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Diastereoselective Mukaiyama-Michael Reaction of *O,S*-Ketene Silyl Acetal

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Abstract: The highly diastereoselective Mukaiyama-Michael reaction has been realized by use of *O,S*-ketene silyl acetals. Of special importance in this reaction is the effective tuning of the stereochemical course simply by changing the double bond geometry of ketene silyl acetals. Thus, both *syn*- and *anti*-Michael adducts can be obtained on the synthetically useful levels of stereochemical purity. Copyright © 1996 Elsevier Science Ltd

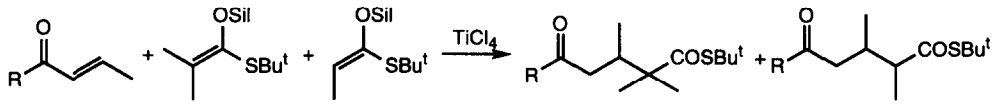
INTRODUCTION

In the preceding paper, we disclosed that the diastereoselective Mukaiyama-Michael reaction can be designed if appropriate conditions were fulfilled.[1] The most crucial one among them was to suppress electron transfer from ketene silyl acetal to Lewis acid. Use of bulky ketene silyl acetals served for this purpose because of the high ionization potentials of these compounds in solution. Previously, we had disclosed that *O,S*-ketene silyl acetals possessed higher ionization potentials than the corresponding *O,O*-ketene silyl acetals.[2] Consequently, it is conceivable that the Mukaiyama-Michael reaction of *O,S*-ketene silyl acetals proceeds by the nucleophilic mechanism leading to the high diastereoselectivity. In fact, Mukaiyama et al. communicated the high diastereoselection in trityl perchlorate-catalyzed Michael reaction.[3] In this paper, we present a full account of this sort of reaction in the presence of Lewis acids.

RESULTS AND DISCUSSION

Whether the reaction proceeds by the nucleophilic mechanism or the electron-transfer initiated radical mechanism can be probed by competition reaction between ketene silyl acetals bearing a different number of methyl group(s) at the β-position.[4] To confirm the validity of the nucleophilic mechanism in Michael reaction of *O,S*-ketene silyl acetal, $TiCl_4$-promoted competition reactions with various α-enones were conducted at -78 ℃ in CH_2Cl_2. The results are given in Table 1-3. In the competitions employing a β,β-dimethylsubstituted ketene silyl acetal as one of the reactants, the less substituted components always react preferentially (Table 1,2) while the competition between monomethyl and unsubstituted compounds leads to decreased selectivities and even a reversed preference occurs in one case (entry 3, Table 3). These results can be reasonably interpreted in terms of the nucleophilic mechanism based on Mayr's nucleophilicity assessment.[5] Although the effect of β-methyl substitution for ketene silyl acetals has not been elucidated, nucleophilicity of allylsilanes was fully examined. The nucleophilicity parameter slightly increases by changing from allyl- (1.62) to crotylsilane (1.99) due to a somewhat prevailing inductive effect of the methyl group over a steric demand. By contrast, the dimethyl substitution induces a severe steric hindrance to cause a drastic decrease of nucleophilicity for the prenyl analog (0.84). As a whole, there is a small gap between unsubstituted and monomethyl derivatives but the nucleophilicity of the dimethyl compound is greatly reduced from those of the other two compounds. The

Table 1. Competition Reaction between β,β-Dimethyl and β-Monomethyl *O,S*-Ketene Silyl Acetals.[a]

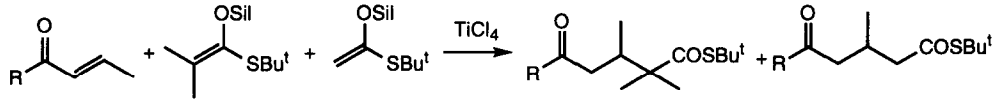


1 2

			yield (%)		ratio[b]
entry	R	Sil	**1**	**2**	**1:2**
1	^{t}Bu	TBS	1	57	1:99
2		TBS[c]	1	52	1:99
3		TMS	5	52	8:92
4	Ph	TBS	2	58	3:97
5		TMS	6	61	9:91
6	Anis	TBS	1	70	1:99
7		TMS	1	72	1:99
8	Mes	TBS	1	66	1:99
9		TMS	1	50	2:98

[a] Reaction conditions: enone:ketene silyl acetal:ketene silyl acetal: $TiCl_4$ = 1.0:1.0:1.0:1.0; CH_2Cl_2, -78 °C; 3 h. [b] Determined by GLC. [c] The (*E*)-isomer of the monomethyl *O,S*-ketene silyl acetal was employed in place of the (*Z*)-counterpart.

