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Design and Synthesis of Novel Propellanes by Using Claisen Rearrangement and Ring-Closing Metathesis as the Key Steps

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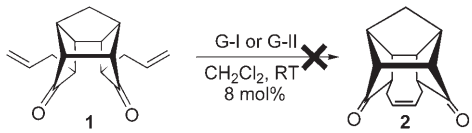
Abstract: Novel hexacyclic caged compounds are prepared by a combination of Claisen rearrangement and ring-closing metathesis (RCM). Additionally, a Grignard reaction in conjugation with RCM produced intricate hexacyclic caged molecules.

Keywords: cage compounds · Claisen rearrangement · metathesis · polycycles

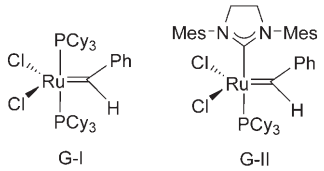
Introduction

Caged polycyclic molecules play an important role in the design and synthesis of natural and non-natural products.[1] Lack of conformational mobility, their molecular symmetry,[2a] and their intricate molecular structure prompted us to synthetically investigate these compounds. They are also useful building blocks for high-energy materials.[2b] In connection with our interest in the preparation of annulated polyquinane we have prepared diallylated tetracyclic dione, 3,6-diallyltetracyclo[6.3.0.0^{4,11}.0^{5,9}]undecan-2,7-dione (**1**) by using fragmentation methodology, which involves a four-step sequence starting with 1,3-cyclopentadiene and 1,4-benzoquinone.[3–5] It was anticipated that the two allyl groups present in **1** would undergo ring-closing metathesis (RCM) to generate a new novel pentacyclic system **2** (Scheme 1).

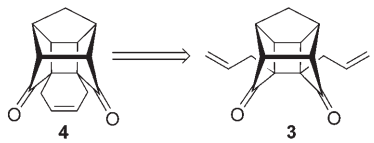


Scheme 1. Nonparticipation of allyl groups in RCM under **G**-I and **G**-II conditions.

However, we observed that even under forcing reaction conditions compound **1** failed to give a RCM product with Grubbs first- and second-generation catalysts.[6,7]



Inspection of the molecular models revealed that the presence of the C1–C7 bond in pentacyclic system **3** (Scheme 2) would force the two allyl groups in close proximity; however, the two allyl groups are far apart in tetracyclic system **1**, which is not suitable for RCM. It appears that the transannular "proximity effect" between the two carbonyl groups in **1** is responsible for hemiketal formation instead of the expected diol during the allyl and vinyl Grignard addition sequence.[1b]



Scheme 2. Retrosynthetic analysis of hexacyclic propellane.

Results and Discussion

As a result of the conformation of pentacyclic system **3**, in which the two allyl groups are much closer in space, we reasoned that this system may undergo RCM to generate a new

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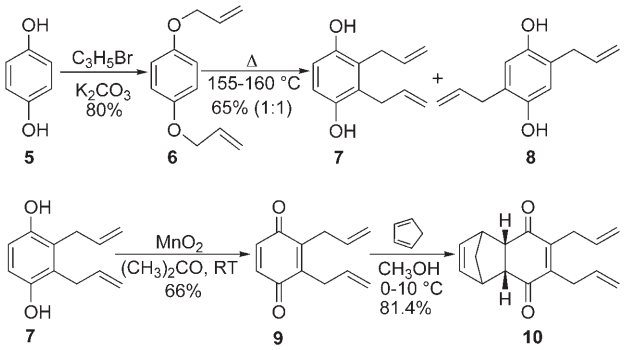
hexacyclic propellane,[8] system **4**. Retrosynthetic analysis of **4** (Scheme 2) indicates that the required diallylated pentacyclic dione **3** could be obtained from [2+2] photocycloaddition of adduct **10**, produced by Diels–Alder (DA) cycloaddition of 2,3-diallyl-1,4-benzoquinone with 1,3-cyclopentadiene (Scheme 3).



