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Stereoselectivity in Trimethylenemethane (TMM) Diyl Mediated Cycloaddition Reaction to Angularly Fused Triquinanes

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Dedicated to Professor Eiichi Nakamura on the occasion of his 60th birthday

Abstract: A thorough study on the diastereoselectivity in the TMM diyl mediated [2+3] cycloaddition reaction of monosubstituted linear substrates to form angularly fused triquinanes was carried out. Substitution at position 3 provided complete diastereoselectivity, while positions 1 and 4 induced marginal stereoselectivity. Position 2 did not show any influence on the diastereoselectivity. Position 4 turned out to be incompatible with the cycloaddition reaction as the carbene intermediate underwent O−Si bond insertion to form a dihydrofuran ring.

Keywords: carbenes · cycloaddition · stereoselectivity · trimethylenemethane · triquinane

Introduction

Trimethylenemethane (TMM) had been a theoretically interesting species before its first observation by Dowd in 1966.[1] Since then, TMM has attracted the interest of physical organic and synthetic chemists owing to its unique electronic state and seemingly high reactivity.[2] The first synthetically useful TMM was discovered by Köbrich[3] as the TMM diyl diradical, and thorough study of this TMM diyl by Berson has revealed various properties of TMM diyl including [2+3] cycloaddition reaction with multiple bonds.[4] Little and Ott later further developed this TMM diyl [2+3] cycloaddition reaction and applied it to the total synthesis of linearly fused triquinane natural products (Figure 1 a).[5] The TMM diyl was also utilized in the diradical cyclization reactions to form medium-size rings.[6] In this case, two radicals of TMM diyl reacted separately to form diradical intermediates that undergo immediate recombinative bond formation.

Though TMM diyl is highly reactive and reacts with any type of multiple bonds to form five-membered rings, it has shown limited synthetic applicability owing to restrictions in the preparation of precursor compounds. As supplements to the TMM diyl diradical, several synthetic methodologies have been developed. Methylene cyclopropane was used in the Pd- or Ni-mediated cycloaddition reaction though the reaction did not generate TMM intermediates or TMM metal complexes.[7] Methylenecyclopropane could be replaced with acetate of silylated methallyl alcohol in a Pd-mediated cycloaddition reaction.[8] A more stable form of TMM as a zwitterion was also developed by Yamago and Nakamura and was applied to [2+3] cycloaddition reaction (Figure 1).[9]

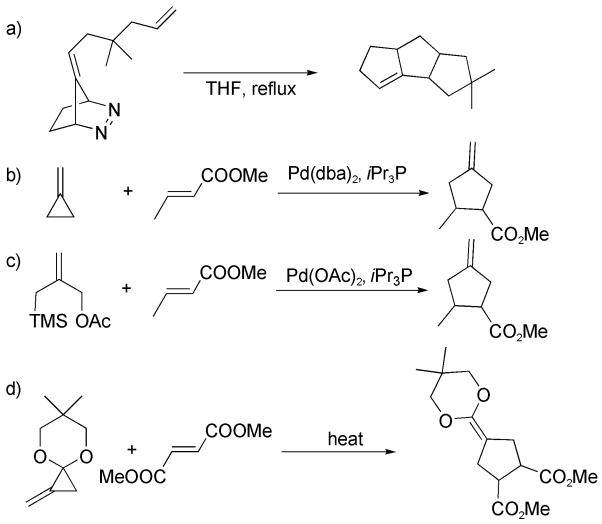

Figure 1. Various ways of TMM-mediated [2+3] cycloaddition reactions.

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Recently, we reported an alkylidene carbene initiated cycloaddition reaction of TMM diyl.[10a] This new strategy not only offers a unique synthetic strategy as the alkylidene carbene reacts with olefin to turn the double bond into a TMM diradical while cleaving the double bond completely, but also adds versatility to the existing synthetic methodology by Little and Ott, as the new methodology extends the TMM diyl mediated cycloaddition reaction to the synthesis of angularly fused triquinanes (Figure 2).[11] The alkylidene

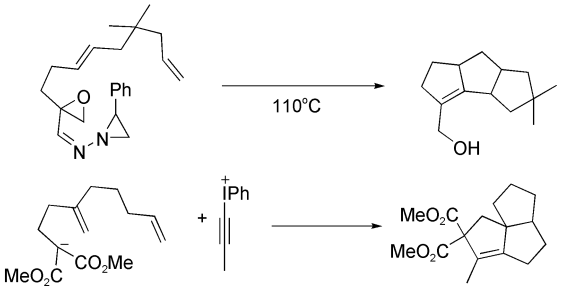


Figure 2. Alkylidene carbene mediated TMM diyl cycloaddition reactions.

