DOI 10.5012/bkcs.2010.31.03.683

Gold-Catalyzed Cycloisomerization of (2-Alkynyl-1-cycloalkenyl)methanols to Highly Substituted Furans†

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Received December 23, 2009, Accepted February 2, 2010

A new and efficient Au-catalyzed alkoxycyclization of conjugated enynols offers a general entry to a wide range of highly substituted furans in good to excellent yields. These furans were subjected to diethyl acetylenedicarcoxylate to afford the interesting cycloadducts in good to excellent yields.

Key Words: Gold catalysis, Furan, Cyclization, Alkynol

Introduction

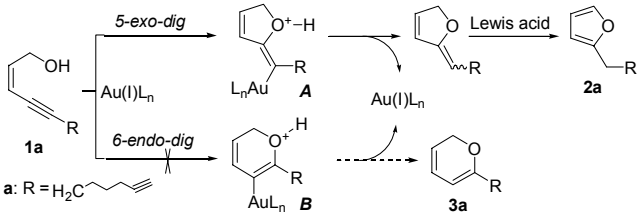
Substituted furan derivatives are found as structural units in many natural products such as pheromones or polyether antibiotics,[1] and are useful and versatile synthetic intermediates.[2] Due to their many applications in pharmaceutical fields, synthetic investigations to furan derivatives have continuously attracted attentions to many organic chemists.[3] Among various strategies, transition metal catalyzed transformation such as palladium-catalyzed processes are the modern approaches for the syntheses of substituted furan derivatives from cyclization of alkyne- or allene-containing substrates.[4] The potential of late-transition metal-based Lewis acid has recently been witnessed for powerful synthetic versatility for total synthesis of complex natural products.[5] Activating alkynes by coordination to electrophilic transition-metal complexes plays a key role in carbon-carbon or carbon-heteroatom bond formation for a variety of cyclizations.[6] The Echavarren group extended the scope of this reaction in detail for hydroxyl- or alkoxy cyclization of enynes, which was particularly attractive because it allowed the sequential formation of a C-C and a C-O bond from enynes.[7] The Larock group reported a novel method of highly substituted furans by $AuCl_3$-catalyzed nucleophilic addition followed by cyclization reaction, although it was limited to specific substrate classes.[8] To circumvent such substrate limitation and enhance the scope of the reaction, we studied catalytic efficacy of Pt(II) complexes in hydroxyl- or alkoxy cyclization of 2-(1-alkynyl)-2-alkene-1-ones.[9] In addition, Cu-[10] and Ru-catalyzed cyclizations,[11] and base-promoted cyclization of (*Z*)-enynols[12] were reported. These methodologies were applicable to structurally diverse substrates with different substitution patterns and provided the corresponding furans in good to excellent yields. Very recently, the Liu group reported that gold compounds catalyzed cycloisomerization of a variety of secondary (*Z*)-2-en-4-yn-1-ols into the corresponding furans in good to excellent yields.[13] The substrate scope in the Liu's paper was limited only to the secondary acyclic (*Z*)-enynols. In continuing our interest in tandem cycloisomerizations of various primary (*Z*)-enynols under gold catalysis, we here wish to report our results on Au-catalyzed cyclization to the furans and their cycloadditions with an electrophile.

†This paper is dedicated to Professor Sunggak Kim on the occasion of his honorable retirement.

Result and Discussion

We prepared (*Z*)-undec-2-en-4,10-diyn-1-ol (**1a**) and surveyed various Au-based catalytic conditions as summarized in Table 1. All reactions were performed in the presence of 3 mol % of gold compounds in various solvents. As found in Table 1, most of our trials afforded the corresponding furan **2a** in varying yields. Gold(I) compounds such as AuCl, $AuCl(PPh_3)$, and AuCl(CO) catalyzed this reaction in ethylene dichloride within 10 min at room temperature affording **2a** in 64%, 11%, and 26% yields, respectively. Gold(III) compounds exhibited better catalytic activity for this reaction: $NaAuCl_4$, $AuCl_3$, and $AuBr_3$ catalyzed this reaction to afford the furan **2a** in 65%, 52%, 76%

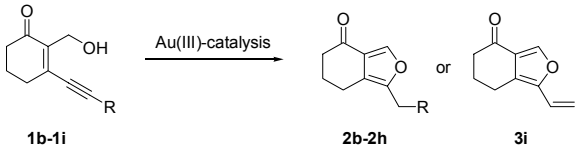
Table 1. Cyclizations of **1a** under various conditions