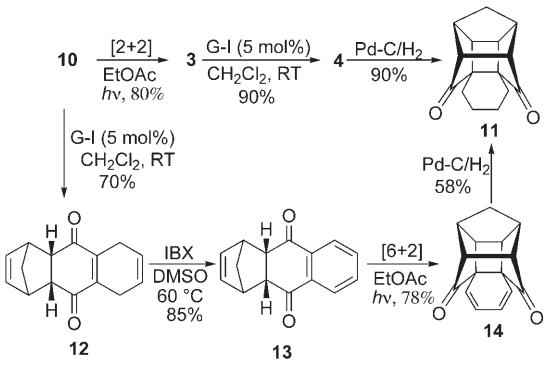
Scheme 3. Base-catalyzed allylation of 1,4-hydroquinone, *o*-Claisen rearrangement, MnO_2 oxidation, and Diels–Alder reaction with 1,3-cyclopentadiene.

Thus, the preparation of diallyl benzoquinone **9** begin with 1,4-hydroquinone (**5**).[9] Diallylation of hydroquinone followed by Claisen rearrangement gave two rearranged allylated hydroquinones **7** and **8** in a 1:1 ratio which could be separated by column chromatography.[10] Oxidation of the 2,3-diallylated derivative **7** with MnO_2 gave 2,3-diallyl-1,4-benzoquinone (**9**) in 66% isolated yield after column chromatography. Cycloaddition of **9** with freshly cracked 1,3-cyclopentadiene at 0–10°C produced low melting DA adduct **10**. The structure of the DA adduct has been established based on high field ^1H NMR spectroscopy (400 MHz) and is further supported by ^{13}C NMR spectral data (100 MHz, $\delta =$ 30.7, 48.2, 48.7, 48.9, 116.6, 133.3, 135.1, 148.6, 198.1 ppm).

The stereochemistry of the DA product was expected to be *endo* and this assumption has been confirmed by the photochemical behavior of the DA adduct, which undergoes a smooth [2+2] photocycloaddition upon exposure to light.[11] The pentacyclic system **3** has displayed the required number of signals in the ^{13}C NMR spectrum (100 MHz, $\delta = 30.2$, 41.4, 41.5, 43.7, 54.1, 55.6, 118.6, 132.7, 213.0 ppm).

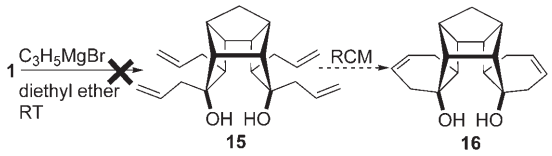
Having prepared the pentacyclic dione **3**, the stage was set for RCM. Exposure of compound **3** to Grubbs first-generation catalyst[6] produced hexacyclic propellane **4** in 90% yield after column chromatography. Additional proof of the structure has been obtained by its chemical conversion to the known hexacyclic system **11** (Scheme 4). The spectral properties of the compound obtained by this route are identical to that in the reported data.[12] Alternatively, compound **11** was also prepared by another sequence involving the intermediates **12** and **13**.

Thus, the DA adduct **10** underwent RCM [13] to generate the tetracyclic derivative **12** in 70% yield. IBX-mediated dehydrogenation[14] followed by [2+2] (or [6+2]) photocycloaddition gave compound **14**, reported by the Kushner et al.[15]



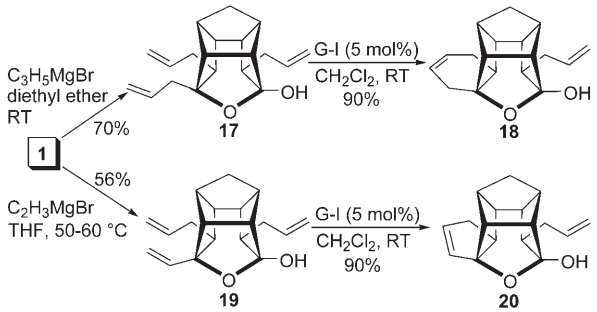
Scheme 4. [2+2] photocycloaddition, RCM with **G**-I, Pd-catalyzed hydrogenation and RCM with **G**-I, IBX-mediated dehydrogenation (IBX = *o*-iodoxybenzoic acid), [6+2] or [2+2] photocycloaddition, and Pd-catalyzed hydrogenation.

The initial observation that the tetracyclic system **1** did not undergo RCM could be turned into an exciting opportunity to design new caged systems, for example, a double Grignard reaction (GR) with allyl magnesium bromide would be expected to give **15**. RCM[16,17] of this tetrallylated derivative **15** in principle can generate the hexacyclic system **16** with two new additional rings (Scheme 5).



