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STEREOSELECTIVE SYNTHESIS OF (*Z*)-α-PHENOXYMETHYLENE-γ-BUTYROLACTONE AND ITS SULFUR ANALOGUES FROM 2-PROPYNYLOXY- OR 2-PROPYNYLTHIOBENZENE

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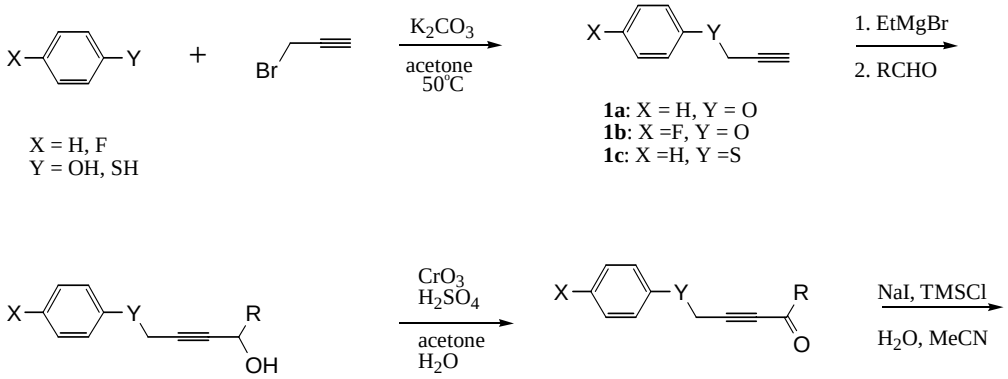
Abstract – The preparations of (Z)-α-phenoxymethylene-γ-butyrolactone, α-phenoxymethyl-γ-butyrolactone, (Z)-α-phenylthiomethylene-γ-butyrolactone, and α-phenylthiomethyl-γ-butyrolactone derivatives from 2-propynyloxy-benzene and 2-propynylthiobenzene were described.

Recently, we have developed an efficient method for the preparation of (*Z*)-α-alkylidene-γ-butyrolactone from 2-alkyn-1-one *via* a deconjugated hydroiodination process.[1] The stereo- selective synthesis of (*Z*)-α-alkylidene-γ-butyrolactone has become attractive since these compounds can be used as a plant growth regulator,[2] or as an important intermediate to the synthesis of obtusilactone isolated from *Lindela obtusiloba*, a cytotoxic natural product.[3] Although several methods have been reported for the introduction of an alkylidene group at the α-position of a γ-butyrolactone with (*E*)- or (*Z*)-configuration,[4] there is no general procedure being reported in the literature for the stereoselective synthesis of the α-exocyclic double bond of γ-butyrolactone with phenoxy or phenylthio group on the exocyclic double bond.[5] In addition, the sulfonate functionalized on the α-exocyclic double bond of γ-butyrolactone has been reported to enhance a Michael-type nucleophilic addition-elimination more rapidly than simple enones so that it may become a possible *irreversible* alkylation agents for cellular nucleophiles and may be employed as a cancer chemoterapeutic agents.[6] In view of the leaving group property of either phenoxy or phenylthio group substituted on the β-position of the α-exocyclic double bond of γ-butyrolactone and their potential application as the alkylating agents for DNA cleavage, we now report the synthesis of (*Z*)-α-phenoxymethylene-γ-butyrolactone and (*Z*)-α-phenylthio-methylene-γ-butyrolactone derivatives from 2-propynyloxybenzene and 2-propynylthiobenzene, respectively, as shown in **Scheme 1**.

The preparation of (*Z*)-5-methyl-3-phenoxymethylene-4,5-dihydrofuran-2-one (**8a**) from 2-propynyl-oxybenzene (**1a**) was representative as follows. Thus, **1a**, obtained in 94% yield from phenol and

Scheme 1. Preparation of α-Phenoxymethylene or Phenoxymethyl-Substituted γ-Butyrolactones and Their Sulfur Analagues.

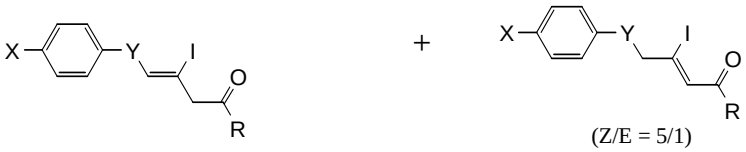


X = H, F
Y = OH, SH

1a: X = H, Y = O
1b: X =F, Y = O
1c: X =H, Y =S

2a: X = H, Y = O, R = Me
2b: X = F, Y = O, R = Me
2c: X = H, Y = O, R = 3,4,5-trimethoxyphenyl
2d: X = F, Y = O, R = 3,4,5-trimethoxyphenyl
2e: X = H, Y = S, R = Me

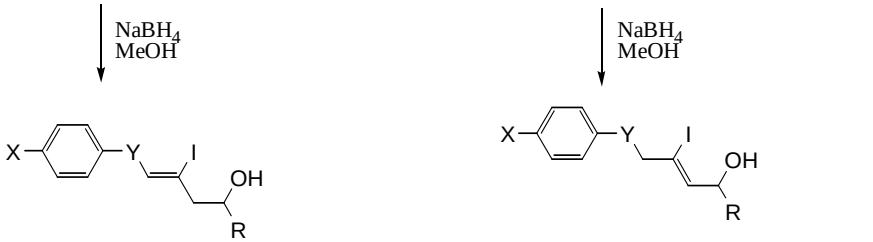
3a: X = H, Y = O, R = Me
3b: X = F, Y = O, R = Me
3c: X = H, Y = O, R = 3,4,5-trimethoxyphenyl
3d: X = F, Y = O, R = 3,4,5-trimethoxyphenyl
3e: X = H, Y = S, R = Me



(Z/E = 5/1)

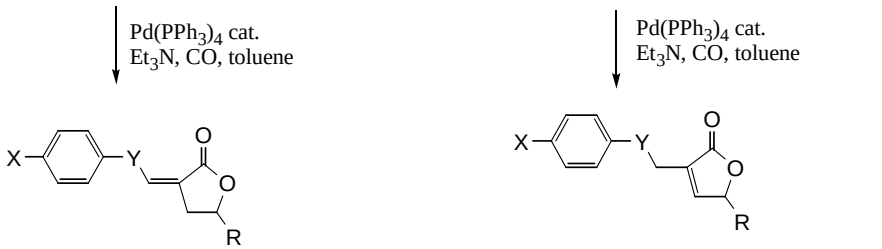
4a: X = H, Y = O, R = Me
4b: X = F, Y = O, R = Me
4c: X = H, Y = O, R = 3,4,5-trimethoxyphenyl
4d: X = F, Y = O, R = 3,4,5-trimethoxyphenyl
4e: X = H, Y = S, R = Me

5a: X = H, Y = O, R = Me
5b: X = F, Y = O, R = Me
5c: X = H, Y = O, R = 3,4,5-trimethoxyphenyl
5d: X = F, Y = O, R = 3,4,5-trimethoxyphenyl
5e: X = H, Y = S, R = Me