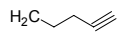
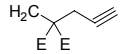
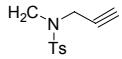
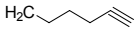
entry	substrates	catalyst	solvent, temp, time (min)	product (% yield)[a]
1	**1a**	**AuCl**	**EDC**, **rt**, **10**	**2a** (**64**)
2	**1a**	$AuCl(PPh_3)$	EDC, rt, 10	**2a** (11)
3	**1a**	$AuCl_3$	EDC, rt, 10	**2a** (65)
4	**1a**	**$NaAuCl_4$**	**EDC**, **rt**, **10**	**2a** (**52**)
5	**1a**	AuCl(CO)	EDC, rt, 10	**2a** (26)
6	**1a**	**$AuBr_3$**	**EDC**, **rt**, **10**	**2a** (**76**)
7	**1a**	$AuBr_3$	toluene, rt, 10	**2a** (42)
8	**1a**	$AuBr_3$	methanol, rt, 10	**2a** (16)
9	**1a**	$AuBr_3$	acetonitrile, rt, 10	**2a** (34)
10	**1a**	$AuBr_3$	*p*-dioxane, rt, 10	**2a** (50)

EDC = 1,2-dichloroethane, [a]Isolated yield.

Table 2. Cyclizations of 6-membered ring fused substrates

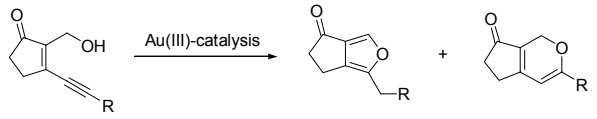


1b-1i **2b-2h** **3i**

entry	substrates		product	yield(%)[a]
1	R = H	**(1b)**	**2b**	73
2	R = Ph	**(1c)**	**2c**	86
3	R = COOEt	**(1d)**	**2d**	71
4		**(1e)**	**2e**	**71**
5		**(1f)**	**2f**	76
6		**(1g)**	**2g**	**76**
7		**(1h)**	**2h**	67
8	CH_2OTBS	**(1i)**	**3i**	68

The reaction was carried out in the presence of 3 mol % of $AuBr_3$ in 1 mL of $ClCH_2CH_2Cl$ at room temperature for 10 min under argon atmosphere. [a]Isolated yield.

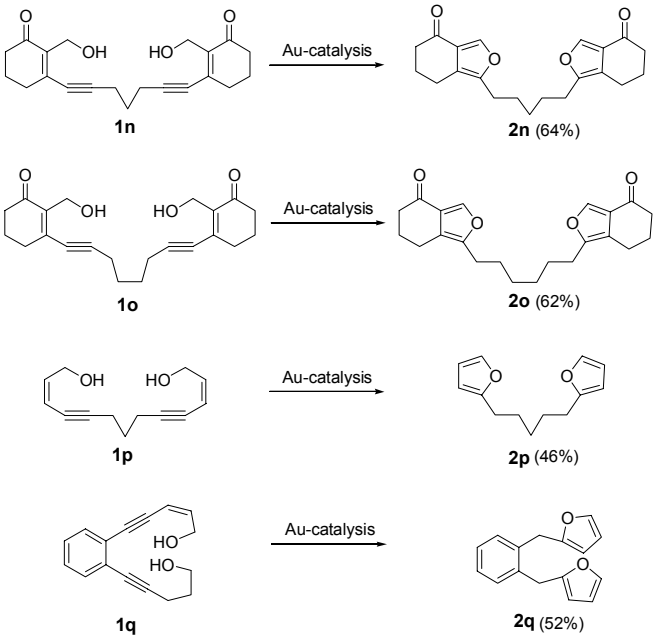
Table 3. Cyclizations of 5-membered ring fused substrates



1j-1m **2j-2m** **4l-4m**

entry	substrates		product	yield(%)[a]
1	R = H	**(1j)**	**2j**	73
2	R = COOEt	**(1k)**	**2k**	86
3	R = Ph	**(1l)**	**2l**, **4l**	15^a, 50^b
4		**(1m)**	**2m**, **4m**	7^a, 40^b

[a]Yields of **2l** and **2m**. [b]Yields of **4l** and **4m**. [c]Isolated yield.



Scheme 1. The reaction was carried out in the presence of 3 mol % of $AuBr_3$ in 1 mL of $ClCH_2CH_2Cl$ at room temperature for 40 min.

yields, respectively. Ethylene dichloride(EDC) turned out to be the best solvent among EDC, methanol, acetonitrile, and 1,4-dioxane.