Table 2. Competition Reaction between β,β-Dimethyl and Unsubstituted *O,S*-Ketene Silyl Acetals.[a]

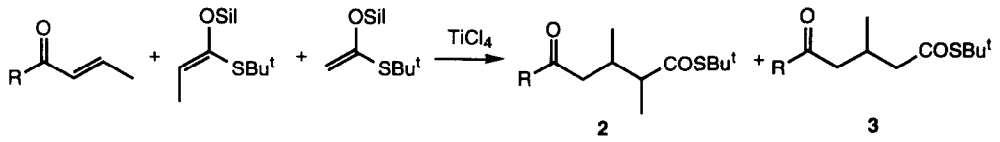


1 3

			yield (%)		ratio[b]
entry	R	Sil	**1**	**3**	**1:3**
1	^{t}Bu	TBS	10	48	17:83
2		TMS	19	40	33:67
3	Ph	TBS	4	55	7:93
4		TMS	18	41	31:69
5	Anis	TBS	1	62	1:99
6		TMS	1	62	1:99
7	Mes	TBS	10	56	15:85
8		TMS	9	47	16:84

[a] Reaction conditions: enone:ketene silyl acetal:ketene silyl acetal: $TiCl_4$ = 1.0:1.0:1.0:1.0; CH_2Cl_2, -78 °C; 3 h. [b] Determined by GLC.

Table 3. Competition Reaction between β-Monomethyl and Unsubstituted *O,S*-Ketene Silyl Acetals.[a]



2 3

			yield (%)		ratio[b]
entry	R	Sil	**2**	**3**	**2:3**
1	^{t}Bu	TBS	20	40	34:66
2		TBS[c]	16	47	25:75
3		TMS	44	22	66:34
4	Ph	TBS	23	40	36:64
5		TMS	26	33	44:56
6	Anis	TBS	18	51	26:74
7		TMS	37	40	48:52
8	Mes	TBS	14	52	21:79
9		TMS	1	53	2:98

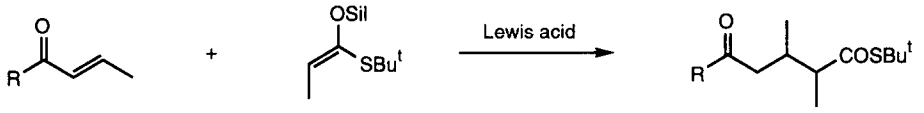
[a] Reaction conditions: enone:ketene silyl acetal:ketene silyl acetal: $TiCl_4$ = 1.0:1.0:1.0:1.0; CH_2Cl_2, -78 °C; 3 h. [b] Determined by GLC. [c] The (*E*)-isomer of the monomethyl *O,S*-ketene silyl acetal was employed in place of the (*Z*)-counterpart.

results of our competition reactions are qualitatively compatible with the nucleophilic mechanism based on this nucleophilicity assessment.

Next, we investigated the diastereoselectivity of the Michael reaction. The reaction was carried out in CH_2Cl_2 at -78 °C. The stereochemistry and diastereomeric ratio were straightforwardly determined by ^{1}H NMR spectra for the *tert*-butyl and methyl enone adducts. The Michael adducts derived from the phenyl, anisyl, and mesityl enones were converted to keto benzoates as described in the preceding paper. The results are summarized in Table 4. A substantially high level of diastereocontrol is achievable. As observed with bulky ketene silyl acetals in the preceding paper, the mesityl (Mes) enone behaves differently from other α-enones, giving rise to the constant *syn* preference (entries 15-18). The stereochemical course is governed primarily by the mesityl group again. With *tert*-butyl, phenyl, anisyl (Anis), and methyl enones, good to excellent anti-selectivities are attained when (*E*)-*O,S*-ketene silyl acetals are employed (entries 1,3,5,7,9,11,13). Notably, even less sterically demanding TMS derivatives exhibit better than an 18:82 *syn/anti* ratio. When the *Z*-counterparts are subjected to the same reaction, the *anti*-selectivity decreases (entries 4,8,12,14) or the reaction is changed to *syn*-preference (entry 6). Furthermore, the selectivity reaches to a 91:9 ratio at best (entries 2,10). It should be noted that analogous stereochemical reversal was observed in trityl perchlorate-catalyzed reaction: from 95:5 to 31:69 for the phenyl enone adduct.[3a] Significantly, we have now succeeded in switching the diastereoselectvity on the synthetically useful level, particularly in view of acyclic stereoselection. Comparison of TBS and TMS groups clearly indicates that the former is superior to the latter for both *syn*- and *anti*-selectivities, suggesting the importance of steric bulk of the siloxy group. The effect of the acyl group of α-enone is rather difficult to be interpreted straightforwardly. It is basically obvious that the bulkiness plays an important role, yet the anisyl enone exhibits the selectivities as high as the *tert*-butyl enone with the TBS ketene

