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Facile Synthesis and Ring-Opening Cross Metathesis of Carbo- and Heterocyclic Bicyclo[3.2.1]oct-6-en-3-ones Using Gaseous Olefinic Reaction Partners

Marko D. Mihovilovic,[a,*] Birgit Grötzl,[a] Wolfgang Kandioller,[a] Radka Snajdrova,[a] Adél Muskotál,[a,b] Dario A. Bianchi,[a] Peter Stanetty[a]

[a] Vienna University of Technology, Institute of Applied Synthetic Chemistry, Getreidemarkt 9/163-OC, 1060 Vienna, Austria
Fax: (+43)-1-58801-15499, e-mail: mmihovil@pop.tuwien.ac.at
[b] Current address: Department of Nanotechnology, University of Veszprém, Veszprém, Hungary

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In memoriam Prof. Roland Schmid.

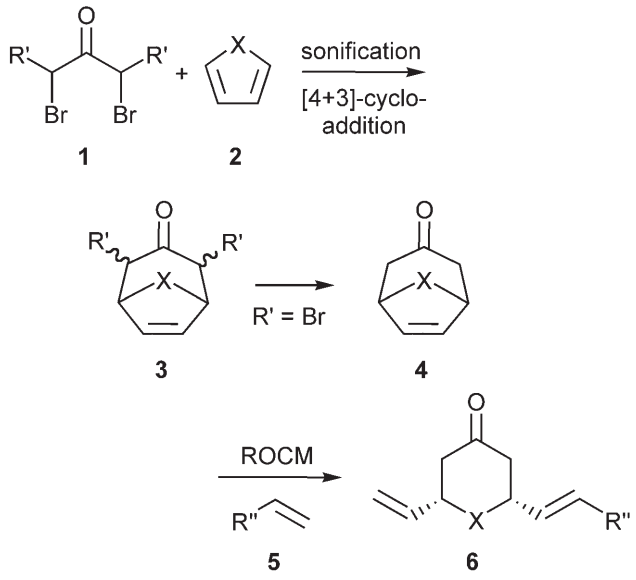
Abstract: The title compounds were prepared by a facile [4+3]-cycloaddition strategy involving sonochemistry. The oxyallyl species required for the reaction with the corresponding diene was generated from a suitable perbromo ketone with activated zinc under sonification conditions. The resulting dibromo bicyclo compounds were reduced to the target products using a Cu/Zn couple. Ring-opening cross metathesis of the resulting bicyclic species was established as an efficient method for the diastereoselective preparation of *cis*-3,5-disubstituted cycloketones. Especially gaseous olefins gave symmetrical and unsymmetrical products as versatile platforms for subsequent transformations. This is the first example of such a ring-opening reaction of a non-strained ring system.

Keywords: [4+3]-cycloaddition; gaseous alkenes; Grubbs catalyst; ring-opening cross metathesis; ruthenium; sonochemistry

Introduction

In the course of an ongoing research program, we have been investigating the microbial Baeyer–Villiger oxidation of prochiral ketones by recombinant whole-cells to form chiral lactones.[1,2] Both carbocyclic[3] and heterocyclic[4] six-membered systems are interesting substrates for the biooxidative formation of valuable asymmetric building blocks. Continuing this project and increasing the structural complexity of our fermentation precursors, we required a rapid and facile method for the construction of carbo- and heterocyclic bicyclo[3.2.1]oct-6-en-3-ones **3** and **4**, respectively (Scheme 1).

In addition, we considered such compounds as attractive precursors to access *cis*-3,5-disubstituted cycloketones in high diastereoselectivity. The implementation of such olefins into the side chain of biooxidation substrates may serve as a functional basis for subsequent transformations, as C=C double bonds are inert to microbial Baeyer–Villiger oxidations.[5] The transformation of bicyclic systems **4** into compounds of type **6** was envisioned by ring-opening cross metathesis (ROCM) with terminal alkenes **5**.



Scheme 1.

[4+3]-Cycloadditions

Bicyclo[3.2.1]ketones are interesting scaffolds and potentially versatile platforms for subsequent transformations. These kinds of compounds are important building blocks in organic chemistry and precursors for a broad range of pharmacological active compounds.[6] The [4+3]-cycloaddition reaction is an interesting tool for the construction of such bicyclic systems. This cyclization involves a perbromo ketone as dienophile, which generates the reactive oxyallyl species in the course of the reaction. Mechanistically, α,α′-dehydrohalogenation generates a *zwitterionic* oxyallyl cation that acts as an electrophile in the cycloaddition. This discovery of the electrophilic reactivity of an oxyallyl cation, and the subsequent utilization of heterosubstituted allyl cations as three-carbon components in [4+3]-cycloaddition reactions, provided an important innovation in the preparation of seven-membered ring systems.[7] A variety of methods for the generation of such oxyallyl species has been reported.[8]

