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A new protocol for synthesis of 3-hydroxymethyl-4-methoxy-2*H*-pyrone derivatives

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Dedicated to Professor Barry M. Trost on the occasion of his 60th birthday

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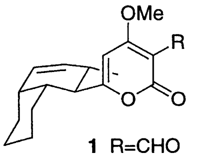
Abstract—The title compounds have been prepared by treatment of 4-methoxy-3-phenylsulfinylmethyl-2*H*-pyrone derivatives with trifluoroacetic anhydride, followed by basic work-up. © 2001 Elsevier Science Ltd. All rights reserved.

Among polyketide natural products, there exist many 4-alkoxy-2*H*-pyrone derivatives, some of which have 3-alkoxy or 3-formyl substituents. Solanapyrones A **1** and B **2** were isolated by Oikawa and Ichihara[1] from phytogenic fungi *Altenaria solani* and *Ascochyta rabiei* as unique phytotoxic polyketides which possess decaline frameworks with a 3-formyl- or a 3-hydroxymethyl-4-methoxy-2*H*-pyrone moiety, respectively (Fig. 1). In the course of our independent synthetic study of solanapyrones, one major issue was the construction of the 3-hydroxymethyl-4-methoxy-2*H*-pyrone moiety at the later stage of the synthetic sequence according to our synthetic design (Scheme 1). Introduction of the 4-alkoxy-2*H*-pyrone moiety to the decaline framework would be feasible by cyclization of β,δ-diketo-ester **3** installed by Claisen condensation. However, to our knowledge, procedures for introduction of a hydroxymethyl or formyl group at C-3 of the 4-alkoxy-2*H*-pyrone derivatives **4** or **5** (R′=H or Me) are quite limited.

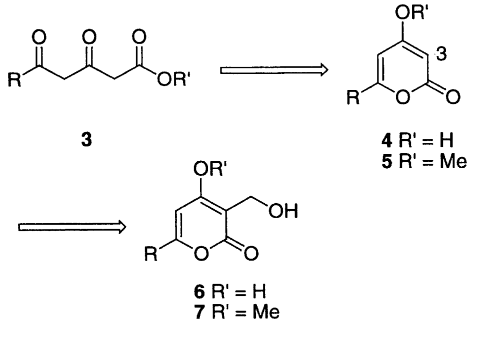


1 R=CHO
2 R=CH_2OH

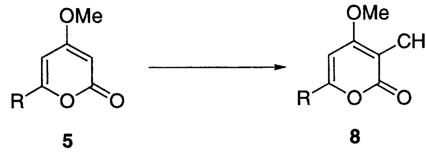
Figure 1.

Only one known example to date for our purpose is the reaction of 4-methoxy-2*H*-pyrone derivatives **5** with dichloromethylmethyl ether in the presence of titanium tetrachloride leading to 3-formyl-4-methoxy-2*H*-pyrone derivatives **8** (Scheme 2),[2] although we found that the application of this procedure to solanapyrone synthesis was difficult.

Consequently, we started our investigation on this issue and delineate a new protocol to introduce a hydroxymethyl unit at C-3 of the 4-hydroxy-2*H*-pyrone derivatives **4** or **5**. Our initial attempts of direct condensation of 4-hydroxy-2*H*-pyrones **4** with formaldehyde provided dimeric compounds under either acidic or basic conditions.[3] Our attempts to



Scheme 1.



Scheme 2.

Keywords: hydroxymethylation; 2*H*-pyrones; solanapyrones; sulfinyl compounds.

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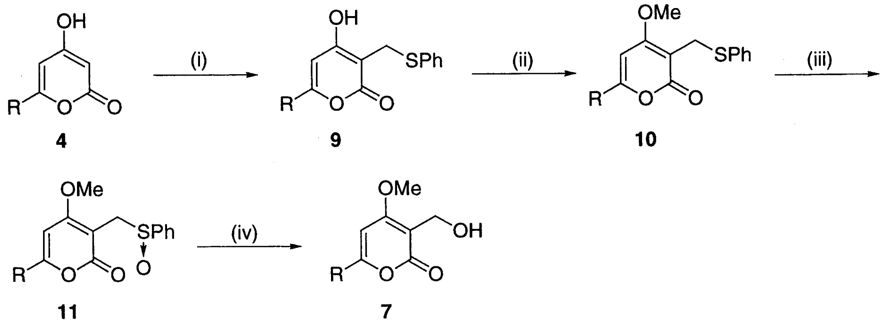


