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Ring-Closing Enyne Metathesis of Terminal Alkynes with Propargylic Hindrance

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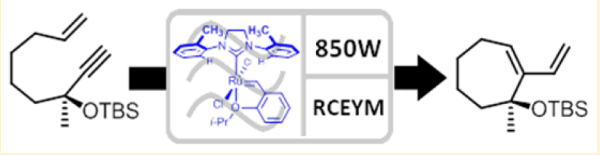
Supporting Information

ABSTRACT: The ring closing enyne metathesis of substrates with propargylic hindrance was investigated, revealing the successful combination of the Stewart-Grubbs catalysts and microwave heating sometimes up to 170 °C for oxacycles. Medium-sized rings were obtained from terminal alkynes previously reputed as reluctant substrates. This unmatched combination was applied to the synthesis of carbocycles and oxacycles. In addition, this is the first report on the use of the Stewart Grubbs catalyst in ring closing enyne metatheses.



Ring-closing enyne metathesis (RCEYM) is a powerful synthetic tool compatible with a wide range of substrates for the preparation of ring-embedded 1,3-dienes and highly functionalized chemical entities.[1] To perform such transformations, the first- and second-generation Grubbs (**1**, **2**) and Hoveyda-Grubbs (**3**, **4**) catalysts have been routinely used (Figure 1). Yet in some cases, the efficiency of these nowadays

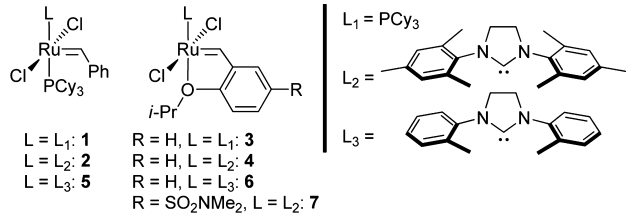


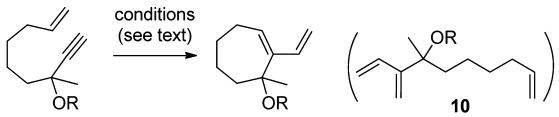
Figure 1. Structure of some ruthenium-based metathesis catalysts used in this study (in total, 14 catalysts were tested, the structures of which are provided in Figure S1).

classical catalysts can be limited, particularly when hindered substrates are implemented.[2] This may discourage the use of this methodology in synthetic strategies where hindered alkynes are required.

With olefin metatheses, this problem has been solved by the use of less hindered ruthenium catalysts compatible with sterically crowded olefins, either for ring-closing or cross metathesis. Grubbs and co-workers developed an *o*-tolyl substituted catalyst (**6**) and reported its efficiency toward the formation of tetrasubstituted olefins by RCM.[3] They also highlighted cross metathesis improvement when this catalyst was used for the formation of disubstituted olefins containing one or more allylic substituents.[4] The drawbacks associated with the RCEYM of alkynes with hindered propargylic positions[2] compelled us to test catalyst **6** in this transformation. Curiously the use of **6** in RCEYM has never been reported in the literature even if it was previously found effective, along with other catalysts drawn in Figure 1, in enyne cross-metathesis with strained geminally substituted alkenes.[5] Herein, we report the efficacy of the *o*-tolyl substituted Stewart-Grubbs catalyst **6** when combined with microwave heating for the RCEYM of substrates hindered at the propargylic position, leading to the synthesis of carbocyclic and oxacyclic 1,3-dienes.

RCEYMs toward seven-membered rings (**9a**–**c**) were first investigated in the course of a natural product synthesis.[6] After having synthesized the 1,8-enyne substrates **8a**–**c** (Scheme 1)

Scheme 1. RCEYM toward Vinylcycloheptenes 9a–c from Enynes Substrates 8a–c



in two steps from 4-pentenal,[7] RCEYMs were attempted in a wide range of conditions, including the use of an ethylene atmosphere (Mori's conditions)[8] which only resulted in the formation of acyclic dienes (**10**). Most of the 14 commercially available catalysts which were screened in this preliminary study (see the Supporting Information for a complete list, Figure S1)