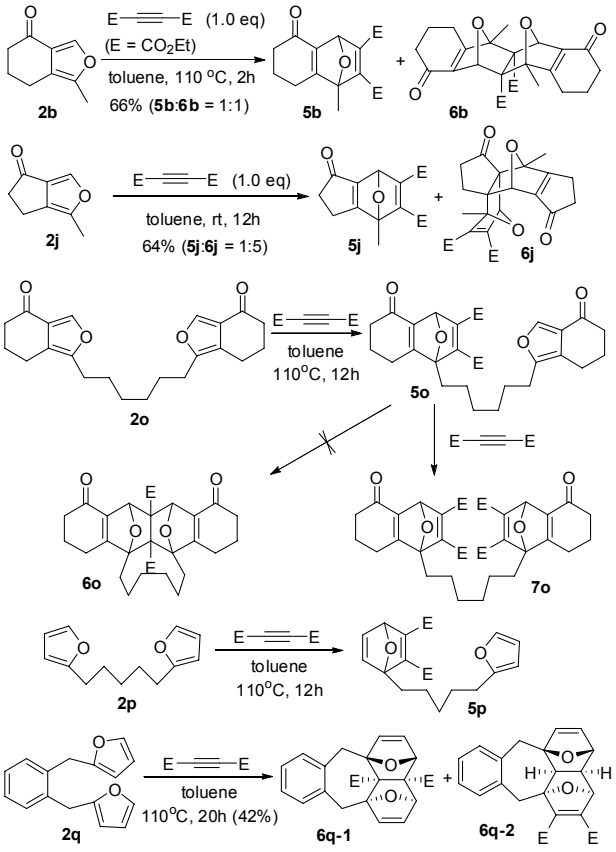
Thus, the optimal experiment was conducted by addition of EDC solution of **2a** into an EDC slurry containing gold(III) bromide at 0 °C under argon atmosphere (entry 6). The resulting orange mixture was stirred at room temperature for 10 min, quenched with a drop of triethylamine, concentrated under reduced pressure, and separated through silica gel chromatography to afford the furan **2a** as a colorless oil. Delighted with this initial success, we prepared several analogs **1b-1i** and cyclized those to the furans under the above conditions (Table 2).

H (**1b**), Ph (**1c**), and electron-withdrawing COOEt (**1d**) group in the alkyne substituent R of enynols did not affect the present reaction to afford the corresponding furans **2b**, **2c**, and **2d**, respectively. We initially prepared **1a** to examine one-pot multicomponent assembly with a dienophile intramolecularly. For this purpose, we prepared several substrates **1e-h** bearing a terminal alkyne group. The alkyl substituted **1e** to **1h** also underwent this *5-exo-dig* cyclization to provide furans **2e-h** in high yields, but further intramolecular Diels-Alder reaction did not occur. Presumably due to the acidity of the reaction medium, the substrate **1i** containing CH_2OTBS group initially gave the initial product **2i** which would undergo elimination to give **3i** in high yield.

Cyclopentenone-fused systems were also studied (Table 3). Different from the cyclohexenone-fused systems, the cyclopentenone-fused systems were hard to cyclize to give the fused furans under these conditions, presumably due to their intrinsic ring tension arisen from bicycle[3,3,0] systems. While enynanol **1j** and **1k** were cyclized to the furans **2j** and **2k** in 55% and 55% yields, respectively, alkyl- or aryl-substituted substrates **1l** and **1m** afforded the expected products in low yields. Instead, their six-membered ring analogs **4l** and **4m** were isolated in 50% and 40% yields, respectively.

In order to demonstrate the substrate diversity, we examined four more substrates having two reacting components **1n**, **1o**, **1p**, and **1q**. These four substrates under the present conditions cyclized to bicyclic furans **2n**, **2o**, **2p**, and **2q** in 64%, 62%, 46% and 52% yields, respectively (Scheme 1).

The furans prepared from this method were further transformed into other valuable compounds by [2+4] cycloadditions with



Scheme 2

diethyl acetylenedicarboxylate as shown in Scheme 2.

Diels-Alder cycloaddition of **2b** and **2j** with diethyl acetylenedicarboxylate (DEAC) in toluene proceeded well at different temperature. Furan **2b** showed lower reactivity toward DEAC than **2j**. Those cycloadducts **5b** and **5j** were even more reactive than DEAC, so that **6b** and **6j** were isolated as major products.