Scheme 3. *Reagents and conditions*: (i) $(HCHO)_n$, PhSH, AcOH, piperidine, EtOH, 55°C; (ii) Me_2SO_4, K_2CO_3, acetone; (iii) MCPBA, CH_2Cl_2; (iv) $(CF_3CO)_2O$, CH_2Cl_2, 0°C then 1 N NaOH, THF.

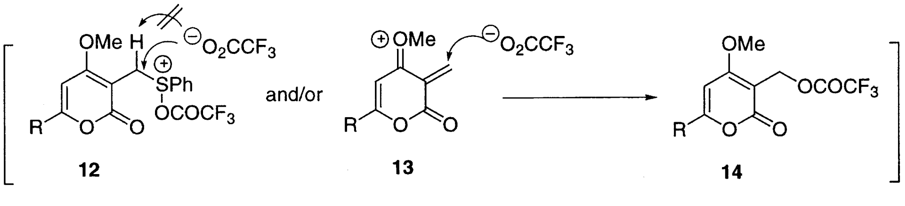
generate a carbanion at C-3[4] of **5** and react it with formaldehyde did not produce the desired product **7**.

We then turned our attention to an alternative strategy utilizing a phenylthiomethyl group as a synthetic equivalent of a hydroxymethyl group (Scheme 3). The starting 4-hydroxy-2*H*-pyrone derivatives **4** were procured or prepared via 1,8-diazabicyclo[2.2.2]undec-7-ene (DBU)[5] promoted cyclization of β,δ-diketoesters.[6] A phenylthiomethyl group was introduced to the 4-hydroxy-2*H*-pyrone derivatives **4** according to the procedure by Moreno-Manas et al.[7] to give 4-hydroxy-3-phenylthiomethyl-2*H*-pyrone derivatives **9**. After conventional *O*-methylation with dimethyl sulfate, the resulting 4-methoxy-3-phenylthiomethyl-2*H*-pyrone derivatives **10** were oxidized with *m*-chloroperoxybenzoic acid (MCPBA) to give 4-methoxy-3-phenylsulfinylmethyl-2*H*-pyrone derivatives **11**. Treatment of the sulfoxides **11** with trifluoroacetic anhydride followed by quenching with 1 N aq. NaOH and THF furnished 3-hydroxymethyl-4-methoxy-2*H*-pyrone derivatives **7** in good yields. Addition of THF was crucial to make the solution homogeneous during hydrolysis. These results are summarized in Table 1. The yield of **10e** was low due to repeated chromatography. Under the reaction conditions, no Pummerer reaction occurred[8] and no 3-formyl-4-methoxy-2*H*-pyrone derivatives **8** were produced. It is important to use dichloromethane (CH_2Cl_2) without ethanol (EtOH) contamination in the last experiment. Also important is the use of apparatus without a rubber septum and balloon. Reaction with acetic anhydride was very sluggish and provided only 16% of 3-acetoxymethyl-4-methoxy-6-nonyl-2*H*-pyrone even at 160°C along with recovery of a large amount of the starting sulfoxide **11b**. More reactive reagents such as trimethylsilyl trifluoromethanesulfonate gave complex mixtures.