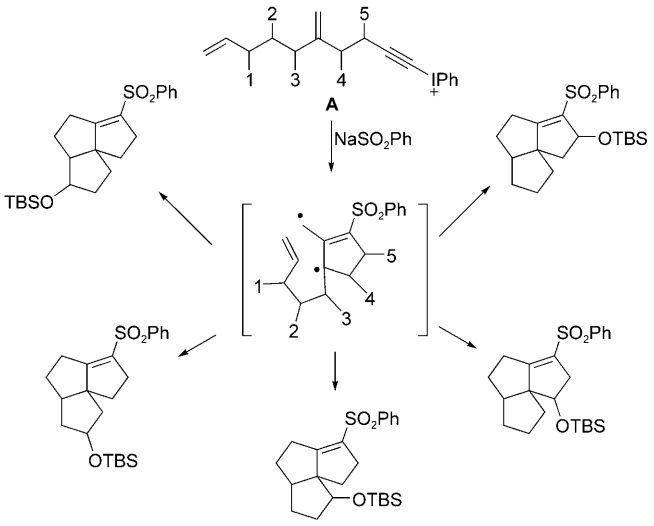
carbene mediated TMM diyl cycloaddition reaction becomes versatile as several different ways to generate alkylidene carbene can be applied to produce TMM diyls[10] and thus allows a stereoselectivity study during [2+3] cycloaddition reaction in the formation of triquinane compounds. While transition-metal-mediated enantioselective [2+3] cycloaddition through a TMM-like intermediate has been successfully explored,[12] diastereoselectivity in the formation of triquinanes through [2+3] cycloaddition reaction has not been systematically studied.[13] For angularly fused triquinanes, no such study had been possible before the alkylidene carbene route was developed. Understanding of stereoselectivity in the cycloaddition reaction to angularly fused triquinanes would provide valuable information for designing and planning the total synthesis of natural products possessing the triquinane structure.[14]

Results and Discussion

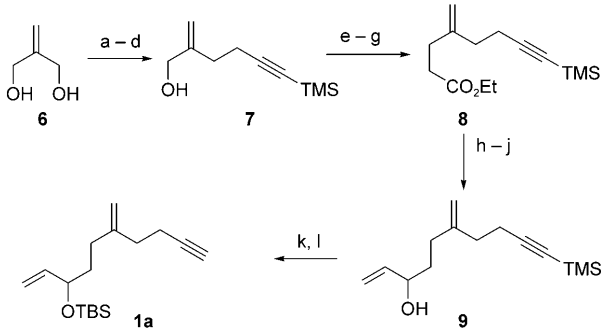
There are five positions in the dieneyne precursor **A** that can induce stereoselectivity during the tandem cycloaddition reaction to form angularly fused triquinanes. A silylated hydroxy group was introduced into each of these five positions to examine the stereoselectivity during the [2+3] cycloaddition reaction (Scheme 1).

Preparation of the Substrates for Tandem Cycloaddition Reaction

The synthesis of **1a** started from **6** (Scheme 2). Selective monoprotection of a hydroxy group with a *tert*-butyldimethylsilyl group[15] and activation of the remaining alcohol as mesylate, followed by copper-catalyzed propargylation, produced **7** after deprotection of the silyl group. The alcohol was activated as mesylate, and malonate ester synthesis protocol produced **8**. The ester of **8** was converted into the corresponding aldehyde and then vinyl Grignard addition to the aldehyde produced **9**. Protection of the alcohol of **9** followed by the liberation of terminal alkyne produced **1a**.

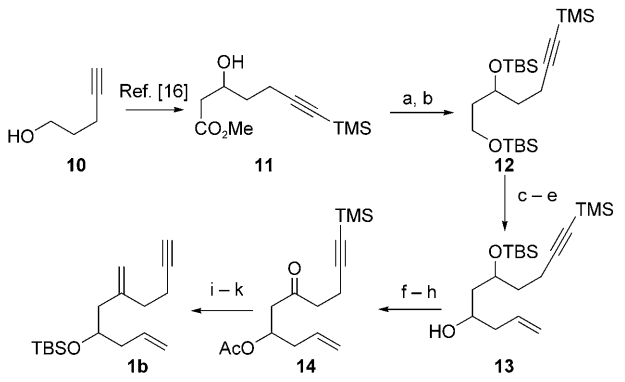


Scheme 1. Asymmetric induction in the TMM diyl [2+3] cycloaddition reaction.