6a: X = H, Y = O, R = Me
6b: X = F, Y = O, R = Me
6c: X = H, Y = O, R = 3,4,5-trimethoxyphenyl
6d: X = F, Y = O, R = 3,4,5-trimethoxyphenyl
6e: X = H, Y = S, R = Me

7a: X = H, Y = O, R = Me
7b: X = F, Y = O, R = Me
7c: X = H, Y = O, R = 3,4,5-trimethoxyphenyl
7d: X = F, Y = O, R = 3,4,5-trimethoxyphenyl
7e: X = H, Y = S, R = Me



8a: X = H, Y = O, R = Me
8b: X = F, Y = O, R = Me
8c: X = H, Y = O, R = 3,4,5-trimethoxyphenyl
8d: X = F, Y = O, R = 3,4,5-trimethoxyphenyl
8e: X = H, Y = S, R = Me

9a: X = H, Y = O, R = Me
9b: X = F, Y = O, R = Me
9c: X = H, Y = O, R = 3,4,5-trimethoxyphenyl
9d: X = F, Y = O, R = 3,4,5-trimethoxyphenyl
9e: X = H, Y = S, R = Me

propargyl bromide in the presence of potassium carbonate in acetone at 50°C, was treated with ethylmagnesium bromide under nitrogen at 0°C and followed by the addition of acetaldehyde at 0°C to give 5-phenoxypent-3-yn-2-ol (**2a**) in 90% yield. Jones oxidation of **2a** could give the corresponding conjugated ynone (**3a**) in 92% yield. Treatment of the conjugated ynone (**3a**) with sodium iodide, trimethylsilyl chloride, and water in acetonitrile[1,7] at room temperature gave deconjugated (4*Z*)-4-iodo-5-phenoxypent-4-en-2-one (**4a**), conjugated (3*Z*)-4-iodo-5-phenoxypent-3-en-2-one (**5a**), and conjugated (3*E*)-4-iodo-5-phenoxypent-3-en-2-one in 65, 15, and 3% yields, respectively. Their stereochemistry were determined by 2D NOESY ^{1}H NMR spectral analyses. It is noteworthy that treatment of **5a** with catalytic amount of trimethylsilyl chloride could transform **5a** into deconjugated iodo enone (**4a**) in 96% yield as we have reported in the literature.[8] Reduction of **4a** with sodium borohydride in methanol at room temperature gave (*Z*)-3-iodo-3-en-1-ol (**6a**) in 93% yield with no loss of stereochemistry as judged by ^{1}H NMR spectral analyses. In the presence of tetrakis(triphenyl-phosphine)palladium catalyst, triethylamine, and carbon monoxide in toluene, the cyclization of **6a** afforded (*Z*)-5-methyl-3-phenoxymethylene-4,5-dihydrofuran-2-one (**8a**) in 18 h and in 84% yield. In order to test the feasibility and difference of the Michael-type nucleophilic addition-elimination of γ-butyrolactones with either exocyclic or endocyclic conjugated double bond, we also synthesize 5-methyl-3-phenoxymethyl-5-hydrofuran-2-one (**9a**) from the conjugated iodo enone (**5a**) intermediate with (*Z*)-configuration. Thus, treatment of **5a** with sodium borohydride in methanol at room temperature gave (*Z*)-3-iodo-2-en-1-ol (**7a**) in 94% yield without loss of stereochemistry as judged by ^{1}H NMR spectral analyses. The cyclization of **7a** in the presence of tetrakis(triphenylphosphine)palladium catalyst, triethylamine, and carbon monoxide in toluene could afford **9a** in 87% yield. The fluoro- and/or 3,4,5-trimethoxyphenyl substituted, and sulfur-containing analogues of the above mentioned compounds are prepared similarly to the above described procedures. Thus, (*Z*)-5-methyl-3-phenylthiomethylene-4,5-dihydrofuran-2-one (**8e**) and 5-methyl-3-phenylthio-methyl-5-hydrofuran-2-one (**9e**) are prepared from 2-propynylthiobenzene (**1c**) in a total yields of 30 and 15%, respectively, in five steps. Similarly, **8b**-**8d** and **9b**-**9d** can be prepared in reasonable yields from **1a** and **1b**. We have attempted to prepare 6-(4-hydroxyphenyl)-hex-3-yn-2-one and 4-(5-oxohex-3-ynyl)phenyl acetate, i.e. **3a** with hydroxy or acetyloxy group at the *p*-position, *via* various kinds of oxidation conditions to the corresponding propargyl alcohols, but only isolated 1,4-benzoquinone as the major product under these oxidation conditions.

EXPERIMENTAL

Precoated silica gel 60F-254 on aluminum plates made by EM chemical company was used for thin-layer chromatography. Purification by column chromatography was carried out with EM silica gel 60 (70-230 mesh ASTM). HPLC separation was performed at a flow rate of 0.7 mL/min by the use of

two Chemco-Pak 10 x 250 column packed with Chemcosorb 5-ODS-H. GLC analysis were performed by a 3.2 x 3.1 column packed with SE-30 (5% on Chemcosorb W). The purity of each compounds was judged to be > 95% by GLC, ^{1}H-NMR or ^{13}C-NMR spectral analyses. Reactions of organometallic compounds were undertaken in oven- and/or flame-dried glassware. Tetrakis(triphenylphosphine)-palladium catalyst was prepared by published method.[9] All other materials were used without further purification. IR spectra were recorded on a Perkin-Elmer Paragon 1000 or 882 infrared spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC200, AC300, or AMX400 spectrometer, chemical shifts were reported in ppm down field from TMS. MS spectra were obtained on HP 5971, Fisons MD800 GC/MS or VG 70-250S spectrometers. HRMS was recorded on VG 70-250S or VG Autospec double focusing high-resolution mass spectrometer. Elemental analyses were performed on Perkin Elmer EA-2400.

Preparation of 1-fluoro-4-prop-2-ynyloxybenzene (1b) as the representative procedure for the synthesis of phenyl propargyl ethers or sulfide: To a solution of 4-fluorophenol (1.12 g, 10 mmol) in 15 mL of dry acetone were added anhydrous potassium carbonate (1.38 g, 10 mmol) and propargyl bromide (1.19 g, 10 mmol). The resultant mixture was stirred at 50°C for 18 h, then the mixture was cooled and the solvent was removed under reduced pressure. The residue was treated with 15 mL of water and extracted with ethyl acetate. The combined organic phases were washed with water, brine and dried over anhydrous magnesium sulfate and evaporated in vacuum. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate = 15/1) to give a colorless oil **1b** (1.31 g, 87%): ^{1}H NMR ($CDCl_3$, TMS) δ 2.51 (t, *J* = 2.4 Hz, 1 H), 4.63 (d, *J* = 2.4 Hz, 2 H), 6.85-7.05 (m, 4 H) ppm ; ^{13}C NMR ($CDCl_3$, TMS) δ 56.36, 75.57, 78.40, 115.79 (d, *J* = 48 Hz), 116.02, 154.43 (d, *J* = 131 Hz), 160.06 ppm; IR ($CHCl_3$) ν 3287, 2124, 1504, 1206, 1027, 827 cm^{-1}; MS *m/z* 150 (M^+), 149, 148, 122, 121, 111, 83. HRMS calcd for C_9H_7OF 150.0481, found 150.0489.