silyl acetal (entries 9,10). In this sense, the electron donating ability also seems to be responsible for the stereocontrol. However, these two enones behaves somewhat differently from each other towards TMS ketene silyl acetals (entries 3,4; 11,12).

Table 4. Diastereoselective Mukaiyama-Michael Reaction of *O,S*-Ketene Silyl Acetals.[a)]



entry	R	Sil	*E* or *Z*	Lewis acid (equiv)	yield (%)	*syn:anti*[b)]
1	^{t}Bu	TBS	*E*	$TiCl_4$ (1.0)	99	5:95
2			*Z*		83	91:9
3		TMS	*E*		75	18:82
4			*Z*		71	46:54
5	Ph	TBS	*E*		66	7:93
6			*Z*		73	54:46
7		TMS	*E*		93	14:86
8			*Z*		82	45:55
9	Anis	TBS	*E*		71	5:95
10			*Z*		82	91:9
11		TMS	*E*		73	8:92
12			*Z*		72	22:78
13	Me	TBS	*E*		77	8:92
14			*Z*		67	40:60
15	Mes	TBS	*E*		60	89:11
16			*Z*		67	89:11
17		TMS	*E*		75	79:21
18			*Z*		90	82:18
19	^{t}Bu	TBS	*E*	$BF_3{\cdot}OEt_2$ (1.0)	85	12:88
20			*Z*		89	59:41
21			*E*	Et_3SiClO_4 (0.1)	83	38:62
22			*E*	Et_3SiClO_4 (1.0)	96	41:59
23			*Z*	Et_3SiClO_4 (0.1)	81	64:36
24			*Z*	Et_3SiClO_4 (1.0)	92	76:24
25			*E*	$SnCl_4$ (0.1)	90	48:52
26			*E*	$SnCl_4$ (1.0)	96	27:73
27			*Z*	$SnCl_4$ (0.1)	93	41:59
28			*Z*	$SnCl_4$ (1.0)	93	30:70

[a)] Reaction conditions: enone:ketene silyl acetal = 1.0:1.3; CH_2Cl_2, -78 °C; 5 h. [b)] The ratio of Michael adducts derived from *tert*-butyl and methyl enones was determined by ^{1}H NMR spectra. The products derived from phenyl, anisyl, and mesityl enones were converted to the keto benzoates as described in the preceding paper. The diastereomeric ratio was determined by HPLC (see experimental part).

Finally, Lewis acids were screened. Et_3SiClO_4 and $BF_3{\cdot}OEt_2$ give rise to similar results: modest selectivities and reversal of the *syn/anti* selectivity in response to change of the ketene silyl acetal geometry

(entries 19-24). Catalytic $SnCl_4$ exhibits no selectivities (entries 25,27). The use of this Lewis acid in a stoichiometric amount improves the *anti*-preference to some degree (entries 26,28). In both cases, however, no stereochemical reversal with the *E/Z* isomers of ketene silyl acetal is observed. It follows from these results that $TiCl_4$ is superior to the other Lewis acids screened here in all respects.

In conclusion, the highly diastereoselective Mukaiyama-Michael reaction is achieved by use of *O,S*-ketene silyl acetals. Both *syn*- and *anti*-products can be obtained by changing the *E/Z* geometry of the ketene silyl acetals. We hope this will meet versatile synthetic applications.