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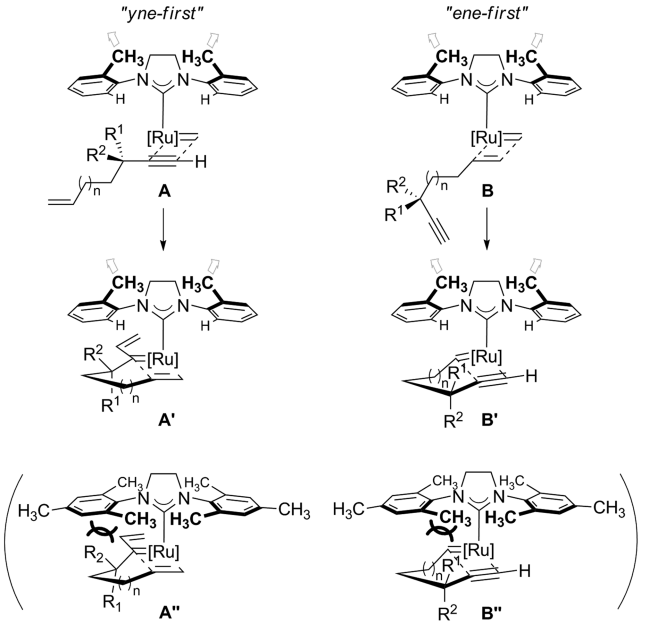
proved unsuccessful with the exception of a few of them. This initial screening was performed with a 5 mol % catalyst loading and resulted in the selection of the five catalysts **2**, **4**, **5**, **6**, and **7** (Figure 1), respectively, providing 8%, 6%, 38%, 38%, and 4% of partial conversion[9] of enyne substrate **8c** (R = TBS) into cycloheptene **9c**, when running the reaction in toluene at 80 °C during 48 h with complete *exo* regioselectivity. With **6**, increasing catalyst loading to 10 mol % only resulted in a slightly better conversion rate of 42% for **9c**. Under similar conditions at 5 mol % catalyst, the tertiary alcohol **8a** was unreactive and the acetate **8b** only poorly reactive, giving **9b** in 7%, 10%, and 5% yields with catalysts **5**, **6**, and **7**, respectively (**2** and **4** did not induce any reaction with **8a** and **8b**), and showing at this stage a slight superiority of the *o*-tolyl substituted Stewart-Grubbs catalysts with this propargylic acetate.

Less bulky NHC-substituants like L_3 (Figure 1) have demonstrated their utility to improve catalyst reactivity toward hindered substrates in olefin metathesis.[3,4] In fact, structural studies on catalyst **6** showed that the *N*-aryl rings are bearing both methyl substituents on the more sterically accessible face. The methyls are squeezed out, thus opening the space near the ruthenium center and enhancing the reactivity of the catalyst toward sterically demanding substrates.[10] With compound **8c**, this would favor the coordination of ruthenium by the hindered alkyne (**A**-**A**′, yne-first mechanism, Scheme 2) or ring closing after alkylidene formation with the alkene (**B**-**B**′, ene-first mechanism), which would not be possible with an *N*-mesityl NHC ligand on ruthenium (**A**″, **B**″).

Scheme 2. Steric Model to Explain the Reactivity of 6 with Hindered Enynes (Grey Arrows Figure out Methyls Drawn Aside)



Yet, dealing with the yield obstacle, the use of microwave irradiation, constituting an attractive alternative to conventional heating,[11,12] was rapidly envisaged in this study. In many cases, microwaves have been shown to dramatically reduce reaction times and increase product yields and purity by preventing side reactions. The outstanding benefit provided with microwaves for olefin metathesis has been well reviewed,[13] while examples of microwave-assisted enyne metathesis also demonstrated their indisputable effect in RCEYM.[14,15] The TBS-protected substrate **8c** was therefore gambled into microwave irradiations. Gratifyingly, performing the reaction in toluene at 120 °C under microwave (850 W) for 1 h in the presence of 10 mol % of the selected catalysts **2**, **4**, **6**, **5**, and **7** dramatically enhanced the reaction yields and reaction times (Table 1). It is worth

Table 1. RCEYM of Enynes 8b and 8c into Cycloheptenes 9b and 9c under Microwave Conditions (see Scheme 1)

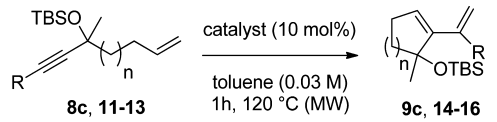
entry	catalyst[a]	substrate[b]	conditions	yields (%)
1	**2**	**8c** (R = TBS)	120 °C, MW, 1 h	13
2	**4**	**8c** (R = TBS)	120 °C, MW, 1 h	24
3	**5**	**8c** (R = TBS)	120 °C, MW, 1 h	79
4	**6**	**8c** (R = TBS)	120 °C, MW, 1 h	88
5	**7**	**8c** (R = TBS)	120 °C, MW, 1 h	17
6	**6**	**8c** (R = TBS)	80 °C (oil bath), 2 d	33
7	**6**	**8c** (R = TBS)	120 °C (sealed tube), 1 h	48
8	**2**	**8b** (R = Ac)	120 °C, MW, 1 h	<1
9	**4**	**8b** (R = Ac)	120 °C, MW, 1 h	<1
10	**6**	**8b** (R = Ac)	120 °C, MW, 1 h	55

[a]Catalyst loading: 10 mol % except Entry 10:15 mol %. [b]Concentration: 0.03 M in toluene.

