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## Graphical Abstract

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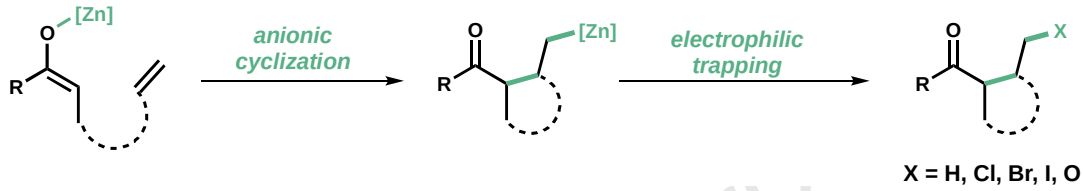

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# Zinc-mediated anionic cyclization of unstabilized ketone enolates with unactivated alkenes

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ABSTRACT

We report herein general conditions for a zinc-mediated anionic cyclization of unstabilized ketone enolates. This anionic cyclization allows access to various carbocyclic architectures by utilizing abundant ketones and unactivated alkenes as precursors. The transformation is enabled by the use of $Zn(TMP)_2$ as base and $Zn(OTf)_2$ as an additive. The resulting alkylzinc species can be intercepted by electrophiles for tandem C–X and C–O bond formation.



## 1. Introduction

The formation of new carbon-carbon bonds via the carbometalation of unactivated olefins is a powerful synthetic strategy for converting cheap and abundant feedstock olefins into higher value products. The carbozincation of alkenes[1] is a particularly useful transformation, as the resulting alkylzinc intermediates can be readily functionalized via transmetalation to other transition metal species (Pd, Ni, Cu, Co, Fe) for further derivatization.[2]

Seminal studies by Normant and Marek demonstrated that carbocyclization reactions of organozinc reagents and unactivated alkenes are valuable synthetic tools for constructing carbocycles.[3] Initial developments in the area of zinc-mediated intramolecular metallo-ene-allene reactions[3a] led to the discovery of an anionic cyclization of zinc enolate derivatives,[3h,4] a contrathermodynamic reaction wherein the resulting alkyl metal species is more basic than the initial enolate.[4] $\alpha$– or $\beta$–amino ester zinc enolates generated by deprotonation with LDA followed by transmetalation with $ZnBr_2$ were shown to diastereoselectively cyclize onto unactivated pendant olefins to give substituted pyrrolidines and piperidines (Figure 1A).[5] Related studies revealed that zinc enolates generated by 1,4-addition of dialkylzinc reagents to unsaturated carbonyls could also undergo carbozincation with a pendant olefin to provide substituted proline and pyrrolidine products.[6]

Concurrent studies by Karoyan and Chassaing also showed that the aminoester enolate carbozincation reaction can be exploited to prepare proline chimeras of proteinogenic amino acids in order to study structure activity relationships of biologically active peptides.[7]

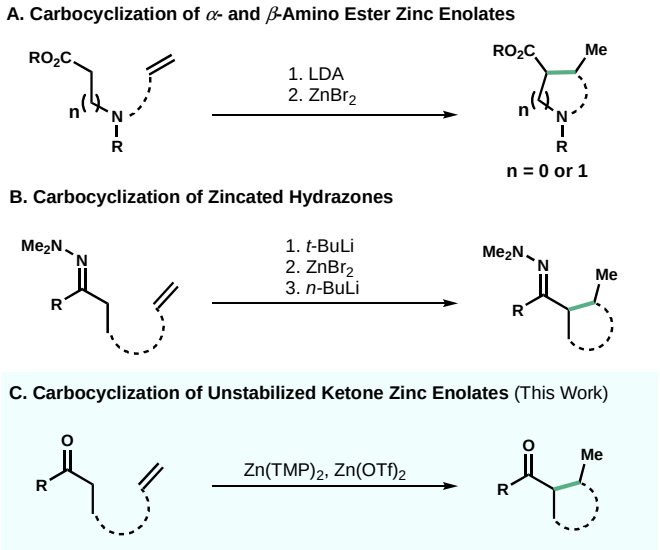



**Figure 1**. Carbocyclization of unactivated alkenes with zinc enolate derivatives.

Another class of intramolecular alkene carbozincation reactions with enolate derivatives include Nakamura's work with zincated hydrazones (Figure 1B).[8] Deprotonation of an *N,N*-dimethylhydrazone with *t*-BuLi, followed by formation of the

zincate via the successive addition of $ZnBr_2$ and *n*-BuLi, enables cyclization with a pendant terminal olefin to give 5- and 6-*exo-trig* cyclization products with good *cis*-diastereoselectivity. Lactams were also found to be suitable substrates for this reaction. These important preliminary studies led to the development of multicomponent alkene functionalization reactions with azaenolates derivatives, including zincated hydrazones and zinc enamides.[9]

In both transformations, the presence of a coordinating *N*-heteroatom on the substrate was crucial for promoting efficient reactivity and stereoselectivity, but limits the scope and availability of starting materials. A general method for the anionic cyclization of unstabilized ketone enolates with unactivated alkenes has not been reported, despite the prevalence of ketones in biologically relevant organic molecules. This transformation would offer significant advantages over the classical thermal Conia-Ene reaction,[10] such as milder reaction conditions, formation of a reactive intermediate that can undergo further derivatization, and does not require the use of precious transition metals such as Pd,[11] Au,[12] Rh,[13] or Ir,[14] for which related enolate alkylations with olefins have been developed.[15] A carbozincation with simple ketone enolates would expand the scope of products that can be accessed, and obviates the need to prepare an activated species, such as a hydrazone, in a separate operation.

We recently reported an anionic cyclization of ketone zinc enolates that may play a role in the nickel-catalyzed cycloalkenylation[16] and alkene difunctionalization reactions of ketone enolates.[17] However, the conditions used in connection with nickel catalysis were not directly applicable to cyclization and electrophile capture. Herein we report general conditions for the anionic cyclization of ketone zinc enolates and an expansion of the scope of ketone scaffolds that can undergo this cyclization reaction. Furthermore, in addition to protonation, we demonstrate that the resulting alkylzinc species can be intercepted for C–X (X = Cl, Br, I) and C–O bond formation.

## 2. Results and Discussion

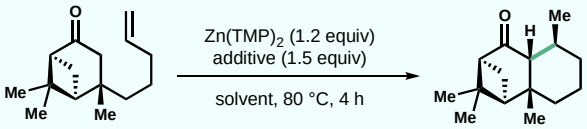
### *2.1. Optimization studies*

In our previous reports,[16,17] we identified that that an anionic cyclization of zinc enolates and alkenes can be effected by heating the substrate in the presence of $Zn(TMP)_2$ as base, albeit in low conversions. Thus, we commenced our optimization using $Zn(TMP)_2$ and **1a**, which was identified as a more challenging model substrate (Table 1) based on our observations that the 6-*exo-trig* cyclization provided lower conversions relative to the corresponding 5-*exo-trig* cyclization using the same verbenone scaffold. In the absence of additives, the zinc cyclization only provided 23% of **2a** (entry 1), with the remainder of the mass balance being unreacted starting material.

