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γ-Regioselectivity of Lithiated 2-Buten-4-olide towards Aromatic Aldehydes: a Simple Synthesis of γ-Arylidenebutenolides

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Abstract: Lithiated 2-buten-4-olide was found to react with aromatic aldehydes regioselectively at γ-position to provide 4-(1-aryl-1-hydroxymethyl)-2-buten-4-olides which could be readily converted into the corresponding (*Z*)-γ-arylidenebutenolides.

Butenolides are an important class of organic compounds existing in natural products and related compounds which exhibit various interesting biological activities. Therefore, considerable efforts for development of new and general synthetic routes for the construction of butenolides have been intensively investigated. Reviews concerning synthetic approaches to this class of compounds including γ–alkylidene-butenolides have recently appeared in the literature.[2-4] Among these methods, trimethylsilyloxy-furan[5] has been of particular interest to be used as an butenolide anion equivalent due to its high γ-regioselectivity towards different types of electrophiles. Thus, use of this reagent as a butenolide building block has led to the synthesis of several complex intermediates and natural products. Our research work, aimed at the preparation of some natural γ–alkylidenebutenolides such as the cytotoxic melodorinol and acetylmelodorinol,[6-9] prompted us to investigate the possibilities of using the anion derived directly from γ–crotonolactone **1**[10] as a butenolide synthon, expecting to receive high γ–regioselectivity. To the best of our knowledge, little is known about the reactions of such anion. The lithiated butenolide **2** has recently been reported to undergo conjugate addition with cyclopentenone derivatives at -78 °C[11] and combined with aliphatic aldehydes regioselectively to afford *ca.* 1:3 ratio of the γ–adduct of type **3** and the α-adduct of type **4**; no yields of the adducts were reported.[12] To extend the synthetic potential of the lithiated butenolide **2**,[13,14] we herein report the highly regioselective reaction of this anion with aromatic aldehydes. We found that the lithiated butenolide **2** (readily generated from γ–crotonolactone/LDA/THF, -78 °C, 30 min) reacted with benzaldehyde (1 equiv) at -78 °C for 1 h, followed by quenching with ammonium chloride solution to provide the γ–adduct **3a** as the sole product in 76% isolated yield as a 80:20 mixture of *syn:anti*-isomers. Optimization of the reaction conditions was briefly investigated.

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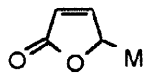
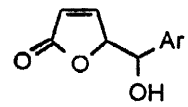


1, M = H
2, M = Li



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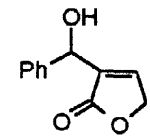

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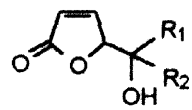
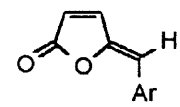


5a, $R_1 = CH_3$; R_2 = Ph (23%)
5b, $R_1 = R_2$ = Ph (10-28%)



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It was found that in the presence of hexamethylphosphoramide (HMPA) at 78 °C for 1 h, a slightly lower yield (64%) of the expected γ–adduct **3a** was obtained. A much lower yield (30%) of **3a** was observed, when the reaction was carried out at -24 °C (1 h). At higher temperature (0 °C, 1 h), no expected product **3a** could be isolated; the reaction led to a mixture of products as revealed by TLC analysis. Under the latter conditions, the failure for the formation of **3a** resulted from the rapid retro-aldol condensation of the initially formed adduct. Accordingly, it seemed to us that the lithiated butenolide **2** was unstable at room temperature. Under the standard conditions, the lithiated butenolide **2** reacted smoothly with several aromatic aldehydes diastereo- and regio-selectively to furnish good yields of the γ–adducts **3b-f** as listed in Table 1. To gain more insight into the scope and limitation of this reaction, the reaction of the lithiated butenolide **2** with other aromatic aldehydes and ketones was studied. It revealed that the lithiated butenolide **2** did not combine with less reactive aromatic aldehydes such as 2,4-dimethoxy- and 2,3,4-trimethoxy-benzaldehydes under the similar conditions. However, the lithiated butenolide **2** reacted with acetophenone and benzophenone to give the expected γ–adducts **5a** and **5b** in 23% and 10-28% yields, respectively.

Table 1: Preparation of compounds **3**.