Experimental Section

General. ^1H NMR (300 or 400 MHz) and ^{13}C NMR (75 or 100 MHz) were measured in $CDCl_3$ solution. Mass spectra were taken on a JEOL JMS-DX 303-HF mass spectrometer using impact ionization. HPLC was measured with a Shimadzu LC-8A machine equipped with a column packed with DEVELOSIL 30-3 (4.6 x 250 mm; NOMURA CHEMICAL CO. LTD.). GLC analysis was performed on a Shimadzu GC-8A gas chromatograph with OV-17 (3.2 mm x 2 m). Elemental analyses were performed with a Perkin-Elemer 2400CHN. All reactions were run under dry nitrogen. CH_2Cl_2 and hexane were distilled from calcium hydride. THF was distilled from a benzophenone ketyl. $SnCl_4$ and $TiCl_4$ were used as received. Et_3SiClO_4 was prepared by the method of Lambert and Sun.[6] 3-Penten-2-one is commercially available and the preparation of other α-enones has been described.[1,4b,7] *O,S*-Ketene silyl acetals were prepared by methods of Gennari[8] and Heathcock.[9] The *E/Z* ratios of β-monomethyl *O,S*-ketene silyl acetals employed in this study were as follows: (*Z*)-TBS acetal: *E* : *Z* = < 1 : 99; (*Z*)-TMS acetal: *E* : *Z* = < 1 : 99; (*E*)-TBS acetal: *E* : *Z* = 93 : 7; (*E*)-TMS acetal: *E* : *Z* = 93 : 7. To assign the diastereochemistry of Michael adducts **2a** (R = ^{t}Bu), the Michael adduct was converted into the keto benzoate **4a**, and this keto benzoate was compared with an authentic sample derived from a known methyl ester. Similarly, the stereochemical assignment of **2d** (R = Mes) was made as the keto benzoate **4d** whose authentic sample was prepared from a known ethyl ester. The *syn/anti* assignments of keto benzoates, **4b** (R = Ph) and **4c** (R = Anis), were made by comparison of their ^1H NMR spectra with those of other well-defined analogs, **4a** and **4d**. The authentic specimen of **2e** (R = Me) was obtained from the corresponding TBS enolate which had been prepared by the trityl perchlorate-catalyzed reaction.[3a]

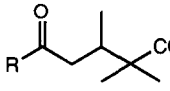
Lewis Acid-Promoted Reaction of O,S-Ketene Silyl Acetal with α-Enone (General Procedure). To a solution of Lewis acid (1.0 or 0.1 mmol) in CH_2Cl_2 (5 mL) was added dropwise α-enone (1.0 mmol) at -78 °C. *O,S*-Ketene silyl acetal (1.3 mmol) was added over a 2 min period. The mixture was stirred for 3 h at this temperature and then H_2O (0.5 mL) was added. The mixture was diluted with EtOAc (60 mL) and washed with H_2O (20 mL). The organic layer was dried over Na_2SO_4, and the solvent was evaporated. The pure Michael adduct was isolated by column chromatography on silica gel.

The Michael adduct **2a-d** were converted to keto benzoates, **4a-d**. To a suspension of $LiAlH_4$ (176 mg, 4.65 mmol) in THF (5 mL) was added a THF solution (5 mL) of the Michael adduct (0.93 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 3 h, and cooled with ice bath, and quenched with 1N-NaOH (2 mL). The mixture was diluted with Et_2O (50 mL), and dried over $MgSO_4$. Filtration and evaporation afforded diol. The resulting crude diol was dissolved in pyridine (5 mL) and 4-dimethylaminopyridine (10 mg, 0.08 mmol). Benzoyl chloride (170 mg, 0.140 mL, 1.21 mmol) was added to this solution at 0 °C. The solution was stirred at room temperature for 8 h, and quenched with H_2O (2 mL). The quenched mixture was diluted with AcOEt (60 mL), and washed with H_2O (20 mL), 3N-HCl (30 mL), saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried over Na_2SO_4, and concentrated to provide the crude products. Column chromatography on silica gel afforded hydroxy benzoate (99 %). To a mixture of PCC (397 mg, 1.84 mmol) and MS 4A (200 mg) in CH_2Cl_2 (5 mL) was added the THF solution (3 mL) of the hydroxy benzoate (0.92 mmol) at 0 °C. The mixture was stirred at room temperature for 3 h and filtered through celite.

The filtrate was evaporated and subjected to column chromatography on silica gel to give the desired keto benzoate (98 %).

General Procedure for Competition Reaction. To a solution of Lewis acid (1.0 mmol) in CH_2Cl_2 (5 mL) at -78 °C was added dropwise α-enone (1.0 mmol). An equimolar mixture of two *O,S*-ketene silyl acetals (1.0 mmol each) was added over a 2 min period. The mixture was stirred for 3 h at this temperature and then H_2O (0.5 mL) was added. The mixture was diluted with EtOAc (60 mL) and washed with H_2O (20 mL). The organic layer was dried over Na_2SO_4, and evaporated. GLC analysis of the crude mixture thus obtained revealed the ratio of Michael adducts.