Surprisingly, an examination of zinc halides as additives (entries 2–4) did not provide an improvement to the conversion, which is in contrast to our observations for the 5-*exo-trig* cyclization wherein $ZnBr_2$ was sufficient for promoting the cyclization.[16] Remarkably, the use of strongly Lewis acidic $Zn(OTf)_2$ as an additive provided a significant increase in the yield of **2a** (75%, entry 5). Surprisingly, the use of other triflate salts (Li, Mg, Cu, Fe, Sc, *n*-$Bu_4N$) were ineffective for promoting this transformation (see Supplementary Data), highlighting the essential role of the zinc cation.[18]

Next, we explored solvents to further optimize the conversion of the carbozincation. The use of solvents such as 1,4-dioxane (entry 6), toluene (entry 7), and trifluorotoluene (entry 8) gave lower conversions, even after attempting to promote conversion

**Table 1.** Optimization of Anionic Cyclization




| Entry | Additive | Solvent | Yield (%) [a] |
|---|---|---|---|
| 1 | none | THF | 23 |
| 2 | $ZnCl_2$ | THF | 20 |
| 3 | $ZnBr_2$ | THF | 10 |
| 4 | $ZnI_2$ | THF | 13 |
| 5 | $Zn(OTf)_2$ | THF | 75 |
| 6 | $Zn(OTf)_2$ | 1,4-dioxane | 52 |
| 7 | $Zn(OTf)_2$ | toluene | 52 |
| 8 | $Zn(OTf)_2$ | $PhCF_3$ | 32 |
| 8 | $Zn(OTf)_2$ | DCE | 87 |
| **10** | **$Zn(OTf)_2$** | **DME** | **92** [b] |
| 11 | none | DME | 48 |

[a] $^1$H-NMR yield was determined using 1,3,5-trimethoxybenzene as an internal standard. [b] Isolated yield.

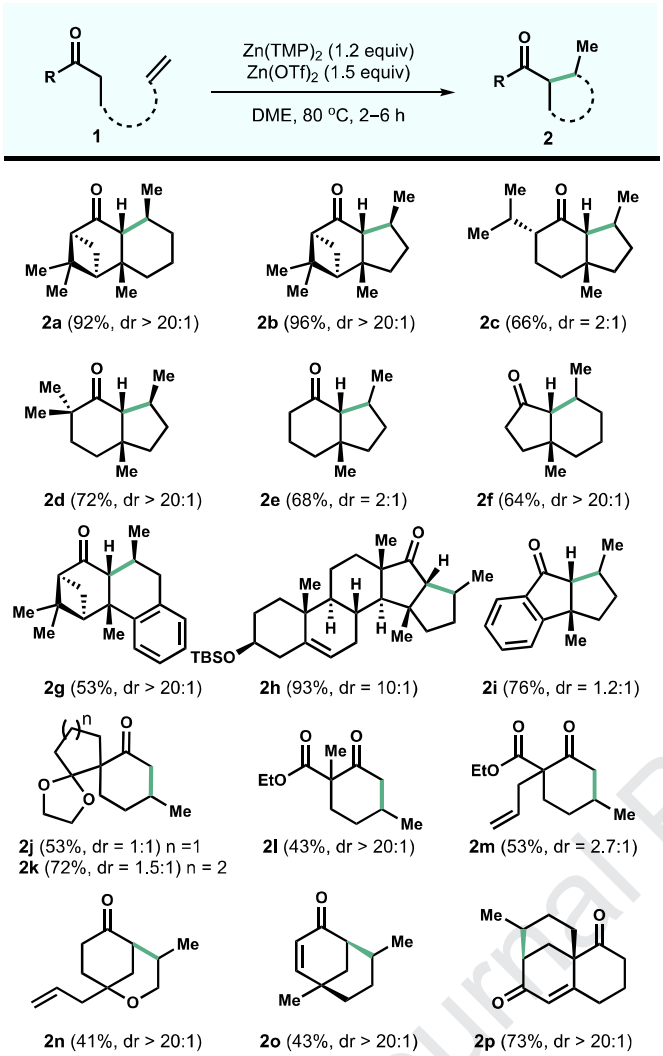
using higher temperatures with these higher boiling solvents. Interestingly, the use of 1,2-dichloroethane (DCE) provided a subtle increase in yield (entry 9). Finally, we found that the optimal conditions required 1,2-dimethoxyethane (DME) as solvent, which afforded **2a** in 92% $^1$H-NMR and isolated yield (entry 10). The use of DME with no Lewis acid additive revealed that the change in solvent from THF alone also provided a dramatic increase in yield (entry 11). Although speculating on the reason for this is challenging, a solvent change may perturb the Schlenk equilibrium, which can result in changes to the aggregation state of the reactive enolates, as well as the ligands bound to zinc, to provide a more efficient reaction. Additionally, solvent-induced conformational changes may also reduce the kinetic barrier to cyclization.

### *2.2. Substrate scope of anionic cyclization*

With the optimized conditions in hand, we explored the scope of the zinc-mediated anionic cyclization (Table 2). 5-*exo-trig* cyclizations were similarly efficient, providing **2b**–**2e** in excellent yields. Remarkably, substrates with two enolizable positions selectively underwent cyclization to form the *cis*-fused bicycle over unproductive pathways or the possible bridged-bicycle (**2e**–**2f**), suggesting that proton transfer between the two enolizable positions occurs. This advancement overcomes the need to have kinetic enolate formation for efficient reactivity, which is a general limitation with our previously reported enolate-initiated carbocyclizations with unactivated alkenes.[16,17] Complex polycyclic products such as **2g**–**2i** were also obtained under the optimized conditions, and highlights the utility of this transformation for late stage functionalization of complex architectures. Acyclic methyl ketones were employed to access spirocyclic products **2j** and **2k** as well as cyclohexanone derivatives **2l** and **2m**. γ,γ-disubstituted cyclohexanones selectively cyclized with the longer *O*-tethered alkene over the shorter allyl group to form the tetrahydropyran containing bicyclo[3.3.1]nonane product **2n**. Access to **2n** is also an additional example of proton transfer being tolerated under the reaction conditions. Cyclohexenones bearing an appropriately long butenyl moiety at the γ-position can cyclize to give the all-carbon bicyclo[3.3.1]nonane product (**2o**). Similarly, the Wieland-Miescher ketone derivative **2p** can be accessed, with cyclization occurring selectively at the more thermodynamically