Since this cyclization occurred well, we tested three bisfurans **2o**, **2p**, and **2q** with DEAC. Bisfurans were expected to cycloadd into diethyl acetylenedicarboxylate affording very interesting fused products. When we used one equivalent of diethyl acetylenedicarboxylate with bisfurans **2o**, only one side cycloadded products **5o** was isolated without detecting a trace of **6o**. Use of excess DEAC resulted in the major formation of **7o** in 54% yield. Structurally simple **2p** exhibited the similar tendency to afford the one-side cycloadduct **5p**. To a big contrast to these, bisfuran **2q** was cycloadded into DEAC to afford an 1:1 mixture of double cycloadducts **6q-1** and **6q-2** in combined 42% yield. Both **6b** and **6q-1** were formed from cycloaddition of the isolated olefin with the pendant furan diene, while both **6j** and **6q-1** were formed from cycloaddition of the conjugated olefin with the pendant furan diene. The anti-stereochemistry of the bridged oxygens in **6q-1** and **6q-2** was speculated with molecular model kit, confirmed with their ^{1}H NMR spectra, and further supported by X-ray structures of **6b** and **6j**.

Conclusion

A new approach to the synthesis of fused bicyclic furan derivatives from a variety of primary (*Z*)-2-en-4-yn-1-ols has been developed using Au(III)-catalysis under very mild condition. Highly characteristic cycloadditions of typical furans obtained from this study with diethyl acetylenedicarboxylate were explored to afford a novel class of fused-cycloadducts in good yields.

Experimental

General procedures. Gold(III) bromide (3 mol %) was added to a mixture of alkynol in dry 1,2-dichloroethane under argon atmosphere. The resulting mixture was stirred for 10 min at room temperature. Upon completion, the reaction was quenched with a drop of triethylamine, the solvent was removed under vacuum and the crude product was subjected for flash column chromatography (EtOAc : *n*-hexane = 1 : 20) to afford the pure product.

2-(Hept-6-ynyl)furan (2a): IR(NaCl, cm^{-1}) 3298, 2935, 2858, 1595, 1006; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 0.8 Hz, 1H), 6.27 (t, J = 2.4 Hz, 1H), 5.97 (d, J = 2.8 Hz, 1H), 2.63 (t, J = 8.0 Hz, 2H), 2.19 (td, J = 7.2 Hz, J = 2.8 Hz, 2H), 1.93 (t, J = 2.8 Hz, 1H), 1.66 (quint, J = 7.6 Hz, 2H), 1.56 (quint, J = 6.8 Hz, 2H), 1.49-1.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.19, 140.67, 110.00, 104.64, 84.46, 68.21, 28.22, 28.17, 27.79, 27.51, 18.29; HRMS calculated for $C_{11}H_{14}NaO$ 185.0914; found, 185.0927.

1-Methyl-6,7-dihydroisobenzofuran-4(5H)-one (2b): IR(NaCl, cm^{-1}) 3267, 2948, 1975, 1149; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 2.57 (t, J = 6.4 Hz, 2H), 2.47 (t, J = 6.4 Hz, 2H), 2.25 (s, 3H), 2.06-2.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.60, 147.10, 141.96, 124.62, 118.80, 39.61, 23.97, 19.72, 11.60; HRMS calculated for $C_9H_{10}NaO_2$ 173.0621; found, 173.0627.

1-Benzyl-6,7-dihydroisobenzofuran-4(5H)-one (2c): IR(NaCl, cm^{-1}) 3136, 2941, 1684, 1546, 1157, 964; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.32-7.18 (m, 5H), 3.96 (s, 2H), 2.55 (t, J = 6.4 Hz, 2H), 2.47 (t, J = 6.4 Hz, 2H), 2.02 (quint, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.44, 149.05, 142.65, 137.42, 128.61, 128.42, 126.64, 124.68, 119.74, 39.56, 32.74, 23.94, 19.77; HRMS calculated for $C_{15}H_{14}NaO_2$ 249.0948; found, 249.0962.

Ethyl 2-(4-oxo-4,5,6,7-tetrahydroisobenzofuran-1-yl)acetate (2d): IR(NaCl, cm^{-1}) 3139, 2924, 2877, 1736, 1543; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 4.19 (quart, J = 7.2 Hz, 2H), 3.65 (s, 2H), 2.63 (t, J = 6.0 Hz, 2H), 2.49 (t, J = 6.0 Hz, 2H), 2.06 (quint, J = 6.4 Hz, 2H), 1.28 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.14, 168.86, 143.17, 143.03, 124.77, 121.84, 61.37, 39.50, 32.59, 23.79, 19.71, 14.12; HRMS calculated for $C_{12}H_{14}NaO_4$ 245.0821; found, 245.0832.