Our proposed mechanism of the substitution reaction is shown in Scheme 4. One possibility is S_N2 substitution of the sulfonium ion **12** by a trifluoroacetoxy anion. Another possibility is S_N1 substitution in which acylation of the phenylsulfinyl group of **11** into sulfonium ions **12** followed by elimination led to oxonium ions **13**. Addition of a trifluoroacetoxy anion to the oxonium ion **13** afforded 4-methoxy-3-trifluoroacetoxymethyl-2*H*-pyrone derivatives **14**. The trifluoroacetates **14** were readily hydrolyzed by weakly basic work-up to give the desired products **7**. An attempt at direct substitution of 4-methoxy-6-nonyl-3-phenylsulfinylmethyl-2*H*-pyrone **11b** with aqueous sodium hydroxide resulted in complete recovery. 4-Methoxy-6-nonyl-3-phenylsulfonylmethyl-2*H*-pyrone gave the same result. Steric hindrance of the methoxy group at C-4 might prevent abstraction of a proton α to the sulfonium ion **12** by trifluoroacetoxy anion (Pummerer reaction pathway)[8] and its electron-donating character might enable rapid elimination to the oxonium ion **13**. Addition of triethylamine resulted in decrease of yield. The reaction was quite fast even at −78 to −40°C and 3-hydroxymethyl-4-methoxy-5-nonyl-2*H*-pyrone derivative **7b** was obtained in 69% yield after basic work-up. Intermediary 4-methoxy-6-nonyl-3-trifluoroacetoxymethyl-2*H*-pyrone **14b** [R=$(CH_2)_8CH_3$] was isolated when the reaction was quenched only with aq.

Table 1. Synthesis of 3-hydroxymethyl-2*H*-pyrone derivatives **7**

4-Hydroxy-2*H*-pyrone **4**	Sulfide **9** (%)	Methyl ether **10** (%)	Sulfoxide **11** (%)	Alcohol **7** (%)
a R=Me	**a** 96	**a** 69	**a** 96	**a** 68
b R=$(CH_2)_8CH_3$	**b** 99	**b** 70	**b** 86	**b** 82
c R=$(CH_2)_2Ph$	**c** 71	**c** 76	**c** 93	**c** 98
d R=cyclohexyl	**d** 67	**d** 86	**d** 90	**d** 93
e R=5,6-benzo	**e** 75	**e** 36	**e** 58	**e** 78



Scheme 4.

NaOH, though it decomposed soon after NMR measurement. When CH_2Cl_2 was contaminated with EtOH, a more nucleophilic ethoxy group was introduced to give only 3-ethoxymethyl-4-methoxy-6-nonyl-2*H*-pyrone derivative in low yields.

In conclusion, we have newly developed a synthetic procedure for the 3-hydroxymethyl-4-methoxy-2*H*-pyrone derivatives **7** via 4 steps starting from the 4-hydroxy-2*H*-pyrone derivatives **4** in acceptable and reproducible yields. Active manganese dioxide oxidation[9] of **7** afforded 3-formyl-2*H*-pyrone **8** in good yield. Application of the present protocol to solanapyrone synthesis will be reported in due course.[10]

1. Experimental

1.1. General

M.p.s were determined with a Yanaco MP hot-stage apparatus and are uncorrected. IR spectra were recorded on a Shimadzu FT/IR-4200 spectrophotometer for solutions in chloroform or Hitachi IR 270-30 spectrophotometer for KBr pellets. ^{1}H-NMR spectra were obtained for solutions in deuteriochloroform with a Varian Gemini 200H (200 MHz) instrument with tetramethylsilane as internal standard. ^{13}C-NMR spectra were measured with a Varian Gemini 200H (50 MHz) instrument. Mass spectral data were run on a JEOL GC-Mate spectrometer. Medium-pressure liquid chromatographies (MPLC) were carried out on a GL Science PU 612 instrument with a silica gel packed column. Microanalyses were carried out in the microanalytical laboratory of the Instrumental Analysis Center for Chemistry, Tohoku University. Compounds **10b**, **11c** and **11d** did not give satisfactory analytical data after repeated analyses.

4-Hydroxy-3-phenylthiomethyl-2*H*-pyrones **9** were prepared according to the modified procedure by Moreno-Manas et al.[7] including non-aqueous work-up by column chromatography and used without purification for further reaction because of stubborn nature towards recrystallization. 4-Hydroxy-6-methyl-2*H*-pyrone **4a** and 5,6-benzo-4-hydroxy-2*H*-pyrone **4e** were procured from Tokyo Kasei Co.

1.1.1. 4-Hydroxy-6-methyl-3-phenylthiomethyl-2*H*-pyran-2-one (9a).[7] 96%; amorphous solid; ν_{max}/cm^{-1} (KBr pellet) 3480, 3000, 2932, 1660, 1636, 1576, 1430, 1408, 1384 and 1258; ^{1}H-NMR (200 MHz, $CDCl_3$) δ (ppm) 2.17 (s, 3H), 4.14 (s, 2H), 5.78 (s, 1H) and 7.17–7.45 (m, 5H).