Entry	ArCHO	% **3** (*syn* : *anti*)[a,b]
1	Benzaldehyde	**3a**, 76% (80 : 20)
2	3-Methoxybenzaldehyde	**3b**, 73% (70 : 30)
3	4-Methoxybenzaldehyde	**3c**, 68% (70 : 30)
4	2,3-Dimethoxybenzaldehyde	**3d**, 78% (86 : 14)
5	3,4-Dimethoxybenzaldehyde	**3e**, 75% (72 : 28)
6	3,4-Methylenedioxybenzaldehyde	**3f**, 82% (70 : 30)

[a] Isolated yields.
[b] Determined by ^{1}H NMR (300 MHz).

Having the γ–adducts **3a-f** in hand, the preparation of γ–arylidenebutenolides could simply be accomplished by elimination of the hydroxyl group at the carbon-6 position. Initially, treatment of **3a** (*syn:anti* = 80:20) with conc. H_2SO_4 (0 °C, 20 min and RT 20 min) gave only the (*Z*)-isomer of the desired γ–benzylidenebutenolide **6a** in 21% yield after chromatography. Similar treatment of **3b** with conc. H_2SO_4 furnished no trace of the expected product **6b**, since decomposition of the starting compound **3b** occurred. We turned our attention to carrying out this conversion by firstly activating the hydroxyl group as the mesylate followed by base-catalyzed elimination. Thus, *in situ* mesylation of **3a** (*syn:anti* = 80:20) at 0 °C employing methanesulfonyl chloride (MsCl) in pyridine for 20 min followed by stirring at room temperature for 11 h afforded 96% yield of **6a** as a 32:68 ratio of (*Z*):(*E*)-isomers. The reaction of **3a** (*syn:anti* = 80:20) under the standard conditions at a longer period of time (48 h at room temperature) increased the (*Z*):(*E*)-ratio of **6a** up to 70:30. Having increased the reaction time and allowed the reaction mixture to reflux, the (*Z*):(*E*)-ratios of **6a** were dramatically increased. The highest (*Z*):(*E*)-ratio was found to be *ca.* 97:3 and good yield of **6a** was achieved. The elimination of the hydroxyl group *via* the *in situ*-generated mesylate leading to γ-benzylidenebutenolide **6a** with high (*Z*)-selectivity proceeded presumably *via* the E1-cb mechanism.[15] By employing the standard reaction conditions as for **6a**, γ-arylidenebutenolides **6b-f** were prepared in good yields with high stereoselectivity as listed in Table 2.

Table 2: Preparation of γ-arylidenebutenolides **6**.

Entry	**3a** (*syn* : *anti*)[c]	Conditions[a]	% **6** (*Z* : *E*)[b,c]
1	**3a** (80 : 20)	RT (11 h)	**6a**, 96% (32 : 68)
2	**3a** (80 : 20)	RT (48 h)	**6a**, 100% (70 : 30)
3	**3a** (80 : 20)	RT (2 h) and 80-90 °C (10 h)	**6a**, 87% (97 : 3)
4	**3b** (70 : 30)	RT (2 h) and 80-90 °C (10 h)	**6b**, 85% (98 : 2)
5	**3c** (70 : 30)	RT (2 h) and 80-90 °C (10 h)	**6c**, 84% (99 : 1)
6	**3d** (86 : 14)	RT (2 h) and 80-90 °C (10 h)	**6d**, 82% (99 : 1)
7	**3e** (72 : 28)	RT (2 h) and 80-90 °C (10 h)	**6e**, 91% (94 : 6)
8	**3f** (70 :30)	RT (2 h) and 80-90 °C (10 h)	**6f**, 97% (94 : 6)

[a] Mesylation was carried out at 0 °C for 20 min (see experimental section).
[b] Isolated yields.
[c] Determined by ^{1}H NMR (300 MHz).

In summary, the present work provides a synthetic utility of the lithiated butenolide as a useful butenolide synthon which reacts regioselectively with aromatic aldehydes at the γ-position. This method affords a simple two-step synthesis of γ–arylidenebutenolides. We are currently investigating the application of the methodology to synthesize some natural products containing the substituted γ–arylidenebutenolide sub-unit.