Michael adducts, **1b** and **2b**, have been reported in our previous paper.[4b] Characterization data for other Michael adducts and keto benzoates are as follows.

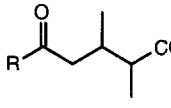


1a: R = ^{t}Bu; **1b**: R = Ph; **1c**: R = Anis; **1d**: R = Mes

1a: ^{1}H NMR δ 0.81 (d, 3H, J=6.71Hz), 1.10 (s, 3H), 1.11 (s, 9H), 1.12 (s, 3H), 1.43 (s, 9H), 2.29-2.52 (m, 3H); ^{13}C NMR δ 14.95, 21.44, 23.09, 26.40, 29.80, 36.07, 39.15, 44.34, 47.17, 53.11, 207.61, 214.52; MS (m/z) 229 (M^+-Bu^t); HRMS calcd for $C_{16}H_{30}O_2S$ (M^+) 286.1967, found 286.2040; Anal. Calcd for $C_{16}H_{30}O_2S$: C, 67.08; H, 10.55. Found: C, 66.78; H, 10.24.

1c: ^{1}H NMR δ 0.80 (d, 3H, J=5.67Hz), 1.08 (s, 3H), 1.10 (s, 3H), 1.37 (s, 9H), 2.47-2.58 (m, 2H), 2.85-2.94 (m, 1H), 3.76 (s, 3H), 6.83 (d, 2H, J=8.85Hz), 7.85 (d, 2H, J=8.85Hz); ^{13}C NMR δ 14.59, 21.07, 22.93, 29.63, 37.08, 40.86, 47.11, 53.15, 55.25, 113.53, 130.02, 130.29, 163.24, 197.99, 207.43; MS (m/z) 247 (M^+-SBu^t); HRMS calcd for $C_{15}H_{19}O_3$ (M^+-SBu^t) 247.1334, found 247.1392; Anal. Calcd for $C_{19}H_{28}O_3S$: C, 67.82; H, 8.38. Found: C, 68.20; H, 8.03.

1d: ^{1}H NMR δ 1.02 (d, 3H, J=7.39Hz), 1.09 (s, 3H), 1.14 (s, 3H), 1.43 (s, 9H), 2.17 (s, 6H), 2.27 (s, 3H), 2.43-2.53 (m, 1H), 2.64-2.76 (m, 2H), 6.82 (s, 2H); ^{13}C NMR δ 14.97, 18.95, 20.55, 20.99, 23.61, 29.77, 35.04, 47.21, 47.89, 53.05, 128.43, 132.32, 138.19, 139.68, 207.44, 209.05; MS (m/z) 259 (M^+-SBu^t); HRMS calcd for $C_{17}H_{23}O_2S$ (M^+-Bu^t) 291.1419, found 291.1481.



2a: R = ^{t}Bu; **2b**: R = Ph; **2c**: R = Anis **2d**: R = Mes; **2e**: R = Me

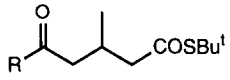
2a: *syn* isomer: ^{1}H NMR δ 0.87 (d, 3H, J=6.21Hz), 1.08 (d, 3H, J=7.00Hz), 1.11 (s, 9H), 1.45 (s, 9H), 2.34-2.63 (m, 4H); ^{13}C NMR δ 13.81, 16.64, 26.28, 29.72, 31.90, 40.77, 44.17, 47.62, 52.82, 204.00, 214.41;*anti* isomer: ^{1}H NMR δ 0.85 (3H, d, J=6.29Hz), 1.10-1.11 (3H, m), 1.11 (9H, s), 1.43 (9H, s), 2.31-2.62 (m, 4H); ^{13}C NMR δ 14.24, 17.41, 26.24, 29.66, 31.84, 40.12, 44.12, 47.56, 52.66, 203.62, 214.49; MS (m/z) 215 (M^+-Bu^t); HRMS calcd for $C_{15}H_{28}O_2S$ (M^+) 272.1810, found 272.1885; Anal. Calcd for $C_{15}H_{28}O_2S$: C, 66.13; H, 10.36. Found: C, 66.39; H, 10.14.