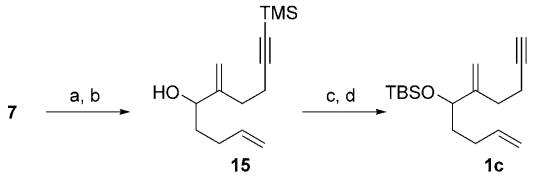


Scheme 2. Reagents and conditions: a) TBSCl, NaH/THF, 86%; b) MsCl, Et_3N/CH_2Cl_2; c) TMS-propargyl Grignard, CuCN/Et_2O, 68% for two steps; d) 1 N HCl/THF, 99%; e) MsCl, Et_3N/CH_2Cl_2; f) diethyl malonate, NaH/THF, 86% for two steps; g) NaCl, H_2O/DMSO, reflux, 66%; h) $LiAlH_4/Et_2O$, 0°C, 99%; i) $(COCl)_2$-DMSO; Et_3N/CH_2Cl_2, −60°C–RT, 96%; j) vinyl Grignard/THF, 0°C, 76%; k) TBSOTf, 2,6-lutidine/CH_2Cl_2, 92%; l) K_2CO_3/MeOH, 97%.

Substrate **1b** was prepared from pentynol (Scheme 3). From pentynol, **11** was prepared by following a literature preparation.[16] The ester group of **11** was reduced using DIBAL-H to form the diol product and both hydroxy groups of the product were protected as silyl ethers to produce **12**. Selective deprotection of the primary alcohol of **12**[17] and subsequent oxidation followed by allyl Grignard addition produced **13**. The free hydroxy group was protected temporarily as an acetate, and deprotection of the silyl group followed by oxidation produced ketone **14**. Olefination of the ketone of **14** under neutral reaction conditions[18] and protecting group exchange yielded **1b**.



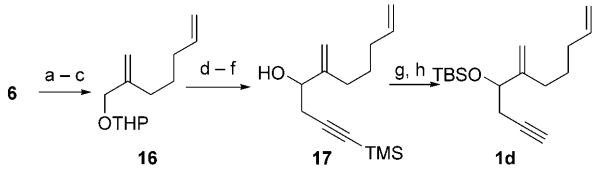
Scheme 3. Reagents and conditions: a) $LiAlH_4/Et_2O$, 85%; b) TBSOTf, 2,6-lutidine/CH_2Cl_2, 96%; c) HF-pyr/THF, 85%; d) $(COCl)_2$-DMSO; Et_3N/CH_2Cl_2, −60°C–RT, 96%; e) allyl Grignard/Et_2O, 0°C, 74% for two steps; f) Ac_2O, Et_3N, DMAP/CH_2Cl_2, 95%; g) 1N HCl/THF, 71%; h) PCC/CH_2Cl_2, 92%; i) CH_2I_2, Zn, $TiCl_4$/THF, 42%; j) K_2CO_3/MEOH, 92% k) TBSOTf, 2,6-lutidine/CH_2Cl_2, 86%.



Scheme 4. Reagents and conditions: a) TPAP, NMO/CH_2Cl_2; b) 3-butenyl Grignard/Et_2O, 84% for two steps; c) TBAF/THF, 91%; d) TBSOTf, 2,6-lutidine/CH_2Cl_2, 98%.

Substrate **1c** was prepared from **7** (Scheme 4). Oxidation of the alcohol to the corresponding aldehyde followed by the addition of 3-butenyl Grignard reagent produced **15**. Silyl protection after desilylation of the alkyne produced **1c**.