Prop-2-ynyloxybenzene (1a)[10]: colorless oil; 94% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.49 (t, *J* = 2.4 Hz, 1 H), 4.66 (d, *J* = 2.4 Hz, 2 H), 6.9-7.0 (m, 3 H), 7.25-7.35 (m, 2 H) ppm; MS *m/z* 132 (M^+), 131, 130, 103.

Prop-2-ynylthiobenzene (1c)[11]: colorless oil; 83% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.21 (t, *J* = 2.4 Hz, 1 H), 3.59 (d, *J* = 2.4 Hz, 2 H), 7.15-7.35 (m, 3 H), 7.4-7.5 (m, 2 H) ppm; MS *m/z* 148 (M^+), 147, 115, 109.

Preparation of 5-phenoxypent-3-yn-2-ol (2a) as the representative procedure for the synthesis of propargy alcohols: To a stirred solution of phenyl propargyl ether (**1a**) (1.32 g, 10 mmol) in THF (4 mL) was added ethylmagnesium bromide (1.1 equiv, 11 mmol) under nitrogen at 0°C. The mixture was stirred at 0°C for 3 h, then allowed to react with acetaldehyde at 0°C for 4 h and quenched by the addition of saturated solution of NH_4Cl (5 mL). The aqueous layer was extracted with ethyl acetate. The combined organic layer was dried over magnesium sulfate and was concentrated under reduced pressure.

The resultant crude product was purified by flash chromatography (silica gel, ethyl acetate/hexane = 1/8) to give **2a**[12] (1.59 g, 90%) as a colorless oil: ^{1}H NMR ($CDCl_3$, TMS) δ 1.33 (d, *J* = 4.5 Hz, 3 H), 2.32 (br s, 1 H), 4.43 (q, *J* = 4.5 Hz, 1 H), 4.60 (s, 2 H), 6.85-6.9 (m, 3 H), 7.2-7.25 (m, 2 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 23.99, 56.01, 58.24, 78.85, 89.20, 114.88, 121.45, 129.42, 157.62 ppm; IR ($CDCl_3$) ν 3403, 2357, 1594, 1241 cm^{-1}; MS m/z 176 (M^+), 158, 131, 103, 94.

5-(4-Fluorophenoxy)pent-3-yn-2-ol (2b): colorless oil; 84% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 1.42 (d, *J* = 6.5 Hz, 3 H), 2.32 (br s, 1 H), 4.55 (q, *J* = 6.5 Hz, 1 H), 4.66 (s, 2 H), 6.8-7.05 (m, 4 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 23.96, 56.44, 58.14, 78.59, 89.38, 115.88 (d, *J* = 49 Hz) 116.03 , 154.46 (d, *J* = 122 Hz), 160.03 ppm; IR ($CHCl_3$) ν 3373, 1505, 1452, 1203, 1019 cm^{-1}; MS *m/z* 194 (M^+), 176, 149, 122, 121, 112. Anal. Calcd for $C_{11}H_{11}O_2F$: C, 68.03; H, 5.71. Found: C, 68.22; H, 5.92.

4-Phenoxy-1-(3,4,5-trimethoxyphenyl)but-2-yn-1-ol (2c): colorless oil; 90% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.90 (br s, 1 H), 3.66 (s, 6 H), 3.80 (s, 3H), 5.26 (s, 1 H), 4.75 (s, 2 H), 5.41 (s, 1 H), 6.68 (s, 2 H), 6.9-7.0 (m, 3 H), 7.2-7.3 (m, 2 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 55.77, 55.88, 60.67, 64.41, 81.47, 86.93, 103.59, 114.70, 121.40, 129.38, 135.70, 137.73, 153.11, 157.42 ppm; IR ($CHCl_3$) ν 3438, 1597, 1495, 1221, 1123, 1010, 755 cm^{-1}; FAB MS: 328 (M^+). Anal. Calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.68; H, 6.21.

4-(4-Fluorophenoxy)-1-(3,4,5-trimethoxyphenyl)but-2-yn-1-ol (2d): colorless oil; 85% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.62 (br s, 1 H), 3.77 (s, 6 H), 3.84 (s, 3 H), 4.73 (s, 2 H) , 5.42 (s, 1 H), 6.69 (s, 2 H), 6.9-7.0 (m, 4 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 55.97, 55.60, 60.73, 64.52, 81.32, 87.11, 103.65, 115.87 (d, *J* = 33 Hz) , 115.98, 135.66, 137.93, 153.23, 154.81 (d, *J* =185 Hz), 159.23 ppm; IR ($CHCl_3$) ν 3454, 1594, 1506, 1463, 1232, 1200, 1007, 829 cm^{-1}; FAB MS: 346 (M^+); HRFABMS calcd for $C_{19}H_{20}O_5F$ 347.1295 (MH^+), found 347.1285.

5-Phenylthiopent-3-yn-2-ol (2e)[13]: colorless oil; 83% yield; ^{1}H NMR ($CDCl_3$ TMS) δ 1.36 (d, *J* = 6.7 Hz, 3 H), 2.14 (br s, 1 H), 3.62 (s, 2 H), 4.47 (q, *J* = 6.7 Hz, 1 H), 7.2-7.45 (m, 5 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 22.85, 24.14, 58.20, 79.72, 85.53, 126.87, 128.83, 130.25, 134.97 ppm; IR ($CHCl_3$) ν 3390, 1480, 1438, 1155, 1077, 1002, 891 cm^{-1}; MS *m/z* 192 (M^+), 174, 147, 110, 109.

Preparation of 5-phenoxypent-3-yn-2-one (3a) as the representative procedure for the synthesis of conjugated ynones: To a solution of **2a** (0.53 g, 3 mmol) in acetone (3 mL) was added dropwise Jones reagent (1.2 equiv), while keeping the temperature between 0-5°C, the mixture was stirred at rt for 2 h. It was diluted with 5 mL of water and extracted with ethyl acetate. The organic layer was washed by water, brine, and dried over magnesium sulfate. The solvent was removed under reduced pressure. The residue was purified by chromatography (silica gel, ethyl acetate/hexane = 1/8) to give **3a**[14] (0.48 g, 92%) as a colorless oil: ^{1}H NMR ($CDCl_3$, TMS) δ 2.31 (s, 3 H), 4.81 (s, 2 H), 6.9-7.0 (m, 3H), 7.25-7.35 (m, 2 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 22.54, 32.39, 55.50, 85.80, 85.88, 114.80, 121.90, 129.14, 129.51, 157.20, 183.60 ppm; IR ($CHCl_3$) ν 2218, 1681, 1598, 1495, 1360, 1212, 1047, 755 cm^{-1}; MS *m/z* 174

(M^+), 159, 131, 103.