Especially, access to the unsubstituted enones seems to be troublesome. Previously published approaches, particularly to oxygen-containing systems of type **4b** (X=O) as precursor for several natural products,[9] involved toxic [$Fe_2(CO)_9$],[10] pyrophoric (Et_2Zn),[11] or expensive (Cu/Ag couple)[12] reagents or elaborate work-up protocols were required as reported by Hoffmann.[13]

Montana and co-worker recently reported a comparative study of [4+3]-cycloadditions under thermal and sonochemical conditions.[14] Ultrasound chemistry offers the advantage of very mild conditions in heterogeneous reactions.[15] Encouraged by these results, we envisioned the synthesis of unsubstituted enones **4** utilizing such a sonification protocol.

Ring-Opening Cross Metathesis (ROCM)

Olefin metathesis is a unique carbon skeleton reconfiguration reaction in which unsaturated carbon-carbon bonds are rearranged in the presence of metal-carbene complexes.[16] Two strategies have been developed in recent years as versatile methods in organic synthesis and polymer chemistry: ring-closing metathesis (RCM) is a highly efficient entry to macrocycles and has been utilized in a number of natural compound and bioactive product syntheses.[17] ROCM as a complementary strategy has not been elaborated to such an extent. However, ROCM has the potential of being a useful tool for the preparation of terminal diolefins and has been used for the synthesis of highly functionalized rings.[18]

The challenge of this type of metathesis is two-fold: (i) suppression of the ring-opening polymerization, which can be achieved by working in high dilution; (ii) equilibrium shift unfavoring the re-cyclization process, feasible by working with an excess of the cross coupling partner. Up to now, ring-opening metathesis was only performed with highly strained bicycles such as norbornenes and cyclobutadienes.[19,20]

Based on an improved access to bicyclic precursor **4** as outlined above, ROCM became an appealing strategy to prepare dialkenes **6** in the presence of gaseous, as well as liquid olefins. According to the literature,[19] gaseous olefins can be used as partners in ring-opening metathesis and polymerization was not observed. We were further encouraged by a report by Wright and co-workers, who performed ring-opening metathesis with the corresponding oxabicycle derivative **4a**,[21] and a very recent account by Hoveyda et al., who reported on an asymmetric version of ROCM on **4a** and structurally related compounds.[22,23]

Consequently, the aim of this study was to develop an efficient and facile access to bicyclic compounds of type **4** and investigate their potential in ROCM reactions with representative gaseous and liquid olefins to ultimately generate prochiral biooxidation precursors of the general structure **6**.

Results and Discussion

We started our study with the synthesis of carbocyclic system **4a** using tetrabromoacetone **1a**[24] (R′=Br; TBA) as precursor for the oxyallyl species generation and freshly monomerized cyclopentadiene **2a** (X=CH_2) as diene (Table 1). Due to the limited stability of dibromo intermediates **3** (R=Br), the crude product

Table 1. Cyclization conditions using dienophile **1a** and Cu/Zn-mediated debromination to bicyclic compounds **4a–c** under sonification conditions.

Entry	R	Diene (equivs.)	X	Metal species (equivs.)	Temp.	Sonification time	Product	Yield [%][a]
1	Br	**2a** (15)	CH_2	Cu/Zn (3.1)	−20 °C	1 h	**4a**	30
2	Br	**2a** (3)	CH_2	Cu/Zn (3.1)	5 °C	1 h	**4a**	40
3	Br	**2a** (5)	CH_2	Zn (3)	r.t.	1 h	**4a**	62
4	Br	**2b** (4.1)	O	Zn (3)	r.t.	1 h	**4b**	50
5	Br	**2b** (10)	O	Cu/Zn (3)	r.t.	1 h	**4b**	60
6	Br	**2b** (10)	O	Cu/Zn (20)	r.t.	5 h	**4b**	40
7	Br	**2c** (3)	NCOOMe	Zn (5)	r.t.	2 h	**4c**	45

[a] Yield of isolated product, purity >95% determined by GC.

of the cyclization after work-up was immediately reduced using a Cu/Zn-couple[25] in a methanolic solution of ammonium chloride.[13] Based on the preceding work by Montana and co-worker, we used the Cu/Zn-couple for the generation of the oxyallyl species. However, we observed some dimerization of the cyclopentadiene already at $-20\,^{\circ}C$ (entry 1), which became the dominant reaction above $5\,^{\circ}C$ (entry 2). Conversion to **4a** was in both cases not satisfactory. These findings prompted us to use the less reactive zinc, which was activated according to a protocol by Hoffmann et al.[13] This approach turned out to be highly successful, since less than 5% of cyclopentadiene dimer was observed upon full conversion. The reaction was completed after 1 h of sonification at room temperature and **4a** was isolated in 62% yield after subsequent debromination using the Cu/Zn couple (entry 3).