noting that the best yields were still obtained with the *o*-tolyl substituted catalysts **5** and **6** (entries 3 and 4), confirming our previous observations, with the Stewart-Grubbs catalyst **6** being the most efficient, affording diene **9c** in 88% isolated yield (entry 4). Comparatively, the second generation Grubbs (**2** and **4**) and Zhan-1B (**7**) catalysts only provided low yields between 13% and 24% (entries 1, 2, and 5). In addition, the more challenging acetate substrate **8b** could also be converted into diene **9b** in a reasonable 55% yield, yet in the presence of 15 mol % of the Stewart-Grubbs catalyst **6** (entry 10). This successful combination of a microwave facility and *o*-tolyl substituted ruthenium catalysts (**5** and **6**) on the RCEYM of challenging substrates would thus allow swift access to highly functionalized dienes in excellent yields and purity. To extend the scope of these conditions, the methodology was applied to the synthesis of small to medium-sized rings in the carbo- and oxacycle series.

As depicted in Table 2, the synthesis of various carbocycles was achieved and allowed comparing the reactivity of catalysts **2** and **4** with the less-hindered one **6** under our optimized conditions. The reactions ran through in every case with these

Table 2. Synthesis of Various Carbocycles through RCEYM Involving Catalysts 2, 4, and 6



8c, **11-13**
R = H or Me

9c, **14-16**
R = H or Me

				yield per cat. (%)		
entry	n	R	product	**2**	**4**	**6**
1	1 (**11**)	H	**14**	13	40	51
2	2 (**12**)	H	**15**	68	74	74
3	3 (**8c**)	H	**9c**	13	24	88
4	3 (**13**)	Me	**16**	59	63	63

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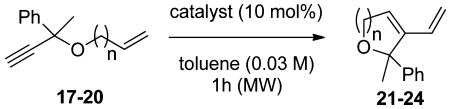
three catalysts. For terminal alkynes **8c**, **11**, and **12** (entries 1−3), the best yields were observed for 5- (**14**) and 7-membered (**9c**) carbocycles with the Stewart-Grubbs catalyst **6**, again showing its versatility. With the propynyl derivative **13** (R = Me, entry 4), **6** did not bring a real advantage compared to **2** and **4**, as expected from the existing literature on the reactivity of propynyl substrates, especially in the oxacycle series.[16] The scope of this RCEYM was extended to oxacycles **21**−**24** with monosubstituted alkynes **17**−**20**, showing again the advantage of **6** when a propargylic hindrance is present (Table 3). In

Table 3. Synthesis of Various Oxacycles through RCEYM Involving Catalysts 2, 4, and 6



17-20 21-24

				yield per catalyst[a] (%)		
entry	n	product	T (°C)	**2**	**4**	**6**
1	1 (**17**)	**21**	120	42	28	95
2	3 (**18**)	**22**	170	55	64	70
3	4 (**19**)	**23**	170	28	13	63
4	5 (**20**)	**24**	170	n.r.	n.r.	n.r.

[a]n.r.: no reaction.

addition to providing good to excellent yields, the combination of catalyst **6** and microwave heating at 170 °C allowed for the first time the access to a eight-membered oxacyclic diene (**23**) by RCEYM from a terminal alkyne[17] with a yield of 63% (entry 3, n = 4) strikingly contrasting with the results obtained with **2** and **4**. Even though these results could not be transposed to the formation of a nine-membered ring like **24** (entry 4, n = 5), this tremendous reactivity confirmed the efficacy of the Stewart-Grubbs catalyst **6** for the microwave-assisted RCEYM of hindered substrates in the oxacycle series.

In summary, we have investigated the application of RCEYM to alkyne substrates with steric hindrance at the propargylic position. The conversion into the corresponding vinyl cycloalkenes was achieved with exclusive *exo* selectivity by combining the attractive reactivity of the Stewart-Grubbs catalyst **6** with microwave irradiations. This method was extended to the synthesis of carbocycles and oxacycles and in most cases demonstrated its superiority by comparison with other available catalysts, while in the worst case, the catalyst showed equivalent efficacy as **2** and **4**. Consequently, we suggest that these conditions could be generalized as first-to-use with such hindered alkynes.