2c: ^{1}H NMR δ 0.93 (d, 3Hx0.45, J=6.41Hz), 0.98 (d, 3Hx0.55, J=6.53Hz), 1.12 (d, 3Hx0.45, J=6.66Hz), 1.15 (d, 3Hx0.55, J=6.83Hz), 1.44 (s, 9Hx0.45), 1.45 (s, 9Hx0.55), 2.45-2.72 (m, 3H), 3.03-3.16 (m, 1H), 3.85 (s, 3H), 6.91 (d, 2Hx0.45, J=8.97Hz), 6.92 (d, 2Hx0.55, J=8.91Hz), 7.92 (d, 2Hx0.45, J=8.97Hz), 7.93 (d, 2Hx0.55, J=8.91Hz); ^{13}C NMR δ 14.03 (*syn* and *anti*), 16.55 (*syn*), 17.58 (*anti*), 29.59 (*syn* and *anti*), 32.86 (*anti*), 32.96 (*syn*), 41.68 (*anti*), 42.77 (*syn*), 47.61 (*syn* and *anti*), 53.19 (*syn* and *anti*), 55.23 (*syn* and *anti*), 113.50 (*anti*), 113.53 (*syn*), 129.97 (*syn*), 130.09 (*anti*), 130.19 (*anti*), 130.25 (*syn*),

163.22 (*syn* and *anti*), 197.62 (*syn*), 197.74 (*anti*), 203.54 (*anti*), 203.94 (*syn*); MS (m/z) 233 (M^+-SBu^t); HRMS calcd for $C_{14}H_{17}O_3S$ (M^+-Bu^t) 265.0899, found 265.0976.

2d: ^1H NMR δ 1.04 (d, 3H, J=5.86Hz), 1.09 (d, 3Hx0.10, J=6.11Hz), 1.12 (d, 3Hx0.90, J=6.60Hz), 1.44 (s, 9H), 2.17 (s, 6H), 2.27 (s, 3H), 2.48-2.63 (m, 2H), 2.78-2.91 (m, 1H), 6.82 (s, 2H); ^{13}C NMR δ 13.39 (*anti*), 14.26 (*syn*), 16.93 (*syn*), 17.96 (*anti*), 18.88 (*syn*), 18.91 (*anti*), 20.91 (*syn* and *anti*), 29.64 (*syn* and *anti*), 31.27 (*syn*), 31.36 (*anti*), 47.68 (*syn*), 47.92 (*anti*), 49.20 (*syn* and *anti*), 52.73 (*anti*), 52.94 (*syn*), 128.38 (*syn* and *anti*), 132.25 (*syn* and *anti*), 138.07 (*syn* and *anti*), 139.49 (*syn* and *anti*), 203.48 (*anti*), 203.85 (*syn*), 208.97 (*syn*), 209.09 (*anti*); MS (m/z) 245 (M^+-SBu^t); HRMS calcd for $C_{20}H_{30}O_2S$ (M^+) 334.1967, found 334.2009; Anal. Calcd for $C_{20}H_{30}O_2S$: C, 71.87; H, 9.04. Found: C, 71.84; H, 9.18.

2e: ^1H NMR δ 0.88 (d, 3Hx0.40, J = 6.15Hz), 0.92 (d, 3Hx0.60, J = 6.59Hz), 1.06 (d, 3Hx0.40, J = 6.96Hz), 1.08 (d, 3Hx0.60, J = 7.02 Hz), 1.42 (s, 9Hx0.60), 1.43 (s, 9Hx0.40), 2.11 (s, 3Hx0.40), 2.12 (s, 3Hx0.60), 2.15-2.62 (m, 4H); ^{13}C NMR δ 13.64 (*syn*), 13.93 (*anti*), 16.33 (*syn*), 17.31 (*anti*), 29.40 (*syn* and *anti*), 29.93 (*syn*), 30.07 (*anti*), 31.87 (*syn* and *anti*), 46.95 (*syn* and *anti*), 47.41 (*anti*), 47.81 (*syn*), 52.44 (*anti*), 52.54 (*syn*), 203.16 (*anti*), 203.42 (*syn*), 207.27 (*syn*), 207.34 (*anti*); MS (m/z) 141 (M^+-SBu^t); HRMS calcd for $C_8H_{13}O_2$ (M^+-SBu^t) 141.0916, found 141.0921.



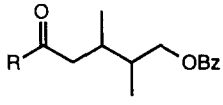
3a: R = ^{t}Bu; **3b**: R = Ph;
3c: R = Anis; **3d** R = Mes

3a: ^1H NMR δ 0.94 (d, 3H, J=6.29Hz), 1.11 (s, 9H), 1.44 (s, 9H), 2.27-2.59 (m, 5H); ^{13}C NMR δ 19.59, 26.17, 26.79, 29.62, 42.47, 43.99, 47.72, 50.53, 199.30, 214.24; MS (m/z) 201 (M^+-Bu^t); HRMS calcd for $C_{10}H_{17}O_2S$ (M^+-Bu^t) 201.0949, found 201.0909; Anal. Calcd for $C_{14}H_{26}O_2S$: C, 65.07; H, 10.14. Found: C, 64.98; H, 10.16.

