 Hz), 5.92 (1H, dd, J = 2.2 Hz, 2.8 Hz), 5.91 (1H, s), 3.5 (2H, t, J = 6.3 Hz), 3.17 (2H, s, -O<u>H</u>), 2.60

(2H, t, J = 7.6Hz), 1.75 (2H, m) ppm; MS m/z (relative intensity): 238 (M^+, 23), 220 (100), 203 (29), 189 (81), 111 (41); Anal. calcd. for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92; S, 13.46; Found: C, 60.37; H, 5.68; S, 13.12.

α-(2-thienyl)-5-(4-hydroxybutyl)-2-furanmethanol **7b**: Following the typical procedure I described above, treatment of 4-(2'-furyl)-butan-1-ol **6b** with 2-thiophenecaroxaldehyde afforded **7b**: 71% yield; oil; IR (film, cm^{-1}): 3407, 2945, 1650, 1580; ^1H NMR (600 MHz, CD_3COCD_3): δ 7.29 (1H, dd, J = 1.2 Hz, 5.0 Hz), 6.93 (1H, m), 6.90 (1H, dd, J = 3.5 Hz, 5.0 Hz), 6.07 (1H, d, J = 3.0 Hz), 5.92 (1H, d, J = 3.0 Hz), 5.91 (1H, s), 3.48 (2H, t, J = 6.4 Hz), 3.17 (2H, s, -OH), 2.54 (2H, t, J = 7.6 Hz), 1.6 (2H, m), 1.49 (2H, m) ppm; MS m/z (relative intensity): 235 (M^++1 H_2O, 18), 234 (M^+-H_2O, 100), 178 (19), 176 (39), 150 (21), 124 (26); Anal. Calcd. for $C_{13}H_{16}O_3S$: C, 61.88; H, 6.39; S, 12.71; Found: C, 61.92; H, 6.47; S, 13.20.

7c-7j were prepared according to the typical procedure described above for the synthesis of **7a**.

α-phenyl-5-(3-hydroxypropyl)-2-furanmethanol **7c**: 71% yield; mp: 62-63 °C; IR (film, cm^{-1}): 3352, 3064, 3031, 2945, 2880, 1603, 1558, 1494, 1452; ^1H NMR (600 MHz, CD_3COCD_3): δ 7.42 (2H, d, J = 7.2 Hz), 7.31 (2H, m), 7,24 (1H, m), 5.95 (1H, d,J = 2.6 Hz), 5.93 (1H, d, J = 2.6 Hz), 5.70 (1H, s), 3.53 (2H, t, J = 6.3 Hz), 3.21 (2H, s, -OH), 2.61 (2H, t, J = 7.5 Hz), 1.76 (2H, m) ppm; MS m/z (relative intensity): 232 (M^+, 40), 215 (182), 214 (77), 197 (35), 183 (1000, 173 (42), 105 (73), 77 (47); HR-MS: Calcd. for $C_{14}H_{16}O_3$: 232.1099; Found: 232.1126.

α-(p-chlorophenyl)-5-(3-hydroxypropyl)-2-furanmethanol **7d**: 70% yield; mp: 89-90 °C; IR (KBr, cm^{-1}): 3396, 3216, 2954, 1557, 1475, 1437; ^1H NMR (300 MHz, $CDCl_3$): δ 7.35 (4H, m), 5.96 (1H, d, J = 3.2 Hz), 5.93 (1H, d, J = 3.1 Hz), 5.75 (1H, s), 3.66 (2H, t, J = 6.3 Hz), 2.70 (2H, t, J = 7.4 Hz), 2.50 (1H, br, -OH), 1.87 (2H, m), 1.52 (1H, br,-OH) ppm; MS m/z (relative intensity): 266 (M^+, 19), 248 (73), 231 (28), 217 (100), 207 (30), 139 (67) ppm; Anal. Calcd. for $C_{14}H_{15}ClO_3$: C, 63.04; H, 5.67; Cl, 13.29; Found: C, 62.86; H, 5.51; Cl, 13.32.

α, α-diphenyl-5-(3-hydroxypropyl)-2-furanmethanol **7e**: 59% yield; mp: 99.5-100 °C; IR (KBr, cm^{-1}): 3356, 3184, 3061, 3036, 2937, 1599, 1585, 1548, 1493, 1447; ^1H NMR (300 MHz, CD_3COCD_3): δ 7.24-7.36 (10H, m), 5.98 (1H, m), 5.81 (1H, d, J = 3.2 Hz), 3.54 (2H, t, J = 6.3 Hz), 3.17 (1H, s, -OH), 3.14 (1H, s, -OH), 2.64 (2H, t, J = 7.5 Hz), 1.78 (2H, tt, J = 6.3 Hz, 7.5 Hz) ppm; MS m/z (relative intensity): 308 (M^+, 15), 291 (87), 290 (83), 259 (29), 231 (57), 105 (100); Anal. Calcd. for $C_{20}H_{20}O_3$: C, 77.90; H, 6.54; Found: C, 77.82; H, 6.54.