Scheme 5. Allyl Grignard addition to **1** followed by RCM.

To prepare the hexacyclic caged system **16**, the diallyl dione **1** was treated with the excess amount of allyl magnesium bromide, generating triallyated hemiketal **17** instead of the tetrallylated derivative **15**. The proximity of the carbonyl groups is responsible for hemiketal formation. In view of earlier observations[18] this result is not surprising. The structure of pentacyclic hemiketal derivatives **17** and **19** (Scheme 6) has been firmly established by ^{13}C NMR spectral



Scheme 6. Allyl and vinyl Grignard addition to **1** followed by RCM.

data. In particular, the presence of a signal at $\delta = 115.6$ ppm in the ^{13}C NMR spectrum of **17** indicates the carbon atom attached to two oxygen atoms. Molecular models indicate that the formation of the hemiketal did not aid in bringing the two initial allyl groups closer (Figure 1). RCM of triallyl compound **17** gave **18** as a sole product.

Along similar lines, addition of vinyl magnesium bromide produced **20** from the corresponding hemiketal derivative **19** (Scheme 6). Later on, it was found that the optimization by ChemDraw and distances between allyl-bearing carbon atoms in **1**, **3**, and **17** were measured by Rasmol visualization software (Figure 1). The distance between the allyl-bearing carbon atoms in **1** ($d_1 = 3.16$ Å) is approximately double the distance between the allyl-bearing carbon atoms in **3** ($d_3 = 1.57$ Å). Even in hemiketal **17** ($d_{17} = 3.06$ Å) this distance has not decreased as much as that between the two allyl groups present in **1**. Participation of the allyl group in ring formation in **3** and **17** clearly shows that the large separation of allyl groups in **1** is responsible for our observations.

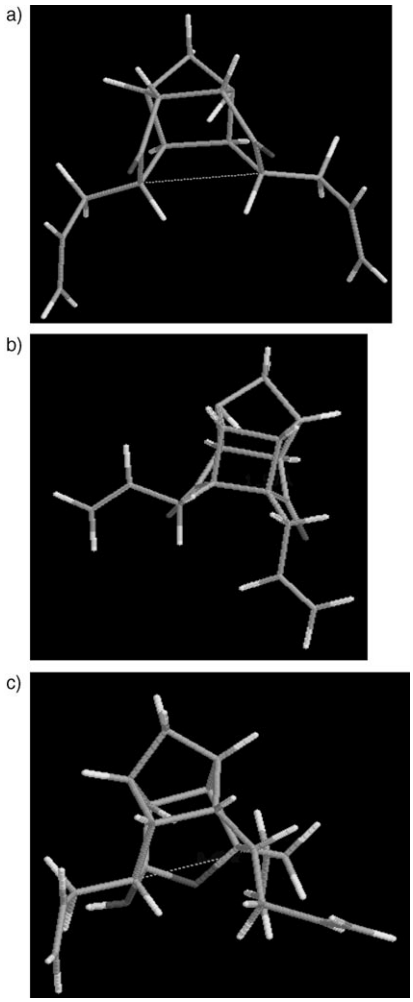


Figure 1. Distance between allyl-bearing carbon atoms in **1**, **3**, and **17**, $d_1 = 3.16$, $d_3 = 1.57$, and $d_{17} = 3.06$ Å.

Conclusion

We have shown that Claisen rearrangement in combination with RCM provides a useful method for the synthesis of hexacyclic caged propellanes such as **4**, which is suitable for studying stereoelectronic effects.[19] This methodology opens up a new route to novel caged compounds of higher order ring systems for example; compound **1** may be an ideal candidate to study the cross-metathesis reaction. A Grignard reaction in combination with RCM gave access to polycyclic caged ether derivatives (e.g. **18** and **20**). These two approaches clearly demonstrate that RCM in combination with other carbon–carbon bond-forming processes, such as Claisen rearrangement and the Grignard reaction, provide exciting opportunities to create novel molecular frames. We have also demonstrated that the presence of suitably disposed olefinic moieties at appropriate distance is necessary for the success of RCM. The strategy demonstrated here has distinct advantages. The cycloaddition reaction and RCM protocol have mostly been employed without the need for protecting groups. Expansion of these strategies to other intricate molecular frames will be reported in near future.