Experimental Section

General: Melting points were determined either by an Electrothermal or a Büchi 510 melting point apparatus and were uncorrected. ^{1}H NMR spectra were measured with Varian EM-360L and Bruker DPX300 spectrometers, using TMS as an internal reference and reported in parts per million (ppm). IR spectra were recorded on a Jasco A-302 or a Perkin Elmer 2000 NIR FT Raman. Mass spectra were obtained on a Finnigan MAT INCOS 50 mass spectrometer at 70 eV. Elemental analyses were performed by using a Perkin Elmer elemental analyzer 2400 CHN. All solvents were dried by using standard methods prior to use.

Preparation of 4-(1-aryl-1-hydroxymethyl)-2-buten-4-olide (3).

General procedure: Preparation of 4-(1-Hydroxy-1-phenylmethyl)-2-buten-4-olide (3a).

A solution of γ-crotonolactone (0.17 g, 2.0 mmol) in THF (2 ml) was added dropwise at -78 °C to a THF solution of lithium diisopropylamide (LDA) in THF under an argon atmosphere [prepared by reacting diisopropylamine (0.31 ml, 2.2 mmol) in THF (10 ml) with BuLi (1.07 M in hexane, 2.35 ml, 2.2 mmol) at -78†°C for 30 min]. After stirring at -78 °C for 30-40 min, a solution of benzaldehyde (0.22 g, 2.2 mmol) in THF (2 ml) was added dropwise. The resulting mixture was stirred at -78 °C for 1 h, and quenched with a solution of NH_4Cl. It was diluted with water (25 ml) and extracted with ethyl acetate (4 x 25 ml). The combined extracts were washed with water, brine and dried over anh. Na_2SO_4. After removal of solvent under reduced pressure, the crude product obtained was purified by radial chromatography (30% ethyl acetate in hexane) to give a colorless viscous liquid of **3a** (0.29 g, 76% yield) as a mixture of *syn*- and *anti*-isomers (80:20). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44-7.31 [m, COCH=C*H* (*syn*) and Ar*H* of *syn*- and *anti*-isomers], 7.17 [dd, J = 5.8, 1.4 Hz, COCH=C*H* (*anti*)], 6.16 (*syn*) and 6.10 (*anti*) (each dd, J = 5.8, 2.0 and 5.8, 1.7 Hz respectively, 1H, COC*H*=CH), 5.19-5.15 (m, 1H, CH=CHC*H*O), 5.09 (*syn*) and 4.70 (*anti*) (each d, J = 4.4 and 7.1 Hz respectively, 1H, ArC*H*OH), 2.65 (br. s, 1H, O*H*). IR (neat): ν_{max} 3431, 3090, 3032, 1780, 1754, 1600, 1495, 1453, 1335, 1267, 1195, 1167, 1104, 1087, 1040, 905, 836, 815, 766, 702 cm^{-1}. MS: m/z (%) relative intensity 190 (M^+, 0.39), 177 (0.28), 172 (2), 161 (0.15), 149 (1) 147 (0.39), 144 (0.7), 128 (0.4), 115 (2), 107 (100), 105 (10), 84 (9), 79 (59), 77 (31), 55 (4). Anal. Calcd. for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.47; H, 4.96.

4-[1-Hydroxy-1-(3-methoxyphenyl)methyl]-2-buten-4-olide (3b).

According to the general procedure described for **3a**, the solution of the lithiated butenolide **2** (2 mmol) in THF (12 ml) was treated with 3-methoxybenzaldehyde (0.27 g, 2.0 mmol) to give a viscous liquid of **3b** (0.32 g, 73% yield; *syn:anti* = 70:30). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35-7.27 [m, Ar*H* and COCH=C*H* (*syn*)], 7.18 [dd, J = 5.8, 1.6 Hz, COCH=C*H* (*anti*)], 6.99-6.95 (m, 3H, Ar*H*), 6.17 (*syn*) and 6.11 (*anti*) (each dd, J = 5.8, 2.0 and 5.8, 2.1 Hz respectively, 1H, COC*H*=CH), 5.19-5.14 (m, 1H, CH=CHC*H*O), 5.08 (*syn*) and 4.67 (*anti*) (each d, J = 4.3 and 7.1 Hz respectively, 1H, ArC*H*OH), 3.83 (s, 3H, O*Me*), 2.90 (br. s, 1H, O*H*). IR (neat): ν_{max} 3447, 3100, 3020, 2939, 1780, 1753, 1602, 1595, 1491, 1480, 1457, 1436, 1263, 1162, 1110, 1090, 1039, 897, 827, 756, 701 cm^{-1}. MS: m/z (%) relative intensity 220 (M^+, 8), 202 (4), 174 (1), 137 (100), 115 (2), 109 (92), 94 (26), 84 (7), 77 (23), 65 (6), 55(5). Anal. Calcd. for $C_{12}H_{12}O_4$: C, 65.44; H, 5.49. Found: C, 65.15; H, 5.20.