5-(4-Fluorophenoxy)pent-3-yn-2-one (3b): colorless oil; 85% yield ; ^{1}H NMR ($CDCl_3$, TMS) δ 2.32 (s, 3 H), 4.79 (s, 2 H), 6.85-7.05 (m, 4 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 32.29, 56.26, 85.45, 85.95, 115.97 (d, *J* = 47 Hz), 116.12, 154.38 (d , *J* = 164 Hz), 160.24, 183.46 ppm; IR ($CHCl_3$) ν 2217, 1686, 1504, 1360, 1221, 1045, 830 cm^{-1}; MS *m/z* 192 (M^+), 177, 149, 121, 111, 83. Anal. Calcd for $C_{11}H_9O_2F$: C, 68.74; H, 4.72. Found: C, 68.91; H, 4.85.

4-Phenoxy-1-(3,4,5-trimethoxyphenyl)but-2-yn-1-one (3c): mp 79-80°C (EtOAc/EtOH); 94% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 3.69 (s, 6 H) , 3.89 (s, 3 H), 4.98 (s, 2 H), 7.01 (d, J = 5.2 Hz, 3 H), 7.28 (s, 2 H), 7.3-7.35 (m, 2 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 55.23, 55.87, 60.81, 84.66, 88.46, 106.71, 114.57, 121.79, 129.57, 131.27, 143.63, 152.92, 157.02, 175.79 ppm; IR ($CHCl_3$) ν 2230, 1650, 1588, 1457, 1331, 1209, 1127, 1041 cm^{-1}; FAB MS: 327 (M^+ + 1). HRMS calcd for $C_{19}H_{18}O_5$ 326.1154; found 326.1162.

4-(4-Fluorophenoxy)-1-(3,4,5-trimethoxyphenyl)but-2-yn-1-one (3d): mp 125-126°C (EtOAc/EtOH); 92% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 3.76 (s, 6 H), 3.91 (s, 3 H), 4.96 (s, 2 H), 6.95-7.05 (m, 4 H), 7.28 (s, 2 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 55.87, 56.00, 60.80, 84.67, 87.94, 106.74, 115.78 , 115.99 (d, *J* = 16 Hz), 131.15, 143.74, 152.90, 154.60 (d , *J* = 229 Hz), 159.34, 175.69 ppm; IR ($CHCl_3$) ν 2233, 1645, 1591, 1506, 1469, 1417, 1334, 1221, 1129, 994, 825 cm^{-1}; MS *m/z* 344 (M^+), 205, 172; HRFABMS calcd for $C_{19}H_{18}O_5F$ 345.1138 (MH^+); found 345.1041.

5-Phenylthiopent-3-yn-2-one (3e): colorless oil; 82% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.25 (s, 3 H), 3.70 (s, 2 H), 7.25-7.4 (m, 3 H), 7.45-7.5 (m, 2 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 23.00, 32.51, 82.74, 87.86, 127.60, 129.03, 131.06, 133.78, 183.97 ppm; IR ($CHCl_3$) ν 2210, 1674, 1358, 1223, 740 cm^{-1}; MS *m/z* 190 (M^+), 176, 155, 136. HRMS calcd for $C_{11}H_{10}OS$ 190.0452; found 190.0461.

Preparation of (4*Z*)-4-iodo-5-phenoxypent-4-en-2-one (4a) as the representative procedure for the synthesis of deconjugated iodo enones: To a solution of anhydrous sodium iodide (0.68 g, 4.5 mmol) in MeCN (3 mL) in a dry flask under nitrogen atmosphere was added TMSCl (0.46 mL, 3.6 mmol) and the mixture was stirred at rt for 20 min followed by the addition of 0.5 equiv of water (27 μL, 1.5 mmol). After stirring for another 10 min at rt, 1 equiv of **3a** (0.52 g, 3 mmol) was added quickly into the flask. After stirring for another 4 h, the reaction mixture was quenched with saturated solution of sodium thiosulfate and extracted with ethyl acetate (10 mL x 3). The organic layer was dried over magnesium sulfate followed by filtration and concentration. The crude product was purified by column chromatography (silica gel, ethyl acetate/hexane = 1/10) to give **4a** (0.59 g, 65%) as a colorless oil: ^{1}H NMR ($CDCl_3$, TMS) δ 2.21 (s, 3 H), 3.65 (s, 2 H), 6.73 (s, 1 H), 7.0-7.4 (m, 5 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 29.29, 51.78, 73.37, 116.75, 123.68, 129.61, 146.39, 156.04, 204.70 ppm; IR ($CHCl_3$) ν 1716, 1590, 1490, 1226, 1162, 1126, 755 cm^{-1}; MS *m/z* 302 (M^+), 259, 132, 131, 105, 104, 103. HRMS calcd for $C_{11}H_{11}O_2I$ 301.9804; found 301.9822.

(3*Z*)-4-Iodo-5-phenoxypent-3-en-2-one (5a): colorless oil; 15% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.26 (s, 3 H), 4.75 9 (s, 2 H), 6.88 (d, *J* = 7.4, 2 H), 7.01 (t, *J* = 7.4 Hz, 1 H), 7.14 (t, *J* = 1.5 Hz, 1 H), 7.30 (t, *J* = 7.4 Hz, 2 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 31.58, 76.85, 109.26, 114.80, 121.87, 129.52, 129.65, 157.21, 195.76 ppm; IR ($CHCl_3$) ν 1755, 1684, 1594, 1491, 1235, 1209, 1177, 754 cm $^{-1}$; MS *m/z* 302 (M^+), 259, 175, 132, 131, 94. Anal. Calcd for $C_{11}H_{11}O_2I$: C, 43.73; H, 3.67. Found: C, 43.85; H, 3.78.

(4*Z*)-5-(4-Fluorophenoxy)-4-iodopent-4-en-2-one (4b): colorless oil; 61% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.24 (s, 3 H), 3.67 (s, 2 H), 6.67 (s, 1 H), 7.0-7.05 (m, 4 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 29.51, 51.88, 73.37, 116.28 (d, *J* = 23 Hz), 118.32, 146.81, 152.36, 159.03 (d, *J* = 241 Hz), 204.48 ppm; IR ($CHCl_3$) ν 1716, 1652, 1498, 1241, 1203, 831 cm^{-1}; MS *m/z* 320 (M^+) 277, 150, 122, 83. HRMS calcd for $C_{11}H_{10}O_2FI$ 319.9710; found 319.9722.

(3*Z*)-5-(4-Fluorophenoxy)-4-iodopent-3-en-2-one (5b): colorless oil; 18% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.42 (s, 3 H), 4.86 (s, 2 H), 6.95-7.2 (m, 4 H), 7.27 (s, 1 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 31.57, 77.58, 108.93, 115.90 (d, *J* = 6 Hz), 116.22 (d, *J* = 16 Hz), 129.71, 154.40 (d, *J* = 152 Hz), 160.18, 195.80 ppm; IR ($CHCl_3$) ν 1697, 1504, 1434, 1196, 1023 cm^{-1}; MS *m/z* 320 (M^+), 277, 193, 150, 112. Anal. Calcd for $C_{11}H_{10}O_2FI$: C, 41.27; H, 3.15. Found: C, 41.40; H, 3.33.