Experimental Section

General: Reactions involving organometallic species were carried out under nitrogen by using oven-dried glassware and syringes. THF and Et_2O were distilled from sodium/benzophenone under nitrogen immediately prior to use. Dichloromethane was distilled over P_2O_5. TLC was performed by using (10×5 cm) glass plates coated with Acme's silica gel GF254 (containing 13% calcium sulphate as a binder). Flash-column chromatography was performed by using Aceme silica gel (100–200 mesh). Solvents were concentrated at reduced pressure on a Büchi R-114 rotary evaporator. ^1H NMR (300, 400 MHz) and ^{13}C NMR (75, 100 MHz) spectra were recorded at room temperature on Varian VXR 300 instruments or AX 400 with TMS ($\delta = 0.0$ ppm, ^1H NMR spectra) and $CDCl_3$ ($\delta = 77.0$ ppm, ^{13}C NMR spectra) as internal standards. IR spectra were recorded on a Nicolet Impact-400 FTIR spectrometer. HRMS were determined on a Micromass Q-Tof spectrometer.

Materials: Vinyl magnesium bromide (1 M solution in THF) and Grubbs first-generation catalyst were purchased from Aldrich, Milwaukee (USA).

4,5-Diallyltricyclo[6.2.1.0^{2,7}]undeca-4,9-diene-3,6-dione (10): Cyclopentadiene (0.2 mL, 0.34 mmol) was added dropwise to a cooled solution of 2,3-diallyl-1,4-benzoquinone **9** (60 mg, 0.32 mmol) at 0 °C in methanol (15 mL). At the end of the reaction (3.5 h, TLC monitoring), the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (3% EtOAc/petroleum ether) to give **10** (66 mg, 81.4% yield) as a thick yellow liquid. $R_f = 0.45$ (petroleum ether/EtOAc 9:1); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.42$–1.52 (dd, $J_1 = J_2 = 9.7$ Hz, 2H; bridge CH_2), 3.06–3.20 (m, 4H; 2×CH_2–CH=CH_2), 3.24–3.26 (m, 2H; 2×CH bridge head), 3.52 (s, 2H; 2×CH ring junction), 5.01–5.08 (m, 4H; 2×CH_2–CH=CH_2), 5.66–5.76 (m, 2H; 2×CH_2–CH=CH_2), 6.00 ppm (s, 2H; CH=CH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 30.7$, 48.2, 48.7, 48.9, 116.6, 133.3, 135.1, 148.6, 198.1 ppm; IR (neat): $\tilde{\nu} = 3079$ (=CH_2 st), 2992 (=CH st), 1664 (C=O conjugated), 1608 (C=C st), 915 cm^{-1} (HC=CH δ); HRMS (QTOF ES+): m/z: calcd for $C_{17}H_{18}O_2Na$: 277.1204; found: 277.1215 $[M+Na]^+$.

1,7-Diallylpentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undeca-8,11-dione (3): Tricyclic dione **10** (125 mg, 0.49 mmol) was dissolved in dry EtOAc (500 mL) and irradiated in a Pyrex immersion well by using an 125 W UV lamp (homemade) for 1.5 h under nitrogen at RT. At the conclusion of the reaction

(TLC monitoring), the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (5% EtOAc/petroleum ether) to give **3** (80 mg, 80%) as a white crystalline solid. $R_f = 0.39$ (petroleum ether/EtOAc 9:1); m.p. 80–81 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.90$–2.00 (dd, $J_{AB} = 12.0$, 11.0 Hz, 2H; bridge CH_2), 2.18–2.26 (dd, $J = 9.0$, 8.9 Hz, 2H; 2×CH bridge head), 2.47–2.55 (m, 2H; 2×CH bridge), 2.74–2.79 (m, 4H; 2×CH_2–CH=CH_2), 2.90 (s, 2H; 2×CH, ring junction), 5.00–5.10 (m, 4H; 2×CH_2–CH=CH_2), 5.50–5.60 ppm (m, 2H; 2×CH_2–C*H*=CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 30.2, 41.4, 41.5, 43.7, 54.2, 55.6, 118.6, 132.7, 213.0 ppm; IR (KBr): $\tilde{\nu} =$ 3069 (=CH_2 st), 2970 (=CH st), 1751 (C=O), 1636 (C=C st), 924 cm^{-1} (HC=CH δ); HRMS (QTOF ES+): *m/z*: calcd for $C_{17}H_{19}O_2$: 255.1385; found: 255.1397 $[M+H]^+$.