4-[1-Hydroxy-1-(4-methoxyphenyl)methyl]-2-buten-4-olide (3c).

According to the general procedure described for **3a**, the solution of the lithiated butenolide **2** (2.2 mmol) in THF (12 ml) was treated with 4-methoxybenzaldehyde (0.27 g, 2 mmol) to give a pale yellow solid of **3c** (0.33 g, 68% yield; *syn:anti* = 70:30; mp 91-95 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31 (*syn*) and 7.09 (*anti*) (each dd, J = 5.8, 1.4 Hz, 1H, COCH=C*H*), 7.25-7.18 (m, 2H, Ar*H*), 6.86-6.80 (m, 2H, Ar*H*), 6.07 (*syn*) and

6.02 (*anti*) (each dd, J = 5.8, 1.8 and 5.8, 1.6 Hz respectively, 1H, COC*H*=CH), 5.08-5.04 (m, 1H, CH=CHC*H*O), 4.92 (*syn*) and 4.58 (*anti*) (each d, J = 4.6 and 7.1 Hz respectively, 1H, ArC*H*OH), 3.83 (s, 3H, O*Me*), 2.83 (br. s, 1H, O*H*). IR (nujol): ν_{max} 3471, 1743, 1610, 1583, 1512, 1317, 1302, 1249, 1200, 1171, 1117, 1102, 1085, 1038, 920, 880, 842, 818, 800, 770, 741, 701 cm^{-1}. MS: m/z (%) relative intensity 220 (M^+, 1), 202 (4), 137 (100), 109 (20), 94 (18), 83 (5), 77 (20), 66 (8), 65(6), 55 (7). Anal. Calcd. for $C_{12}H_{12}O_4$: C, 65.44; H, 5.49. Found: C, 65.40; H, 5.55.

4-[1-Hydroxy-1-(2,3-dimethoxyphenyl)methyl]-2-buten-4-olide (3d).

According to the general procedure described for **3a**, the solution of the lithiated butenolide **2** (2.1 mmol) in THF (12 ml) was treated with 2,3-dimethoxybenzaldehyde (0.35 g, 2.1 mmol) to give a white solid of **3d** (0.41 g, 78% yield; *syn:anti* = 86:14); mp 109-111 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31 (*syn*) and 7.22 (*anti*) (d and dd, J = 5.7 Hz and 5.7, 1.4 Hz respectively, 1H, COCH=C*H*), 7.15-6.89 (m, 3H, Ar*H*), 6.13 (*syn* and *anti*) (br. d, J = 5.7 Hz, 1H, COC*H*=CH), 5.34 (m, 2H, CH=CHC*H*O and ArC*H*OH), 3.92 and 3.88 (each s, 6H, O*Me*), 3.15 (br. s, 1H, O*H*). IR (nujol): ν_{max} 3429, 1748, 1720, 1600, 1585, 1335, 1280, 1172, 1115, 1083, 1038, 1000, 924, 900, 865, 832, 791, 760, 723, 698 cm^{-1}. MS: m/z (%) relative intensity 250 (M^+, 3), 232 (1), 219 (1), 167 (100), 152 (29), 139 (77), 137 (65), 124 (38), 109 (31), 95 (8), 92 (15), 81 (25), 77 (42), 65 (27), 55 (61). Anal. Calcd. for $C_{13}H_{14}O_5$: C, 62.39; H, 5.63. Found: C, 62.21; H, 5.67.

4-[1-Hydroxy-1-(3,4-dimethoxyphenyl)methyl]-2-buten-4-olide (3e).