EXPERIMENTAL SECTION

General Information. All reactions were carried out in oven-dried reaction vessels under an atmosphere of argon and in anhydrous solvents. Reactions under microwave conditions were carried out in an Anton Paar Microwave 300 apparatus (850) equipped with an infrared external temperature sensor and a stirrer. Reactions and purifications were monitored by TLC on silica gel 60 F254 aluminum, using UV absorption, then vanillin−H_2SO_4 (1% vanillin in ethanol +2% H_2SO_4) as staining system. The products were purified by flash chromatography on silica gel Si 60, 40−63 μm. NMR spectra were recorded on 400 and 600 MHz spectrometers. Chemical shifts (δ) are quoted in ppm with internal calibration from the residual solvent peak ($CHCl_3$: 7.27, 77.0 ppm for ^{1}H and ^{13}C NMR, respectively). All coupling constants (J) are quoted in Hertz. The following abbreviations are used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet, br = broad. High resolution mass spectra (HRMS) of synthesized compounds were measured on a Qq-ToF spectrometer using electrospray ionization (ESI). Infrared spectra were recorded on a FTIR spectrometer. The following compounds used in this study were prepared according to the literature: *tert*-butyldimethyl[(4-methyldeca-9-en-2-yn-4-yl)oxy]silane (**13**),[20] hept-6-en-2-one,[21] 3-phenylbut-1-yn-3-ol,[22] [3-(allyloxy)but-1-yn-3-yl]-benzene (**17**),[23] [3-(pent-4-en-1-yloxy)but-1-yn-3-yl]benzene (**18**),[22] and [3-(hex-5-en-1-yloxy)but-1-yn-3-yl]benzene (**19**).[22]

*3-Methylnon-8-en-1-yn-3-ol (**8a**).* To a solution of oct-7-en-2-one[18,19] (114.8 mg, 0.91 mmol) in THF (10 mL) was added sodium acetylide (18% slurry in xylene, 0.56 mL, 1.82 mmol) and the mixture was stirred at room temperature for 16 h. The reaction mixture was slowly quenched using a saturated aqueous solution of NH_4Cl (8 mL), extracted with Et_2O (3 × 10 mL), washed with brine (10 mL), and concentrated under reduced pressure. The crude material was purified by chromatography on silica gel (pentane/ether 8:2), to afford **8a** as a pale yellow liquid (123.6 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39−1.59 (m, 7H), 1.64−1.71 (m, 2H), 1.84 (brs, 1H), 2.05−2.13 (m, 2H), 2.43 (s, 1H), 4.91−5.06 (m, 2H), 5.75−5.88 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.1, 29.0, 29.7, 33.7, 43.3, 68.1, 71.3, 87.7, 114.5, 138.8. IR (NaCl): ν = 3391, 3078, 2978, 2936, 2858, 2110, 1643, 1373, 1265, 910, 741 cm^{-1}. HRMS (ESI+) m/z calc. for $C_{10}H_{15}$ $[M-OH^-]^+$ 135.1168; found: 135.1164.

*3-Methylnon-8-en-1-yn-3-yl acetate (**8b**).* To a solution of oct-7-en-2-one[18,19] (1 g, 7.92 mmol) in THF (79 mL) was added sodium acetylide (18% slurry in xylene, 7.33 mL, 23.8 mmol) and the mixture was stirred at room temperature for 16 h. The reaction mixture was quenched using acetic anhydride (2.25 mL, 15.85 mmol) while the mixture turned from yellow to white and was stirred 30 min at room temperature until complete conversion. Water (50 mL) was then added and the mixture was extracted with Et_2O (3 × 50 mL), washed with brine (50 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The crude material was purified by silica gel chromatography (pentane/ether 95:5), to afford **8b** as a colorless liquid (1.34 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.37−1.57 (m, 4H), 1.67 (s, 3H), 1.76−2.00 (m, 2H), 2.03 (s, 3H), 2.04−2.12 (m, 2H), 2.54 (s, 1H), 4.92−5.06 (m, 2H), 5.75−5.87 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.0, 23.5, 26.4, 28.7, 33.6, 41.1, 68.1, 73.3, 75.0, 114.5, 138.7, 169.4. IR (NaCl): ν = 3296, 3077, 2978, 2935, 2857, 2118, 1740, 1639, 1368, 1240 cm^{-1}. HRMS (ESI+) m/z calc. for $C_{12}H_{18}NaO_2$ $[M + Na]^+$ 217.1199; found: 217.1190.

*tert-Butyldimethyl[(3-methylnon-8-en-1-yn-3-yl)oxy]silane (**8c**).* To a solution of oct-7-en-2-one[18,19] (106.2 mg, 0.84 mmol) in dry THF (10 mL) was added sodium acetylide (18% slurry in xylene, 0.52 mL, 1.68 mmol) and the mixture was stirred at room temperature for 16 h. The reaction mixture was quenched using TBSOTf (0.39 mL, 1.68 mmol) while the mixture turned from yellow/orange suspension to clear yellow solution. After stirring for 10 min a saturated aqueous solution of NH_4Cl was added (10 mL), and the two phases were separated. The aqueous phase was extracted with Et_2O (3 × 15 mL), the combined layers were washed with brine (15 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was passed through a short silica gel pad (pentane) to afford **8c** as a colorless liquid (212 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.17 (s, 6H), 0.87 (s, 9H), 1.36−1.67 (m, 9H), 2.03−2.10 (m, 2H), 2.39 (s, 1H), 4.89−5.05 (m, 2H), 5.76−5.88 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ −3.1, −2.9, 18.0, 24.0, 25.7, 29.0, 30.9, 33.7, 45.0, 69.0, 71.7, 88.4, 114.3, 139.0. IR (NaCl): ν = 3310, 3078, 2978, 2953, 2930, 2907, 2888, 2857, 2110, 1642, 1472, 1464, 1252 cm^{-1}. HRMS (ESI+) m/z calc. for $C_{16}H_{30}OSi$ $[M + H]^+$.267.2139; found: 267.2153.