1.1.2. 4-Hydroxy-6-nonyl-3-phenylthiomethyl-2*H*-pyran-2-one (9b). >99%; amorphous solid; m.p. 74–76°C; ν_{max}/cm^{-1} (KBr pellet) 3480, 2932, 1666, 1632, 1588, 1558, 1436, 1416 and 1258; ^{1}H-NMR (200 MHz) δ (ppm) 0.88 (t, 3H, *J* 6.3 Hz), 1.19–1.38 (m, 12H), 1.46–1.71 (m, 2H), 2.40 (t, 2H, *J* 7.5 Hz), 4.13 (s, 3H), 5.80 (s, 1H) and 7.19–7.42 (m, 5H).

1.1.3. 4-Hydroxy-6-(2-phenylethyl)-3-phenylthiomethyl-2*H*-pyran-2-one (9c). 71%; amorphous solid; m.p. 181–183°C; ν_{max}/cm^{-1} (KBr pellet) 3464, 3036, 2928, 1660, 1636, 1590, 1556, 1436, 1414 and 1262,; ^{1}H-NMR (200 MHz) δ (ppm) 2.65–2.77 (m, 2H), 2.87–2.99 (m, 2H), 4.14 (s, 2H), 5.70 (s, 1H) and 7.07–7.42 (m, 10H).

1.1.4. 6-Cyclohexyl-4-hydroxy-3-phenylthiomethyl-2*H*-pyran-2-one (9d). 67%; amorphous solid; m.p. 157–159°C; ν_{max}/cm^{-1} (KBr pellet) 3428, 3084, 2936, 1672, 1630, 1576, 1434, 1422, and 1262; ^{1}H-NMR (200 MHz) δ (ppm) 1.17–1.48 (m, 5H), 1.63–1.98 (m, 5H), 2.32 (m, 1H), 4.16 (s, 2H), 5.75 (s, 1H), 7.20–7.42 (m, 5H) and 8.32 (s, 1H).

1.1.5. 5,6-Benzo-4-hydroxy-3-phenylthiomethyl-2*H*-pyran-2-one (9e). 75%; amorphous solid; ν_{max}/cm^{-1} (KBr pellet) 3480, 3088, 3008, 2930, 1654, 1632, 1566, 1500, 1482, 1456, 1396, 1260 and 1176; ^{1}H-NMR (200 MHz) δ (ppm) 4.31 (s, 2H), 7.20–7.65 (m, 7H), 7.84 (dd, 1H, *J* 8.2, 1.6 Hz) and 8.01 (m, 1H).

Representative procedure of methylation is as follows:

1.1.6. 4-Methoxy-6-methyl-3-phenylthiomethyl-2*H*-pyran-2-one (10a). A suspension of 4-hydroxy-2*H*-pyrone **9a** (1.70 g, 6.9 mmol), dimethyl sulfate (3.3 ml, 34 mmol) and potassium carbonate (4.74 g, 34 mmol) in acetone (50 ml) was stirred at room temperature for 4 h. H_2O (3 ml) was added and the resulting solution was stirred at room temperature for 2 h. After addition of aqueous ammonium chloride, the reaction mixture was extracted with CH_2Cl_2 twice. The combined organic extracts were washed with water and brine. Evaporation of the solvent followed by column chromatography of the residue provided 4-methoxy-6-methyl-3-phenylthiomethyl-2*H*-pyran-2-one **10a** (1.24 g, 69%) as crystals.

69%; blocks; m.p. 54–55°C; ν_{max}/cm^{-1} ($CHCl_3$) 2998, 1703, 1647, 1566, 1466, 1441, 1247 and 1022; ^{1}H-NMR (200 MHz) δ (ppm) 2.27 (s, 3H), 3.72 (s, 3H), 3.98 (s, 2H), 5.96 (s, 1H), 7.12–7.31 (m, 3H) and 7.40–7.50 (m, 2H); ^{13}C-NMR (50 MHz) δ (ppm) 20.5, 28.1, 56.3, 94.8, 101.4, 126.3, 128.5, 130.9, 136.5, 162.7, 164.1 and 167.0; (Found: C, 63.92, H, 5.38, S, 12.23; $C_{14}H_{14}O_3S$ requires: C, 64.1, H, 5.58, S, 12.22%).