According to the general procedure described for **3a**, the solution of the lithiated butenolide **2** (2.2 mmol) in THF (12 ml) was treated with 3,4-dimethoxybenzaldehyde (0.36 g, 2.1 mmol) to give a pale yellow solid of **3e** (0.415 g, 75% yield; *syn:anti* = 72:28), mp 100-108 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38 (*syn*) and 7.17 (*anti*) (each dd, J = 5.8, 1.3 and 5.8, 1.5 Hz respectively, 1H, COCH=C*H*), 6.98-6.83 (m, 3H, Ar*H*), 6.16 (*syn*) and 6.10 (*anti*) (each dd, J = 5.8, 1.8 and 5.8, 1.9 Hz respectively, 1H, COC*H*=CH), 5.18-5.14 (m, 1H, CH=CHC*H*O), 5.02(*syn*) and 4.65 (*anti*) (each d, J = 4.5 and 7.0 Hz respectively, 1H, ArC*H*OH), 3.90 (s, 6H, O*Me*), 2.80 (br. s, 1H, O*H*). IR (nujol): ν_{max} 3464, 1750, 1747, 1600, 1594, 1519, 1465, 1422, 1286, 1159, 1130, 1043, 1025, 905, 835, 809, 800, 764, 734, 698 cm^{-1}. MS: m/z (%) relative intensity 250 (M^+, 6), 232 (2), 167 (100), 151 (9), 139 (66), 124 (23), 119 (4), 108 (23), 95 (24), 79 (16), 77 (28), 65 (16). Anal. Calcd. for $C_{13}H_{14}O_5$: C, 62.39; H, 5.63. Found: C, 62.26; H, 5.92.

4-[1-Hydroxy-1-(3,4-methylenedioxyphenyl)methyl]-2-buten-4-olide (3f).

According to the general procedure described for **3a**, the solution of the lithiated butenolide **2** (2.1 mmol) in THF (12 ml) was treated with 3,4-methylenedioxybenzaldehyde (0.33 g, 2.2 mmol) to give a pale yellow solid of **3f** (0.41 g, 82% yield; *syn:anti* = 70:30; mp 65-72 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39 (*syn*) and 7.19 (*anti*) (each dd, J = 5.8, 1.5 and 5.8, 1.6 Hz respectively, 1H, COCH=C*H*), 6.90-6.80 (m, 3H, Ar*H*), 6.18 (*syn*) and 6.13 (*anti*) (each dd, J = 5.8, 2.0 and 5.8, 1.9 Hz respectively, 1H, COC*H*=CH), 5.99 (s, 2H, OCH_2O), 5.13-5.10 (m, 1H, CH=CHC*H*O), 4.96 (*syn*) and 4.62 (*anti*) (each d, J = 4.7 and 7.0 Hz respectively, 1H, ArC*H*OH), 2.60 (br. s, 1H, O*H*). IR ($CHCl_3$): ν_{max} 3598, 3422, 1758, 1602, 1504, 1490, 1455, 1248, 1098, 1006, 933, 898, 829, 813, 717, 702 cm^{-1}. MS: m/z (%) relative intensity 234 (M^+, 12), 216, (3), 152 (20), 151 (97), 149 (42), 135 (4), 123 (32), 102 (5), 93 (90), 83 (39), 77 (21), 65 (100), 55 (48). Anal. Calcd. for $C_{12}H_{10}O_5$: C, 61.54; H, 4.30. Found: C, 61.42; H, 4.66.

4-(1-Hydroxy-1-methyl-1-phenylmethyl)-2-buten-4-olide (5a).

According to the general procedure described for **3a**, the solution of the lithiated butenolide **2** (2.0 mmol) in THF(12 ml) was treated with acetophenone (0.25 g, 2.1 mmol) to give a pale yellow viscous liquid of **5a** (0.0952 g, 23% yield). ^{1}H NMR (60 MHz, $CDCl_3$): δ 7.70-7.23 (m, 5H, Ar*H*), 7.03 (dd, J = 6, 2 Hz, 1H, COCH=C*H*), 6.10 (dd, J = 6, 2 Hz, 1H, COC*H*=CH), 5.13 (app. t, J = 2 Hz, 1H, CH=CHC*H*O), 2.63, (br. s,

1H, O*H*), 1.73 (s, 3H, *Me*). IR (neat): ν_{max} 3448, 1753, 1601, 1495, 1447, 1376, 1317, 1168, 1093, 1080, 1040, 1026, 912, 866, 830, 761, 702 cm^{-1}. MS: m/z (%) relative intensity 186 (M^+-H_2O, 48), 169 (5), 158 (6), 129 (10), 121 (71), 105 (100), 91 (8), 84 (5), 77 (47), 65 (4), 55 (9). Anal. Calcd. for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found: C, 70.23; H, 6.08.