1-(Hex-5-ynyl)-6,7-dihydroisobenzofuran-4(5H)-one (2e): IR(NaCl, cm^{-1}) 3297, 2944, 2902, 1699, 1551; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 2.64-2.57 (m, 4H), 2.48 (t, J = 6.4 Hz, 2H), 2.22 (td, J = 7.2 Hz, J = 2.4 Hz, 2H), 2.04 (quint, 6.0 Hz, 2H), 1.96 (t, J = 2.4 Hz, 1H), 1.76 (quint, J = 7.2 Hz, 2H), 1.55 (quint, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.61, 150.63, 142.19, 124.52, 118.83, 83.99, 68.52, 39.62, 27.72, 27.03, 25.78, 24.01, 19.78, 18.08; HRMS calculated for $C_{14}H_{16}NaO_2$ 239.1024; found, 239.1082.

Diethyl 2-(2-(4-oxo-4,5,6,7-tetrahydroisobenzofuran-1-yl) ethyl)-2-(prop-2-ynyl)malonate (2f): IR(NaCl, cm^{-1}) 2984, 2941, 1683, 1546, 1207; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 4.26-4.14 (m, 4H), 2.88 (d, J = 2.8 Hz, 2H), 2.62-2.57 (m, 4H), 2.47 (t, J = 7.2 Hz, 2H), 2.41-2.37 (m, 2H), 2.07-2.01 (m, 3H), 1.26 (t, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.50, 169.77, 149.34, 142.39, 124.62, 119.31, 78.45, 71.64, 61.81, 56.13, 39.63, 30.34, 23.92, 22.87, 21.39, 19.70, 14.03; HRMS calculated for $C_{20}H_{24}NaO_6$ 383.1541; found, 383.1520.

4-Methyl-N-(2-(4-oxo-4,5,6,7-tetrahydroisobenzofuran-1-yl)ethyl)-N-(prop-2 ynyl) benzenesulfonamide (2g): IR(NaCl, cm^{-1}) 3276, 2921, 2875, 1684, 1549, 1157; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.69 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 4.04 (d, J = 2.4 Hz, 2H), 3.44 (t, J = 5.6 Hz, 2H), 3.27 (t, J = 9.2 Hz, 2H), 2.94 (t, J = 7.2 Hz, 2H), 2.60 (d, J = 6.4 Hz, 2H), 2.46 (t, J = 6.0 Hz, 2H), 2.41 (s, 3H), 2.07-2.00 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.34, 147.19, 143.68, 142.72, 135.67, 129.55, 127.55, 124.70, 120.84, 76.78, 73.81, 45.11, 39.58, 37.19, 26.12, 23.90, 21.49, 19.67; HRMS calculated for $C_{20}H_{21}NNaO_4S$ 394.1134; found, 394.1120.

1-(Hept-6-ynyl)-6,7-dihydroisobenzofuran-4(5H)-one (2h): IR(NaCl, cm^{-1}) 3300, 2940, 2897, 1684, 1549, 1122; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 2.62-2.57 (m, 4H), 2.47 (t, J = 6.8 Hz, 2H), 2.20 (td, J = 6.8 Hz, J = 2.4 Hz, 2H), 2.04 (quint, J = 6.0 Hz, 2H), 1.94 (t, J = 2.8 Hz, 1H), 1.65 (quint, J = 7.2 Hz, 2H), 1.55 (quint, J = 7.2 Hz, 2H), 1.47-1.39 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.66, 150.94, 124.53, 118.71, 84.34, 68.30, 39.65, 28.10, 28.06, 27.50, 26.15, 24.04, 19.82, 18.28; HRMS calculated for $C_{15}H_{18}NaO_2$ 253.1264; found, 253.1271.

1-Vinyl-6,7-dihydroisobenzofuran-4(5H)-one (3i). IR(NaCl, cm^{-1}) 3287, 2929, 2888, 1654, 1540, 1120; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 6.50 (dd, J = 17.2, 11.6 Hz, 1H), 5.65 (d, J = 17.2 Hz, 1H), 5.25 (d, J = 11.6 Hz, 1H), 2.70 (t, J = 6.0 Hz, 2H), 2.51 (t, J = 6.8 Hz, 2H), 2.08 (quint, J = 5.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.33, 148.49, 143.21, 125.55, 123.27, 122.04, 113.26, 39.80, 23.98, 20.26; HRMS calculated for $C_{10}H_{10}NaO_2$ 185.0664; found, 185.0642.

1-Methyl-5,6-dihydrocyclopenta[c]furan-4-one (2j): IR(NaCl, cm^{-1}) 3115, 3074, 2964, 1714, 1550. 1131; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (s, 1H), 2.93-2.90 (m, 2H), 2.84-2.81 (m, 2H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.27, 144.99, 135.61, 130.53, 130.30, 43.59, 17.78, 12.02; HRMS calculated for $C_8H_8NaO_2$ 159.0449; found, 159.0439.