α-(p-nitrophenyl)-5-(3-hydroxypropyl)-2-furanmethanol **7f**: 40% yield; mp: 114-115 °C; IR (KBr, cm^{-1}): 3330, 3195, 2955, 2883, 1602, 1553, 1521; ^1H NMR (600 MHZ, CD_3COCD_3): δ 8.20 (2H, d, J = 8.6 Hz), 7.71 (2H, d, J = 8.6 Hz), 6.06 (1H, d, J = 2.7 Hz), 5.95 (1H, d, J = 2.7 Hz), 5.88 (1H, s), 3.52 (2H, t, J = 6.3

Hz), 3.20 (2H, s, -OH), 2.61 (2H, t, J = 7.5 Hz), 1.75 (2H, m) ppm; MS m/z (relative intensity): 277 (M^+, 14), 260 (29), 259 (52), 242 (29), 228 (100), 212 (20), 196 (110), 150 (37); Anal. Calcd. for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05; Found: C, 60.19; H, 5.28; N, 4.83.

α-(p-methoxyphenyl)-5-(3-hydroxypropyl)-2-furanmethanol **7g**: 65% yield; mp: 55-57 °C; IR (film, cm^{-1}): 3378, 2937, 2838, 1611, 1585, 1559, 1512, 1463, 1442; ^1H NMR (600 MHz, CD_3COCD_3): δ 7.33 (2H, d, J = 8.5 Hz), 6.87 (2H, d, J = 8.5 Hz), 5.93 (2H, m), 5.64 (1H, s), 3.76 (3H, s), 3.53 (2H, t, J = 6.3 Hz), 3.20 (2H, s, -OH), 2.61 (2H, t, J = 7.5 Hz), 1.77 (2H, m) ppm; MS m/z (relative intensity): 262 (M^+,31), 245 (64), 244 (100), 227 (17), 216 (36), 213 (41), 160 (31), 135 (70); HR-MS: Calcd. for $C_{15}H_{18}O_4$: 262.1205; Found: 262.1248.

α-(3,4-methylenedioxylphenyl)-5-(3-hydroxypropyl)-2-furanmethanol **7h**: 62% Yield; oil; IR (film, cm^{-1}): 3420, 2591, 2893, 1604, 1559, 1503, 1488, 1444; ^1H NMR (600 MHz, CD_3COCD_3): δ 6.93 (1H, s), 6.88 (1H, d J = 7.3 Hz), 6.77 (1H, d, J = 7.9 Hz), 5.98 (1H, d J = 2.5 Hz), 5.94 (3H, m), 5.62 (1H, s), 3.54 (2H, t, J = 6.3 Hz), 3.27 (2H, s, -OH), 2.61 (2H, t, J = 7,5 Hz), 1.77 (2H, tt, J = 6.5 Hz, 7.4 Hz) ppm; MS m/z (relative intensity): 276 (M^+, 9), 259 (31), 258 (100), 241 (6), 230 (38), 227 (47), 174 (28) 149 (29); HR-MS: Calcd. for $C_{15}H_{14}O_4$ (M^+-H_2O): 258.0892; Found: 258 0879.

α-(trans-propenyl)-5-(3-hydroxypropyl)-2-furanmethanol **7i**: 64% yield; oil; IR (film, cm^{-1}): 3367, 2939, 2881, 1671, 1559, 1509, 1447; ^1H NMR (600 MHz, CD_3COCD_3): δ 6.05 (1H, d, J = 2.8 Hz), 5.93 (1H, d, J = 2.6 Hz), 5.74~5.68 (2H, m), 5.00 (1H, d, J = 3.5 Hz), 3.55 (2H, t, J = 6.1 Hz), 3.33 (2H, s, -OH), 2.63 (2H, t, J = 7.6 Hz), 1.78 (2H, m), 1.66 (3H, d, J = 4.2 Hz) ppm; MS m/z (relative intensity): 196 (M^+, 71), 179 (44) 178 (75), 163 (52), 147 (65), 137 (80), 68 (100), 43 (74); HR-MS: Calcd. for: $C_{11}H_{16}O_3$: 196.1099; Found: 196.1085.