This Zn-assisted [4+3]-cycloaddition protocol utilizing sonification conditions could also be successfully applied to the reaction of **1a** and furan (**2b**); oxabicyclic ketone **4b** was isolated in 50% yield after dehalogenation without additional purification (entry 4). This represents a significantly simplified approach to this compound with similar yield compared to the best documented synthesis in the literature.[13] The Cu/Zn-mediated cyclization gave even better results, since dimerization is not causing any problems with furan as diene (entry 5). Again, the crude compound **4b** was obtained without further purification after debromination in >95% purity (GC). When analyzing the crude mixture of intermediate dibromo-**3b**, we observed a minor amount of dehalogenated product **4b**. Obviously, under sonification conditions *in situ* debromination can be achieved when using the Cu/Zn couple, which was not reported for the classical thermal reaction. Consequently, a one-pot procedure for the synthesis of **4a** was realized using excess Cu/Zn and prolonged sonification time. However, the yields achieved were not superior to the two-step protocol.

We could demonstrate that also activated pyrrole derivatives (**2c**)[26] can be converted in the presence of activated Zn to the corresponding azabicycloketone (**4c**) in acceptable yields.

In order to demonstrate the applicability of the Zn-mediated cyclization to other dienophiles, we carried out a set of experiments with dibromopentanone **1b**[27] and the results are compiled in Table 2.

Again, cyclopentadiene dimerization could be effectively suppressed by carrying out the reaction in the presence of activated Zn (entry 1). All cyclizations gave exclusive formation of the *cis*-dimethyl product of bicycloketones **3d–f**. Addition of NaI further improved the conversion by increasing the yield and shortening the sonification time (entry 2). Oxa- and azabicyclic ketones **3e** and **3f** could be successfully prepared by this convenient method (entries 3 and 4). The diastereomeric ratio was approximately 2:1 for all conversions using dienophile **1b** favoring the *endo*-product.

After having established a facile access to bicyclic compounds **4**, we turned our attention to studying the behavior of these products in ROCM reactions. While the principal possibility of such a transformation on bicyclic systems of type **4** had been demonstrated,[21,22] we were particularly interested in the reaction with gaseous olefins. According to the literature,[19] gaseous olefins can be used as partners in ring-opening metathesis without polymerization.

An initial set of experiments was carried out on carbocyclic precursor **4a** using Grubbs catalysts 1 and 2 (Table 3, entries 1–8). Different reaction conditions were investigated using ethylene and 1-hexene as representative model olefins for the conversion with gaseous and liquid alkenes. Regarding gaseous olefins, a balloon of the cross coupling partner was usually attached to the reaction vessel and the solvent was saturated with ethylene. Afterwards the catalyst was added. Bubbling ethylene through the reaction mixture for the duration of the reaction did not lead to an increase of the conversion rate as the catalyst seems to favor the oligomerization of ethylene.

Working with propylene and butylene showed a general trend: substitution of the double bond increased the electron density at the olefin, leading to reduced reaction times and higher conversion rates. Using Grubbs 2 catalyst for the experiments with gaseous alkene partners did not lead to shorter reaction times. In all cases of transformations with gaseous olefins to produce compounds **6** we observed formation of an equilibrium of bicyclic compound and diolefin.

Blechert and co-workers investigated different procedures for the addition of *trans*- and *cis*-3-hexene in ring-opening cross metathesis with norbornene derivatives.[20] In our case, this kind of slow addition of the partner olefin over 5 hours did not lead to the desired high

Table 2. Cyclization using dienophile **1b** to dimethyl bicyclic ketones **3d–f** under sonification conditions.

Entry	R	Diene (equivs.)	X	Equivs. of Zn	Temp.	Additive	Time	Product	Yield [%][a]	*cis/trans*	*endo/exo*
1	Me	**2a** (3)	CH_2	3	r.t.	—	1 h	**3d**	61	100:0[b]	58:42[b]
2	Me	**2a** (3)	CH_2	3	r.t.	NaI	45 min	**3d**	72	100:0[b]	62:38[b]
3	Me	**2b** (3)	O	3	r.t.	—	1 h	**3e**	84	100:0[b]	70:30[b]
4	Me	**2c** (1)	NCOOMe	3	r.t.	—	1 h	**3f**	60	100:0[b]	62:38[b]

[a] Yield of isolated product, purity >95% determined by GC.
[b] Determined by GC.

Table 3. Ring-opening metathesis using gaseous and liquid olefins.