stable enolate. Attempts to form bicyclo[3.2.1]octane products from γ,γ-

**Table 2.** Substrate Scope of Anionic Cyclization




disubstituted cyclohexenones bearing an allyl group were unsuccessful due to poor conversion. Furthermore, poor conversion was observed if a quaternary center is not present on the tethered alkene, or when internal alkenes were employed. The failure of internal olefins to participate in this transformation suggests that a radical cyclization is unlikely. While the cyclization reaction exclusively provided *cis*-fused products for bicyclic systems,[5a,5b] the relative stereochemistry of the resulting methyl group on the newly formed ring depends on the structure of the ketone scaffold. More structurally rigid motifs provided better diastereoselectivity for the more thermodynamically favored product, wherein the methyl group is situated on the less-hindered, convex face of the resulting bicyclic system.

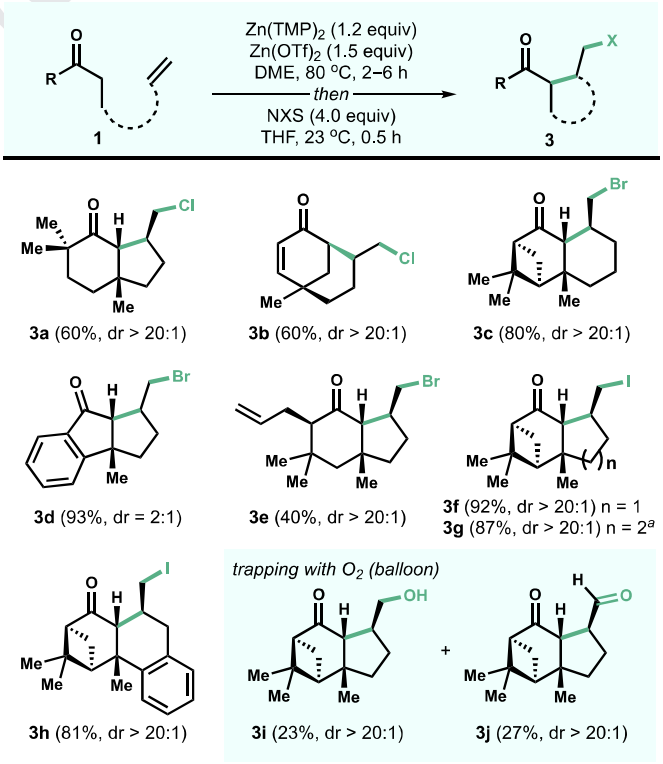
### *2.3. Substrate Scope of Alkene Difunctionalization*

With the scope of the anionic cyclization established, we hypothesized that the resulting alkylzinc species could be trapped by the addition of electrophiles to allow for an alkene difunctionalization reaction (Table 3). We were particularly interested in exploring the use of electrophilic halogenating reagents as electrophiles, as the resulting alkyl halide products are versatile and valuable intermediates that can be used for subsequent derivatization via substitution or cross-coupling reactions. While the cyclized alkylzinc species could directly be used for further substrate elaboration through Negishi-type cross-coupling reactions,[2] having access to both the alkylzinc and alkyl halide species broadens the range of reactions that are accessible. We found that the addition of four equivalents of commercially available and operationally convenient *N*-halosuccinimides was necessary for complete conversion of the organozinc intermediate to the desired carbohalogenation product.

Using *N*-chlorosuccinimide, carbochlorination products **3a**–**3b** could be obtained. *N*-Bromosuccinimide could also be used to give carbohalogenation products **3c**–**3e**, and generally proceeded more efficiently than the corresponding chlorination reactions. Carboiodination with *N*-iodosuccinimide to give products **3f** and **3h** was also successful. Carboiodination using $I_2$ as the halogen source was similarly efficient, providing **3g** in excellent yield, and represents a more atom economical halogenating source. Importantly, alkene functionality (**3b, 3e**) which are well known to undergo halogenation reactions in the presence of *N*-halosuccinimides, was tolerated under the reaction conditions.

Alkylzinc halides have also been demonstrated in the literature to undergo oxidation in the presence of $O_2$.[19] Therefore, we hypothesized that aerobic oxidation of the alkylzinc species generated by our anionic cyclization conditions should also be feasible. Indeed, stirring the alkylzinc species under an oxygen atmosphere provided the corresponding alcohol (**3i**) and aldehyde (**3j**) products with a combined yield of 50%, and demonstrates the possibility of tandem C–C/C–O bond formation by this approach.

**Table 3.** Substrate Scope of Alkene Difunctionalization




[a]$I_2$ was used as the halogen source.

### *2.4. Mechanistic studies*

Preliminary mechanistic studies were conducted to further investigate the nature of the zinc cyclization. Upon complete consumption of **1a** under the reaction conditions, the resulting intermediate can be quenched with $D_2O$ to afford the deuterated product **2a-*d*$_1$** in 68% isolated yield with 60% deuterium incorporation (Figure 2A), confirming the presence of an alkylzinc intermediate.

In order to understand why only 60% deuterium incorporation was observed, we wanted to probe whether radical intermediates[6,20] could be involved. If a radical process was operative, deuterated product **2a-*d*$_1$** should be observed when a