(3*Z*)-3-Iodo-4-phenoxy-1-(3,4,5-trimethoxyphenyl)but-3-en-1-one (4c): pale yellow oil; 62% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 3.92 (s, 6 H), 3.93 (s, 3 H), 4.20 (s, 2 H), 6.74 (s, 1 H), 7.03 (d, *J* = 7 Hz, 2 H), 7.10 (t, *J* = 7 Hz, 1 H), 7.33 (t , *J* = 7 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$, TMS) δ 46.90, 56.36, 60.95, 73.76, 105.66, 106.07, 115.26, 116.94, 123.74, 129.73, 131.44, 146.55, 153.11, 156.33, 194.72 ppm; IR ($CHCl_3$) ν 1678, 1581, 1491, 1337, 1228, 1126, 754 cm^{-1}; MS *m/z* 454 (M^+), 328, 235, 196. HRMS calcd for $C_{19}H_{19}O_5I$ 454.0277; found 454.0285.

(2*Z*)-3-Iodo-4-phenoxy-1-(3,4,5-trimethoxyphenyl)but-2-en-1-one (5c): colorless oil; 17% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 3.77 (s, 6 H), 3.92 (s, 3 H), 4.86 (s, 2 H), 6.95-7.4 (m, 5 H), 7.59 (s, 2 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 56.04, 60.80, 76.24, 105.64, 109.86, 114.65, 121.74, 128.63, 129.70, 131.63, 142.92, 152.99, 157.10, 188.72 ppm; IR ($CHCl_3$) ν 1658, 1581, 1491, 1453, 1408, 1331, 1228, 1163, 1127, 1001, 757 cm^{-1}; MS *m/z* 454 (M^+), 328, 290, 235, 196, 155. HRMS calcd for $C_{19}H_{19}O_5I$ 454.0277; found 454.0282.

(3*Z*)-4-(4-Fluorophenoxy)-3-iodo-1-(3,4,5-trimethoxyphenyl)but-3-en-1-one (4d): colorless oil; 64% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 3.93 (s, 9 H), 4.20 (s, 2 H), 6.68 (s, 1 H), 7.01 (d, *J* = 6.2 Hz, 4 H), 7.26 (s, 2 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 44.28, 56.39, 61.31, 62.53, 112.89, 115.47 (d, *J* = 26 Hz), 118.68 (d, *J* = 8 Hz), 135.19, 142.64, 143.25, 153.19, 155.67, 157.41 (d, *J* = 280 Hz), 192.74 ppm; IR ($CDCl_3$) ν 1670, 1581, 1500, 1337, 1201, 1120, 833 cm^{-1}; MS *m/z* 472 (M^+), 344, 234, 219, 206, 195, 191; HRMS calcd for $C_{19}H_{18}O_5FI$ 472.0183, found 472.0179.

(2*Z*)-4-(4-Fluorophenoxy)-3-iodo-1-(3,4,5-trimethoxyphenyl)but-2-en-1-one (5d): colorless oil; 13% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 3.81 (s, 6 H), 3.90 (s, 3 H), 4.85 (s, 2 H), 6.9-7.0 (m, 4 H), 7.08 (s, 2 H),

7.58 (s, 1 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 56.43, 61.25, 76.38, 112.34, 114.64 (d, *J* = 28 Hz), 117.25 (d, *J* = 8 Hz), 135.69, 139.68, 144.39, 153.97, 154.63, 157.29 (d, *J* = 272 Hz), 186.37 ppm; IR ($CHCl_3$) ν 1664, 1575, 1504, 1331, 1203, 1126, 830 cm^{-1}; HRFABMS calcd for $C_{19}H_{19}O_5FI$ 473.0261 (MH^+), found: 473.0240.

(4*Z*)-4-Iodo-5-phenylthiopent-4-en-2-one (4e): colorless oil; 53% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.20 (s, 3 H), 3.74 (s, 2 H), 6.84(s, 1 H), 7.25-7.45 (m, 5 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 29.47, 58.24, 90.11, 127.79, 129.18, 130.85, 133.57, 137.67, 203.95 ppm; IR ($CHCl_3$) ν 1716, 1579, 1475, 1354, 1156, 740 cm^{-1}; FAB MS *m/z* 318 (M^+). Anal. Calcd for $C_{11}H_{11}OIS$: C, 41.52; H, 3.48. Found: C, 41.65; H, 3.59.

(3*Z*)-4-Iodo-5-phenylthiopent-3-en-2-one (5e): colorless oil; 25% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.13 (s, 3 H), 3.94 (s, 2 H), 6.54 (s, 1 H), 7.2-7.4 (m, 5 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 30.71, 47.69, 110.00, 127.59, 129.65, 131.59, 133.71, 140.11, 195.81 ppm; IR ($CHCl_3$) ν 1703, 1575, 1478, 1177 cm^{-1}; FAB MS *m/z* 318 (M^+). HRMS calcd for $C_{11}H_{11}OIS$ 317.9575, found 317.9583.

Preparation of (4*Z*)-4-iodo-5-phenoxypent-4-en-2-ol (6a) as the representative procedure for the reduction of deconjugated and conjugated iodo enones: To a cooled (0-5°C) solution of **4a** (0.30 g, 1 mmol) in 2 mL of methanol was added in one portion of sodium borohydride (0.05 g, 1.2 mmol), the mixture was then stirred at room temperature and monitored by TLC. After the disappearance of the iodo enone, the reaction mixture was added to 2 mL of water and was extracted with ethyl acetate. The combining organic extracts were washed with brine and dried over magnesium sulfate. After filtration and evaporation of the solvent, the crude product was purified by chromatography (silica gel, ethyl acetate/ hexane = 1/6) to give **6a** (0.28 g, 93%) as a colorless oil: ^{1}H NMR ($CDCl_3$, TMS) δ 1.25 (d, *J* = 6.3 Hz, 3 H), 2.2-2.4 (m, 2 H), 2.5-2.6 (m, 1 H), 4.05-4.15 (m, 1 H), 6.68 (s, 1 H), 6.95-7.35 (m, 5 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 22.74, 54.86, 66.89, 68.55, 112.15, 124.50, 129.40, 143.60, 157.20; IR ($CHCl_3$) ν 1658, 1588, 1485, 1229, 1119, 1074, 748 cm^{-1}; MS *m/z* 304 (M^+), 303, 260, 259, 131, 104. Anal. Calcd for $C_{11}H_{13}O_2I$: C, 43.44; H, 4.31. Found: C, 43.56; H, 4.43.

(3*Z*)-4-Iodo-5-phenoxypent-3-en-2-ol (7a): colorless oil; 94% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 1.25 (d, J = 6.3 Hz, 3 H), 2.56 (s, 1 H), 4.45-4.55 (m, 1 H), 4.62 (s, 2 H), 6.09 (d, *J* = 7.8 Hz, 1 H), 6.8-7.0 (m, 3 H), 7.26 (t, *J* = 7 Hz, 2 H) ppm**;** ^{13}C NMR ($CDCl_3$, TMS) δ 21.73, 71.91, 75.28, 100.11, 115.04, 121.48, 129.43, 140.64, 157.58 ppm; IR ($CHCl_3$) ν 3390, 1594, 1491, 1229, 1061, 748 cm^{-1}; MS *m/z* 304 (M^+), 260, 159, 133, 94. HRMS calcd for $C_{11}H_{13}O_2I$ 303.9960; found 303.9973.