4-(1-Hydroxy-1,1-(diphenylmethyl)-2-buten-4-olide (5b).

According to the general procedure described for **3a**, the solution of the lithiated butenolide **2** (2.0 mmol) in THF (12 ml) was treated with benzophenone (0.44 g, 2.4 mmol) to give a white solid of **5b** (0.15 g, 28% yield; mp 172-173 °C, from ethyl acetate in hexane). ^1H NMR (60 MHz, $CDCl_3$): δ 8.0-7.22 (m, 10H, Ar*H*), 7.13 (dd, J = 6, 2 Hz, 1H, COCH=C*H*), 6.07 (dd, J = 6, 2 Hz, 1H, COC*H*=CH), 5.90 (app. t, J = 2 Hz, 1H, CH=CHC*H*O), 2.78 (br. s, 1H, O*H*). IR (nujol): ν_{max} 3394, 1732, 1694, 1596, 1492, 1470, 1447, 1376, 1343, 1320, 1200, 1190, 1180, 1172, 1100, 1054, 958, 839, 803, 758, 748, 704 cm^{-1}. MS: m/z (%) relative intensity 248 (M^+-H_2O, 0.2), 223 (0.3), 202 (0.4), 183 (75), 165 (3), 152 (4), 139 (1), 115 (2), 105 (100), 83 (4), 77 (78), 63 (2), 55 (7). This compound was characterized as its elimination product, 5-(diphenylmethylene)-2(5*H*)-furanone, which was readily prepared by using the general procedure described for compound **6**: mp 109-111 °C (ethyl acetate/hexane); ^1H NMR (60 MHz, $CDCl_3$): δ 8.03-6.73 (m, 11H, Ar*H* and COCH=C*H*), 6.20 (d, J = 6 Hz, 1H, COC*H*=CH). IR (nujol): ν_{max} 1769, 1745, 1546, 1445, 1231, 1191, 1155, 1115, 1086, 1036, 957, 878, 824, 774, 757, 719, 698 cm^{-1}. MS: m/z (%) relative intensity 248 (M^+, 92), 219 (51), 192 (38), 165 (100), 139 (15), 115 (20), 95 (4), 82 (17), 77 (3), 63 (10). Anal. Calcd. for $C_{17}H_{12}O_2$: C, 82.24; H, 4.87. Found: C, 82.17; H, 4.73.

Preparation of 5-arylidene-2(5H)-furanone (6).

General procedure: Preparation of 5-benzylidene-2(5H)-furanone (6a).

To a solution of compound **3a** (*syn:anti* = 80:20) (0.046 g, 0.24 mmol) in dry pyridine (1 ml) was added at 0 °C freshly distilled methanesulfonyl chloride (0.04 ml, 0.5 mmol) under an argon atmosphere. The reaction mixture was stirred at 0 °C for 20 min and at room temperature for 2 h, followed by heating at 80-90 °C for 10†h. The resulting mixture was diluted with water and extracted with ethyl acetate. The combined extracts were washed with water, brine and dried over anh. Na_2SO_4. Filtration and evaporation of solvent afforded a crude product of **3a**, which was purified by preparative thin-layer chromatography (SiO_2, 20% ethyl acetate in hexane) to provide a white solid of **3a** (0.036 g, 87% yield), mp 86-87 °C (ether) (lit.[16] mp 86-87 °C) as a >97:3 ratio of (*Z*):(*E*)-isomers. ^1H NMR (300 MHz, $CDCl_3$): δ 7.79 (d, J = 7.1 Hz, 2H, Ar*H*), 7.50 (d, J = 5.3 Hz, 1H, COCH=C*H*), 7.47-7.30 (m, 3H, Ar*H*), 6.34 *(E)* and 6.22 *(Z)* (each d, J = 5.3 Hz, 1H, COC*H*=CH), 6.8 *(E)* and 6.04 *(Z)* (each s, 1H, C=C*H*Ar). IR (nujol): ν_{max} 1785, 1747, 1549, 1448, 1368, 1345, 1229, 1186, 1117, 1071, 951, 934, 921, 892, 880, 822, 759, 689 cm^{-1}. MS: m/z (%) relative intensity 172 (M^+, 100), 144 (36), 131 (4), 115 (55), 89 (23), 63 (9).