Ethyl 2-(4-oxo-5,6-dihydro-4H-cyclopenta[c]furan-1-yl) acetate (2k): IR(NaCl, cm^{-1}) 3139, 2937, 2876, 1714, 1541, 1261; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 4.21 (quart, J = 7.2 Hz, 2H), 3.70 (s, 2H), 2.96-2.89 (m, 4H), 1.29 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.77, 168.75, 140.77, 136.76, 132.94, 130.92, 61.40, 43.39, 33.03, 18.20, 14.15; HRMS calculated for $C_{11}H_{12}NaO_4$ 231.0659; found, 231.0654.

1-Benzyl-5,6-dihydrocyclopenta[c]furan-4-one (2l): IR(NaCl, cm^{-1}) 3032, 2871, 1584, 1446, 1157, 951; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.35-7.32 (m, 2H), 7.28-7.23 (m, 3H), 4.00 (s, 2H), 2.83 (t, J = 6.4 Hz, 2H), 2.54 (t, J = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.36, 147.26, 137.05, 136.39, 131.45, 130.99, 129.12, 128.89, 127.09, 43.65, 33.77, 18.28; HRMS calculated for $C_{14}H_{12}NaO_2$ 235.0722; found, 235.0719.

3-Phenyl-5,6-dihydrocyclopenta[c]pyran-7(1H)-one (4l): IR (NaCl, cm^{-1}) 3001, 2572, 1334, 1121, 899; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 7.6 Hz, 2H), 7.35 (t, J = 8.0 Hz, 2H), 7.24-7.02 (m, 1H), 5.72 (s, 1H), 5.15 (d, J = 0.8 Hz, 2H), 2.97-2.95 (m, 2H), 2.78-2.75 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.60, 174.16, 154.18, 147.62, 134.87, 128.51, 126.98, 103.64, 71.64, 41.56, 21.01; HRMS calculated for $C_{14}H_{12}NaO_2$ 235.0722; found, 235.0726.

1-Pentyl-5,6-dihydrocyclopenta[c]furan-4-one (2m): IR(NaCl, cm^{-1}) 3202, 2763, 1256, 782; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 2.93-2.90 (m, 2H), 2.87-2.85 (m, 2H), 2.64 (t, J = 7.6 Hz, 2H), 1.67 (quint, J = 7.2 Hz, 2H), 1.38-1.29 (m, 4H), 0.91 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.62, 149.49, 135.86, 130.73, 130.12, 43.75, 31.62, 27.37, 27.18, 22.58, 18.41, 14.23; HRMS calculated for $C_{12}H_{16}NaO_2$ 215.1027; found, 215.1011.

3-Butyl-5,6-dihydrocyclopenta[c]pyran-7(1H)-one (4m): IR (NaCl, cm^{-1}) 3012, 2478, 1234, 912; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (s, 1H), 5.00 (s, 2H), 2.56-2.54 (m, 2H), 2.47-2.45 (m, 2H), 2.19 (t, J = 7.2 Hz, 2H), 1.53 (t, J = 7.2 Hz, 2H), 1.41-1.31 (m, 2H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.25, 168.02, 167.84, 121.98, 97.86, 64.83, 35.40, 33.91, 28.82, 26.66, 22.09, 13.66; HRMS calculated for $C_{12}H_{16}NaO_2$ 215.1027; found, 215.1021.

1,1'-(Pentane-1,5-diyl)bis(6,7-dihydroisobenzofuran-4(5H)-one) (2n): IR(NaCl, cm^{-1}) 3029, 2947, 2914, 1671, 1526, 1217; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 2H), 2.61-2.55 (m, 8H), 2.47 (t, J = 6.8 Hz, 4H), 2.03 (quint, J = 6.4 Hz, 4H), 1.65 (quint, J = 7.6 Hz, 4H), 1.34 (quint, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.60, 150.94, 142.13, 124.55, 118.71, 39.64, 28.50, 27.69, 26.17, 24.04, 19.81; HRMS calculated for $C_{21}H_{24}NaO_4$ 363.1622; found, 363.1621.

1,1'-(Hexane-1,6-diyl)bis(6,7-dihydroisobenzofuran-4(5H)-one) (2o): IR(NaCl, cm^{-1}) 3130, 2935, 2896, 1684, 1549, 1147; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 2H), 2.60-2.55 (m, 8H), 2.47 (t, J = 6.8 Hz, 4H), 2.03 (quint, J = 6.4 Hz, 4H), 1.63 (t, J = 7.6 Hz, 4H), 1.33 (quint, J = 3.6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.63, 151.05, 142.05, 124.52, 118.62, 39.63, 28.69, 27.87, 26.21, 24.03, 19.79; HRMS calculated for $C_{22}H_{26}NaO_4$ 377.1741; found, 377.1739.