α-(trans-styryl)-5-(3-hydroxypropyl)-2-furanmethanol **7j**: 71%; oil; IR (film, cm^{-1}): 3366, 3027, 2944, 2880, 1636, 1600, 1559, 1496, 1449; ^1H NMR (600 MHz, CD_3COCD_3): δ 7.44 (2H, d, J = 7.3 Hz), 7.32 (2H, m), 7.22 (1H, m), 6.70 (1H, d, J = 15.9 Hz), 6.49 (1H, dd, J = 6,2 Hz, 15,8 Hz), 6.15 (1H, d, J = 2,7 Hz), 5.97 (1H, d, J = 2.7 Hz), 5.26 (1H, J = 6.0 Hz), 3.56 (2H, t, J = 6.3 Hz), 3,21 (2H, s, -OH), 2.65 (2H, t, J = 7.5 Hz), 1.80 (2H, tt, J = 6.5 Hz, 7.4 Hz) ppm; MS m/z (relative intensity): 258 (M^+, 6), 241 (13), 240 (46), 153 (15), 139 (18), 115 (30), 71 (40), 43 (100); HR-MS: Calcd. for $C_{16}H_{16}O_2$ (M^+-H_2O): 240.1150; Found: 240.1160.

Typical procedure II --- *2-(2-thienylmethylene)-1,6-dioxaspiro[4.4]non-3-ene* **3**: To a solution of furandiol **7a** (1.0 g, 4.2 mmol) in 30 mL of dry toluene was added 1.05 g of $CuSO_4 \cdot 5H_2O$ (4.2 mmol). The reaction mixture was stirred at 60 °C for 3 h, then the copper salts was separated. The organic phase was concentrated *in vacuo*, the residue was purified by flash chromatography (neutral alumina oxide, 100 : 1 petroleum ether/ethyl acetate) to give 900 mg (97%) of **3** as an oil. Recrystalization of the product afforded

colorless crystal: mp: 59-60 °C; IR (KBr, cm^{-1}): 2978, 2900, 1651, 1590, 1490; ^1H NMR (600 MHz, $CDCl_3$): 7.17 (1H, d, J = 5.1 Hz), 7.05 (1H, d, J = 3.3 Hz), 6.96 (1H, dd, J = 3.3 Hz, 5.1 Hz), 6.34 (1H, d, J = 5.6 Hz), 6.11 (1H, d, J = 5.6 Hz), 5.74 (1H, s), 4.27 (1H, m), 4,03 (1H, dd, J = 7.6 Hz, 15.3 Hz), 2.37 (1H, m), 2.22 (1H, m), 2.09 (2H, m) ppm; MS m/z (relative intensity): 220 (M^+, 100), 203 (3), 189 (36), 178 (20), 150 (11), 136 (30); Anal. calcd. for $C_{12}H_{12}O_2S$: C, 65.43; H, 5.49; S, 14.56; Found: C, 65.77; H, 5.43; S, 14.33.

Following the typical procedure II, spiroketal-enol ether **4**, **8c-8j** were prepared.

2-(2-thienylmethylene)-1,6-dioxaspiro[4.5]dec-3-ene **4**: 97% yield; oil; IR(film, cm^{-1}): 3098, 2945, 2877, 16459, 1582, 1648, 1244; ^1H-NMR (600MHz, C_6D_6): δ 7.27 (1H, d, J = 3.4 Hz), 7.22 (1H, d, J = 5.1 Hz), 7.05 (1H, dd, J = 3.4 Hz, 5.1 Hz), 6.08 (1H, d, J = 5.6 Hz), 6.02 (1H, d, J = 5.6 Hz), 5.82 (1H, s), 4.47 (1H, m), 3.91 (1H, m), 2.35 (1H, m), 1.85-1.66 (5H, m) ppm; MS m/z (relative intensity): 234 (M^+, 100), 217 (4), 189 (13) ,176 (27), 150 (15), 123 (19); Anal. calcd. for $C_{13}H_{14}O_2S$: C, 66.64; H, 6.02; S, 13.68; Found: C, 66.64; H, 6.26; S, 13.66.

2-benzylidene-1,6-dioxaspiro[4.4]non-3-ene **8c**: 97% yield; oil; IR (film, cm^{-1}): 3086, 3022, 2984. 2981, 1653, 1594, 1492, 1449; ^1H NMR (300 MHz, C_6D_6): δ 7.88 (2H, m), 7.31 (2H, m), 7.11 (1H, m), 5.96 (1H, d, J = 5.5 Hz), 5.72 (1H, dd, J = 0.7 Hz, 5.6 Hz), 5.34 (1H, s), 4.00 (1H, m), 3.67 (1H, m), 2.00-1.88 (2H, m), 1.62-1.46 (2H, m) ppm; MS m/z (relative intensity): 215 (M^++1, 29), 214 (M^+, 58), 184 (25), 172 (13), 158 (17), 127 (21), 115 (100), 53 (86); HR-MS: Calcd. for $C_{14}H_{14}O_2$: 214.0994; Found: 214.0955.