Entry	Bicyclic compound	X	Olefin	R	Reaction time	Catalyst	Conversion [%]	Product	Yield [%][a]	*E/Z*
1	**4a**	CH_2	**5a**	H	26 h	Grubbs 1 (1 mol %)	75	**6a**	50	n.a.[d]
2	**4a**	CH_2	**5b**	CH_3	75 min	Grubbs 1 (1 mol %)	95	**6b**	40	3.6:1
3	**4a**	CH_2	**5c**	CH_2CH_3	60 min	Grubbs 1 (1 mol %)	95	**6c**	65	6.3:1
4	**4a**	CH_2	**5d**	$(CH_2)_3CH_3$	20 min	Grubbs 1 (1 mol %)	95	**6d**	50	7.5:1
5	**4a**	CH_2	**5e**	Ph	6 h	Grubbs 1 (1 mol %)	90	**6e**	61	100:1
6	**4a**	CH_2	**5f**	Bn	19 h	Grubbs 2 (1 mol %)	90	**6f**	50	1:1.9
7	**4a**	CH_2	**5g**	CH_2Br	48 h	Grubbs 2 (1 mol %)	15	**6g**	n.i.[b]	n.a.
8	**4a**	CH_2	**5h**	CH_2OAc	48 h	Grubbs 2 (1 mol %)	34	**6h**	n.i.	n.a.
9	**4b**	O	**5a**	H	26 h	Grubbs 1 (1 mol%)	75	**6i**	43	n.a.
10	**4b**	O	**5b**	CH_3	4 h	Grubbs 1 (1 mol %)	86	**6j**	40	3.6:1
11	**4b**	O	**5c**	CH_2CH_3	1 h	Grubbs 1 (1 mol %)	87	**6k**	42	8.5:1
12	**4c**	NCOOMe	**5a**	H	29 h	Grubbs 2 (2 mol %)	0	**6l**	n.r.[c]	n.a.
13	**4c**	NCOOMe	**5b**	CH_3	29 h	Grubbs 2 (2 mol %)	0	**6m**	n.r.	n.a.
14	**4c**	NCOOMe	**5c**	CH_2CH_3	27 h	Grubbs 2 (2 mol %)	0	**6n**	n.r.	n.a.

[a] Yield of isolated product after column chromatography.
[b] n.i. = not isolated.
[c] n.r. = no reaction.
[d] n.a. = not applicable.

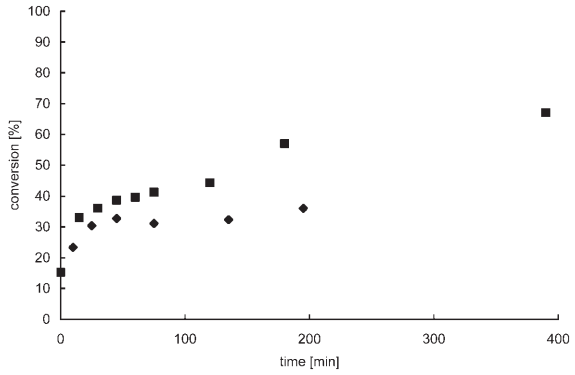


Figure 1. Effect of the mode of addition on the ROCM of **4a** with ethylene **5a** (administration of gaseous olefin *via* balloon [■] or continuous bubbling [◆]).

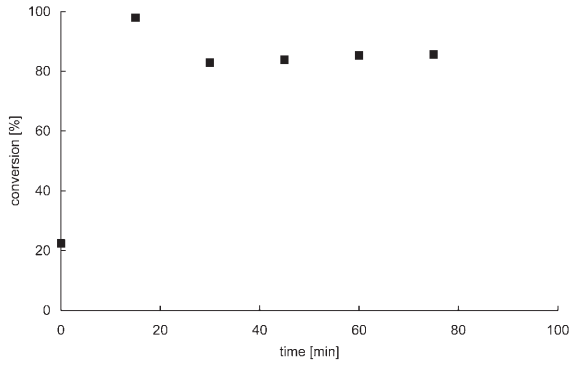


Figure 2. Conversion progress for ROCM of **4a** with 1-hexene **5d**.

conversion. Therefore, mixing of the bicyclo[3.2.1]oct-6-en-3-one with 5 equivalents of 1-hexene and fast addition of the catalyst was performed and monitored by GC. This procedure led to a conversion of 98% after 15 minutes.

This reaction procedure was established with all other liquid olefins. A first screening was carried out with Grubbs 1 catalyst. In those cases where only low to moderate reactivity was observed, experiments were re-run with Grubbs 2 catalyst. Generally, Grubbs 1 – if it catalyses the reaction – shows rather short reaction times and Grubbs 2 takes longer (entry 6).