Hexacyclo[10.2.1.0^{4,9}.0^{4,14}.0^{9,13}]pentadeca-6-ene-3,10-dione (4): Grubbs first-generation catalyst (10 mg, 5 mol%) was added to a solution of diallyl pentacyclic dione **3** (100 mg, 0.39 mmol) in dry dichloromethane (15 mL) under argon at RT. At the end of the reaction (4 h, TLC monitoring), the solvent was evaporated by using a water bath and the residue was purified by silica gel column chromatography (8% EtOAc/petroleum ether) to give **4** (80 mg, 90%) as a white crystalline solid. $R_f = 0.25$ (petroleum ether/EtOAc 9:1); m.p. 109–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.81$–1.89 (m, 2H; 2×CH bridge head), 1.90–2.04 (dd, $J_1 = J_2 =$ 11 Hz, 2H; bridge CH_2), 2.30–2.40 (d, $J = 16$ Hz, 2H; 2×CH bridge), 2.60–2.70 (m, 4H; 2×CH_2–CH=CH), 2.90 (d, $J = 1.6$ Hz, 2H; 2×CH bridge adjacent to carbonyl group), 5.90 ppm (t, $J = 3$ Hz, 2H; CH=CH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.8$, 41.1, 43.0, 43.5, 51.9, 54.8, 126.1, 212.8 ppm; IR (KBr): $\tilde{\nu} = 2930$ (=CH st), 1741 (C=O), 1725 (C=C st), 1094 cm^{-1} (HC=CH δ); HRMS (QTOF ES+): *m/z*: calcd for $C_{15}H_{15}O_2$: 227.1072; found: 227.1068 $[M+H]^+$.

Hydrogenation of hexacyclo[10.2.1.0^{4,9}.0^{4,14}.0^{9,13}]pentadeca-6-ene-3,10-dione (4): Palladium/charcoal (10%, 300 mg) was added to a solution of **4** (11.3 mg, 0.05 mmol) in EtOAc (10 mL) under hydrogen (1 atm) at RT. At the end of the reaction (3 h, TLC monitoring), the reaction mixture was filtered off by using a Celite pad. The solvent then evaporated under reduced pressure and the residue was purified by silica gel column chromatography (5% EtOAc/petroleum ether) to give **11** (8 mg, 90%) as an off-white solid. M.p. 67–68 °C (lit.[12] m.p. 70 °C).

^{1}H and ^{13}C NMR spectroscopic chemical shift values matched with literature values.[12]

1,4,4a,5,8,9a-Hexahydro-1,4-methanoanthracene-9,10-dione (12): Grubbs first-generation catalyst (15 mg, 5 mol%) was added to a solution of tricyclicdione **10** (160 mg, 0.62 mmol) in dry dichloromethane (15 mL) under nitrogen and stirred at RT for 3.5 h. At the end of the reaction (4 h, TLC monitoring), the solvent was evaporated and the residue was purified by silica gel column chromatography (5% EtOAc/petroleum ether) to give **12** (98 mg, 70%) as a white crystalline solid. $R_f = 0.35$ (petroleum ether/EtOAc 9:1); m.p. 126–128 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.40$–1.50 (m, 2H; bridge CH_2), 2.90 (m, 4H; 2×CH_2–CH=CH_2), 3.20 (dd, $J = 2.0$, 1.0 Hz, 2H; 2×CH bridge head), 3.50 (dd, $J = 2.0$, 1.0 Hz, 2H; 2×CH ring junction), 5.70 (s, 2H; CH=CH), 6.00 ppm (t, $J = 2.0$ Hz, 2H; norbornene CH=CH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 24.6$, 48.1, 48.9, 49.6, 122.6, 135.3, 145.6, 198.3 ppm; HRMS (QTOF ES+): *m/z*: calcd for $C_{15}H_{15}O_2$: 227.1077; found: 227.1072 $[M+H]^+$.