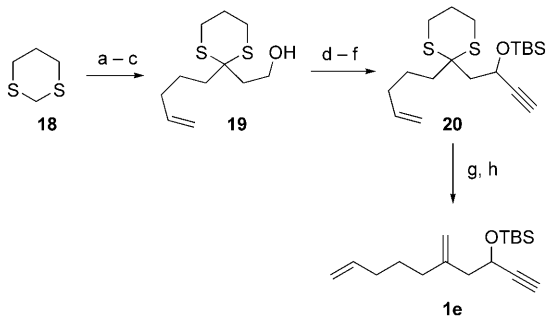
Substrate **1d** also was preprared from hydroxymethallyl alcohol **6** (Scheme 5). Selective protection of one of the two



Scheme 5. Reagents and conditions: a) DHP, PPTS/CH_2Cl_2, 50%; b) MsCl, Et_3N/CH_2Cl_2; c) 3-butenyl Grignard, CuCN/Et_2O, 87% for two steps; d) TsOH/MeOH, 95%; e) TPAP, NMO/CH_2Cl_2; f) TMS-propargyl Grignard/Et_2O, 69% for two steps; g) TBAF/THF, 90%; h) TBSOTf, 2,6-lutidine/CH_2Cl_2, 93%.

alcohols as the THP ether and butenylation after activation of the remaining alcohol as mesylate afforded **16**. The alcohol that was obtained from deprotection of the THP group of **16** was oxidized to the aldehyde, and propargyl Grignard addition to the aldehyde produced **17**. Silyl protection of the alcohol after the desilylation of alkyne produced **1d**.

The synthesis of **1e** started from 1,3-dithiane anion alkylation reactions (Scheme 6).[19] 1,3-Dithiane was alkylated

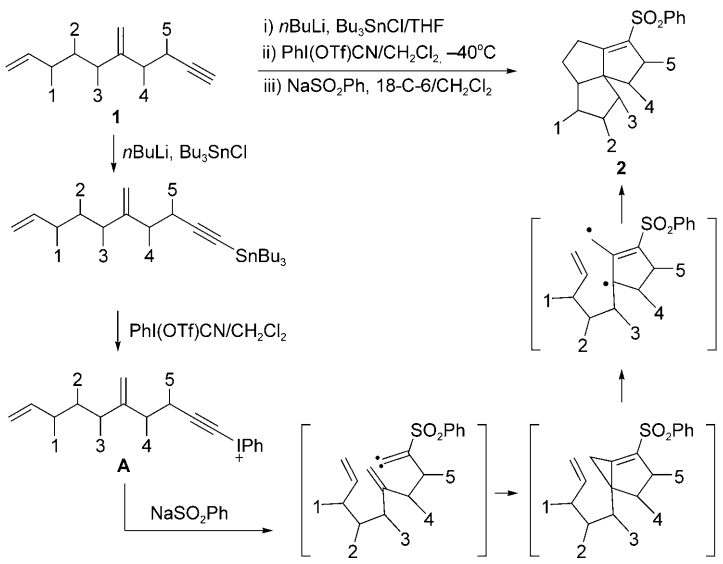


Scheme 6. Reagents and conditions: a) *n*BuLi, 5-bromopent-1-ene/THF 95%; b) *n*BuLi, $BrCH_2CH_2OTBS$/THF, 68%; c) TBAF/THF, 90%; d) TFAA-DMSO; Et_3N/CH_2Cl_2, −60°C–RT, 67%; e) HCCMgBr/Et_2O, 0°C, 66%; f) TBSOTf, 2,6-lutidine/CH_2Cl_2, 95%; g) $PhI(TFA)_2/CH_3CN$-H_2O, 70%; h) CH_2I_2, Zn, $TiCl_4$/THF, 33%.

twice with 5-bromopent-1-ene and silyl-protected bromoethanol to afford **19** after deprotection of the silyl protecting group. The alcohol of **19** was oxidized to the corresponding aldehyde, and acetylide anion addition to the aldehyde produced **20** after protection of the resulting alcohol. The thioacetal of **20** was liberated to the ketone,[20] and olefination of the ketone furnished **1e**.

Stereoselectivity in the Tandem Cycloaddition Reaction of Linear Substrates with OTBS Substituents in the Formation of Angularly Fused Triquinanes

The prepared substrates **1a–e** were converted into alkynyl iodonium salts, and alkylidene carbenes were generated from the alkynyl iodonium salts by the addition of phenylsulfinate anion to the β-position of the alkynes. The alkylidene carbenes underwent tandem cycloaddtion reaction to form angularly fused triquinanes (Scheme 7) and the results are summarized in the Table 1.



Scheme 7. Preparation of iodonium salts and tandem cycloaddition reaction.