As observed in the case of gaseous reaction partners, also in the case of liquid partner olefins the reactivity depended on the electron density of the alkene double bond: Conversion is significantly speeded up by the presence of electron-donating substituents (entries 1–5). All such reactions gave conversions beyond 75% and products **6a**–**f** were isolated in moderate to good chemical yields. In the case of gaseous olefins, addition of ethyl vinyl ether (EVE) minimizes reverse reaction upon work-up (entries 1–3). Olefins carrying additional functional groups such as allyl bromide and vinyl acetate were poor reaction partners and transformations commenced very sluggishly (entries 7 and 8).

In the case of unsymmetrically substituted products (entries 2–6) varying *E/Z* ratios were obtained. Only in the case of styrene-derived compound **6e** was exclusive *E*-selectivity observed.

Based on the successful conversion with gaseous olefins, we extended our study to the heterobicyclic compounds **4b** and **4c**. The oxygen-containing system **4b** behaved quite similar to carbocylic precursor **4a** and transformations with olefins **5a**–**c** gave the expected products **6i**–**k**. Equilibrium conversions were comparable to the carbocyclic series. Also *E/Z* ratios were in a similar range as in the carbocyclic series.

However, in the case of methyl carbamate **4c** we were not able to achieve any ROCM with gaseous olefins (entries 12–14) either using 1st or 2nd generation Grubbs catalyst. The expected products **6l**, **m** were not formed and only starting material **4c** was recovered. This may be explained by the very ready RCM of the corresponding systems of type **6** containing a protected nitrogen heteroatom, as recently reported by Martin and coworker.[28]

Conclusion

Summarizing, we have developed a convenient method for the synthesis of carbo- and heterocyclic bicyclo[3.2.1]octenones using sonochemistry. The presented protocol only requires activated zinc and readily available/commercial chemicals. It allows access to elusive and poorly described ketones **4a–c** in a two-step sequence without elaborate work-up and purification in yields comparable to or surpassing previous methods and is scalable to gram-quantities.

With this facile entry to such bridged bicycles we also developed a diastereoselective access to 3,5-difunctionalized six-membered cycloketones by ROCM with liquid and especially gaseous olefins. This work represents one of the few studies of the latter transformation and valuable precursors for subsequent investigations in the field of enantioselective Baeyer–Villiger oxidation are currently under development in our laboratory.

Experimental Section

General Remarks

Unless otherwise noted, chemicals and solvents were purchased from commercial suppliers and used without further purification. All solvents were distilled prior to use. Sonochemical transformations have been performed in a Bandelin Sonorex super RK102H ultrasound bath or utilizing a Bandelin Sonoplus HD3200 sonificator. Flash column chromatography (FCC) was performed on silica gel 60 from Merck (40–63 μm). Melting points were determined using a Kofler-type Leica Galen III micro hot stage microscope and are uncorrected. Reaction control and product purity was determined on a ThermoQuest Trace GC 2000 chromatograph with FID (240 °C) using a standard capillary column DB5 (30 m × 0.32 mm ID). NMR spectra were recorded from $CDCl_3$ or DMSO-d_6 solutions on a Bruker AC 200 (200 MHz) or Bruker Avance UltraShield 400 (400 MHz) spectrometer and chemical shifts are reported in ppm using Me_4Si as internal standard.

General Procedure for the Zn-Mediated [4 + 3]-Cycloaddition

One drop of dibromomethane was added to a suspension of zinc dust (3 equivs.) in dry MeCN (30% suspension) under nitrogen. The suspension was cooled in an ice-bath and treated with perbromo compound **1a**/**b** (1 equiv.) in MeCN (40% solution). Subsequently, the reaction vessel was immersed in an ultrasound bath, sonification was initiated and freshly distilled diene **2a–c** (5 equivs.) was added quickly. The reaction was monitored by GC until full conversion was observed (approx. 1 h) and subsequently quenched by addition of water. The solids were separated by filtration and the layers were separated. The aqueous layer was repeatedly extracted with Et_2O and the combined organic layers were dried (Na_2SO_4), filtered and concentrated (evaporator bath < 30 °C). Crude products **3d–f** were purified by column chromatography. Dibromo intermediates **3a–c** were dissolved in MeOH and 10% of this solution was added dropwise to a well-stirred suspension of freshly prepared Cu/Zn-couple[25] (10 equivs.) in a methanolic NH_4Cl solution (25%) at −80 °C. The mixture was stirred at this temperature for 15 min, then addition was continued maintaining a reaction temperature below −10 °C. After complete addition the mixture was stirred at r.t. for 2–12 h (GC control). The solids were removed by filtration and the organic solution was concentrated. The residue was dissolved in a small amount of Et_2O and carefully treated with saturated $NaHCO_3$ solution. The precipitated salts were removed by filtration and the aqueous phase was repeatedly extracted with Et_2O. The combined organic phases were dried (Na_2SO_4), filtered, and concentrated (evaporator bath < 30 °C) to give pure compounds **3a–c** without further purification.