*3-Methyloct-7-en-1-yn-3-ol (**25**).* To a solution of hept-6-en-2-one[21] (201 mg, 1.78 mmol) in THF (18 mL) was added sodium acetylide (18% slurry in xylene, 0.66 mL, 2.15 mmol), and the mixture was stirred at room temperature for 6 h. The reaction mixture was quenched using a saturated aqueous solution of NH_4Cl (18 mL), extracted with Et_2O (3 × 20 mL), washed with brine (20 mL), and concentrated under reduced pressure. The crude material was purified by silica gel chromatography (pentane/ether 8:2), to afford the 3-methyloct-7-en-1-yn-3-ol **25** as a pale yellow liquid (77 mg, 31%). ^{1}H

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NMR (400 MHz, $CDCl_3$): δ 1.49 (s, 3H), 1.52−1.72 (m, 4H), 1.91 (s, 1H), 2.10 (dd, J = 6.9, 13.9 Hz, 2H), 2.43 (s, 1H), 4.94−5.06 (m, 2H), 5.75−5.87 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.8, 29.8, 33.6, 42.9, 68.0, 71.3, 87.6, 114.8, 138.4. IR (NaCl): ν = 3391, 3306, 3078, 2978, 2943, 2866, 2843, 2110, 1643, 1492, 1443, 1373, 1157, 1119, 914 cm^{-1}. HRMS (ESI$^+$) m/z calc. for C_9H_{13} [M−OH$^-$]$^+$ 121.1012; found: 121.1018.

*tert-Butyldimethyl[(3-methyloct-7-en-1-yn-3-yl)oxy]silane (**12**).* To a solution of 3-methyloct-7-en-1-yn-3-ol **25** (42.1 mg, 0.31 mmol) in CH_2Cl_2 (3 mL) were added 2,4,6-collidine (81 μL, 0.61 mmol) and TBSOTf (70 μL, 0.31 mmol). The reaction mixture was stirred for 1.5 h before adding a saturated aqueous solution of NH_4Cl (3 mL). The layer were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by silica gel chromatography (pentane) as eluent, to afford compound **12** as a colorless liquid (61.4 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.16 (s, 6H), 0.86 (s, 9H), 1.43 (s, 3H), 1.53−1.67 (m, 4H), 2.06 (dt, J = 6.5, 12.9 Hz, 2H), 2.39 (s, 1H), 4.90−5.07 (m, 2H), 5.75−5.88 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ −3.1, −2.9, 18.0, 23.7, 25.7, 31.0, 33.7, 44.6, 69.0, 71.8, 88.3, 114.4, 138.9. IR (NaCl): ν = 3310, 3078, 2951, 2931, 2859, 2112, 1474, 1254, 1119, 1084, 837, 775 cm^{-1}. HRMS (ESI$^+$) m/z calc. for $C_{15}H_{29}OSi$ [M + H]$^+$ 253.1982; found: 253.1980.

General Procedure for Tertiary Alcohol Alkylation of 3-Phenylbut-1-yn-3-ol.[16] To a solution of NaH (60% in mineral oil, 1.2 equiv) in DMF at 0 °C was slowly added a solution 3-phenylbut-1-yn-3-ol[22] (1 equiv) in DMF (final concentration: 0.1 M). After 2 h at the same temperature, the bromoalkene (1.2 equiv) was added dropwise. The reaction mixture was then stirred at room temperature for 13 h, quenched with water, and then extracted with Et_2O (3 × 10 mL). Combined extracts were washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude material was purified by silica gel chromatography to afford compounds **17**,[23] **18**,[22] **19**,[22] and **20**.

*[3-(Hept-6-en-1-yloxy)but-1-yn-3-yl]benzene (**20**).* Obtained as a colorless liquid (322.4 mg, 92%) from 3-phenylbut-1-yn-3-ol (212.0 mg, 1.45 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30−1.42 (m, 4H), 1.58 (pseudoquint., J = 7.1 Hz, 2H), 1.73 (s, 3H), 2.04 (m, 2H), 2.69 (s, 1H), 3.07−3.15 (m, 1H), 3.52−3.60 (m, 1H), 4.88−5.03 (m, 2H), 5.73−5.85 (m, 1H), 7.29 (m, 1H), 7.36 (m, 2H), 7.60 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.7, 28.7, 29.8, 32.9, 33.7, 64.9, 75.1, 75.6, 84.3, 114.2, 125.9, 127.7, 128.2, 139.0, 142.9. IR (NaCl): ν = 3302, 3063, 3028, 2990, 2932, 2862, 2112, 1447, 1223, 1096, 1072, 910, 764, 698 cm^{-1}. HRMS (ESI$^+$) m/z calc. for $C_{17}H_{23}O$ [M + H]$^+$ 243.1743; found: 243.1758.