2-(p-chlorobenzylidene)-1,6-dioxaspiro[4.4]non-3-ene **8d**: 92% yield; mp: 82.5-84 °C; IR (KBr, cm^{-1}): 3080, 2993, 1645, 1578, 1451; ^1H NMR (300 MHz, $CDCl_3$): δ 7.53 (2H, m), 7.24 (2H, m), 6.33 (1H, d, J = 5.5 Hz), 6.06 (1H, d, J = 5.5 Hz), 5.35 (1H, s), 4.25 (1H, m), 4.02 (1H, m), 2.36-2.20 (2H, m), 2.16-2.06 (2H, m) ppm; MS m/z (relative intensity): 250 (M^++2, 35), 248 (M^++1, 22), 248 (M^+, 100), 220 (48), 206 (18), 178 (12), 129 (22), 115 (28); Anal. calcd. for $C_{14}H_{13}ClO_2$: C, 67.61; H, 5.27; Cl, 14.25; Found: C. 67.49; H. 5.25; Cl, 14.31.

2-diphenylmethylene-1,6-dioxaspiro[4.4]non-3-ene **8e**: 97% yield; mp: 143.5-144.5 °C; IR (KBr, cm^{-1}): 3060, 3030, 2990, 2880, 1627, 1595, 1585, 1491, 1442; ^1H NMR (300 MHz, C_6D_6): δ 7.80 (2H, m), 7.28-7.05 (8H, m), 6.23 (1H, d, J = 5.6 Hz), 5.72 (1H, d, J = 5.6 Hz), 3.98 (1H, m), 3.67 (1H, dd, J = 7.6 Hz, 15.2 Hz), 2.00-1.87 (2H, m), 1.69-1.47 (2H, m) ppm; MS m/z (relative intensity): 291 (M^++1, 24), 290 (M^+, 100), 272 (15), 262 (48), 206 (56), 191 (29), 165 (40); Anal. calcd. for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25; Found: C, 82.79; H, 6.24.

2-(p-nitrobenzylidene)-1,6-dioxaspiro[4.4]non-3-ene **8f**: 95% yield; mp: 88-90 °C; IR (KBr, cm^{-1}): 3100, 2871, 1646, 1585, 1505, 1338,; ^1H NMR (300 MHz, C_6D_6): δ 8.02 (2H, dd, J = 1.7 Hz, 8.9 Hz), 7.47 (2H, dd, J = 1.8 Hz, 8.9 Hz), 5.85 (1H, d, J = 5.6 Hz), 5.77 (1H, d, J = 5.6 Hz), 5.08 (1H. s), 3.98 (1H, m),

3.67 (1H, m), 1.97-1.82 (2H, m), 1.61-1.50 (2H, m) ppm; MS m/z (relative intensity): 259 (M^+, 100), 243 (12), 231 (45), 217 (5), 187 (5), 171 (4), 153 (5), 115 (32); HR-MS: Calcd. for: $C_{14}H_{13}NO_4$: 259.0846; Found: 259.0833.

2-(p-methoxybenzylidene)-1,6-dioxaspiro[4.4]non-3-ene **8g**: 96% yield; oil; IR (film, cm^{-1}): 3080, 2895, 2837, 1654, 1606, 1583, 1510, 1463, 1364; ^1H NMR (300 MHz, C_6D_6): δ 7.84 (2H, dd , J = 2.1 Hz, 7.0 Hz), 6.93 (2H, dd, J = 2.1 Hz, 6.8 Hz), 6.01 (1H, d, J = 5.5 Hz), 5.72 (1H, d, J = 5.5 Hz), 5.36 (1H, s), 4.04 (1H, m), 3.70 (1H, m), 3.35 (3H, s), 1.99-1.95 (2H, m), 1.69-1.59 (2H, m) ppm; MS m/z (relative intensity): 245 (M^++1, 70), 244 (M^+, 91), 217 (71), 214 (36), 199 (45), 160 (100), 136 (54), 76 (62); HR-MS: Calcd. for $C_{15}H_{16}O_3$: 244.1099; Found: 244.1055.

2-(3,4-methylenedioxybenzylidene)-1,6-dioxaspiro[4.4]non-3-ene **8h**: 92% yield; mp: 92-93 °C; IR (KBr, cm^{-1}): 3080, 2898, 1655, 1586, 1504, 1484, 1442; ^1H NMR (300 MHz, C_6D_6): δ 7.78 (1H, s), 7.10 (1H, dd, J = 1.0 Hz, 8.0 Hz), 6.79 (1H, d, J = 8.1 Hz), 5.95 (1H, d, J = 5.5 Hz), 5.69 (1H, d, J = 5.5 Hz), 5.35 (2H, d, J = 3.7 Hz), 5.27 (1H, s), 3.92 (1H, m), 3.63 (1H, m), 1.93-1.82 (2H, m), 1.69-1.44 (2H, m) ppm; MS m/z (relative intensity): 259 (M^++1), 258 (M^+, 100), 230 (26), 216 (4), 188 (5), 174 (17), 144 (10), 116 (10), 115 (10); Anal. calcd. for $C_{15}H_{14}O_4$: C, 69.77; H, 5.46; Found: C, 69.77; H, 5.45.