(4*Z*)-5-(4-Fluorophenoxy)-4-iodopent-4-en-2-ol (6b): colorless oil; 83% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 1.27 (d, *J* = 7.2 Hz, 3 H), 1.97 (br s, 1 H), 2.53 (d, *J* = 6.2 Hz, 2 H), 4.0-4.2 (m, 1 H), 6.64 (s, 1 H), 6.98 (s, 2 H), 7.01 (d, *J* = 2.2 Hz, 2 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 22.13, 47.29, 66.10, 81.35, 116.22 (d, J = 57 Hz), 118.37 (d, J = 28 Hz), 145.00, 154.48 (d, *J* = 305 Hz), 161.34 ppm; IR ν 3377, 1645, 1498, 1203, 1126, 831 cm^{-1}; MS *m/z* 322 (M^+), 278, 112, 83. Anal. Calcd for $C_{11}H_{12}O_2FI$: C,

41.02; H, 3.75. Found: C, 41.22; H, 3.91

(3*Z*)-5-(4-Fluorophenoxy)-4-iodopent-3-en-2-ol (7b): colorless oil; 87% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 1.29 (d, J = 6.6 Hz, 3 H), 1.86 (s, 1 H), 4.5-4.6 (m, 1 H), 4.62 (s, 2 H), 6.09 (d, *J* = 7.5 Hz, 1 H), 6.8-7.0 (m, 4 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 21.86, 72.05, 76.19, 100.21, 116.08 (d, *J* = 49 Hz), 116.22, 140.26, 153.82, 157.71 (d, *J* = 238 Hz) ppm; IR ($CHCl_3$) ν 3364, 1505, 1202, 1019, 828 cm^{-1}; MS *m/z* 323 (M^+ + 1), 290, 231, 179, 155, 136, 112. HRMS calcd for $C_{11}H_{12}O_2FI$ 321.9866; found 321.9876.

(3*Z*)-3-Iodo-4-phenoxy-1-(3,4,5-trimethoxyphenyl)but-3-en-1-ol (6c): colorless oil; 92% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.2 (br s, 1 H), 2.7-2.9 (m, 2 H), 3.81 (s, 3 H), 3.83 (s, 6 H), 4.9-4.95 (m, 1 H), 6.58 (s, 1 H), 6.62 (s, 2 H), 6.90 (d , *J* = 7.8 Hz, 2 H), 7.10 (t, *J* = 7 Hz, 1 H), 7.73 (t, *J* = 7 Hz, 2 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 47.77, 56.04, 60.73, 72.47, 80.75, 102.78, 116.61, 123.52, 129.47, 137.31, 138.59, 145.15, 153.17, 156.20 ppm; IR ($CHCl_3$) ν 3456, 1593, 1491, 1231, 1125, 1005, 757 cm^{-1}; MS *m/z* 456 (M^+), 439, 307, 197, 154, 136; HRMS calcd for $C_{19}H_{21}O_5I$ 456.0434, found 456.0445.

(2*Z*)-3-Iodo-4-phenoxy-1-(3,4,5-trimethoxyphenyl)but-2-en-1-ol (7c): colorless oil; 89% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.62 (br s, 1 H), 3.81 (s, 6 H), 3.83 (s, 3 H), 4.68 (s, 2 H), 5.42 (d, *J* = 8 Hz, 1 H), 6.28 (d, *J* = 8 Hz, 1 H), 6.64 (s, 2 H), 6.7-7.3 (m, 5 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 56.02, 60.70, 75.32, 77.43, 99.57, 102.22, 102.94, 114.92, 121.54, 129.45, 137.26, 138.07, 153.28, 157.57 ppm; IR ($CHCl_3$) ν 3454, 1588, 1491, 1460, 1414, 1324, 1228, 1126, 1004, 754 cm^{-1}; MS *m/z* 457 (M^+ + 1), 440, 308, 219, 198, 154; HRMS calcd for $C_{19}H_{21}O_5I$ 456.0434, found 456.0445.

(3*Z*)-4-(4-Fluorophenoxy)-3-iodo-1-(3,4,5-trimethoxyphenyl)but-3-en-1-ol (6d): colorless oil; 94% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 1.82 (br s, 1 H), 2.7-2.9 (m, 2H), 3.81 (s, 3 H), 3.84 (s, 6 H), 4.92 (t, *J* = 5.5 Hz, 1 H), 6.51 (s, 1 H), 6.63 (s, 2 H), 6.85-7.0 (m, 4 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 47.83, 56.20, 60.85, 72.62, 80.89, 102.96, 115.99 (d, *J* = 47 Hz), 116.46, 118.12 (d, *J* = 12 Hz), 138.62, 145.54, 152.45, 153.39 (d, *J* = 361 Hz), 161.37 ppm; IR ($CHCl_3$) ν 3461, 1592, 1202, 1126, 1007, 831 cm^{-1}; MS *m/z* 474 (M^+). HRMS calcd for $C_{19}H_{20}O_5FI$ 474.0340; found 474.0352.

(2*Z*)-4-(4-Fluorophenoxy)-3-iodo-1-(3,4,5-trimethoxyphenyl)but-2-en-1-ol (7d): colorless oil; 78% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.32 (br s, 1 H), 3.83 (s, 9 H), 4.65 (s, 2 H), 5.43 (d, *J* = 7.9 Hz, 1 H), 6.26 (d, *J* = 7.9 Hz, 1 H), 6.65 (s, 2H), 6.8-6.95 (m, 4 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 56.09, 60.78, 76.16, 77.53, 102.33, 102.95, 115.90 (d, *J* = 23 Hz), 116.35 (d, *J* = 8 Hz), 137.22, 137.64, 138.34, 153.40, 153.71, 157.69 (d, *J* = 238 Hz) ppm; IR ($CHCl_3$) ν 3461, 1589, 1498, 1460, 1421, 1325, 1229, 1203, 1126, 998, 831 cm^{-1}. HRMS calcd for $C_{19}H_{20}O_5FI$ 474.0340; found 474.0348.

(4*Z*)-4-Iodo-5-phenylthiopent-4-en-2-ol (6e): colorless oil; 90% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 1.24 (d, *J* = 6.2 Hz, 3 H), 1.75 (s, 1 H), 2.63 (d, *J* = 6.2 Hz, 2 H), 4.0-4.15 (m, 1 H), 6.80 (s, 1 H), 7.25-7.45 (m, 5 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 22.01, 54.03, 66.46, 99.02, 127.60, 129.28, 130.62, 133.89, 135.08 ppm; IR ($CHCl_3$) ν 3356, 1578, 1474, 1241, 1063, 728 cm^{-1}; MS *m/z* 320 (M^+), 302, 276, 220,

148, 147, 109. HRMS calcd for $C_{11}H_{13}OIS$ 319.9732; found 319.9741.