General Procedure for Microwave-Assisted Ring-Closing Enyne Metathesis. To a microwave tube containing the enyne (**8a**−**c**, **11**−**13**, **16**−**20**) in dry toluene (0.03 M) was added the catalyst (10 mol %) under a positive pressure of argon. The resulting reaction mixture was stirred at 120 °C for 1 h (or 170 °C for enyne **19**) under microwave irradiations at 850 W and the solvent was then evaporated. The crude material was purified by silica gel chromatography to afford the corresponding vinylcycloalkene.

*1-Methyl-2-vinylcyclohept-2-en-1-yl acetate (**9b**).* Obtained as a yellow oil (55 mg, 55%) from **8b** (106 mg, 0.55 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.50 (s, 3H), 1.52−1.60 (m, 1H), 1.62−1.89 (m, 4H), 2.06−2.17 (m, 1H), 1.96 (s, 3H), 2.26−2.37 (m, 1H), 2.65−2.77 (m, 1H), 4.88 (dd, J = 1.9, 11.0 Hz, 1H), 5.25 (dd, J = 1.9, 17.1 Hz, 1H), 5.89−5.94 (m, 1H), 6.25−6.37 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.1, 23.3, 25.6, 25.8, 26.8, 36.3, 85.0, 113.1, 129.6, 138.1, 144.4, 169.7. HRMS (ESI$^+$) m/z calc. for $C_{12}H_{18}NaO_2$ [M + Na]$^+$ 217.1199; found: 217.1205. IR (NaCl): ν = 2978, 2932, 2866, 1740, 1366, 1246, 1227 cm^{-1}.

*tert-Butyldimethyl[(1-methyl-2-vinylcyclohepta-2-en-1-yl)oxy]-silane (**9c**).* Obtained as a colorless oil (95 mg, 88%) from **8c** (108 mg, 0.40 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.08 (s, 3H), 0.09 (s, 3H), 0.87 (s, 9H), 1.33 (s, 3H), 1.49−1.67 (m, 3H), 1.70−1.87 (m, 2H), 1.88−2.02 (m, 1H), 2.04−2.15 (m, 1H), 2.16−2.28 (m, 1H), 4.85 (dd, J = 10.7, 2.2 Hz, 1H), 5.21 (dd, J = 17.1, 2.2 Hz, 1H), 5.88 (t, J = 6.6 Hz, 1H), 6.46−6.62 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ −0.04, −0.03, 20.2, 25.2, 27.8, 27.8, 28.3, 30.1, 42.5, 80.1, 113.6, 126.6, 141.2, 150.2. IR (NaCl): ν = 3082, 2928, 2855, 1462, 1254, 1103, 1037, 995, 837, 775, 744 cm^{-1}. HRMS (ESI$^+$) m/z calc. for $C_{16}H_{30}OSi$ [M + H]$^+$ 267.2139; found: 267.2153.

*tert-Butyldimethyl(1-methyl-2-vinylcyclopent-2-en-1-yloxy)silane (**14**).* Obtained as a colorless oil (11 mg, 51%) from **11** (21 mg, 0.086 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.06 (s, 3H), 0.10 (s, 3H), 0.87 (s, 9H), 1.39 (s, 3H), 1.96−2.11 (m, 2H), 2.15−2.27 (m, 1H), 2.30−2.41 (m, 1H), 5.08 (d, J = 11.0 Hz, 1H), 5.60 (d, J = 17.5 Hz, 1H), 5.69 (t, J = 2.9 Hz, 1H), 6.22−6.33 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ −2.5, −2.0, 18.4, 26.0, 27.8, 29.1, 42.2, 85.4, 115.2, 128.3, 130.9, 148.4. HRMS (ESI+) m/z calc. for $C_{14}H_{26}NaOSi$ [M + Na]$^+$ 261.1645; found: 261.1635. IR (NaCl): ν = 2955, 2928, 2855, 1254, 1088, 1030, 837, 775, 745 cm^{-1}.