Bicyclo[3.2.1]oct-6-en-3-one (4a): TBA (3.80 g, 10.6 mmol) was converted with freshly monomerized cyclopentadiene in an ultrasound bath according to the above protocol and conditions outlined in Table 1 to give **4a**[29] as beige crystals (purity > 95%/GC); yield: 0.80 g (62% over 2 steps); mp 98–100 °C.

8-Oxabicyclo[3.2.1]oct-6-en-3-one (4b): TBA (3.80 g, 10.6 mmol) was converted with freshly distilled furan in an ultrasound bath according to the above protocol and conditions outlined in Table 1 to give **4b**[13] as a beige oil (purity > 95%/GC); yield: 0.75 g (60% over 2 steps); which slowly crystallizes in a freezer to give colorless crystals, mp 36–38 °C.

8-Methoxycarbonyl-8-azabicyclo[3.2.1]oct-6-en-3-one (4c): TBA (1.40 g, 3.7 mmol) was converted with protected pyrrole **2c** in an ultrasound bath according to the general protocol and conditions outlined in Table 1 to give of **4c**[8] as a yellow oil (purity > 95%/GC); yield: 0.30 g (45% over 2 steps).

***cis*-2,4-Dimethylbicyclo[3.2.1]oct-6-en-3-one (3d):** 2,4-Dibromopentanone (0.40 g, 1.6 mmol) was converted with freshly monomerized cyclopentadiene upon addition of NaI (0.48 g, 2 equivs.) in an ultrasound bath according to the general protocol and conditions outlined in Table 2 to give **3d**[8] as a colorless oil after FCC (10 g silica gel, LP/Et_2O, 4:1); yield: 0.18 g (72%).

***cis*-2,4-Dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (3e):** 2,4-Dibromopentanone (1.60 g, 6.07 mmol) was converted with furan in an ultrasound bath according to the general protocol and conditions outlined in Table 2 to give **3e**[8] as a colorless crystals after FCC (25 g silica gel, LP/Et_2O, 2:1); yield: 0.84 g (84%).

***cis*-2,4-Dimethyl-8-methoxycarbonyl-8-azabicyclo[3.2.1]oct-6-en-3-one (3f):** 2,4-Dibromopentanone (1.60 g, 6.07 mmol) was converted with protected pyrrole in an ultrasound bath according to the general protocol and conditions outlined in Table 2 to give **3f**[8] as yellow oil after FCC (40 g silica gel, LP/Et_2O, 4:1); yield: 0.70 g (60%).

Scale-Up (10-fold) of the Transformation to Compound 4b Using a Sonicator Probe

A few drops of dibromomethane were added to a suspension of Cu/Zn couple (20.6 g, 320 mmol, 3 equivs.) and furan (100 mL) in dry MeCN (80 ml) under nitrogen. Subsequently, a solution of TBA (38.0 g, 100.6 mmol) in dry MeCN (50 mL) was added dropwise during 15 minutes. The reaction was sonificated for 30 minutes at room temperature and monitored by GC to confirm full conversion. Afterwards, the reaction was quenched by addition of water (100 mL). The solids were separated by filtration and layers were separated. The aqueous layer was extracted with dichloromethane and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. Crude intermediate **3b** was dissolved in EtOH (200 mL) and debrominated by dropwise adding an initial 10% of the solution to a well-stirred suspension of freshly prepared Cu/Zn couple (75.0 g, 1147 mmol) and NH_4Cl (26.0 g, 486 mmol) in EtOH (300 mL) at $-78\,^{\circ}C$. The mixture was stirred at this temperature for 15 min, warmed to 0–10 °C, and continuously treated dropwise with the solution of **3b**. After complete addition the mixture was stirred for approximately 1 h until GC control showed full conversion. The solids were removed by filtration. The precipitate was washed thoroughly with dichloromethane and the obtained organic solution was concentrated. The residue was dissolved in a mixture of saturated $NaHCO_3$ solution and dichloromethane. The organic layer was separated and the aqueous layer was repeatedly extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered and concentrated to give **4b** as a beige oil which solidifies upon standing in the refrigerator (purity >95%/GC); yield: 7.25 g (58% over 2 steps); physical properties were identical to the material obtained from the small-scale transformation.

General Procedure for the ROCM with Gaseous Olefins

Bicyclic ketone **4a–c** (1 equiv., 100 mg) was dissolved in dichloromethane (20 mL) and the gaseous olefin **5a–c** was bubbled through the reaction mixture using a balloon. The catalyst (Grubbs 1 or 2) was dissolved in dichloromethane (2 mL) and added in one shot. The gaseous olefin was bubbled through the reaction mixture every 3 hours. The metathesis reaction was carried out according to conditions outlined in Table 3 and conversion was monitored by GC. After reaching the equilibrium, an excess of ethyl vinyl ether was added and the mixture was stirred for 30 minutes. The solvent was evaporated, followed by purification *via* column chromatography (1/80 silica gel, LP/EtOAc, 40:1).