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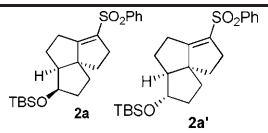
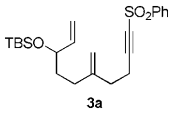
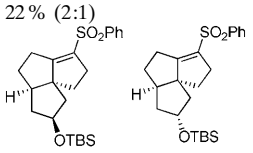
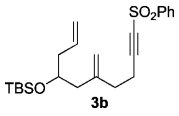
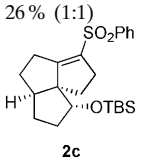
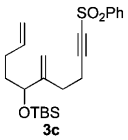
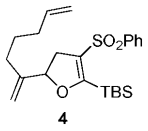
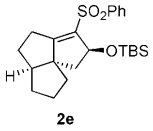
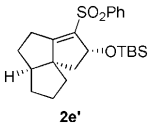
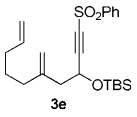
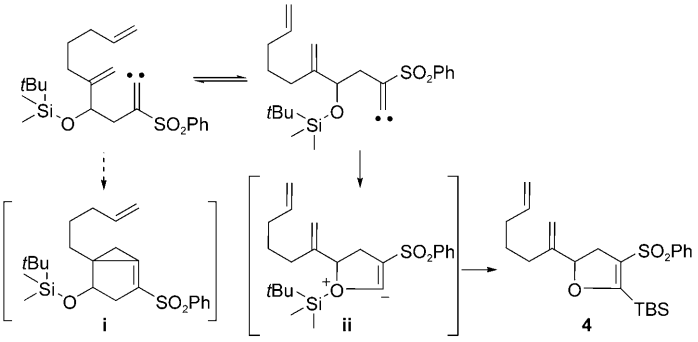
Table 1. Products from tandem cycloaddition reaction of alkylidene carbenes.

Precursor	Products and yield[a]		
1a			
	22% (2:1)		26%
1b			
	26% (1:1)		28%
1c			
	21%		33%
1d			
	74%		
1e			
	36%	15%	13%

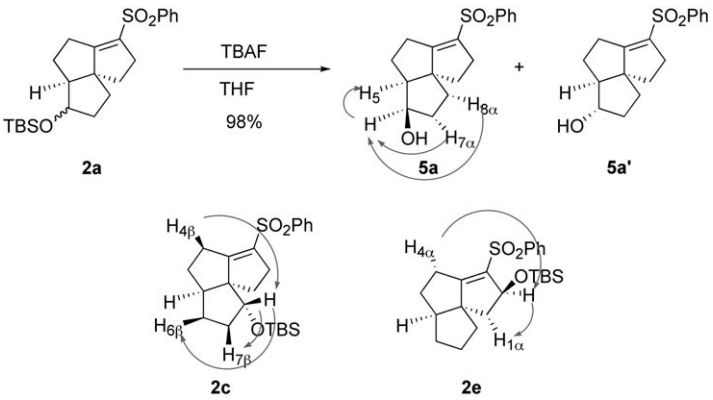
[a] Yield of isolated product. The product ratios in the parenthesis were determined by ^{1}H NMR integration of the crude product mixtures.

Synthesis of angularly fused triquinanes from linear substrates **1a–e** was initiated by the introduction of an iodophenyl group to the end of the terminal alkynes via $SnBu_3$ substitution. When the phenylsulfinate anion was added to the alkynyl iodonium salts, the alkylidene carbenes were generated, and subsequent cyclopropanation followed by TMM formation set the stage for a possible stereoselective [2+3] cycloaddition reaction. Though the triquinane formation through alkylidene cabene formation was accompanied by rearrangement of the alkylidene carbene to phenyl sulfone, this side reaction would not affect the stereoselectivity during the cycloaddition reaction. The cycloaddition reaction of **1a** produced a mixture of two diastereomeric products in 2:1 ratio. When the substitution was moved to position 2, no stereoselecitivity was observed, as the cycloaddition reaction of **1b** produced an equal amount of two diastereomeric products. To our delight, when the substituent was moved to position 3, only a single isomeric triquinane product was obtained. In the case of the substrate **1e**, the cycloaddition reaction produced a mixture of two diastereomeric products in 2:1 ratio. Contrary to other substrates, **1d** produced a completely different type of product through carbene insertion reaction (Scheme 8). Alkylidene carbene was inserted into the O–Si bond to form a dihydrofuran[21] instead of undergoing cyclopropanation reaction. The insertion reaction into the O–Si bond appears to be as facile as the insertion reaction into the C–H bond. This result indicates that position 4 cannot accommodate substituents where carbene insertion could occur.