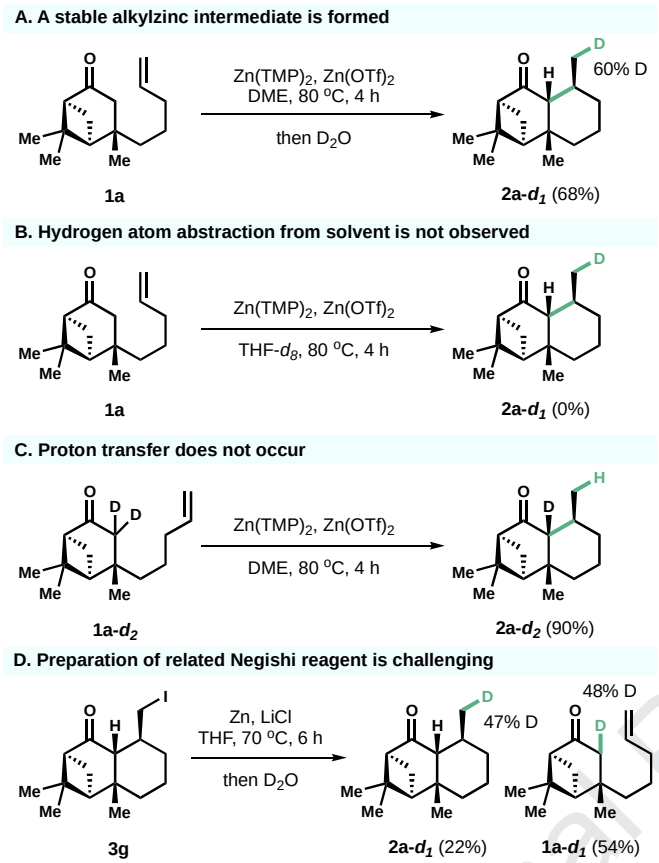



**Figure 2.** Mechanistic studies.

deuterated solvent is used for the cyclization reaction, as the primary alkyl radical formed after cyclization should quickly abstract a deuteride from the deuterated solvent. While no deuterated products were obtained using THF-$d_8$ as solvent (Figure 2B), which argues against an intermediate alkyl radical undergoing hydrogen atom abstraction, we cannot rule out the possibility that the radical formed after cyclization is rapidly reduced by a Zn(II) species[20c] to prevent deuterium transfer from the solvent.

Compound **1a-*d*$_2$** was prepared to investigate whether the incomplete deuterium incorporation was the result of proton exchange between the cyclized alkylzinc species and the more acidic ketone $\alpha$-protons (Figure 2C). However, after dideuterated compound **1a-*d*$_2$** was subjected to the standard conditions and an aqueous quench, compound **2a-*d*$_2$** was obtained with no deuterium incorporation at the methyl group, suggesting that proton transfer does not occur, despite the primary alkylzinc species being more basic than the carbonyl $\alpha$-protons. Furthermore, these results suggest that the TMP-D formed after deprotonation also did not undergo proton transfer with the primary alkylzinc species, as no dideuterated products were observed after the reaction. The incomplete deuteration previously observed is likely the result of the alkylzinc species being quenched by adventitious water. Longer reaction times or higher reaction temperatures with $D_2O$ did not result in higher levels of deuterium incorporation.

Attempts to prepare the related Negishi reagent in THF from alkyl iodide **3g** by direct zinc insertion, followed by quenching with $D_2O$ afforded hydrodehalogenation product **2a-*d*$_1$** in 22% yield with 47% deuterium incorporation (Figure 2D), demonstrating the feasibility of forming similar organozinc species by conventional approaches. However, ring opened product **1a-*d*$_1$** was obtained in 54% yield and determined to have 48% deuterium incorporation at the $\alpha$-position. The analogous reaction conducted in DME as solvent resulted in the formation of dehalogenated species **2a** in 11% yield and ring opened product **1a** in 89% yield. Attempts to achieve alkylzinc formation from **3g** via zinc-halide exchange using $Et_2Zn$ resulted in 4% ring opened product **1a** and 90% unreacted halide (see Supplementary Data).[20] These results highlight the challenge of zinc enolate cyclizations with unactivated alkenes due to the thermodynamically favored reverse reaction. The ring opening reaction may proceed via anionic opening with transfer of the zinc ion from C to O, or via a radical-mediated mechanism involving homolytic fragmentation of the carbon-zinc bond.[21] In contrast, the zinc cyclization under our optimized conditions provides a straightforward and operationally simple method to access functionalized alkylzincs in high yields and conversions, and suggests the structure of the ZnX species (either ZnTMP, ZnOTf, or some other aggregate) is important for driving the equilibrium between the zinc enolate and alkylzinc towards the cyclized product.

## 3. Conclusion

In conclusion, we have developed an efficient anionic cyclization of unactivated ketone zinc enolates and unactivated alkenes using $Zn(TMP)_2$ as base and $Zn(OTf)_2$ as an additive. The choice of DME as solvent provided a significant increase in the efficiency of the carbozincation reaction. This specific combination of additive and solvent was crucial for achieving a broad substrate scope. The reaction provides access to a variety of carbocyclic skeletons and generates a reactive and conventionally challenging to access alkylzinc species that can undergo further reaction with electrophiles to give products that have undergone protonation, halogenation, or hydroxylation. We anticipate this strategy for C–C bond formation to have broad utility in multistep synthesis as it provides an approach to construct cyclic systems using commonly found ketone and unactivated alkene functional groups, while also forming stable and reactive functionalized organozinc species for further derivatization.

## 4. Experimental Section

### *4.1. General Experimental Procedures*

All reactions were carried out under an inert nitrogen atmosphere with dry solvents under anhydrous conditions unless otherwise stated. All reactions were capped with a rubber septum, or Teflon-coated silicon microwave cap unless otherwise stated. Stainless steel cannula or syringe was used to transfer solvent, and air- and moisture sensitive liquid reagents. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica gel plates (60F-254) using UV light as the visualizing agent and potassium permanganate, an acidic solution of *p*-anisaldehyde, phosphomolybdic acid, or $I_2$ on $SiO_2$ as developing agents. Flash column chromatography employed SiliaFlash® P60 (40-60 μm, 230-400 mesh) silica gel purchased from SiliCycle, Inc.

### *4.2. Materials*

All reaction solvents were purified using a Seca solvent purification system by Glass contour. $CuBr \cdot SMe_2$ was prepared and purified according to the literature procedure.[22] $Zn(TMP)_2$

(0.5 M in toluene) was purchased from Sigma-Aldrich or prepared according to the literature procedure.[17] 4-bromo-1-butene was purchased from Oakwood Products, Inc and purified via neat filtration through a 2 cm pad of dry silica in a 5.75 inch pipette prior to use. All other reagents were used as received without further purification, unless otherwise stated.

*4.3. Instrumentation*

All new compounds were characterized by means of $^{1}$H-NMR, $^{13}$C-NMR, FT-IR (thin film), and GC-MS. Copies of the $^{1}$H- and $^{13}$C-NMR spectra can be found at the end of each experimental procedure. NMR spectra were recorded using a Varian 400 MHz NMR spectrometer, Varian 500 MHz NMR spectrometer, or a Varian 600 MHz NMR spectrometer. All $^{1}$H-NMR data are reported in δ units, parts per million (ppm), and were calibrated relative to the signals for residual chloroform (7.26 ppm) in deuterochloroform ($CDCl_3$). All $^{13}$C-NMR data are reported in ppm relative to $CDCl_3$ (77.16 ppm) and were obtained with $^{1}$H decoupling unless otherwise stated. The following abbreviations or combinations thereof were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, abq = ab quartet, br = broad, m = multiplet, and a = apparent. All IR spectra were taken on an FT-IR/Raman Thermo Nicolet 6700. Gas chromatography mass spectra (GC-MS) were recorded on an Agilent Technologies 6890N Network Gas Chromatograph System with an Agilent Technologies 5973N Mass Selective Detector. Optical rotation data was obtained using a Perkin-Elmer 341 polarimeter or a Rudolph Autopol IV polarimeter.