***cis*-3,5-Diethenylcyclohexan-1-one (6a):** Bicyclic compound **4a** (100 mg, 0.819 mmol) was converted with ethylene according to the above general protocol to give **6a** as a colorless oil; yield: 62 mg (50%); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.11–1.40$ (m, 1H), 1.85–2.20 (m, 3H), 2.28–2.50 (m, 4H), 4.98–5.05 (m, 4H), 5.62–5.83 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta =$ 37.4 (t), 41.3 (d), 46.5 (t), 113.7 (t), 141.1 (d), 209.9 (s).

***cis*-5-Ethenyl-3-propenylcyclohexan-1-one (6b):** Bicyclic compound **4a** (100 mg, 0.819 mmol) was converted with propylene according to the above general protocol to give **6b** as a beige oil; yield: 52 mg (40%); ^{1}H NMR (200 MHz, $CDCl_3$; *E/Z*-isomers): $\delta = 1.20–1.30$ (m, 1H), 1.59 (d, $J = 5.5$ Hz, 3H), 1.85–2.37 (m, 7H), 4.91–5.00 (m, 2H), 5.05–5.50 (m, 2H), 5.64–5.80 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$; *E*-isomer): $\delta = 17.8$ (q), 38.0 (t), 40.6 (d), 41.3 (d), 46.5 (t), 47.2 (t), 113.5 (t), 124.2 (d), 134.0 (d), 141.2 (d), 210.3 (s); (*Z*-isomer): $\delta =$ 12.9 (q), 35.8 (d), 37.8 (t), 41.5 (d), 46.5 (t), 47.3 (t), 113.6 (t), 124.3 (d), 133.3 (d), 141.2 (d), 210.1 (s).

***cis*-5-Butenyl-3-propenyl-cyclohexan-1-one (6c):** Bicyclic compound **4a** (100 mg, 0.819 mmol) was converted with 1-butylene according to the above general protocol to give **6c** as a beige oil; yield: 85 mg (65%); ^{1}H NMR (200 MHz, $CDCl_3$; *E/Z*-isomers): $\delta = 0.97$ (t, $J = 7.5$ Hz, 3H), 1.16–1.42 (m, 2H), 1.85–2.60 (m, 8H), 4.97–5.07 (m, 2H), 5.55–5.71 (m, 2H), 5.72–5.88 (m, 1H); ^{13}C-NMR (50 MHz, $CDCl_3$; *E*-isomer): $\delta = 13.7$ (q), 25.4 (t), 38.1 (t), 41.3 (d), 41.5 (d), 46.5 (t), 47.3 (t), 113.5 (t), 131.8 (d), 141.2 (d), 210.4 (s); (*Z*-isomer): $\delta =$ 14.4 (q), 20.8 (t), 29.2 (t), 36.1 (d), 41.5 (d), 46.5 (t), 47.5 (t), 113.5 (t), 131.9 (d), 141.2 (d), 210.4 (s).

***cis*-2,6-Diethenylperhydro-4-pyranone (6i):** Bicyclic compound **4b** (100 mg, 0.806 mmol) was converted with ethylene according to the above general protocol to give **6i** as a colorless oil; yield: 52 mg (43%); ^{1}H-NMR (200 MHz, $CDCl_3$): $\delta = 2.31–2.51$ (m, 4H), 4.13–4.23 (m, 2H), 5.18–5.38 (m, 4H), 5.86–6.02 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 47.2$ (t), 77.2 (d), 116.2 (t), 137.0 (d), 205.9 (s).

***cis*-2-Ethenyl-6-propenylperhydro-4-pyranone (6j):** Bicyclic compound **4b** (100 mg, 0.806 mmol) was converted with propylene according to the above general protocol to give **6j** as a beige oil; yield: 53 mg (40%); ^{1}H NMR (200 MHz, $CDCl_3$; *E/Z*-isomers): $\delta = 1.73$ (d, $J = 6.2$ Hz, 3H), 2.37–2.42 (m, 4H), 4.07–4.20 (m, 2H), 5.18–5.36 (m, 2H), 5.52–6.02 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 17.7$ (q), 47.3 (t), 47.7 (t), 77.3 (d), 116.4 (t), 128.7 (d), 130.2 (d), 137.0 (d), 206.2 (s).