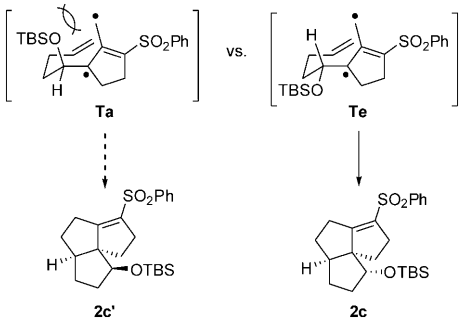
Scheme 8. Cyclopropanation versus insertion reaction.

The stereochemistry of the products was confirmed by NOE experiments (Scheme 9). Since **2a** and **2a′** were not separable, the corresponding diastereomeric alcohols **5a** and **5a′** were prepared through deprotection of the silyl groups and then separated. The NOE experiment on **5a** showed that the carbinol proton has interactions with protons H_5, $H_{7\alpha}$, and $H_{8\alpha}$, which confirmed the relative stereochemistry of **5a**. In the case of **2c**, interaction of the carbinol proton with $H_{4\beta}$ clearly confirmed the relative stereochemistry. Interaction of the carbinol proton of **2e** with $H_{4\alpha}$ also confirmed the relative stereochemistry of **2e**. This result showed that only position 3 can induce a good diastereoselectivity during the [2+3] cycloaddition reaction while positions 1 and 5 have little influence in the diastereoselectivity. Position 2 did not appear to influence the stereochemical outcome of the cycloaddition reaction.



Scheme 9. Confirmation of stereochemistry of the products by NOE experiments.

The diastereoselectivity of the cycloaddition reaction can be explained through the transition-state model (Scheme 10). The transition-state model clearly distinguishes the pseudo-equatorially positioned OTBS group from the



Scheme 10. Transition-state model of the [2+3] cycloaddition reaction.

pseudo-axially positioned one at position 3. The pseudo-axially oriented OTBS group shows a 1,3-diaxial interaction with the methyl group of the five-membered ring. This steric bias led to the complete stereoselectivity of the cycloaddition reaction of **1c**. On the other hand, substitution at position 2 would be far from the other part of the molecule and thus shows no influence on the diastereoselectivity. The current model also explains why there is only a small bias for the two diastereomeric products in the transition state during the cycloaddition reactions of **1a** and **1e**. The substituent at position 1 or 5 does not appear to provide substantial steric bias in the transition state to distinguish the two products.

Conclusions

In summary, substituent effects on the diastereoselectivity during TMM diyl [2+3] cycloaddition reaction were investigated. Among five positions for a substituent effect, only position 3 provides a good diastereoselectivity. Position 4 turned out to be incompatible with the alkylidene carbene mediated TMM diyl [2+3] cycloaddition reaction. Substituents at the other positions showed little or no stereoselectivity during the cycloaddition reaction.

This result provides a good guideline for the alkylidene-mediated TMM diyl [2+3] cycloaddtion reaction in application to the stereoselective total synthesis of many angularly fused triquinane natural products as most of angularly fused triquinanes in nature have substituents at position 3.[22] Application of this diastereoseletive cycloaddition reaction to the total synthesis of angularly fused triquinane natural products will be communicated in due course.

Experimental Section

General experimental procedure for cycloaddition reaction: To a stirred solution of alkyne **1a–e** (1 equiv) in THF (20 mL mmol^{-1}) was added *n*BuLi (1.2 equiv) at −78 °C. After the reaction mixture was stirred for 1 h, tributyltin chloride (1.1 equiv) was added. The reaction mixture was allowed to warm to room temperature and stirred overnight. The resulting mixture was quenched with saturated NH_4Cl solution and extracted with EtOAc. The organic layers were combined and dried over $MgSO_4$. The filtrate was concentrated in vacuo to yield the tin compound, which was used for the next step. To a stirred solution of tin compound in CH_2Cl_2 (100 mL mmol^{-1}) was added a solution of phenyl(cyano)iodonium triflate (1.2 equiv) at −40 °C under argon. The reaction mixture was stirred for 15 min and formed a clear solution at −40 °C. Then, the reaction mixture was added to a solution of benzenesulfinic acid sodium salt (2 equiv) and [18]crown-6 (2 equiv) in CH_2Cl_2 (200 mL mmol^{-1}) at room temperature. The resulting reaction mixture was stirred and was quenched with saturated NH_4Cl solution and extracted with CH_2Cl_2. The organic layers were combined and dried over $MgSO_4$. The filtrate was concentrated in vacuo, and the residue was purified by flash column chromatography on silica gel to give the products.