*4.4. General Procedures*

*4.4.1. General Procedure for Anionic Cyclization*

To a flame-dried, 10 mL microwave vial equipped with a magnetic stir bar was added $Zn(OTf)_2$ (109.1 mg, 0.30 mmol, 1.5 equiv). The vial was capped, evacuated, and flame-dried under vacuum for 10 seconds (this process was repeated 3 times). The reaction vessel was backfilled with $N_2$ before 1,2-dimethoxyethane (2 mL, 0.1 M) was added. To the stirred mixture was added ketone **1** (0.2 mmol, 1.0 equiv) and $Zn(TMP)_2$ (0.48 mL, 0.5 M in toluene, 0.24 mmol, 1.2 equiv). The reaction vessel was sealed with parafilm, and placed in an 80 °C preheated oil bath and stirred until complete conversion was observed by thin layer chromatography (2–6 hours).

The reaction vessel was removed from the oil bath and cooled to ambient temperature before sat. aq. $NH_4Cl$ (1 mL) and $Et_2O$ (1 mL) was added. The organic phase was separated and the aqueous phase was extracted with $Et_2O$ (2 x 1 mL). The combined organic extracts were filtered over a small pad of dry silica gel and concentrated under reduced pressure by rotary evaporation. The crude mixture was purified by flash column chromatography on silica gel.

*4.4.2. General Procedure for Carbohalogenation*

To a flame-dried, 10 mL microwave vial equipped with a magnetic stir bar was added $Zn(OTf)_2$ (109.1 mg, 0.30 mmol, 1.5 equiv). The vial was capped, evacuated, and flame-dried under vacuum for 10 seconds (this process was repeated 3 times). The reaction vessel was backfilled with $N_2$ before 1,2-dimethoxyethane (2 mL, 0.1 M) was added. To the stirred mixture was added ketone **1** (0.2 mmol, 1.0 equiv) and $Zn(TMP)_2$ (0.48 mL, 0.5 M in toluene, 0.24 mmol, 1.2 equiv). The reaction vessel was sealed with parafilm, and placed in an 80 °C preheated oil bath and stirred until complete conversion was observed by thin layer chromatography (2–6 hours).

The reaction vessel was removed from the oil bath and placed into a 0 °C ice-water bath and stirred for 10 minutes before NXS (0.8 mmol, 4.0 equiv) in THF (2.0 mL, 0.4 M) was added dropwise. The reaction vessel was removed from the ice-water bath and the reaction mixture was stirred at ambient temperature for 30 minutes.

To the reaction mixture was added sat. aq. $NH_4Cl$ (1 mL) and $Et_2O$ (1 mL). The organic phase was separated and the aqueous phase was extracted with $Et_2O$ (2 x 1 mL). For carboiodination reactions, the combined organic extracts were washed with sat. aq. $Na_2S_2O_3$ (2 mL) until the red color of iodine faded. The organic extracts were filtered over a small pad of dry silica gel and concentrated under reduced pressure by rotary evaporation. The crude mixture was purified by flash column chromatography on silica gel.

*4.5. Substrate Synthesis*

Ketones **1a**, **1b**, **1c**, **1d**, **1h**, **1i**, **1j**, **1k**, **1l**, **1m**, **1n**, **1o**, **1p,** and **1q** were prepared according to our previously reported procedures.[16,17] Ketones **1e**[23] and **1f**[24] were prepared according to the literature procedure. See the Supplementary Data for more details.

*4.5.1. (1S,4S,5R)-4-(2-allylphenyl)-4,6,6-trimethylbicyclo[3.1.1] heptan-2-one (**1g**)*

To a flame-dried 20 mL microwave vial was added magnesium turnings (52.8 mg, 2.2 mmol, 1.2 equiv) and a catalytic amount of $I_2$ (ca 5 mg). The reaction vessel was capped, evacuated, and backfilled with $N_2$ and THF (4.0 mL, 0.5 M) was added to the reaction vessel. The reaction vessel was then moved to a 70 °C pre-heated oil bath and stirred for 10 minutes. The reaction vessel was then removed from the oil bath and to the reaction mixture was added 1-allyl-2-bromobenzene (0.3 mL, 2.0 mmol, 1.1 equiv) dropwise over 15 minutes as to maintain a gentle reflux. The reaction vessel was then moved back to a 70 °C oil bath and stirred for 30 minutes. The reaction vessel was then removed from the oil bath and cooled to ambient temperature.

In a separate flame-dried 20 mL microwave vial equipped with a magnetic stir bar was added $CuBr{\bullet}SMe_2$ (41.3 mg, 0.2 mmol, 10 mol %). The reaction vessel was evacuated and backfilled with $N_2$ before THF (4 mL, 0.45 M) was added to the reaction vessel. The reaction mixture was then cooled to −40 °C in a dry ice-acetonitrile bath and the previously prepared Grignard solution was added dropwise over 15 minutes. The reaction mixture was stirred at −40 °C for 30 minutes before it was cooled to −78 °C in a dry ice-acetone bath and **SI-1** (0.28 mL, 1.8 mmol, 1.0 equiv) was added dropwise. The reaction mixture was stirred for 12 hours and slowly warmed to ambient temperature.

To the reaction mixture was added sat. aq. $NH_4Cl$ (10 mL) and $Et_2O$ (10 mL). The organic phase was separated and the aqueous phase was extracted with $Et_2O$ (2 x 10 mL). The combined organic extracts were washed with brine (30 mL), dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure by rotary evaporation. Purification by flash column chromatography on silica gel (10% $Et_2O$/hexanes) afforded **1g** (270.3 mg, 56%) as a yellow oil. $\mathbf{R_f}$: 0.36 (10% $Et_2O$/hexanes) $[\alpha]^{20}_{D}$: −16.0° (*c* 1.0, $CHCl_3$) **$^{1}$H NMR** (400 MHz, $CDCl_3$): δ 7.28 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.19–7.10 (m, 2H), 7.00 (d, *J* = 7.2 Hz, 1H), 5.99 (ddt, *J* = 16.4, 10.0, 6.0 Hz, 1H), 5.14–5.05 (m, 2H), 3.51 (d, *J* = 6.0 Hz, 2H), 2.99 (s, 2H), 2.75–2.70 (m, 2H), 2.55 (at, *J* = 4.8 Hz, 1H), 1.54 (s, 3H), 1.53–1.51 (m, 1H), 1.50 (s, 3H), 1.14 (s, 3H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 213.4, 149.6, 138.1, 137.8, 132.9, 126.0, 125.9, 124.9, 116.5, 55.9, 52.8, 50.6, 40.1, 39.7, 38.5, 30.2, 27.9, 27.0, 25.9 **IR** ($cm^{-1}$): 2925, 1711, 1637, 1483, 1255, 1202, 987, 914, 760, 503, 467 **GC-MS** (m/z): [M] calc'd for $C_{19}H_{24}O$: 268.2; found: 268.1.