5-(3-Methoxybenzylidene)-2(5H)-furanone (6b).

According to the general procedure as described for **6a**, compound **3b** (*syn:anti* = 70:30) (0.0687 g, 0.31 mmol) was reacted with MsCl (0.04 ml, 0.5 mmol) in pyridine (1 ml) to give a pale yellow solid of **6b** (0.053 g, 85% yield; mp 65-71 °C) as a 98:2 mixture of (*Z*):(*E*)-isomers. ^1H NMR (300 MHz, $CDCl_3$): δ 7.47 (d, J = 5.5 Hz, 1H, COCH=C*H*), 7.35-7.26 (m, 3H, Ar*H*), 6.91-6.87 (m, 1H, Ar*H*), 6.32 (*E*) (dd, J = 5.5, 1.75 Hz) and 6.19 (*Z*) (d, J = 5.5 Hz) (1H, COC*H*=CH), 6.74 *(E)* and 5.98 *(Z)* (each s, 1H, C=C*H*Ar), 3.83 (s, 3H, O*Me*). IR (nujol): ν_{max} 1770, 1747, 1720, 1654, 1597, 1574, 1551, 1481, 1455, 1437, 1364, 1345, 1316, 1293, 1262, 1200, 1161, 1121, 1067, 1051, 940, 900, 880, 818, 779, 690 cm^{-1}. MS: m/z (%) relative intensity 202 (M^+, 100), 187 (4), 174 (25), 159 (10), 146 (21), 131 (47), 115 (20), 103 (31), 97 (7), 91 (15), 83 (8), 77 (24), 71 (15), 63 (8), 57 (16). Anal. Calcd. for $C_{12}H_{10}O_3$: C, 71.27; H, 4.98. Found: C, 71.23; H, 4.64.

5-(4-Methoxybenzylidene)-2(5H)-furanone (6c).

According to the general procedure as described for **6a**, compound **3c** (*syn:anti* = 78:22) (0.110 g, 0.5 mmol) was reacted with MsCl (0.08 ml, 1.0 mmol) in pyridine (2 ml) to give a pale yellow solid of **6c** (0.085 g, 84% yield; mp 107-110 °C) as a 99:1 mixture of (*Z*):(*E*)-isomers. ^{1}H NMR of (*Z*)-isomer (300 MHz, $CDCl_3$): δ 7.76-7.73 (m, 2H, Ar*H*), 7.46 (d, J = 5.3 Hz, 1H, COCH=C*H*), 6.95-6.89 (m, 2H, Ar*H*), 6.14 (dd, J = 5.3, 0.7 Hz, 1H, COC*H*=CH), 5.98 (s, 1H, C=C*H*Ar), 3.84 (s, 3H, O*Me*). IR (nujol): ν_{max} 1787, 1750, 1738, 1651, 1604, 1552, 1509, 1367, 1334, 1318, 1258, 1187, 1175, 1119, 1078, 1025, 930, 894, 882, 848, 832, 813, 770, 680, cm^{-1}. MS: m/z (%) relative intensity 202 (M^+, 100), 187 (10), 174 (10), 159 (23), 148 (9), 131 (70), 120 (24), 115 (18), 103 (63), 91 (34), 89 (30), 77 (84), 74 (17), 63 (31), 57 (4). Anal. Calcd. for $C_{12}H_{10}O_3$: C, 71.27; H, 4.98. Found: C, 71.41; H, 5.05.

5-(2,3-Dimethoxybenzylidene)-2(5H)-furanone (6d).