2-(2E-but-2-enylidene)-1,6-dioxaspiro[4.4]non-3-ene **8i**: 44% yield; oil; IR(film, cm^{-1}): 3080, 2900, 1650, 1585, 1440; ^1H NMR (600 MHz, C_6D_6): **8i-E,Z**: 6.85-6.78 (1H, m, J = 11.6 Hz, 13.2 Hz), 5.95 (1H, d, J = 5.5 Hz), 5.74 (1H, d, J = 5.4 Hz), 5.60 (1H, m, J = 6.7 Hz, 13.6 Hz), 5.19 (1H, d, J = 11.0 Hz), 4.02 (1H, m), 3.71 (1H, m), 1.97 (2H, m), 1.71-1.54 (5H, m) ppm; **8i-E,E**: 6.40 (1H, d, J = 5.7 Hz), 6.20 (1H, m, J = 12.0 Hz, 13.3 Hz), 5.78 (1H, d, J = 5.7 Hz), 5.47 (1H, d, J = 12.1 Hz), 5.42 (1H, m, J = 6.9 Hz, 14.7 Hz), 4.02 (1H, m), 3.71 (1H, m), 1.97 (2H, m), 1.71-1.54 (5H, m) ppm; MS m/z (relative intensity): 179 (M^++1, 16), 178 (M^+, 21), 167 (12), 149 (70), 141 (100), 135 (26), 123 (74), 87 (20); HR-MS: Calcd. for $C_{11}H_{14}O_2$: 178.0994; Found: 178.0965.

2-(2E-3-phenylprop-2-enylidene)-1,6-dioxaspiro[4.4]non-3-ene **8j**: 90% yield; oil; IR (film, cm^{-1}): 3080, 3028, 2983, 2891, 1675, 1634, 1582, 1493, 1449; ^1H-NMR: **8j-E,Z** (600MHz, C_6D_6): δ 7.58 (1H, dd, J = 11.3 Hz, 15.1 Hz), 7.31 (2H, d, J = 7.8 Hz), 7.11 (2H, dd, J = 7.0 Hz, 7.5 Hz), 7.03 (1H, d, J = 6.7 Hz), 6.51 (1H, d, J = 15.8 Hz), 5.95 (1H, d, J = 5.0 Hz), 5.73 (1H, d, J = 5.3 Hz), 5.34 (1H, d, J = 11.2 Hz), 4.05 (1H, m), 3.69 (1H, m), 1.99 (2H, m), 1.66-1.51 (2H, m) ppm; **8j-E,E** (300MHz, C_6D_6): δ 7.31 (2H,m), 7.18-7.03 (3H, m), 6.95 (1H, dd, J = 11.6 Hz, 15.4 Hz), 6.38 (1H, d, J = 5.9 Hz), 6.33 (1H, d, J = 15.4 Hz), 6.06 (1H, dd, J = 1.0 Hz, 11,1 Hz), 5.79 (1H, dd, J =1.8 Hz, 5.8 Hz), 4.10-4.00 (1H, m), 3.72-3.64 (1H, m), 2.01-1.93 (2H, m), 1.64-1.48 (2H, m) ppm; MS m/z (relative intensity): 241 (M^++1, 51), 240 (M^+, 58), 184 (145), 150 (45), 149 (69), 131 (35), 115 (39), 77 (100); HR-MS: Calcd. for $C_{16}H_{16}O_2$: 240.1150; Found: 240.1179.

5-(3-acetoxypropyl)-2-furaldehyde **10a**: Acetic anhydride (4.95 g, 48.5 mmol) and 4-(dimethylamino)pyridine (1.0 g, 8.1 mmol) were added to a solution of 3-(2-furyl)propan-1-ol **6** (5.05 g, 40 mmol) in pyridine (6.1 mL) at 0 °C. The reaction mixture was stirred at room temperature for 12 h and then concentrated *in vacuo*. Ether (80 mL) and water (30 mL) were added, the layers were partitioned, and the organic layer was washed with saturated aqueous $CuSO_4$ (50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography afforded 6.10 g (91%) of acetate **9a** as an oil. Phosphorus oxychloride (6.82 g, 43.9 mmol) and CH_2Cl_2 (22 mL) were added slowly to DMF (3.20 g, 43.9 mmol) at 0 °C, the reaction mixture was stirred at 0 °C for 0.5 h and furan acetate **9a** (6.10 g, 36.2 mmol) in CH_2Cl_2 (44 mL) was added dropwise. After addition was completed, the reaction mixture was allowed to warm to room temperature and was stirred for 4 h. Saturated aqueous Na_2CO_3 (120 mL) and CH_2Cl_2 (120 mL) were added and the layers were seperated. The organic layer was washed with saturated brine, dried ($MgSO_4$), and cocentrated *in vacuo*. Purification by flash chromatography afforded 6.47 g (91%) of furan aldehyde **10a** as an oil: ^{1}H NMR (CCl_4, 90 MHz): 9.35 (1H, s), 6,95 (1H, d, J = 3.5 Hz), 6.13 (1H, d, J = 3.5 Hz), 3.95 (2H, t, J = 6.0 Hz), 2.66 (2H, t, J = 7.3 Hz), 2.03 (3H, s), 1.70 (2H, m) ppm.