(3*Z*)-4-Iodo-5-phenylthiopent-3-en-2-ol (7e): colorless oil; 92% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 1.01 (d, *J* = 6.4 Hz, 3 H), 1.69 (br s, 1 H), 3.83 (br s, 2 H), 4.3-4.4 (m, 1 H), 5.53 (d, *J* = 7.4 Hz, 1 H), 7.25-7.4 (m, 5 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 21.58, 49.75, 72.50, 102.44, 127.51, 128.88, 132.21, 134.00, 141.09 ppm; IR ($CHCl_3$) ν 3364, 1581, 1472, 1434, 1401, 1248, 1062, 889, 741 cm^{-1}; MS *m/z* 320 (M^+), 276, 218, 149, 110. HRMS calcd for $C_{11}H_{13}OIS$ 319.9732; found 319.9739.

Preparation of (*Z*)-5-methyl-3-phenoxymethylene-4,5-dihydrofuran-2-one (8a) as the representative procedure for the palladium-catalyzed CO insertion and lactonization of iodo enols: To a flask were charged under nitrogen with **6a** (0.31 g, 1 mmol), triethylamine (0.14 mL, 1 mmol), tetrakis(triphenylphosphine)palladium (0.12 g, 0.1 mmol), and 3 mL of toluene. A balloon was flushed three times with carbon monoxide and connected *via* a needle to a condenser attached to the above reaction flask. The system was flushed with a gentle steam of carbon monoxide for 1 min and then placed in an oil bath at 50°C for 3-18 h. Upon completion of the reaction, the reaction mixture was quenched with 10% ammonium hydroxide aqueous solution. Extraction (ethyl acetate), washing (brine), drying (magnesium sulfate), concentration, and chromatography (silica gel, ethyl acetate/hexane = 1/8) gave **8a** (0.17 g, 84%) as a colorless oil: ^{1}H NMR ($CDCl_3$, TMS) δ 1.43 (d, *J* = 6.2 Hz, 3 H), 2.56 (ddd, *J* = 15.1, 8.6, 2.1 Hz, 1 H), 3.06 (ddd, J = 15.1, 7.5, 1.7 Hz, 1 H), 4.6-4.7 (m, 1 H), 6.91 (s, 1 H), 7.11 (d, *J* = 8.9 Hz, 2 H), 7.16 (t, *J* = 7.5 Hz, 1 H), 7.37 (t, *J* = 7.9 Hz, 2 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 21.72, 33.02, 74.02, 106.29, 117.53, 124.63, 129.76, 148.69, 157.08, 167.87 ppm; MS m/*z* 204 (M^+), 160, 132, 131, 104, 103. Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found: C, 70.77; H, 5.99.

5-Methyl-3-phenoxymethyl-5-hydrofuran-2-one (9a): colorless oil, 87% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 1.43 (d, *J* = 6.9 Hz, 3 H), 4.77 (t, *J* = 1.9 Hz , 2 H), 5.05-5.15 (m, 1 H), 6.86 (d, *J* = 8.1 Hz, 2 H), 6.97 (t, *J* = 7.2 Hz, 1 H), 7.30 (t, *J* = 8.1 Hz, 2 H), 7.39 (s, 1 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 18.83, 61.86, 78.46, 114.50, 121.48, 129.59, 129.94, 151.49, 157.82, 171.69 ppm; IR ($CHCl_3$) ν 1755, 1683, 1599, 1496, 1234, 1201, 1083, 1022, 755 cm^{-1}; MS *m/z* 204 (M^+), 159, 111, 110, 94. HRMS calcd for $C_{12}H_{12}O_3$ 204.0786; found 204.0798.

(*Z*)-3-[(4-Fluorophenoxy)methylene]-5-methyl-4,5-dihydrofuran-2-one (8b): colorless oil; 86% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 1.44 (d, *J* = 6.2 Hz , 3 H) , 2.55 (ddd, *J* = 15.2 , 6.5, 2.1 Hz, 1 H), 3.06 (ddd, *J* = 15.2, 7.5, 1.7 Hz , 1 H) , 4.6-4.75 (m , 1 H) , 6.82 (t, *J* = 1.7 Hz, 1 H) , 7.0-7.15 (m, 4 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 21.79, 33.05, 74.08, 106.59, 116.40 (d, *J* = 24 Hz), 119.15 (d, *J* = 8 Hz), 148.83, 153.29, 159.57 (d, *J* = 242 Hz), 167.79 ppm; IR ($CHCl_3$) ν 1751, 1674, 1501, 1202, 1080, 835 cm^{-1}; MS *m/z* 222 (M^+), 150, 124, 112, 83. Anal. Calcd for $C_{12}H_{11}O_3F$: C, 64.86; H, 4.99. Found: C, 64.98; H, 5.10.

3-[(4-Fluorophenoxy)methyl]-5-methyl-5-hydrofuran-2-one (9b): colorless oil; 95% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 1.47 (d, *J* = 6.9 Hz, 3 H), 4.76 (t, *J* = 1.8 Hz, 2 H), 5.1-5.15 (m, 1 H), 6.85-6.9 (m, 2 H),

6.95-7.0 (m, 2 H), 7.40 (s, 1 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 18.84, 62.57, 78.47, 115.67 (d, *J* = 8 Hz), 116.01 (d, *J* = 23 Hz), 130.23, 151.64, 154.01, 157.65 (d, *J* = 238 Hz), 171.63 ppm; IR ($CHCl_3$) ν 1748, 1504, 1209, 1087, 1017, 825 cm^{-1}; MS *m/z* 222 (M^+), 176, 166, 154, 136. HRFABMS calcd for $C_{12}H_{12}O_3F$ 223.0770 (MH^+), found 223.0760.

(*Z*)-3-Phenoxymethylene-5-(3,4,5-trimethoxyphenyl)-4,5-dihydrofuran-2-one (8c): colorless oil; 63% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.92 (ddd, *J* = 15.3, 7.4, 2.1 Hz, 1 H), 3.35 (ddd, *J* = 15.3, 7.8, 1.4 Hz, 1 H), 3.85 (s 3 H), 3.87 (s, 6 H), 5.48 (t, *J* = 7.5 Hz, 1 H), 6.57 (s, 2 H), 6.96 (t, *J* = 1.8 Hz, 1 H), 7.1-7.4 (m, 5 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 34.38, 56.23, 60.82, 78.11, 102.28, 105.44, 117.60, 124.87, 129.87, 135.73, 137.96, 149.23, 153.57, 157.08, 167.58 ppm; IR ($CHCl_3$) ν 1756, 1501, 1202, 1126 cm^{-1}; MS *m/z* 356 (M^+), 263, 189, 136; HRFABMS calcd for $C_{20}H_{21}O_6$ 357.1338 (MH^+), found 357.1353.

3-Phenoxymethyl-5-(3,4,5-trimethoxyphenyl)-5-hydrofuran-2-one (9c): colorless oil; 78% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 3.81 (s, 6 H), 3.83 (s, 3 H), 4.62 (s, 2 H), 5.6-5.7 (m, 1 H), 6.60 (s, 2 H), 6.8-7.1 (m, 5 H), 7.68 (d, *J* = 6 Hz, 1 H); ^{13}C NMR ($CDCl_3$, TMS) δ 56.25, 61.63, 63.67, 79.96, 103,04, 115.36, 121.40, 130.04, 137.90, 143.43, 150.89, 155.78, 159.86, 168.90 ppm; IR ($CHCl_3$) ν 1750, 1509, 1226, 831 cm^{-1}; MS *m/z* 356 (M^+), 341, 263, 136; HRFABMS calcd for $C_{20}H_{21}O_6$ 357.1338 (MH^+), found 357.1351.