*4.6. Product Characterization*

*4.6.1. (1R,3S,5S,8aR)-2,2,5,8a-tetramethyloctahydro-1,3-methan-onaphthalen-4(1H)-one (**2a**)*

Compound **2a** was prepared from **1a** (44.1 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (4 hours). Purification by flash column chromatography on silica gel (3% $Et_2O$/hexanes) afforded **2a** (40.6 mg, 92%) as a colorless oil. $\mathbf{R_f}$: 0.45 (10% $Et_2O$/hexanes): $[\alpha]^{20}_D$: −62.0° (*c* 1.0, $CHCl_3$) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 2.51 (at, *J* = 5.2 Hz, 1H), 2.44 (adt, *J* = 10.8, 6.4 Hz, 1H), 1.89–1.82 (m, 1H), 1.80 (at, *J* = 6.0 Hz, 1H), 1.75–1.54 (m, 6H), 1.34 (s, 3H), 1.27–1.21 (m, 1H), 1.19 (s, 3H), 1.11 (d, *J* = 6.4 Hz, 3H), 1.04 (s, 3H), 0.99–0.95 (m, 1H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 215.7, 59.3, 58.8, 55.0, 40.6, 35.9, 32.2, 31.5, 30.5, 28.0, 27.7, 25.8, 25.2, 22.4, 16.7 **IR** ($cm^{-1}$): 2946, 2870, 1463, 1378, 1259, 1203, 1097, 1033, 804, 517 **GC-MS** (m/z): [M] calc'd for $C_{15}H_{24}O$: 220.2; found: 220.2.

*4.6.2. (1S,3aR,4R,6S)-1,3a,5,5-tetramethyloctahydro-7H-4,6-methanoinden-7-one (**2b**)*

Compound **2b** was prepared from **1b** (41.3 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (2 hours). Purification by flash column chromatography on silica gel (2% $Et_2O$/hexanes) afforded **2b** (39.7 mg, 96%) as a pale-yellow oil. $\mathbf{R_f}$: 0.43 (10% $Et_2O$/hexanes) $[\alpha]^{20}_D$: −59.0° (*c* 1.0, $CHCl_3$) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 2.50 (at, *J* = 5.2 Hz, 1H), 2.42 (adt, *J* = 10.8, 6.4 Hz, 1H), 2.00 (at, *J* = 6.0 Hz, 1H), 1.95–1.89 (m, 1H), 1.84 (d, *J* = 10.0 Hz, 1H), 1.84–1.78 (m, 1H), 1.71–1.61 (m, 2H), 1.44–1.37 (m, 2H), 1.35 (s, 3H), 1.25 (d, *J* = 6.4 Hz, 3H), 1.21 (s, 3H), 0.98 (s, 3H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 216.4, 62.9, 58.4, 52.3, 44.6, 44.5, 42.9, 41.1, 34.5, 29.3, 27.4, 25.8, 25.2, 21.4 **IR** ($cm^{-1}$): 2947, 2871, 1700, 1462, 1376, 1269, 1201, 1041, 1006, 828, 751, 524 **GC-MS** (m/z): [M] calc'd for $C_{14}H_{22}O$: 206.2; found: 206.2.

*4.6.3. (3S,5R,7aR)-5-isopropyl-3,7a-dimethyloctahydro-4H-inden-4-one (**2c**)*

Compound **2c** was prepared from **1c** (41.7 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (4 hours). Purification by flash column chromatography on silica gel (2% $Et_2O$/hexanes) afforded **2c** (27.7 mg, 66%, dr = 2:1) as a colorless oil. $\mathbf{R_f}$: 0.50 (10% $Et_2O$/hexanes) $[\alpha]^{20}_D$: −13.0° (*c* 1.0, $CHCl_3$) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 2.45–2.33 (m, 0.33H), 2.26–2.13 (m, 2H), 2.09–2.00 (m, 0.33H), 1.97–1.75 (m, 3.67H), 1.73–1.60 (m, 1.67H), 1.57–1.52 (m, 1H), 1.50–1.43 (m, 1H), 1.41–1.20 (m, 2H), 1.10 (s, 2H), 1.04 (s, 1H), 1.03 (d, *J* = 6.4 Hz, 2H), 0.96 (d, *J* = 6.4 Hz, 1H), 0.92 (d, *J* = 6.8 Hz, 2H), 0.90 (d, *J* = 6.4 Hz, 1H), 0.85–0.83 (m, 3H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 215.7, 215.3, 70.0, 68.0, 55.5, 52.1, 48.3, 45.0, 40.7, 40.4, 38.9, 38.7, 36.0, 34.7, 33.7, 32.7, 30.9, 28.5, 26.5, 26.3, 24.7, 21.6, 21.3, 21.3, 20.4, 20.3, 19.4, 18.6 **IR** ($cm^{-1}$): 2952, 2868, 1694, 1458, 1377, 1368, 1169, 986, 659, 563 **GC-MS** (m/z): [M] calc'd for $C_{14}H_{24}O$: 208.2; found: 208.2.

*4.6.4. 3,5,5,7a-tetramethyloctahydro-4H-inden-4-one (**2d**)*

Compound **2d** was prepared from **1d** (38.9 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (4 hours). Purification by flash column chromatography on silica gel (5% $Et_2O$/hexanes) afforded **2d** (28.1 mg, 72%) as a colorless oil. $\mathbf{R_f}$: 0.60 (10% $Et_2O$/hexanes) **$^1$H NMR** (500 MHz, $CDCl_3$): δ 2.37–2.25 (m, 1H), 1.90–1.83 (m, 1H), 1.82 (d, *J* = 11.5 Hz, 1H), 1.76–1.65 (m, 2H), 1.60–1.56 (m, 1H), 1.53–1.44 (m, 2H), 1.33–1.21 (m, 2H), 1.11 (s, 3H), 1.09 (s, 3H), 1.08 (s, 3H), 1.03 (d, *J* = 8.0 Hz, 3H) **$^{13}$C NMR** (151 MHz, $CDCl_3$): δ 219.0, 66.5, 45.3, 43.5, 40.7, 39.2, 35.1, 33.7, 33.5, 29.8, 27.1, 26.7, 20.5 **IR** ($cm^{-1}$): 2952, 2866, 1693, 1458, 1381, 1116, 1072, 555 **GC-MS** (m/z): [M] calc'd for $C_{13}H_{22}O$: 194.2; found: 194.2.