5-(4-acetoxybutyl)-2-furaldehyde **10b** was prepared according to the same procedure: ^{1}H NMR (CCl_4, 90 MHz): 9.50 (1H. S), 7.17 (1H, d, J = 3.5 Hz), 6.25 (1H, d, J = 3.5 Hz), 4.10 (2H, t, J = 6.0 Hz), 2.77 (2H, t, J = 7.0 Hz), 2.05 (3H, s), 1.75 (4H, m) ppm.

Typical procedure III *α-(phenylethynyl)-5-(3-acetoxypropyl)-2-furan-methanol* **11**: To a solution of phenylacetylene (0.63 g, 6.2 mmol) in 10 mL of dry THF and 1.07 mL of TMEDA cooled to -78 °C under a nitrogen atmosphere, was added dropwise a 2.5 M solution of n-butyllithium in hexanes (2.6 mL, 6.5 mmol). The reaction mixture was stirred for 30 minutes at -78 °C, warmed to room temperature, and then added dropwise to a solution of furanaldehyde **10a** (1.00 g, 5.1 mmol) in 15 mL of dry THF over 30 min. The reaction mixture was stirred for 3 h and was then quenched with saturated NH_4Cl solution (10 mL). The organic layer was separated and the aqueous phase was extracted with ethyl acetate (25 mL × 3). The combined organic layer was washed with brine (20 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel; 6 : 1 petroleum ether/ethyl acetate) to give 1.26 g (82%) of **11** as an oil: IR (film, cm^{-1}): 3425, 2961, 2202, 1737, 1599, 1557, 1491, 1444, 1368, 1247; ^{1}H NMR (300 MHz, CD_3COCD_3): δ 7.47~7.35 (5H, m), 6.37 (1H, d, J = 3.0 Hz), 6.05 (1H, d, J = 3.0 Hz), 5.60 (1H, s), 4.07 (2H, t, J = 6.5 Hz), 3.16 (1H, s), 2.70 (2H, t, J = 7.5Hz), 2.05~1.92 (5H, m) ppm; MS m/z (relative intensity): 298 (M^+, 3), 281 (41), 238 (12), 220 (100), 191 (13), 165 (17), 129 (13), 115 (13); Anal. calcd. for $C_{18}H_{18}O_4$: C, 72.74; H, 6.08; Found: C, 72.00; H, 6.02.

α-(1,3-pentadiynyl)-5-(3-acetoxypropyl)-2-furan-methanol **14a**: To a solution of 1,3-pentadiyne (0.64 g, 10 mmol) in 20 mL of dry THF and 1.73 mL of TMEDA cooled to -78 °C under a nitrogen atmosphere was added dropwise a 2.5 M solution of n-butyllithium in hexane (4.2 mL, 10.5 mmol). The reaction mixture was stirred for 30 min at -78 °C, warmed to room temperature, and then added dropwise to a solution of furanaldehyde **10a** (1.78 g, 9.07 mmol) in 20 mL of dry THF over 30mins. The reaction mixture was stirred for 3 h, and was then quenched with saturated NH_4Cl solution (15 mL), the organic layer was separated and the aqueous phase was extracted with ethyl acetate (25 mL × 3). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel; 6 : 1 petroleum ether/ethyl acetate) to give 1.77 g (75%) of **14a** as an oil: IR (film, cm^{-1}): 3418, 2962, 2260, 1737, 1556, 1434, 1380, 1368, 1246; ^1H NMR (300 MHz, CD_3COCD_3): δ 6.28 (1H, d, J = 3.1 Hz), 6.04 (1H, d, J = 3.1 Hz), 5.43 (1H, s), 4.07 (2H, t, J = 6.5 Hz), 3.19 (1H, s,-OH), 2.69 (2H, t, J = 7.4 Hz), 1.99~1.89 (8H, m) ppm; HR-MS: Calcd. for $C_{15}H_{14}O_3$ (M^+-H_2O): 242.0943; Found: 242.0951.