3b: ^1H NMR δ 1.04 (d, 3H, J=6.54Hz), 1.46 (s, 9H), 2.40-2.60 (m, 2H), 2.65-2.85 (m, 2H), 3.06-3.13 (m, 1H), 7.44-7.59 (m, 3H), 7.96 (d, 2H, J=7.33Hz); ^{13}C NMR δ 19.74, 27.58, 29.65, 44.62, 47.88, 50.79, 127.99, 128.47, 132.91, 136.92, 198.91, 199.30; MS (m/z) 189 (M^+-SBu^t); HRMS calcd for $C_{12}H_{13}O_2S$ (M^+-Bu^t) 221.0636, found 221.0660.

3c: ^1H NMR δ 1.01 (d, 3H, J=6.43Hz), 1.44 (s, 9H), 2.38-2.57 (m, 2H), 2.62-2.76 (m, 2H), 2.99-3.04 (m, 1H), 3.85 (s, 3H), 6.91 (d, 2H, J=8.94Hz), 7.92 (d, 2H, J=8.94Hz); ^{13}C NMR δ 19.70, 27.78, 29.62, 44.30, 47.80, 50.85, 55.27, 113.57, 130.04, 130.24, 163.30, 197.43, 199.28; MS (m/z) 219 (M^+-SBu^t); HRMS calcd for $C_{13}H_{15}O_3S$ (M^+-Bu^t) 251.0742, found 251.0679; Anal. Calcd for $C_{17}H_{24}O_3S$: C, 66.20; H, 7.84. Found: C, 66.16; H, 7.87.

3d: ^1H NMR δ 1.08 (d, 3H, J=6.29Hz), 1.45 (s, 9H), 2.18 (s, 6H), 2.64 (s, 3H), 2.38-2.84 (m, 5H), 6.82 (s, 2H); ^{13}C NMR δ 18.89, 19.80, 20.91, 26.42, 29.65, 47.86, 50.48, 50.56, 128.40, 132.30, 138.11, 139.39, 199.21, 208.94; MS (m/z) 232 (M^+-SBu^t+1); HRMS calcd for $C_{15}H_{19}O_2S$ (M^+-Bu^t) 263.1106, found 263.1124.



4a: R = ^{t}Bu; **4b**: R = Ph;
4c: R = Anis; **4d**: R = Mes

4a: ^1H NMR δ 0.86 (d, 3Hx0.56, J = 6.60Hz), 0.91 (d, 3Hx0.44, J = 6.78Hz), 0.95 (d, 3Hx0.56, J = 7.02Hz), 1.02 (d, 3Hx0.44, J = 7.02Hz), 1.12 (s, 9Hx0.44), 1.13 (s, 9Hx0.56), 1.90-2.03 (m, 1H), 2.25-2.41 (m, 1H), 2.42-2.50 (m, 2H), 4.13-4.30 (m, 2H), 7.41-7.58 (m, 3H), 8.02-8.07 (m,2H); *syn* isomer

^{13}C NMR δ 12.50, 15.23, 26.12, 29.62, 36.34, 41.30, 44.25, 68.03, 128.34, 129.55, 130.38, 132.84, 166.64, 214.83; *anti* isomer ^{13}C NMR δ 14.52, 16.70, 26.22, 30.61, 36.96, 40.44, 44.14, 67.41, 128.25, 129.43, 130.30, 132.78, 166.50, 214.82; MS (m/z) 234 (M^+-Bu^t+1); HRMS calcd for $C_{11}H_{21}O_2$ (M^+-COPh) 185.1542, found 185.1540; Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.14; H, 9.25.