IBX-mediated dehydrogenation of 12:[14] IBX (2 equiv) was added to a solution of **12** (80 mg, 0.35 mmol) in DMSO under nitrogen and heated at 60–65 °C. At the end of the reaction (3 h, TLC monitoring), the mixture was extracted with EtOAc (3×10 mL) and the combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. Once dry, the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (5% EtOAc/petroleum ether) to give **13** (67 mg, 85%) as a white crystalline solid. M.p. 116–117 °C (lit.[15] m.p. 117–118 °C).

[2+2] Photocycloaddition of 13: Dehydrogenated product **13** (60 mg, 0.27 mmol) dissolved in EtOAc (150 mL) was irradiated in a Pyrex immersion well by using an 125 W UV lamp (homemade) for 5 h under argon at RT. At the end of the reaction (TLC monitoring), the solvent was evaporated under reduced pressure and the residue obtained was purified by silica gel column chromatography (5% EtOAc/petroleum ether) to give **14** (46.8 mg, 78%) as an off-white solid. M.p. 110–111 °C (lit.[15] m.p. 111–112 °C).

Triallyl pentacyclic hemiketal 17: A solution of tetracyclic dione **1** (105 mg, 0.41 mmol) in diethyl ether (8 mL) was added dropwise to freshly prepared allyl magnesium bromide (327 mg, 2.45 mmol) in ether (10 mL) over a period of 10–15 min at RT under nitrogen. At the end of the reaction (8 h, TLC monitoring), the mixture was quenched with saturated aqueous NH_4Cl solution at 0 °C, and the resulting aqueous layer was extracted with EtOAc (3×25 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and the solvent evaporated under reduced pressure. The resulting residue was purified by silica gel column chromatography (4% EtOAc/petroleum ether) to give **17** (85.5 mg, 70%) as a white solid. $R_f = 0.71$ (petroleum ether/EtOAc 4:1); m.p. 95–96 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.50$–1.60 (m, 2H; 2×CH attached to the allyl-bearing carbon atoms), 1.60–1.90 (m, 2H; bridge CH_2), 2.00–2.20 (m, 2H; 2×CH bridge head), 2.30–2.50 (m, 8H; 3×CH_2–CH=CH_2, 2×CH bridge), 2.50–2.60 (m, 2H; 2×CH bridge adjacent to C=O), 3.30 (d, $J = 8.0$ Hz, 1H; OH), 4.94–5.10 (m, 6H; 3×CH_2–CH=C*H*$_2$), 5.60–6.01 ppm (m, 3H; 3×CH_2-C*H*=CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 34.9$, 35.1, 37.6, 39.1, 45.1, 46.0, 46.4, 46.5, 51.30, 51.34, 57.7, 60.6, 93.0, 115.6, 115.8, 116.3, 117.1, 135.4, 137.8, 138.5 ppm; IR (KBr): $\tilde{\nu} = 3134$ (OH hemiketal), 1638 (C=C st), 1403 (−O− hemiketal), 910 cm^{-1} (C−H δ); HRMS (QTOF ES+): *m/z*: calcd for $C_{20}H_{26}O_2Na$: 321.1833; found: 321.1831 $[M+Na]^+$.

Monoallyl hexacyclic hemiketal 18: Grubbs first-generation catalyst (6 mg, 5 mol%) was added to a solution of **17** (23 mg, 0.076 mmol) under argon at RT. At the end of the reaction (after 5 h, TLC monitoring), the solvent was evaporated, and the resulting residue was purified by silica gel column chromatography (5% EtOAc/petroleum ether) to give **18** (16 mg, 77%) as an off-white solid. $R_f = 0.60$ (petroleum ether/EtOAc 4:1); m.p. 58–59 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.60$ (s, 2H), 1.70–1.90 (m, 2H), 1.90–2.10 (m, 2H; bridge CH_2), 2.30–2.50 (m, 8H; 2×CH_2–CH=CH, 2×CH_2–CH=CH_2, 2×CH bridge), 2.60–2.70 (m, 2H; 2×CH bridge adjacent to C–O), 3.20 (s, 1H; OH), 5.00–5.10 (m, 2H; CH_2–CH=C*H*$_2$), 5.70–5.90 ppm (m, 3H; 2×C*H*=C*H*, CH_2–C*H*=CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 30.5$, 34.0, 35.1, 37.7, 45.0, 46.7, 47.3, 48.3, 51.1, 51.6, 60.5, 61.5, 91.6, 115.9, 116.2, 125.5, 129.2, 138.7 ppm; IR (KBr): $\tilde{\nu} =$ 3116 (OH hemiketal), 1638 (C=C st), 1400 (−O− hemiketal), 916 cm^{-1} (C−H δ); HRMS (QTOF ES+): *m/z*: calcd for $C_{18}H_{22}O_2Na$: 293.1517; found: 293.1526 $[M+Na]^+$.