α-(1,3-pentadiynyl)-5-(4-acetoxybutyl)-2-furanmethanol **14b**: Following the typical procedure III, treatment of 1,3-pentadiyne (0.64 g, 10 mmol) with furaldehyde **10b** (1.9 g, 9.0 mmol) provided 1.65 g (69%) of **14b**: oil; IR (film, cm^{-1}): 3421, 2954, 2260, 2237, 1734, 1557, 1508, 1434, 1246; ^1H NMR (600 MHz, CD_3COCD_3): δ 6.28 (1H, d, J = 2.8Hz), 6.03 (1H, d, J = 2.7 Hz), 5.44 (1H, s), 4.06 (2H, t, J = 6.0 Hz), 3.19 (1H, s, -OH), 2.64 (2H, m), 1.99 (3H, s), 1.94 (3H, d, J = 0.7Hz), 1.68 (4H, m) ppm; MS m/z (relative intensity): 275 (M^++1, 6), 274 (M^+, 32), 257 (45), 196 (48), 169 (54), 115 (57), 91 (59), 43 (100); Anal. Calcd. for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61; Found: C, 70.12; H, 6.75.

Typical procedure IV *α-(phenylacetylenyl)-5-(3-hydroxypropyl)-2-furanmethanol* **12**: A solution of compound **11** (1.00 g, 3.4 mmol) and $KHCO_3$ (2.0 g) in methanol (30 mL) and H_2O (5 mL) was heated at 40°C for 12h, and was then extracted with ethyl acetate (5 × 25 mL), the combined organic layer was washed with brine(25 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel; 2/1 petroleum ether/ethyl acetate containing 0.5% v/v triethylamine) to give 816 mg (95%) of compound **12** as an oil: IR (film,cm^{-1}): 3369, 2948, 2202, 1598, 1558, 1490, 1443; ^1H NMR (600 MHz, CD_3COCD_3): δ 7.42~7.40 (2H, m), 7.33~7.31 (3H, m), 6.32 (1H, d, J = 3.0 Hz), 5.97 (1H, d, J = 3.0 Hz), 5.55 (1H, s), 3.53 (2H, t, J = 6.3 Hz), 3.18 (2H, br, -OH), 2.64 (2H, t, J = 7.6 Hz), 1.77 (2H, m) ppm; MS m/z (relative intensity): 256 (M^+,25), 238 (100), 221 (30), 207 (66), 197 (53), 181 (29), 165 (57), 129 (59); Anal. calcd. for $C_{16}H_{16}O_3$: C, 74.987; H, 6.29; Found: C, 74.44; H, 6.54.

α-(1,3-pentadiynyl)-5-(3-hydroxypropyl)-2-furanmethanol **5a**: Following the typical procedure IV, deacetylation of **14a** (500 mg, 1.92 mmol) in $KHCO_3$-CH_3OH-H_2O solution afforded compound **5a** (385 mg, 92%) as an oil: IR (film, cm^{-1}): 3339, 3165, 2877, 2266, 1557, 1443; ^1H-NMR (600 MHz, CD_3COCD_3): δ 6.41

(1H, d, J = 3.1 Hz), 6.15 (1H, d, J = 3.1 Hz), 5.58 (1H, s), 3.71 (2H, t, J = 6.4 Hz), 3.50 (2H, br, -OH), 2.81 (2H, t, J = 7.7 Hz), 2.08 (3H, s), 1.96 (2H, m) ppm; MS m/z (relatie intensity): 218 (22.3, M^+), 200 (46.5, M^+-H_2O), 187 (91.0), 173 (65.0), 159 (58.8), 145 (46.3), 128 (75.5), 115 (100.0). HR-MS: Calcd. for $C_{13}H_{14}O_3$: 218.0943; Found: 218.0949.

α-(1,3-pentadiynyl)-5-(4-hydroxybutyl)-2-furanmethanol **5b**: Following the typical procedure IV, deacetylation of **14b** (685 mg, 2.5 mmol) in $KHCO_3$-CH_3OH-H_2O solution afforded compound **5b** (52 0mg, 90%): mp: 78-80 °C ; IR (KBr, cm^{-1}): 3408, 3300, 2948, 2872, 2235, 2138, 1581, 1509, 1438, 1370; ^{1}H-NMR (600MHz, CD_3COCD_3): δ 6.41 (1H, d, J = 2.8 Hz), 6.15 (1H, d, J = 2.4 Hz), 5.58 (1H, s), 3.69 (2H, t, J = 6.3 Hz), 3.34 (2H, s, -OH), 2.75 (2H, t, J = 7.2 Hz), 2.08 (3H, s), 1.83 (2H, m), 1.71 (2H, m) ppm; MS m/z (relatie intensity): 215 (M^+-OH, 31), 214 (M^+-H_2O, 100), 199 (9), 185 (28), 169 (19), 156 (38), 129 (21), 115 (25); Anal. calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94; Found: C, 72.33; H, 6.92.