Compound **3a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (2H, d, J = 7.2 Hz), 7.66–7.62 (1H, m), 7.56–7.53 (2H, m), 5.79–5.70 (1H, m), 5.12 (1H, dt, J = 17.2 Hz, J = 1.5 Hz), 5.02 (1H, dd, J = 11.6 Hz, J = 1.2 Hz), 4.73 (1H, s), 4.66 (1H, s), 4.07 (1H, q, J = 6.0 Hz), 2.47 (2H, t, J = 7.4 Hz), 2.23 (2H, t, J = 7.5 Hz), 2.02–1.89 (2H, m), 1.58–1.50 (2H, m), 0.87 (9H, s), 0.01 (3H, s), 0.00 ppm (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.3, 142.0, 141.3, 133.9, 129.2, 127.2, 114.0, 110.6, 97.0, 78.5, 73.3, 36.0, 33.3, 31.0, 25.8, 28.2, 17.7, −4.3, −4.8 ppm.

Compound **5a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.84 (2H, m), 7.58–7.57 (1H, m), 7.53–7.49 (2H, m), 4.36–4.31 (1H, m), 3.05–2.99 (1H, m), 2.85–2.79 (1H, m), 2.56 (1H, dd, J = 14.8 Hz, J = 8.0 Hz), 2.32–2.25 (2H, m), 2.14–2.09 (1H, m), 1.87–1.77 (3H, m), 1.68–1.61 (3H, m), 1.35–1.29 (1H, m), 1.25–1.22 ppm (1H, m)

Compound **5a′**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.84 (2H, m), 7.61–7.49 (3H, m), 4.07–4.05 (1H, m), 3.01 (1H, dd, J = 15.7 Hz, J = 7.0 Hz), 2.90–2.81 (1H, m), 2.58–2.52 (1H, m), 2.29–2.21 (1H, m), 2.17–2.08 (2H, m), 2.02–1.94 (4H, m), 1.89–1.84 (1H, m), 1.78–1.70 ppm (3H, m).

Compound **2b+2b′**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (4H, d, J = 7.3 Hz), 7.59–7.56 (2H, m), 7.52–7.48 (4H, m), 7.52–7.48 (4H, m), 4.34–4.31 (1H, m), 4.07–4.03 (1H, m), 3.04–2.94 (2H, m), 2.82–2.73 (2H, m), 2.57–2.46 (3H, m), 2.28–2.18 (2H, m), 2.14 (2H, dd, J = 12.1 Hz, J = 5.7 Hz), 2.02–1.92 (3H, m), 1.91–1.86 (2H, m), 1.83–1.75 (3H, m), 1.73–1.64 (3H, m), 1.49–1.44 (2H, m), 1.37–1.33 (2H, m), 0.84 (9H, s), 0.82 (9H, s), 0.01 (3H, s), 0.01 (3H, s), 0.00 (3H, s), −0.01 ppm (3H, s).

Compound **3b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.96 (2H, m), 7.66–7.63 (1H, m), 7.57–7.53 (2H, m), 5.81–5.70 (1H, m), 5.03–4.97 (2H, m), 4.78 (1H, s), 4.75 (1H, d, J = 1.1 Hz), 3.78–3.72 (1H, m), 2.48 (2H, t, J = 7.2 Hz), 2.26 (2H, t, J = 7.4 Hz), 2.21–2.03 (4H, m), 0.83 (9H, s), 0.01 (3H, s), −0.03 ppm (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.5, 142.1, 134.9, 133.9, 129.2, 127.2, 117.2, 113.7, 97.0, 78.6, 71.0, 43.1, 41.5, 33.7, 25.8, 18.0, 17.7, −4.5, −4.5 ppm.

Compound **2c**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.84 (2H, m), 7.56–7.54 (1H, m), 7.50–7.46 (2H, m), 3.80 (1H, dd, J = 9.8 Hz, J = 5.8 Hz), 3.05 (1H, dd, J = 18.6 Hz, J = 7.2 Hz), 2.81–2.77 (1H, m), 2.54 (1H, dd, J = 14.4 Hz, J = 9.2 Hz), 2.47 (1H, dd, J = 12.1 Hz, J = 6.6 Hz), 2.34–2.29 (1H, m), 2.09–2.03 (2H, m), 1.96–1.92 (1H, m), 1.82–1.76 (1H, m), 1.69–1.63 (1H, m), 1.57–1.47 (3H, m), 1.16–1.14 (1H, m), 0.74 (9H, s), −0.09 (3H, s), −0.24 ppm (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 141.2, 132.9, 131.0, 129.0, 127.5, 79.1, 71.8, 45.5, 36.4, 36.0, 34.8, 32.7, 28.8, 25.7, 24.3, 17.8, −4.8, −5.3 ppm.