*tert-Butyldimethyl[(1-methyl-2-vinylcyclohex-2-en-1-yl)oxy]-silane (**15**).* Obtained as a colorless oil (13.3 mg, 74%) from **12** (18 mg, 0.072 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.06 (s, 3H), 0.09 (s, 3H), 0.86 (s, 9H), 1.34 (s, 3H), 1.48−2.17 (m, 6H), 4.96 (d, J = 11.1 Hz, 1H,), 5.36 (d, J = 17.9 Hz, 1H), 5.80 (t, J = 4.10 Hz, 1H), 6.33−6.45 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ −2.1, −1.7, 18.5, 20.5, 25.9, 26.1, 29.2, 40.1, 73.3, 113.1, 123.8, 136.2, 143.0. HRMS (ESI+) m/z calc. for $C_{15}H_{28}NaOSi$ [M + Na]$^+$ 275.1802; found: 275.1809. IR (NaCl): ν = 3082, 3013, 2932, 2893, 2859, 2835, 1250, 1126, 1103, 1034, 833, 772 cm^{-1}.

*tert-Butyldimethyl{[1-methyl-2-(propen-2-yl)cyclohept-2-en-1-yl]oxy}silane (**16**).* Obtained as a colorless oil (14.4, 63%) from **13** (23 mg, 0.082 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.09 (s, 6H), 0.87 (s, 9H), 1.43 (s, 3H), 1.45−1.51 (m, 2H), 1.58−1.66 (m, 2H), 1.77−1.87 (m, 2H), 1.88 (s, 3H), 2.01−2.21 (m, 2H), 4.59−4.69 (m, 2H), 5.50 (dd, J = 5.2, 8.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ −1.64, −1.59, 18.5, 25.4, 25.6, 26.1, 27.1, 27.6, 28.4, 42.4, 78.9, 111.5, 125.2, 150.6, 154.7. IR (NaCl): ν = 3078, 2928, 2859, 1250, 833, 775 cm^{-1}. HRMS (ESI$^+$) m/z calc. for $C_{17}H_{32}NaOSi$ [M + Na]$^+$ 303.2115; found: 303.2132.

*2-Methyl-2-phenyl-3-vinyl-2,5-dihydrofuran (**21**).* Obtained as a colorless liquid (10.7 mg, 95%) from **17** (11.3, 0.048 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.81 (s, 3H,), 4.78 (brs, 2H), 5.00−5.13 (m, 2H), 6.00 (brs, 1H), 6.17−6.29 (m, 1H), 7.24−7.28 (m, 1H), 7.31−7.35 (m, 2H), 7.42−7.44 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.5, 73.3, 89.9, 117.1, 124.3, 126.2, 127.6, 128.4, 128.9, 144.6, 144.8. IR (NaCl): ν = 3095, 2986, 1420, 895, 737, 706 cm^{-1}. HRMS (ESI$^+$) m/z calc. for $C_{13}H_{15}O$ [M + H]$^+$ 187.1117; found: 187.1116.

*2-Methyl-2-phenyl-3-vinyl- 2,5,6,7-tetrahydrooxepine (**22**).* Obtained as a colorless liquid (14.5 mg, 70%) from **18** (20.7 mg, 0.097 mmol). Data were consistent with those of the literature.[16]

*(Z)-2-Methyl-2-phenyl-3-vinyl-5,6,7,8-tetrahydro-2H-oxocine (**23**).* Obtained as a colorless liquid (12.7 mg, 63%) from **19** (20.1 mg, 0.088 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42−1.82 (m, 7H), 1.95−2.30 (m, 1H), 2.62−2.88 (m, 1H), 3.63−3.91 (m, 2H), 4.93 (dd, J = 1.9, 10.9 Hz, 1H), 5.21 (d, J = 17.1 Hz, 1H), 5.97 (t, J = 9.0 Hz, 1H), 6.25−6.37 (m, 1H), 7.20−7.25 (m, 1H), 7.29−7.32 (m, 2H), 7.50−7.53 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.2, 26.1, 26.7, 28.4, 64.2, 81.7, 113.9, 126.0, 126.8, 128.0, 130.0, 139.3, 143.1. IR (NaCl): ν = 3082, 3059, 2970, 2924, 2866, 1493, 1447, 1223, 1099, 1072, 1030, 910, 760, 698 cm^{-1}. HRMS (ESI$^+$) m/z calc. for $C_{16}H_{21}O$ [M + H]$^+$ 229.1587; found: 229.1588.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The complete list of catalysts used in this study (Figure S1) and spectral data for all new compounds are provided. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00659.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Diver, S. T.; Giessert, A. J. *Chem. Rev.* **2004**, *104*, 1317−1382. (b) Mori, M. *Materials* **2010**, *3*, 2087−2140. (c) Li, J.; Lee, D. *Eur. J. Org. Chem.* **2011**, 4269−4287.

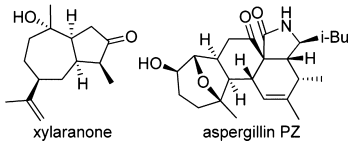
(2) Vedrenne, E.; Royer, F.; Oble, J.; El Kaïm, L.; Grimaud, L. *Synlett* **2005**, *15*, 2379−2381.