1.1.7. 4-Methoxy-6-nonyl-3-phenylthiomethyl-2*H*-pyran-2-one (10b). 70%; amorphous solid; m.p. 48–50°C; ν_{max}/cm^{-1} ($CHCl_3$) 2930, 2857, 1699, 1564, 1469, 1265 and 1028; ^{1}H-NMR (200 MHz) δ (ppm) 0.88 (t, 3H, *J* 6.4 Hz), 1.21–1.38 (m, 12H), 1.55–1.72 (m, 2H), 2.80 (t, 2H, *J* 7.5 Hz), 3.73 (s, 3H), 3.98 (s, 2H), 5.93 (s, 1H), 7.17–7.31 (m, 3H) and 7.40–7.49 (m, 2H); ^{13}C-NMR (50 MHz) δ (ppm) 13.9, 22.4, 26.7, 28.0, 28.8, 29.0, 29.2, 31.6, 34.1, 56.2, 93.9, 101.0, 126.1, 128.3, 130.7, 136.3, 164.0, 166.3 and 166.9.

1.1.8. 4-Methoxy-6-(2-phenylethyl)-3-phenylthiomethyl-2*H*-pyran-2-one (10c). 76%; blocks; m.p. 101–102°C; ν_{max}/cm^{-1} ($CHCl_3$) 2949, 1703, 1645, 1566, 1466, 1264, 1127, 1030 and 1012; ^{1}H-NMR (200 MHz) δ (ppm) 2.73–2.85 (m, 2H), 2.92–3.07 (m, 2H), 3.62 (s, 3H), 3.97 (s, 2H), 5.87 (s, 1H) and 7.10–7.48 (m, 10H); ^{13}C NMR (50 MHz) δ (ppm) 28.2, 33.1, 36.2, 56.3, 94.8, 101.8, 126.4, 126.5, 128.3, 128.5, 128.6, 131.1, 136.4, 139.7, 164.1, 164.8 and 166.8; (Found: C, 71.28, H, 5.87; $C_{21}H_{20}O_3S$ requires: C, 71.56, H, 5.72%).

1.1.9. 6-Cyclohexyl-4-methoxy-3-phenylthiomethyl-2*H*-pyran-2-one (10d). 86%; needles; m.p. 145–146°C; ν_{max}/cm^{-1} ($CHCl_3$) 2938, 1697, 1564, 1464, 1127 and 1033; ^{1}H-NMR (200 MHz) δ (ppm) 1.18–1.53 (m, 5H), 1.65–2.02 (m, 5H), 2.42 (m, 1H), 3.74 (s, 3H), 3.99 (s, 2H), 5.91 (s, 1H) and 7.12–7.48 (m, 5H); ^{13}C-NMR (50 MHz) δ (ppm) 25.6, 25.8, 28.1, 30.5, 42.8, 56.3, 92.0, 101.5, 126.2, 128.5, 130.7, 136.7, 164.2, 167.2 and 170.4; (Found: C, 68.79, H, 6.69, S, 9.78; $C_{19}H_{22}O_3S$ requires: C, 69.06, H, 6.71, S, 9.7%).

1.1.10. 5,6-Benzo-4-methoxy-3-phenylthiomethyl-2*H*-pyran-2-one (10e). 36%; needles; m.p. 93–94°C; ν_{max}/cm^{-1} ($CHCl_3$) 1712, 1625, 1622, 1456, 1354, 1273, 1099 and 1057; ^{1}H-NMR (200 MHz) δ (ppm) 4.02 (s, 3H), 4.18 (s, 2H), 7.17–7.40 (m, 5H), 7.45–7.65 (m, 3H) and 7.67–7.72 (m, 1H); ^{13}C-NMR (50 MHz) δ (ppm) 29.6, 62.4, 112.7, 116.7, 117.0, 123.5, 124.1, 126.9, 128.9, 130.9, 132.0, 136.0, 152.8, 162.8 and 164.7; (Found: C, 68.31, H, 4.77, S, 10.58; $C_{17}H_{14}O_3S$ requires: C, 68.44, H, 4.73, S, 10.75%).