4b: ^{1}H NMR δ 0.98 (d, 3Hx0.31, J=6.78Hz), 1.02 (d, 3H, J=6.84Hz), 1.08 (d, 3Hx0.69, J=7.03Hz), 2.04-2.12 (m, 1H), 2.40-2.53 (m, 1H), 2.79-3.15 (m, 2H), 4.19-4.38 (m, 2H), 7.39-7.59 (m, 6H), 7.91-8.05 (m, 4H); ^{13}C NMR δ 12.41 (*anti*), 14.23 (*syn*), 15.30 (*anti*), 16.98 (*syn*), 30.72 (*anti*), 31.46 (*syn*), 36.54 (*anti*), 37.19 (*syn*), 42.36 (*syn*), 43.58 (*anti*), 67.40 (*syn*), 67.87 (*anti*), 128.03 (*syn*), 128.05 (*anti*), 128.33 (*anti*), 128.35 (*syn*), 128.55 (*syn* and *anti*), 129.53 (*syn* and *anti*), 130.28 (*syn*), 130.29 (*anti*), 132.85 (*anti*), 132.90 (*syn*), 132.91 (*syn* and *anti*), 137.18 (*anti*), 137.23 (*syn*), 166.57 (*syn* and *anti*), 199.76 (*anti*), 199.86 (*syn*); MS (m/z) 205 (M^+-COPh); HRMS calcd for $C_{13}H_{17}O_2$ (M^+-COPh) 205.1229, found 205.1225; Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.68; H, 7.07.

4c: ^{1}H NMR δ 0.96 (d, 3Hx0.26, J=6.77Hz), 1.00 (d, 3Hx0.74, J=6.78Hz), 1.01 (d, 3Hx0.26, J=7.01Hz), 1.06 (d, 3Hx0.74, J=7.02Hz), 2.00-2.13 (m, 1H), 2.36-2.52 (m, 1H), 2.72-2.86 (m, 2H), 2.95-3.09 (m, 2H), 3.83 (s, 3Hx0.74), 3.85 (s, 3Hx0.26), 4.19-4.37 (m, 2H), 6.84-6.91 (m, 2H), 7.40-7.58 (m, 3H), 7.88-8.05 (m, 2H); ^{13}C NMR δ 12.42 (*anti*), 14.00 (*syn*), 15.15 (*anti*), 16.87 (*syn*), 30.78 (*anti*), 31.49 (*syn*), 36.38 (*anti*), 37.05 (*syn*), 41.75 (*syn*), 43.10 (*anti*), 55.20 (*syn* and *anti*), 67.26 (*syn*), 67.74 (*anti*), 113.51 (*syn* and *anti*), 128.16, 128.19, 129.38, 130.15, 132.67 (*syn*), 132.71 (*anti*), 163.19 (*syn* and *anti*), 166.34 (*syn* and *anti*), 198.09 (*anti*), 198.20 (*syn*); MS (m/z) 218 (M^+-OCOPh-1); HRMS calcd for $C_{14}H_{19}O_3$ (M^+-COPh) 235.1334, found 235.1336; Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 73.80; H, 7.39.

4d: ^{1}H NMR δ 0.97 (d, 3Hx0.90, J=7.02Hz), 1.02 (d, 3Hx0.90, J=6.78Hz), 1.03 (d, 3Hx0.10, J=7.01Hz), 1.11 (d, 3Hx0.10, J=6.78Hz), 1.99-2.36 (m, 1H), 2.18 (s, 6Hx0.1), 2.20 (s, 6Hx0.9), 2.27 (s, 3H), 2.46-2.58 (m, 1H), 2.60-2.88 (m, 2H), 4.17-4.31 (m, 2H), 6.83 (s, 2H), 7.41-7.60 (m, 3H), 8.01-8.07 (m, 2H); ^{13}C NMR δ 12.17 (*syn*), 13.92 (*anti*), 15.07 (*syn*), 17.17 (*anti*), 18.92 (*syn* and *anti*), 20.83 (*syn* and *anti*), 28.94 (*syn*), 29.82 (*anti*), 36.33 (*syn*), 36.88 (*anti*), 48.24 (*anti*), 49.59 (*syn*), 67.17 (*anti*), 67.71 (*syn*), 128.18 (*syn* and *anti*), 128.39 (*syn* and *anti*), 129.38 (*syn* and *anti*), 130.06 (*anti*), 130.14 (*syn*), 132.16 (*anti*), 132.21 (*syn*), 132.70 (*syn* and *anti*), 138.04 (*syn* and *anti*), 139.50 (*syn* and *anti*), 166.35 (*syn* and *anti*), 209.19 (*syn*), 209.34 (*anti*); MS (m/z) 353 (M^++1); HRMS calcd for $C_{23}H_{28}O_3$ (M^+) 352.2039, found 252.2061; Anal. Calcd for $C_{23}H_{28}O_3$: C, 78.38; H, 8.01. Found: C, 78.63; H, 8.19.

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