2-(3-phenyl-2-propynyliden)-1,6-dioxaspiro[4.4] non-3-ene **13**: Following the typical procedure II described above, treatment of furandiol **12** (550 mg, 2.15 mmol) with $CuSO_4.5H_2O$ afforded **13** (Z, 250 mg; E, 235 mg, 94%) as oil: IR (film, cm^{-1}): 3095, 3052, 2959, 2894 2192, 1639, 1585, 1582, 1489; ^{1}H-NMR (600MHz, C_6D_6): **13-Z**: 7.73 (2H, m), 7.17 (3H, m), 5.93 (1H, d, J = 5.6 Hz), 5.89 (1H, d, J = 5.6 Hz), 5.02 (1H, s), 4.15(1H, m), 3.79 (1H, dd, J = 7.5 Hz, 15.4 Hz), 2.11 (2H, m), 1.74~1.60 (2H, m); **13-E**: 7.67 (2H, m), 7.27~7.20 (3H, m), 6.93 (1H, d, J = 5.7 Hz), 6.00 (1H, dd, J = 1.7 Hz, 5.7 Hz), 5.62 (1H, d, J = 1.5 Hz), 4.13 (1H, m), 3.82 (1H, dd, J = 7.3 Hz, 15.1 Hz), 2.05 (2H, m), 1.76~1.63 (2H, m) ppm; MS m/z (relative intensity): 238 (M^+, 100), 223 (12), 210 (21), 181 (19), 165 (22), 149 (22), 139 (28), 105 (31); Anal. calcd. for $C_{16}H_{14}O_2$: C, 78.48; H, 6.59; Found: C, 78.94; H, 6.04.

2-(2,4-hexadiynyliden)-1,6-dioxaspiro[4.4] non-3-ene **Tonghaosu 1**: Following the typical procedure II described above, treatment of furandiol **5a** (100 mg, 0.46mmol) with $CuSO_4.5H_2O$ afforded 86 mg (94%) of **1** as an oil (the ratio of Z/E was about 1.5 : 1): IR (film, cm^{-1}): 3035, 2985, 2139, 1630, 1581, 1438; ^{1}H NMR (600 MHz, C_6D_6): **1-E**: δ 6.53 (1H, d, J = 5.6 Hz), 5.69 (1H, dd, J = 1.6 Hz, 5.6 Hz), 5.11 (1H, s), 3.88 (1H, m), 3.58 (1H, dd, J = 7.4Hz 15.0 Hz), 1.85~1.73 (2H, m), 1.52~1.39 (5H, m)ppm; **1-Z**: 5.68 (1H, d, J = 5.6 Hz), 5.64 (1H, d, J = 5.6 Hz), 4.50 (1H, s), 3.88 (1H, m), 3.58 (1H, dd, J = 7.4 Hz, 15.0 Hz), 1.85~1.73 (2H, m), 1.52~1.39 (5H, m) ppm; MS m/z (relative intensity): 200 (M^+, 100), 199 (25), 185 (19), 170 (20), 157 (26), 128 (25), 115 (38); Anal. calcd. for $C_{13}H_{12}O_2$: C, 77.98: H, 6.04; Found: C, 77.93; H, 6.39.

2-(2,4-hexadiynyliden)-1,6-dioxaspiro[4.5] dec-3-ene **2**: Following the typical procedure II described above, treatment of **5b** (232 mg, 1 mmol) with $CuSO_4$·$5H_2O$ afforded 200 mg (92%) of **2** as an oil (the ratio of Z/E was about 2 : 1): IR (film, cm^{-1}): 3095, 3047, 2948, 2882, 2231, 2138, 1631, 1581, 1441; ^{1}H NMR (600 MHz, C_6D_6): **2-E**: 6.50 (1H, d, J = 5.5 Hz), 5.76 (1H, d, J = 5.6 Hz), 5.17 (1H, s), 4.01-3.84 (2H, m), 1.86-1.70

(2H, m), 1.49 (3H, s), 1.47-1.31 (4H, m) ppm; **2-Z**: 5.75(1H, d, J = 5.3 Hz), 5.57 (1H, d, J = 5.6 Hz), 4.52 (1H, s), 4.01-3.84 (2H, m), 1.86-1.70 (2H, m), 1.43 (3H, s),1.47-1.31 (4H, m) ppm; MS m/z (relative intensity): 215 (M^++1, 21), 214 (M^+, 100), 199 (9), 185 (29), 171 (21), 156 (41), 143 (12), 129 (22); HR-MS: Calcd for $C_{14}H_{14}O_2$: 214.0994; Found: 214.1017.

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