Representative procedure of oxidation is as follows:

1.1.11. 4-Methoxy-6-methyl-3-phenylsulfinylmethyl-2*H*-pyran-2-one (11a). To a stirred solution of the sulfide **10a** (1.11 g, 4.2 mmol) in CH_2Cl_2 (30 ml) was added MCPBA (80%, 913 mg, 5.3 mmol) at 0°C. After being stirred for 20 min, aqueous sodium hydrogen carbonate was added and the reaction mixture was extracted with CH_2Cl_2 twice. The combined organic layer was washed with water and brine and evaporated to dryness. The residue was purified by column chromatography to afford 4-methoxy-6-methyl-3-phenylsulfinylmethyl-2*H*-pyran-2-one **11a** (1.13 g, 96%).

96%; blocks; m.p. 128–130°C; ν_{max}/cm^{-1} ($CHCl_3$) 3050, 1705, 1645, 1566, 1468, 1264, 1038 and 1022; ^{1}H-NMR (200 MHz) δ (ppm) 2.29 (s, 3H), 3.68 (d, 1H, *J* 12.2 Hz), 3.73 (s, 3H), 4.11 (d, 1H, *J* 12.2 Hz), 5.99 (s, 1H), 7.44–7.53 (m, 3H) and 7.61–7.71 (m, 2H); ^{13}C-NMR (50 MHz) δ (ppm) 20.4, 53.1, 56.5, 94.1, 94.7, 124.2, 128.6, 130.9, 144.2, 163.9 and 168.8; (Found: C, 60.3, H, 5.12, S, 11.46; $C_{14}H_{14}O_4S$ requires: C, 60.42, H, 5.07, S, 11.52%).

1.1.12. 4-Methoxy-6-nonyl-3-phenylsulfinylmethyl-2*H*-pyran-2-one (11b). 86%; needles; m.p. 85–86°C; ν_{max}/cm^{-1} ($CHCl_3$) 2930, 2857, 1703, 1642, 1564, 1466, 1267 and 1032; ^{1}H-NMR (200 MHz) δ (ppm) 0.89 (t, 3H, *J* 6.4 Hz), 1.22–1.38 (m, 12H), 1.60–1.74 (m, 2H), 2.51 (t, 2H, *J* 7.5 Hz), 3.74 (s, 3H), 3.86 (d, 1H, *J* 12.1 Hz), 4.11 (d, 1H, *J* 12.1 Hz), 5.96 (s, 1H), 7.44–7.52 (m, 3H) and 7.62–7.71 (m, 2H); ^{13}C-NMR (50 MHz) δ (ppm) 14.0, 22.5, 26.8, 28.8, 29.1, 29.3, 31.7, 34.3, 53.3, 56.5, 93.9, 94.5, 124.2, 128.6, 130.9, 144.3, 164.0, 167.7 and 168.8; (Found: C, 67.38, H, 7.80, S, 8.38; $C_{22}H_{30}O_4S$ requires: C, 67.66, H, 7.74, S, 8.21%).

1.1.13. 4-Methoxy-6-(2-phenylethyl)-3-phenylsulfinylmethyl-2*H*-pyran-2-one (11c). 93%; viscous oil; ν_{max}/cm^{-1} ($CHCl_3$) 2951, 1709, 1643, 1564, 1466, 1264, 1040 and 1036; ^{1}H-NMR (200 MHz) δ (ppm) 2.78–2.89 (m, 2H), 2.95–3.06 (m, 2H), 3.60 (s, 3H), 3.87 (d, 1H, *J* 12.1 Hz), 4.09 (d, 1H, *J* 12.1Hz), 5.84 (s, 1H), 7.13–7.36 (m, 5H), 7.37–7.52 (m, 3H) and 7.57–7.69 (m, 2H); ^{13}C-NMR (50 MHz) 32.9, 36.1, 53.2, 56.5, 94.6, 94.7, 124.3, 126.5, 128.2, 128.5, 128.6, 131.0, 139.4, 144.2, 163.9, 166.0 and 168.6.