1,5-Di(furan-2-yl)pentane (2p): IR(NaCl, cm^{-1}) 2933, 2857, 1594, 1507, 1147; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (s, 2H), 6.27 (t, J = 2.8 Hz, 2H), 5.96 (d, J = 2.6 Hz, 2H), 2.62 (t, J = 7.2 Hz, 4H), 1.67 (t, J = 8.0 Hz, 4H), 1.40 (t, J = 8Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.34, 140.67, 110.02, 104.61, 28.64, 27.84, 27.75; HRMS calculated for $C_{13}H_{16}NaO_2$ 227.1023; found, 227.1021.

1,2-Bis(furan-2-ylmethyl)benzene (2q): IR(NaCl, cm^{-1}) 3022, 3001, 1628, 1557, 1172; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 2H), 7.22-7.15 (m, 4H), 6.27 (dd, J = 2.6, 2.0 Hz, 2H), 5.90 (d, J = 2.4 Hz, 2H), 3.99 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.04, 141.40, 141.38, 136.30, 130.09, 127.04, 110.24, 106.33 31.74; HRMS calculated for $C_{16}H_{14}NaO_2$ 261.0931; found, 261.0923.

5b: IR(NaCl, cm^{-1}) 3088, 1712, 1603, 1496, 1298, 1212; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89 (s, 1H), 4.31 (qd, J = 7.2 Hz, J = 2 Hz, 2H), 4.25 (quart, J = 7.2 Hz, 2H), 2.65 (dt, J = 19.2,

2.0 Hz, 1H), 2.54-2.39 (m, 2H), 2.35-2.27 (m, 1H), 2.17-2.04 (m, 2H), 1.77 (s, 3H), 1.32 (quint, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.14, 178.44, 164.11, 161.69, 153.78, 151.54, 148.75, 94.77, 80.40, 61.70, 61.54, 37.03, 23.25, 22.95, 14.09, 14.03, 13.30; HRMS calculated for $C_{17}H_{20}NaO_6$ 343.1211; found, 343.1227.

6b: IR(NaCl, cm^{-1}) 3066, 1687, 1600, 1250, 1233; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (s, 2H), 4.04-3.92 (m, 4H), 2.54-2.40 (m, 4H), 2.39-2.29 (m, 4H), 2.04 (quint, J = 6.0 Hz, 4H), 1.77 (s, 6H), 1.18 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.43, 172.98, 168.42, 145.73, 92.12, 72.52, 61.54, 37.43, 24.03, 23.34, 13.87, 13.34; HRMS calculated for $C_{26}H_{30}NaO_8$ 493.1861; found, 493.1841.

5j: IR(NaCl, cm^{-1}) 3084, 1632, 1601, 1450, 1378, 1252, 1231; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73 (s, 1H), 4.33 (quart, J = 6.8 Hz, 2H), 4.25 (quart, J = 6.8 Hz, 2H), 2.97-2.80 (m, 3H), 2.71-2.64 (m, 1H), 1.80 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H), 1.31 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.59, 195.47, 162.18, 154.72, 151.63, 93.65, 80.01, 61.88, 61.71, 42.57, 23.61, 14.09, 14.04, 13.21; HRMS calculated for $C_{16}H_{18}NaO_6$ 329.1041; found, 329.1021.

6j: IR(NaCl, cm^{-1}) 3096, 1701, 1611, 1521, 1257, 1243; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.83 (s, 1H), 4.64 (s, 1H), 4.32-4.21 (m, 4H), 2.93-2.71 (m, 4H), 2.61-2.46 (m, 2H), 2.38-2.32 (m, 1H), 2.07-1.98 (m, 1H), 1.64 (s, 3H), 1.52 (s, 3H), 1.30 (quart, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.50, 199.10, 188.08, 164.10, 160.72, 154.68, 152.77, 145.52, 93.04, 90.45, 82.96, 78.36, 70.52, 61.96, 61.70, 44.93, 41.56, 25.73, 23.63, 13.97, 13.79, 12.80; HRMS calculated for $C_{24}H_{26}NaO_8$ 465.1561; found, 465.1527.

5o: IR(NaCl, cm^{-1}) 3210, 2931, 2855, 1700, 1212, 977; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 5.92 (s, 1H), 4.29 (quart, J = 7.2 Hz, 2H), 4.24 (quart, J = 7.2 Hz, 2H), 2.66-2.51 (m, 7H), 2.49-2.39 (m, 4H), 2.34-2.25 (m, 2H), 2.22-2.19 (m, 1H), 2.14-2.00 (m, 6H), 1.34-1.28 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.62, 192.11, 178.33, 164.39, 161.61, 153.28, 151.92, 151.05, 149.08, 142.09, 124.56, 118.68, 98.45, 80.43, 61.65, 61.52, 39.65, 37.16, 29.40, 28.78, 27.81, 27.04, 26.22, 24.41, 24.06, 23.40, 23.22, 19.81, 14.06, 14.03; HRMS calculated for $C_{30}H_{36}NaO_8$ 547.2311; found, 547.2351.