***cis*-6-Butenyl-2-ethenylperhydro-4-pyranone (6k):** Bicyclic compound **4b** (100 mg, 0.806 mmol) was converted with 1-butylene according to the above general protocol to give **6k** as a beige oil; yield: 60 mg (42%); ^{1}H NMR (200 MHz, $CDCl_3$; *E/Z*-isomers): $\delta = 1.01$ (t, $J = 7.0$ Hz, 3H), 2.09 (q, $J = 7.0$ Hz, 2H), 2.37–2.42 (m, 4H), 4.11–4.18 (m, 2H), 5.18–5.37 (m, 2H), 5.49–6.02 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 13.0$ (q), 25.1 (t), 47.3 (t), 47.9 (t), 77.3 (d), 77.5 (d), 128.0 (d), 135.0 (d), 137.1 (d), 206.2 (s).

General Procedure for the ROCM with Liquid Olefins

Bicyclic ketone **4a** (1 equiv., 100 mg, 0.819 mmol) and liquid olefin **5d–h** (5 equivs.) were dissolved in dichloromethane (10 mL) and the catalyst (Grubbs 1 or 2) dissolved in dichloromethane (2 mL) was added in one shot to the reaction mixture. The conversion was carried out under conditions specified in Table 3 and was monitored by GC. After reaching the equilibrium, the transformation was stopped by adding an excess of ethyl vinyl ether. The mixture was stirred for 30 minutes. Then the solvent was evaporated and the crude reaction mixture was purified *via* column chromatography (1/80 SiO_2, LP/EtOAc, 40:1).

***cis*-5-Ethenyl-3-hexenylcyclohexan-1-one (6d):** Conversion with 1-hexene according to the above general protocol gave **6d** as a colorless oil; yield: 85 mg (50%); ^{1}H NMR (200 MHz, $CDCl_3$; *E/Z*-isomers): $\delta = 0.85$ (t, $J = 7$ Hz, 3H), 1.15–1.30 (m, 4H), 1.80–2.45 (m, 10H), 4.85–5.00 (m, 2H), 5.15–5.35

(m, 2H), 5.60–5.80 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$; *E*-isomer): δ = 13.8 (q), 22.1 (t), 31.5 (t), 32.1 (t), 38.1 (t), 40.6 (d), 41.3 (d), 46.5 (t), 47.4 (t), 113.5 (t), 129.9 (d), 132.8 (d), 141.2 (d), 210.3 (s); (*Z*-isomer): δ = 13.8 (q), 22.1 (t), 27.1 (t), 31.9 (t), 38.1 (t), 38.1 (d), 41.5 (d), 46.5 (t), 47.4 (t), 113.5 (t), 130.0 (d), 132.2 (d), 141.2 (d), 210.2 (s).

***cis*-5-Ethenyl-3-(2′-phenyl-1′-ethenyl)-cyclohexan-1-one (6e):** Conversion with styrene according to the above general protocol gave **6e** as a colorless oil; yield: 113 mg (61%); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.37–1.56 (m, 1H), 2.04–2.57 (m, 7H), 5.00–5.10 (m, 2H), 5.73–5.90 (m, 1H), 6.08–6.19 (dd, *J* = 6.8 Hz, *J* = 9 Hz, 1H,), 6.40 (d, *J* = 15.8 Hz, 1H), 7.21–7.37 (m, 5H); ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 37.8 (t), 40.9 (d), 41.3 (d), 46.5 (t), 46.9 (t), 113.8 (t), 126.1 (d), 127.4 (d), 128.6 (d), 129.1 (d), 132.7 (d), 136.9 (d), 141.0 (d), 209.7 (s).

***cis*-5-Ethenyl-3-(3′-phenyl-1′-propenyl)-cyclohexan-1-one (6f):** Conversion with allylbenzene according to the above general protocol gave **6f** as a colorless oil; yield: 98 mg (50%); ^{1}H NMR (200 MHz, $CDCl_3$; *E/Z*-isomers): δ = 1.16–1.45 (m, 1H), 1.65–2.55 (m, 6H), 2.81–2.85 (m, 1H), 3.25–3.34 (m, 2H), 4.91–5.01 (m, 2H), 5.23–5.34 (m, 1H), 5.35–5.56 (m, 1H), 5.63–5.80 (m, 1H), 7.06–7.25 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$; *E*-isomer): δ = 33.6 (t), 36.2 (d), 38.4 (t), 40.5 (d), 47.2 (t), 47.3 (t), 113.6 (t), 126.1 (d), 128.2 (d), 128.3 (d), 128.4 (d), 134.3 (d), 141.1 (d), 209.9 (s); (*Z*-isomer): δ = 33.6 (t), 36.2 (d), 37.9 (t), 41.3 (d), 47.2 (t), 47.3 (t), 113.6 (t), 126.1 (d), 128.2 (d), 128.3 (d), 128.4 (d), 133.3 (d), 140.1 (d), 209.8 (s).

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