1.1.14. 6-Cyclohexyl-4-methoxy-3-phenylsulfinylmethyl-2*H*-pyran-2-one (11d). 90%; blocks; m.p. 139–141°C; ν_{max}/cm^{-1} ($CHCl_3$) 2859, 1703, 1640, 1563, 1466, 1260, 1031 and 1024; ^{1}H-NMR (200 MHz) δ (ppm) 1.22–1.35 (m, 5H), 1.78–2.03 (m, 5H), 2.43 (m, 1H), 3.76 (s, 3H), 3.84 (d, 1H, *J* 12.2 Hz), 4.11 (d, 1H, *J* 12.2 Hz), 5.94 (s, 1H), 7.43–7.52 (m, 3H) and 7.62–7.71 (m, 5H); ^{13}C-NMR (50 MHz) 25.6, 25.7, 30.4, 42.9, 53.5, 56.5, 92.0, 94.9, 124.3, 128.7, 130.9, 144.5, 164.1, 169.1 and 171.5.

1.1.15. 5,6-Benzo-4-methoxy-3-phenylsulfinylmethyl-2*H*-pyran-2-one (11e). 58%; needles; m.p. 121–123°C; ν_{max}/cm^{-1} ($CHCl_3$) 1713, 1626, 1613, 1572, 1354, 1101, 1063 and 1043; ^{1}H-NMR (200 MHz) δ (ppm) 4.02 (d, 1H, *J* 12.5 Hz), 4.23 (d, 1H, *J* 12.5 Hz), 4.23 (s, 3H), 7.28–7.42 (m, 2H), 7.50–7.65 (m, 4H) and 7.71–7.80 (m, 3H); ^{13}C-NMR (50 MHz) 55.4, 64.0, 106.1, 116.6, 117.0, 123.8, 123.9, 124.3, 129.2, 131.2, 132.5, 144.1, 152.9, 162.9 and 167.2; (Found: C, 64.76, H, 4.68, S, 10.26; $C_{17}H_{14}O_4S$ requires: C, 64.95, H, 4.49, S, 10.20%).

Representative procedure of hydroxymethylation is as follows:

1.1.16. 3-Hydroxymethyl-4-methoxy-6-methyl-2*H*-pyran-2-one (7a). To a stirred solution of the sulfoxide **11a** (27.7 mg, 0.1 mmol) in CH_2Cl_2 (EtOH free, 4 ml) was added trifluoroacetic anhydride (56 μl, 0.4 mmol) at 0°C. After being stirred for 30 min at 0°C, 1N aqueous NaOH (1 ml) and THF (6 ml) were added and stirring was continued for 1.5 h at room temperature. The reaction mixture was extracted with ethyl acetate twice and the combined organic layer was washed with aqueous ammonium chloride, water and brine. Evaporation of the solvent followed by MPLC purification furnished 3-hydroxymethyl-4-methoxy-6-methyl-2*H*-pyran-2-one **7a** (11.5 mg, 68%). In this experiment, use of a rubber septum and balloon provided a complex mixture of undesired products.

68%; blocks; m.p. 151–153°C; ν_{max}/cm^{-1} ($CHCl_3$) 3472, 2951, 1694, 1645, 1568, 1389, 1260 and 1022; ^{1}H-NMR (200 MHz) δ (ppm) 2.30 (s, 3H), 3.91 (s, 3H), 4.54 (s, 2H), and 6.08 (s, 1H); ^{13}C-NMR (50 MHz) δ (ppm) 20.4, 54.5, 56.4, 95.1, 103.6, 163.3, 165.3 and 166.8; (Found: C, 56.36, H, 5.98; $C_8H_{10}O_4$ requires: C, 56.47, H, 5.92%).

1.1.17. 3-Hydroxymethyl-4-methoxy-6-nonyl-2*H*-pyran-2-one (7b). 82%; needles; m.p. 67–68°C; ν_{max}/cm^{-1} ($CHCl_3$) 3504, 2930, 1692, 1640, 1566, 1402, 1264 and 1030; ^{1}H-NMR (200 MHz) δ (ppm) 0.88 (t, 3H, *J* 6.4 Hz), 1.20–1.42 (m, 12H), 1.52–1.76 (m, 2H), 2.51 (t, 2H, *J* 7.5 Hz), 2.93 (t, 1H, *J* 6.8 Hz), 3.91 (s, 3H), 4.54 (d, 2H, *J* 6.8 Hz) and 6.04 (s, 1H); ^{13}C-NMR (50 MHz) δ (ppm) 14.1, 22.6, 27.0, 29.0, 29.2, 29.4, 31.8, 34.4, 54.7, 56.5, 94.3, 94.5, 103.8, 165.5, 166.7 and 167.2; (Found: C, 68.09, H, 9.23; $C_{16}H_{26}O_4$ requires: C, 68.06, H, 9.28%).