*4.6.5. 3,7a-dimethyloctahydro-4H-inden-4-one (**2e**)*

Compound **2e** was prepared from **1e** (33.2 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (2 hours). Purification by flash column chromatography on silica gel (5% $Et_2O$/hexanes) afforded **2e** (22.6 mg, 68%, dr = 2:1) as a colorless oil. $\mathbf{R_f}$: 0.55 (20% $Et_2O$/hexanes) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 2.45–2.37 (m, 0.33H), 2.36–2.28 (m, 0.33H), 2.25–2.17 (m, 1.67H), 2.09–2.02 (m, 1H), 1.95–1.86 (m, 1.67H), 1.85–1.75 (m, 1.33H), 1.73–1.66 (m, 1.67H), 1.64–1.59 (m, 1H), 1.57–1.56 (m, 0.67H), 1.53–1.52 (m, 0.33H), 1.43–1.28 (m, 1H), 1.15–1.08 (m, 1H), 1.07 (s, 0.67H), 1.00–0.96 (m, 5.33H) **$^{13}$C NMR** (151 MHz, $CDCl_3$): δ 215.6, 215.2, 69.5, 53.8, 50.2, 47.6, 40.5, 40.5, 39.2, 38.1, 37.9, 34.3, 33.9, 33.2, 32.9, 32.3, 30.9, 26.9, 25.3, 22.6, 22.3, 20.2 **IR** ($cm^{-1}$): 2952, 2925, 2868, 1710, 1459, 1379, 1233, 1098, 804, 503 **GC-MS** (m/z): [M] calc'd for $C_{11}H_{18}O$: 166.1; found: 166.2.

*4.6.6. 3a,7-dimethyloctahydro-1H-inden-1-one (**2f**)*

Compound **2f** was prepared from **1f** (33.3 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (4 hours). Purification by flash column chromatography on silica gel (3% $Et_2O$/hexanes) afforded **2f** (21.4 mg, 64%) as a pale-yellow oil. $\mathbf{R_f}$: 0.41 (10% $Et_2O$/hexanes) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 2.36–2.21 (m, 2H), 2.09–2.01 (m, 1H), 1.63–1.29 (m, 8H), 1.00 (s, 3H), 0.98 (d, *J* = 8.0 Hz, 3H), 0.97–0.92 (m, 1H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 220.5, 63.1, 38.7, 34.9, 34.7, 32.8, 30.5, 29.3, 29.3, 20.7, 19.9 **IR** ($cm^{-1}$): 2323, 2870, 1736, 1455, 1379, 1152, 1113, 993, 507 **GC-MS** (m/z): [M] calc'd for $C_{11}H_{18}O$: 166.1; found: 166.2.

*4.6.7. (2S,4R,4aR,10S)-3,3,4a,10-tetramethyl-3,4,4a,9,10,10a-hexahydro-2,4-methanophenanthren-1(2H)-one (**2g**)*

Compound **2g** was prepared from **1g** (53.7 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (4 hours). Purification by flash column chromatography on silica gel (3% $Et_2O$/hexanes) afforded **2g** (28.2 mg, 53%) as a white solid. $\mathbf{R_f}$: 0.42 (10% $Et_2O$/hexanes) $[\alpha]^{20}_D$: −70.0° (*c* 1.0, $CHCl_3$) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.24–7.17 (m, 2H), 7.10 (atd, *J* = 6.8, 1.2 Hz, 1H), 7.03 (d, *J* = 7.2 Hz, 1H), 2.97–2.89 (m, 1H), 2.67–2.60 (m, 2H), 2.51–2.41 (m, 3H), 2.25 (adt, *J* = 11.2, 6.0 Hz, 1H), 1.59 (s, 3H), 1.39 (s, 3H), 1.20 (s, 3H), 1.09 (d, *J* = 7.2 Hz, 3H), 0.94 (d, *J* = 10.8 Hz, 1H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 214.3, 144.5, 135.5, 129.4, 126.8, 126.3, 125.8, 58.2, 58.1, 56.0, 40.4, 39.3, 35.0, 31.0, 28.9, 27.7, 26.0, 25.2, 20.9 **IR** ($cm^{-1}$): 2944, 2843, 1702, 1447 1381, 1254, 1181, 973, 760, 729, 520, 487 **GC-MS** (m/z): [M] calc'd for $C_{19}H_{24}O$: 268.2; found: 268.1

*4.6.8. (2S,4aR,4bS,6aS,8S,10aR,10bR,10cR)-2-((tert-butyldimethylsilyl)oxy)-4a,6a,8,10a-tetramethyl-2,3,4,4a,4b,5,6,6a,7a,8,9,10,10a,10b,10c,11-hexadecahydropentaleno[1,2-a]phenanthren-7(1H)-one (**2h**)*

Compound **2h** was prepared from **1h** (47.1 mg, 0.10 mmol, 1.0 equiv) according to the general procedure (4 hours). Purification by flash column chromatography on silica gel (3% $Et_2O$/hexanes) afforded **2h** (43.8 mg, 93%) as a white solid. $\mathbf{R_f}$: 0.45 (10% $Et_2O$/hexanes) $[\alpha]^{20}_D$: −44.0° (*c* 1.0, $CHCl_3$) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 5.35 (bs, 1H), 3.51–3.45 (m, 1H), 2.59 (d, *J* = 7.6 Hz, 0.33 H), 2.30–2.23 (m, 2H), 2.20–2.14 (m, 2.67 H), 1.95–1.86 (m, 1H), 1.84–1.80 (m, 2H), 1.76–1.72 (m, 3H), 1.67–1.59 (m, 3H), 1.46–1.35 (m, 2H), 1.31–1.13 (m, 6H), 1.11–1.02 (m, 11H), 0.89 (s, 9H), 0.06 (s, 6H) **$^{13}$C NMR** (151 MHz,

$CDCl_3$): δ 221.6, 141.7, 120.8, 72.7, 66.7, 57.6, 51.0, 50.9, 47.6, 43.5, 42.8, 37.6, 37.2, 37.1, 35.2, 33.8, 32.8, 32.2, 30.1, 26.1, 25.1, 21.0, 20.0, 19.5, 18.4, 17.9, −4.4 **IR** ($cm^{-1}$): 2930, 2857, 1733, 1462, 1383, 1251, 1088, 870, 834, 773, 737, 666, 617 **GC-MS** (m/z): [M] calc'd for $C_{30}H_{50}O_2Si$: 470.4; found: 469.4.