According to the general procedure as described for **6a**, compound **3d** (*syn:anti* = 86:14) (0.220 g, 0.9†mmol) was reacted with MsCl (0.15 ml, 1.5 mmol) in pyridine (2 ml) to give a pale yellow solid of **6d** (0.172 g, 82% yield; mp 65-67 °C) as a 99:1 mixture of (*Z*):(*E*)-isomers. ^{1}H NMR of (*Z*)-isomer (300 MHz, $CDCl_3$): δ 7.82 (br. d, J = 8.0 Hz, 1H, Ar*H*), 7.53 (d, J = 5.3 Hz, 1H, COCH=C*H*), 7.09 (app. t, J = 8.0 Hz, 1H, Ar*H*), 6.91 (dd, J = 8.0, 1.2 Hz, 1H, Ar*H*), 6.52 (s, 1H, C=C*H*Ar), 6.20 (d, J = 5.3 Hz, 1H, COC*H*=CH), 3.87 and 3.86 (each s, 6H, O*Me*). IR (nujol): ν_{max} 1772, 1735, 1650, 1575, 1550, 1477, 1428, 1351, 1338, 1303, 1276, 1232, 1204, 1168, 1108, 1064, 1004, 955, 916, 881, 788, 765, 749, 731, 675 cm^{-1}. MS: m/z (%) relative intensity 232 (M^+, 100), 217 (1), 201 (12), 189 (10), 161 (34), 146 (5), 115 (13), 92 (6), 89 (5), 77 (5), 63 (5). Anal. Calcd. for $C_{13}H_{12}O_4$: C, 67.23; H, 5.20. Found: C, 66.90; H, 5.25.

5-(3,4-Dimethoxybenzylidene)-2(5H)-furanone (6e).

According to the general procedure as described for **6a**, compound **3e** (*syn:anti* = 72:28) (0.254 g, 1.0 mmol) was reacted with MsCl (0.15 ml, 1.5 mmol) in pyridine (4 ml) to give a yellow solid of **6e** (0.21 g, 91% yield; mp 114-117 °C) as a 94:6 mixture of (*Z*):(*E*)-isomers. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47 (d, J = 5.4 Hz, 1H, COCH=C*H*), 7.45 (d, J = 2 Hz, 1H, Ar*H*), 7.29 (dd, J = 8.3, 2.0 Hz, 1H, Ar*H*), 6.88 (d, J = 8.3 Hz, 1H, Ar*H*), 6.31 (*E*) and 6.15 (*Z*) (each dd, J = 5.4, 1.8 Hz and 5.4, 0.8 Hz, respectively, 1H, COC*H*=CH), 6.73 (*E*) and 5.98 (*Z*) (each br. s, 1H, C=C*H*Ar), 3.94 and 3.92 (each s, 6H, O*Me*). IR (nujol): ν_{max} 1775, 1750, 1732, 1651, 1596, 1543, 1516, 1327, 1269, 1214, 1184, 1169, 1142, 1116, 1079, 1022, 962, 922, 887, 854, 806, 779, 676 cm^{-1}. MS: m/z (%) relative intensity 232 (M^+, 100), 217 (23), 204 (2), 189 (8), 171 (5), 161 (10), 143 (3), 133 (17), 116 (7), 105 (8), 97 (3), 92 (6), 89 (5), 77 (7), 69 (3), 63 (5), 55 (6). Anal. Calcd. for $C_{13}H_{12}O_4$: C, 67.23; H, 5.20. Found: C, 67.08; H, 5.30.

5-(3,4-Methylenedioxybenzylidene)-2(5H)-furanone (6f).

According to the general procedure as described for **6a**, compound **3f** (*syn:anti* = 70:30) (0.233 g, 1.0 mmol) was reacted with MsCl (0.12 ml, 1.5 mmol) in pyridine (4 ml) to give a pale yellow solid of **6f** (0.21 g, 97% yield; mp 138-140 °C) as a 94:6 mixture of (*Z*):(*E*)-isomers. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47-7.45 (m, 2H, Ar*H* and COCH=C*H*), 7.17 (dd, J = 8.1, 1.9 Hz, 1H, Ar*H*), 6.82 (d, J = 8.1 Hz, 1H, Ar*H*), 6.16 (d, J = 4.9 Hz, 1H, COC*H*=CH), 6.02 (*E*) and 6.01 (*Z*) (each s, 2H, OCH_2O), 6.7 (*E*) (d, J = 1.6 Hz) and 5.95 (*Z*) (s) (1H, C=C*H*Ar). IR (nujol): ν_{max} 1773, 1741, 1651, 1619, 1600, 1546, 1488, 1447, 1338, 1276, 1261, 1209, 1191, 1119, 1067, 1039, 936, 883, 821, 722, 681 cm^{-1}. MS: m/z (%) relative intensity 216 (M^+, 100), 188 (13), 162 (6), 134 (14), 130 (20), 102 (32), 93 (5), 76 (23), 63 (3), 50 (12). Anal. Calcd. for $C_{12}H_8O_4$: C, 66.66; H, 3.73. Found: C, 66.66; H, 3.60.

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