(3) (a) Stewart, I. C.; Ung, T.; Pletnev, A. A.; Berlin, J. M.; Grubbs, R. H.; Schrodi, Y. *Org. Lett.* **2007**, *9*, 1589−1592. (b) White, D. E.; Stewart, I. C.; Grubbs, R. H.; Stoltz, B. M. *J. Am. Chem. Soc.* **2008**, *130*, 810−811.

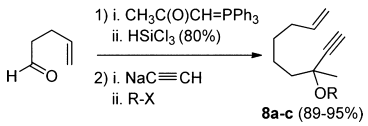
(4) Stewart, I. C.; Douglas, C. J.; Grubbs, R. H. *Org. Lett.* **2008**, *10*, 441−444.

(5) Clark, D. A.; Basile, B. S.; Karnofel, W. S.; Diver, S. T. *Org. Lett.* **2008**, *10*, 4927−4929.

(6) Seven-membered rings are widely distributed in terpenoids like xylaranone Amand, S.; Langenfeld, A.; Blond, A.; Dupont, J.; Nay, B.; Prado, S. *J. Nat. Prod.* **2012**, *75*, 798−801. or in polyketides like aspergillin PZ (Zhang, Y.; Wang, T.; Pei, Y.; Hua, H.; Feng, B. *J. Antibiot.* **2002**, *55*, 693−695 .



(7) Two efficient processes were involved, including a one-pot Wittig reaction−enone reduction recently reported in the literature Cao, J.-J.; Zhou, F.; Zhou, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 4976−4980. followed by the addition of ethynylmagnesium bromide to the ketone and *in situ* quench of the resulting tertiary alcohol with an appropriate electrophile (see the Supporting information):.



(8) Mori, M.; Sakakibara, N.; Kinoshita, A. *J. Org. Chem.* **1998**, *63*, 6082−6083.

(9) Estimated by the comparison of starting material and product ratios in the crude reaction mixtures by NMR.

(10) Stewart, I. C.; Benitez, D.; O'Leary, D. J.; Tkatchouk, E.; Day, M. W.; Goddard, W. A., III; Grubbs, R. H. *J. Am. Chem. Soc.* **2009**, *131*, 1931−1938.

(11) Nüchter, M.; Müller, U.; Ondruschka, B.; Tied, A.; Lautenschläger, W. *Chem. Eng. Technol.* **2003**, *26*, 1207−1216.

(12) de la Hoz, A., Loupy, A., Eds. *Microwaves in Organic Synthesis*; Wiley-VCH: Weinheim, 2012.

(13) Coquerel, Y.; Rodriguez, J. *Eur. J. Org. Chem.* **2008**, 1125−1132.

(14) (a) Salim, S. S.; Bellingham, R. K.; Brown, R. C. D. *Eur. J. Org. Chem.* **2004**, 800−806. (b) Debleds, O.; Campagne, J.-M. *J. Am. Chem. Soc.* **2008**, *130*, 1562−1563. (c) Lamberto, M.; Kilburn, J.-D. *Tetrahedron Lett.* **2008**, *49*, 6364−6367.

(15) Samojlowicz, C.; Borré, E.; Mauduit, M.; Grela, K. *Adv. Synth. Catal.* **2011**, *353*, 1993−2002.

(16) Zhang, L.-L.; Zhang, W.-Z.; Ren, X.; Tan, X.-Y.; Lu, X.-B. *Tetrahedron Lett.* **2012**, *53*, 3389−3392.

(17) Terminal alkynes have been known as poor substrates for the synthesis of eight-membered ring by RCEYM: see ref 16 and Teichert, J. F.; Zhang, S.; van Zijl, A. W.; Slaa, J. W.; Minnaard, A. J.; Feringa, B. L. *Org. Lett.* **2010**, *12*, 4658−4660.

(18) Cao, J.-J.; Zhou, F.; Zhou, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 4976−4980.

(19) Rosillo, M.; Arnáiz, E.; Abdi, D.; Blanco-Urgoiti, J.; Domínguez, G.; Pérez-Castells, J. *Eur. J. Org. Chem.* **2008**, 3917−3927.

(20) Egi, M.; Yamaguchi, Y.; Fujiwara, N.; Akai, S. *Org. Lett.* **2008**, *10*, 1867−1870.

(21) Gribkov, D. V.; Hultzsch, K. C.; Hampel, F. *J. Am. Chem. Soc.* **2006**, *128*, 3748−3759.

(22) Schmidt, E. Y.; Cherimickina, N. A.; Bidusenko, I. A.; Protzuk, N. I.; Trofimov, B. A. *Eur. J. Org. Chem.* **2014**, 4663−4670.

(23) Picquet, M.; Bruneau, C.; Dixneuf, P. H. *Chem. Commun.* **1998**, *20*, 2249−2250.

DOI: 10.1021/acs.joc.5b00659
J. Org. Chem. 2015, 80, 5359−5363