(*Z*)-3-[(4-Fluorophenoxy)methylene]-5-(3,4,5-trimethoxyphenyl)-4,5-dihydrofuran-2-one (8d): colorless oil; 68% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 2.92 (ddd, *J* = 15.3, 7.2, 2.2 Hz, 1 H), 3.35 (ddd, *J* = 15.3, 7.9, 1.7 Hz, 1 H), 3.85 (s, 3 H), 3.88 (s, 6 H), 5.49 (t, *J* = 7.5 Hz, 1 H), 6.57 (s, 2 H), 6.88 (t, *J* = 1.9 Hz, 1 H), 7.0-7.15 (m, 4 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 34.36, 56.29, 60.85, 78.14, 102.36, 104.24, 105.73, 116.48 (d, *J* = 35 Hz), 119.16 (d, *J* = 13 Hz), 135.63, 149.29, 153.23, 153.64, 159.69 (d, *J* = 363 Hz), 168.08 ppm; IR ($CHCl_3$) ν 1755, 1673, 1593, 1502, 1463, 1202, 1127, 1025, 835 cm^{-1}; FAB MS *m/z* 374 (M^+), 280, 279, 263. HRMS calcd for $C_{20}H_{19}O_6F$ 374.1166; found 374.1175.

3-[(4-Fluorophenoxy)methyl]-5-(3,4,5-trimethoxyphenyl)-5-hydrofuran-2-one (9d): colorless oil; 72% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 3.81 (s, 6 H), 3.83 (s, 3 H), 4.68 (s, 2 H), 5.65-5.75 (m, 1 H), 6.60 (s, 2 H), 6.8-7.2 (m, 4 H), 7.58 (d, *J* = 6 Hz, 1 H); ^{13}C NMR ($CDCl_3$, TMS) δ 56.80, 61.34, 63.50, 80.34, 102.43, 117.68 (d, *J* = 39 Hz), 119.03 (d, *J* = 8 Hz), 129,67, 137.87, 143.43, 150.34, 153.78, 156.65, 157.89 (d, *J* = 270 Hz), 169.69 ppm; IR ($CHCl_3$) ν 1745, 1666, 1590, 1509, 1468, 1225, 831 cm^{-1}; MS *m/z* 374 (M^+), 359, 280; HRMS calcd for $C_{20}H_{19}O_6F$ 374.1166; found 374.1178.

(*Z*)-5-Methyl-3-phenylthiomethylene-4,5-dihydrofuran-2-one (8e): colorless oil; 93% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 1.42 (d, *J* = 6.3 Hz, 3 H), 2.58 (ddd, *J* = 16.2, 6.2, 2.2 Hz, 1 H), 3.11 (ddd, *J* = 16.2, 7.7, 1.8 Hz, 1 H), 4.65-4.75 (m , 1 H), 7.06 (t, *J* = 2.0 Hz, 1 H) , 7.35-7.5 (m, 5 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 22.01, 36.42, 74.65, 119,57, 128.22, 129.41, 131.04, 135.62, 140.68, 169.76 ppm; IR ($CHCl_3$) ν 1729, 1607, 1440, 1344, 1190, 1081, 1036, 831, 741 cm^{-1}; MS *m/z* 220 (M^+), 147, 109.

HRMS calcd for $C_{12}H_{12}O_2S$ 220.0558; found 220.0563.

5-Methyl-3-phenylthiomethyl-5-hydrofuran-2-one (9e): colorless oil; 95% yield; ^{1}H NMR ($CDCl_3$, TMS) δ 1.33 (d, *J* = 6.8 Hz, 3 H), 3.73 (t, *J* = 1.5 Hz, 2 H), 4.9-5.0 (m, 1 H), 6.99 (dd, *J* = 2.7, 1.2 Hz, 1 H), 7.2-7.35 (m, 5 H) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ 18.90, 28.36, 77.55, 126.99, 129.05, 130.23, 130.46, 134.61, 151.49, 172.27 ppm; IR ($CHCl_3$) ν 1752, 1581, 1497, 1318, 1074, 1024, 743 cm^{-1}; MS *m/z* 220 (M^+), 119, 85, 84. HRMS calcd for $C_{12}H_{12}O_2S$ 220.0558; found 220.0568.

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REFERENCES

1. F. T. Luo, M. W. Wang, and Y. S. Liu, *Heterocycles*, **1996**, *43*, 2725.
2. S. Huneck, K. Schreiber, C. Schulze, and G. Sembdner, Ger. (East) Patent, 1975, 112884 (*Chem. Abstr.*, 1976, **84**, 116942x).
3. M. Niwa, M. Iguchi, and S. Yamamura, *Chem. Lett*., 1975, 655.
4. A. W. Murray and R. G. Reid, *J. Chem. Soc., Chem. Commun*., 1984, 132; K. Tanaka, N. Tamura, and A. Kaji, *Chem. Lett*., 1980, 595; E. Piers and J. S. M. Wai, *J. Chem. Soc., Chem. Commun.*, 1988, 1245; G. L. Larson and R. M. B. Perez, *J. Org. Chem*., 1985, **50**, 5257; F. Bellina, A. Carpita, M. D. Santis, and R. Rossi, *Tetrahedron*, 1994, **50**, 12029; S. Matsui, *Bull. Chem. Soc. Jpn*., 1987, **60**, 1853; L. D. Martin and J. K. Stille, *J. Org. Chem*., 1982, **47**, 3630.
5. G. A. Howie, I. K. Stamos, and J. M. Cassady, *J. Med. Chem.*, **1976**, *19*, 309.
6. P. J. Stang and W. L. Treptow, *J. Med. Chem.*, **1981**, *24*, 468; Z. Rappoport and A. Gal, *J. Org. Chem.*, **1972**, *37*, 1174.
7. F. T. Luo, K. A. Kumar, L. C. Hsieh, and R. T. Wang, *Tetrahedron Lett.*, 1994, **35**, 2553; F. T. Luo, *J. Org. Chem.*, **1998**, *63*, 5656.
8. F. T. Luo and L. C. Hsieh, *Tetrahedron Lett.*, 1994, **35**, 9585.
9. D. R. Coulson, *Inorg. Synth*., **1972**, *13*, 121.
10. M. T. W. Hearn, *Tetrahedron*, **1976**, *32*, 115; G. Pourcelot, P. Cadiot, and C. Georgoulis, *Tetrahedron*, **1982**, *38*, 2123.
11. J. G. Donkervoort, A. R. Gordon, C. Johnstone, W. K. Kerr, and U. Lange, *Tetrahedron*, **1996**, *52*, 7391.
12. G. Frater and H. Schmid, *Helv. Chim. Acta*, **1970**, *53*, 269.
13. F. Kido, S. C. Sinha, T. Abiko, M. Watanabe, and A. Yoshikoshi, *Tetrahedron*, **1990**, *46*, 4887.
14. A. N. Dey, *J. Chem. Soc*., **1937**, 1057.