Compound **3c**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.96 (2H, m), 7.66–7.62 (1H, m), 7.56–7.53 (2H, m), 5.80–5.70 (1H, m), 4.99–4.91 (3H, m), 4.73 (1H, s), 4.03 (1H, t, J = 6.4 Hz), 2.54 (2H, t, J = 7.5 Hz), 2.35–2.28 (1H, m), 2.23–2.15 (1H, m), 2.02–1.87 (2H, m), 1.59–1.42 (2H, m), 0.84 (9H, s), 0.00 (3H, s), −0.07 ppm (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.4, 142.0, 138.3, 133.9, 129.2, 127.3, 114.7, 111.5, 97.2, 78.5, 75.9, 35.7, 29.7, 27.8, 25.8, 18.1, 18.0, −4.6, −5.0 ppm.

Compound **4**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.84 (2H, m), 7.57–7.49 (3H, m), 5.74–5.69 (1H, m), 5.06–4.91 (4H, m), 4.84 (1H, s), 2.90 (1H, dd, J = 14.4 Hz, J = 11 Hz), 2.57 (1H, dd, J = 14.4 Hz, J = 9.8 Hz), 2.02–1.87 (4H, m), 1.51–1.47 (2H, m), 0.99 (9H, s), 0.38 (3H, s), 0.35 ppm (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.8, 147.0, 141.5, 138.2, 132.7, 129.0, 127.2, 124.5, 114.9, 110.9, 86.9, 36.1, 33.4, 30.4, 26.9, 26.6, 17.5, −4.9, −5.0 ppm.

Compound **2e**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.87–7.85$ (2H, m), 7.54–7.50 (1H, m), 7.47–7.44 (2H, m), 5.15 (1H, d, $J = 5.6$ Hz), 3.05–2.98 (1H, m), 2.37–2.28 (1H, m), 2.16–2.04 (2H, m), 1.97–1.85 (3H, m), 1.80–1.65 (4H, m), 1.64–1.56 (1H, m), 1.45–1.37 (1H, m), 0.74 (9H, s), 0.01 (3H, s), −0.03 ppm (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 177.7$, 142.9, 132.5, 131.3, 128.8, 126.8, 80.6, 67.7, 48.9, 46.9, 41.1, 34.9, 34.8, 27.1, 25.7, 24.9, 17.7, −4.8, −5.0 ppm.

Compound **2e′**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.87–7.84$ (2H, m), 7.51–7.43 (3H, m), 5.43–5.39 (1H, m), 2.86 (1H, ddd, $J = 16.8$ Hz, $J = 7.8$ Hz, $J = 2.1$ Hz), 2.46–2.36 (1H, m), 2.29 (1H, dd, $J = 11.6$ Hz, $J = 5.6$ Hz), 2.18–2.11 (1H, m), 2.01–1.91 (2H, m), 1.74–1.59 (4H, m), 1.50–1.46 (1H, m), 1.42–1.34 (2H, m), 0.72 (9H, s), 0.01 (3H, s), −0.01 ppm (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 173.1$, 143.1, 132.3, 131.6, 128.6, 126.8, 79.9, 63.7, 52.2, 47.2, 39.2, 34.9, 33.2, 27.3, 25.9, 25.8, 18.0, −4.7, −4.9 ppm.

Compound **3e**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.98–7.96$ (2H, m), 7.68–7.64 (1H, m), 7.57–7.54 (2H, m), 5.79–5.71 (1H, m), 5.00–4.92 (2H, m), 4.79 (1H, d, $J = 1.2$ Hz), 4.74 (1H, s), 4.52 (1H, t, $J = 6.8$ Hz), 2.36 (2H, d, $J = 6.8$ Hz), 2.02–1.94 (4H, m), 1.49–1.41 (2H, m), 0.79 (9H, s), 0.00 (3H, s), −0.02 ppm (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 143.5$, 141.6, 138.5, 134.1, 129.3, 127.5, 114.7, 113.7, 95.7, 81.3, 62.2, 43.7, 35.5, 33.2, 26.8, 25.5, 18.0, −4.9, −5.2 ppm.

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