Diallyl-monovinyl pentacyclic hemiketal 19: Vinyl magnesium bromide (6 equiv, 1 M solution in THF) was added dropwise to a solution of **1** (105 mg, 0.41 mmol) in dry THF (8 mL). Initially the addition was carried out at RT, but after 3 h the reaction mixture was heated up to 50 °C for the next 10 h. At the end of the reaction (TLC monitoring) the reaction was quenched with a concentrated aqueous solution of NH_4Cl at 0 °C, and the resulting aqueous layer was extracted with EtOAc (3×25 mL). The combined organic layers were then washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the resulting residue was purified by silica gel column chromatography (5% EtOAc/petroleum ether) to give **19** as a white solid (65 mg, 56%). $R_f = 0.65$ (petroleum ether/EtOAc 4:1); m.p. 110–111 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.60$–1.70 (m, 2H), 1.70–2.00 (m, 2H; bridge CH_2), 2.1–2.4 (m, 6H; 2×CH bridge, 2×CH_2–CH=CH_2), 2.50–2.60 (m, 2H), 2.71–2.75 (m, 2H), 3.0 (s, 1H; OH), 4.92–5.12 (m, 4H; 2×CH_2–CH=C*H*$_2$), 5.06–5.07 (dd, $J_1 = J_2 = 1.83$ Hz, 1H; CH=C*H*H), 5.23–5.28 (dd, $J_1 = J_2 = 1.53$ Hz, 1H; CH=CH*H*), 5.61–5.90 (m, 2H; 2×CH_2–C*H*=CH_2), 5.94–6.02 ppm (dd, $J_1 = J_2 = 17.4$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 34.9$, 36.7, 37.6, 45.1, 46.6, 46.7, 46.8, 51.3, 52.7, 58.9, 60.4, 93.5, 112.3, 115.8, 115.9, 116.2, 137.9, 138.6, 138.7 ppm; IR (KBr): $\tilde{\nu} = 3119$ (OH hemiketal), 1638 (C=C st), 1400 (−O− hemiketal), 911 cm^{-1} (C−H δ); HRMS (QTOF ES+): *m/z*: calcd for $C_{19}H_{24}O_2Na$: 307.1674; found: 307.1672 $[M+Na]^+$.

Monoallyl hexacyclic hemiketal 20: Grubbs first-generation catalyst (5 mg, 5 mol%) was added to a solution of **19** (23 mg, 0.080 mmol) under argon at RT. At the end of the reaction (after 5 h, TLC monitoring), the solvent was evaporated by using a water bath and the resulting residue was purified by silica gel column chromatography (6% EtOAc/petroleum

ether) to give **20** (15.6 mg, 76%) as a white crystalline solid. $R_f = 0.58$ (petroleum ether/EtOAc 4:1); m.p. 98–99 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.60$ (br d, $J = 2.0$ Hz, 2H), 1.90–2.08 (m, 2H), 2.12–2.24 (m, 2H), 2.40–2.80 (m, 8H), 5.00–5.20 (m, 2H; $2 \times CH_2{-}CH{=}CH_2$), 5.70–5.90 ppm (m, 3H; $CH_2{-}CH{=}CH_2$, $CH{=}CH$); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 35.2$, 37.0, 37.9, 45.4, 46.1, 46.5, 48.0, 51.2, 52.7, 59.8, 60.0, 103.5, 116.0, 116.7, 132.7, 133.0, 138.8 ppm; IR (KBr): $\tilde{\nu} = 3129$ (OH hemiketal), 1638 (C=C st), 1399 (−O− hemiketal), 905 cm^{-1} (C−H δ); HRMS (QTOF ES+): *m*/*z*: calcd for $C_{17}H_{20}O_2Na$: 279.1361; found: 279.1365 $[M+Na]^+$.

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