7o: IR(NaCl, cm^{-1}) 3013, 2831, 2834, 1699, 1323, 1218, 978; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91 (s, 2H), 4.30 (quart, J = 7.2 Hz, 4H), 4.24 (quart, J = 7.2 Hz, 4H), 2.61-2.59 (m, 2H), 2.54-2.39 (m, 4H), 2.34-2.18 (m, 4H), 2.14-2.01 (m, 6H), 1.35-1.29 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.10, 178.33, 164.36, 161.59, 153.26, 151.86, 149.05, 98.40, 80.37, 61.64, 61.48, 37.14, 29.45, 29.48, 27.00, 24.32, 23.37, 23.20, 14.05, 14.01; HRMS calculated for $C_{38}H_{46}NaO_{12}$ 717.2984; found, 717.2959.

Diethyl 1-(5-(furan-2-yl)pentyl)-7-oxa-bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (5p): IR(NaCl, cm^{-1}) 2983, 2931, 2864, 1708, 1307, 1268; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.28 (d, J = 1.2 Hz, 1H), 7.17 (dd, J = 5.2, 2.0 Hz, 1H), 6.98 (d, J = 5.2 Hz, 1H), 6.27-6.26 (dd, J = 2.8, 2.0 Hz, 1H), 5.96 (d, J = 2.4 Hz, 1H), 5.63 (d, J = 2.0 Hz, 1H), 4.30 (quart, J = 7.2 Hz, 2H), 4.22 (quart, J = 6.8 Hz, 2H), 2.61 (t, J = 8.0 Hz, 2H), 2.22-2.08 (m, 2H), 1.69-1.62 (m, 2H), 1.51-1.38 (m, 4H), 1.35-1.31 (t, J = 7.2 Hz, 3H), 1.29 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.02, 162.50, 156.22, 156.02, 151.06, 145.03, 144.52, 140.65, 109.98, 104.62, 97.74, 83.28, 61.37, 61.16, 29.20, 28.76, 27.78, 27.72, 24.57, 14.09, 14.06; HRMS calculated for $C_{21}H_{26}NaO_6$ 397.1614; found, 397.1624.

6q-1: IR(NaCl, cm^{-1}) 2988, 1700, 1621, 1213; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (s, 4H), 6.66 (d, J = 5.2 Hz, 2H), 6.49 (d, J = 4.8 Hz, 2H), 4.94 (d, J = 1.6 Hz, 2H), 4.17-4.11 (m, 2H), 4.06 (quart, J = 6.8 Hz, 2H), 3.90 (d, J = 11.2 Hz, 2H), 3.30 (d, J = 15.2 Hz, 2H), 1.30-1.26 (m, 3H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.62, 169.82, 144.39, 136.91, 135.56, 130.57, 127.27, 89.83, 83.06, 76.05, 61.23, 60.96, 36.24, 14.17, 14.08, 14.01; HRMS calculated for $C_{24}H_{24}NaO_6$ 431.1514; found, 430.9391.

6q-2: IR(NaCl, cm^{-1}) 2877, 1688, 1601, 1222; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (s, 4H), 6.52 (d, J = 5.2 Hz, 1H), 6.40 (d, J = 5.6 Hz, 1H), 5.04 (s, 1H), 4.84 (s, 1H), 4.34 (quart, J = 6.8 Hz, 2H), 4.23 (quart, J = 6.8 Hz, 2H) 3.76 (dd, J = 24Hz, J = 14.8 Hz, 2H), 3.34 (d, J = 14.8 Hz, 2H), 2.37 (ABq, Δδ = 22.2 Hz, J = 6.0 Hz, 2H), 1.37 (t, J = 7.2 Hz, 3H), 1.29 (t, J = 6.8Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.37, 162.36, 150.07, 144.69, 141.52, 138.92, 135.80, 134.79, 130.76, 130.69, 127.47, 127.29, 88.66, 85.58, 80.96, 80.01, 61.54, 61.30, 55.18, 53.88, 36.57, 34.94, 14.17, 14.09; HRMS calculated for $C_{24}H_{24}NaO_6$ 431.1514; found, 431.1391.

Acknowledgments. We would like to thank the National Research Foundation of Korea (200900000001607) for financial support.

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