1.1.18. 3-Hydroxymethyl-4-methoxy-6-(2-phenylethyl)-2*H*-pyran-2-one (7c). 98%; amorphous solid; m.p. 69–71°C; ν_{max}/cm^{-1} ($CHCl_3$) 3472, 2982, 1692, 1642, 1566, 1466, 1402, 1260, 1037 and 1011; ^{1}H-NMR (200 MHz) δ (ppm) 2.77–3.05 (m, 5H), 3.82 (s, 3H), 4.53 (d, 2H, *J* 6.9 Hz), 5.92 (s, 1H) and 7.12–7.36 (m, 5H); ^{13}C-NMR (50 MHz) δ (ppm) 33.1, 36.2, 54.6, 56.5, 95.1, 104.0, 126.5, 128.3, 128.6, 139.6, 165.4, 165.5 and 166.6; *m/z* 260 (M^+, 37%), 245 (7), 242 (15), 231 (13), 152 (28), 141 (27), 91 (100), 77 (11) and 69 (16) (Found: 260.10843; $C_{15}H_{16}O_4$ requires: 260.10484).

1.1.19. 6-Cyclohexyl-3-hydroxymethyl-4-methoxy-2*H*-pyran-2-one (7d). 93%; needles; m.p. 94–95°C; ν_{max}/cm^{-1} ($CHCl_3$) 3472, 2859, 1688, 1638, 1566, 1466, 1261, 1254 and 1037; ^{1}H-NMR (200 MHz) δ (ppm) 1.20–1.55 (m, 5H), 1.66–2.02 (m, 5H), 2.43 (m, 1H), 2.94 (t, 1H, *J* 6.9 Hz), 3.90 (s, 3H), 4.55 (d, 2H, *J* 6.9 Hz) and 6.01 (s, 1H); ^{13}C-NMR (50 MHz) δ (ppm) 25.6, 25.7, 30.5, 42.9, 54.7, 56.4, 92.3, 103.9, 165.4, 166.8 and 171.0; (Found: C, 65.38, H, 7.70; $C_{13}H_{18}O_4$ requires: C, 65.53, H, 7.88%).

1.1.20. 5,6-Benzo-3-hydroxymethyl-4-methoxy-2*H*-pyran-2-one (7e). 78%; needles; m.p. 112–113°C; ν_{max}/cm^{-1} ($CHCl_3$) 3202, 1698, 1622, 1616, 1358, 1070 and 1007; ^{1}H-NMR (200 MHz) δ (ppm) 2.89 (t, 1H, *J* 7.0 Hz), 4.21 (s, 3H), 4.72 (d, 2H, *J* 7.0 Hz), 7.31–7.40 (m, 2H), 7.54 (ddd, 1H, *J* 1.5, 7.2, 8.6 Hz) and 7.79 (dd, 1H, *J* 1.5, 7.8 Hz); ^{13}C-NMR (50 MHz) δ (ppm) 55.9, 63.1, 112.8, 116.8, 117.1, 123.9, 124.4, 132.3, 152.7, 164.5 and 164.8; (Found: C, 63.85, H, 5.02; $C_{11}H_{10}O_4$ requires: C, 64.07, H, 4.89%).

1.1.21. 3-Trifluoroacetoxymethyl-4-methoxy-6-nonyl-2*H*-pyran-2-one (14b). ^{1}H-NMR (200 MHz) δ (ppm) 0.88 (t, 3H, *J* 6.4 Hz), 1.12–1.45 (m, 12H), 1.55–1.76 (m, 2H), 2.52 (t, 2H, *J* 7.6 Hz), 3.95 (s, 3H), 5.26 (s, 2H) and 6.05 (s, 1H).

This compound decomposed soon after NMR measurement.

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