*4.6.9. 1,3a-dimethyl-2,3,3a,8a-tetrahydrocyclopenta[a]inden-8(1H)-one (**2i**)*

Compound **2i** was prepared from **1i** (40.0 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (2 hours). Purification by flash column chromatography on silica gel (4% $Et_2O$/hexanes) afforded **2i** (30.3 mg, 76%, dr = 1.2:1) as an orange oil. **$R_f$**: 0.35 (10% $Et_2O$/hexanes) **$^1$H NMR** (500 MHz, $CDCl_3$): δ 7.65 (dd, *J* = 7.5, 3.5 Hz, 1H), 7.63–7.59 (m, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.36–7.33 (m, 1H), 2.55 (d, *J* = 10.0 Hz, 0.45H), 2.45–2.35 (m, 0.45H), 2.30–2.27 (m, 0.55 H), 2.06–1.98 (m, 1H), 1.86 (ddd, *J* = 12.5, 6.5, 5.5 Hz, 0.45H), 1.77 (atd, *J* = 13.0, 6.0 Hz, 0.55H), 1.69 (adt, *J* = 12.0, 6.0 Hz, 0.55H), 1.61–1.57 (m, 1H), 1.53 (s, 1.35H), 1.49–1.43 (m, 0.45H), 1.47 (s, 1.65H), 1.22 (d, *J* = 7.0 Hz, 1.35H), 1.09 (d, *J* = 7.0 Hz, 1.65H), 0.93 (ddd, *J* = 24.5, 12.0, 5.5 Hz, 0.55H) **$^{13}$C NMR** (151 MHz, $CDCl_3$): δ 209.1, 208.0, 163.1, 163.0, 137.8, 135.7, 135.5, 135.2, 127.5, 127.5, 124.3, 124.0, 123.5, 122.7, 68.0, 62.9, 51.8, 51.1, 40.7, 39.6, 39.1, 38.7, 34.6, 34.6, 28.5, 27.8, 21.1, 16.1 **IR** ($cm^{-1}$): 2954, 2925, 2857, 1709, 1603, 1462, 1285, 764 **GC-MS** (m/z): [M] calc'd for $C_{14}H_{16}O$: 200.1; found: 200.1.

*4.6.10. 9-methyl-1,4-dioxadispiro[4.0.5$^6$.3$^5$]tetradecan-7-one (**2j**)*

Compound **2j** was prepared from **1j** (44.9 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (6 hours). Purification by flash column chromatography on silica gel (10% $Et_2O$/hexanes) afforded diastereomers **2ja** (12.1 mg, 27%) and **2jb** (11.6 mg, 26%) as colorless oils. **2ja**: **$R_f$**: 0.35 (20% $Et_2O$/hexanes) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 3.99–3.85 (m, 4H), 2.47–2.27 (m, 4H), 1.84–1.63 (m, 4H), 1.62–1.50 (m, 3H), 1.40 (atd, *J* = 12.8, 5.2 Hz, 1H), 1.27–1.20 (m, 1H), 0.98 (d, *J* = 6.4 Hz, 3H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 212.4, 118.1, 64.5, 64.3, 58.1, 50.2, 35.0, 34.5, 34.4, 33.7, 31.2, 22.7, 19.2 **IR** ($cm^{-1}$): 2952, 2874, 1698, 1456, 1442, 1309, 1213, 1152, 1126, 1063, 1016, 945, 931, 584, 528, 473 **GC-MS** (m/z): [M] calc'd for $C_{13}H_{20}O_3$: 224.1; found: 224.2 **2jb**: **$R_f$**: 0.22 (20% $Et_2O$/hexanes) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 3.97–3.88 (m, 4H), 2.51 (ddd, *J* = 14.0, 4.8, 0.4 Hz, 1H), 2.22–2.13 (m, 2H), 2.09–1.93 (m, 3H), 1.90–1.72 (m, 3H), 1.66–1.51 (m, 3H), 1.36–1.27 (m, 1H), 0.96 (d, *J* = 6.8 Hz, 3H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 212.1, 118.3, 65.4, 64.1, 59.9, 47.9, 34.4, 34.1, 32.8, 30.5, 29.9, 21.1, 18.9 **IR** ($cm^{-1}$): 2952, 2874, 1698, 1456, 1442, 1309, 1213, 1152, 1126, 1063, 1016, 945, 931, 584, 528, 473 **GC-MS** (m/z): [M] calc'd for $C_{13}H_{20}O_3$: 224.1; found: 224.2.

*4.6.11. 9-methyl-1,4-dioxadispiro[4.0.5$^6$.4$^5$]pentadecan-7-one (**2k**)*

Compound **2k** was prepared from **1k** (47.7 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (6 hours). Purification by flash column chromatography on silica gel (20% $Et_2O$/hexanes) afforded diastereomers **2ka** (13.7 mg, 29%) and **2kb** (20.5 mg, 43%) as a colorless oil. **2ka**: **$R_f$**: 0.32 (20% $Et_2O$/hexanes) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 3.97–3.86 (m, 4H), 2.43 (dd, *J* = 13.2, 4.8 Hz, 1H), 2.36–2.29 (m, 2H), 2.18–2.11 (m, 1H), 2.00–1.88 (m, 1H), 1.76–1.63 (m, 4H), 1.56–1.47 (m, 3H), 1.44–1.31 (m, 3H), 0.98 (d, *J* = 6.8 Hz, 3H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 213.8, 111.5, 64.4, 64.3, 55.0, 49.7, 34.0, 33.9, 32.7, 31.5, 29.5, 23.2, 21.7, 20.9 **IR** ($cm^{-1}$): 2929, 2869, 1707, 1450, 1298, 1182, 1102, 1085, 1032, 954, 859, 565 **GC-MS** (m/z): [M] calc'd for $C_{14}H_{22}O_3$: 238.2; found: 238.2 **2kb**: **$R_f$**: 0.21 (20% $Et_2O$/hexanes) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 4.03–3.78 (m, 4H), 2.27–2.18 (m, 4H), 1.91–1.79 (m, 3H), 1.72–1.61 (m, 3H), 1.59–1.38 (m, 4H), 1.12–1.01 (m, 1H), 0.98 (d, *J* = 6.4 Hz, 3H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 212.6, 110.9, 65.6, 64.3, 56.8, 48.0, 34.8, 33.4, 32.1, 31.0, 29.0, 23.5, 22.3, 21.5 **IR** ($cm^{-1}$): 2929, 2869, 1707, 1450, 1298, 1182, 1102, 1085, 1032, 954, 859, 565 **GC-MS** (m/z): [M] calc'd for $C_{14}H_{22}O_3$: 238.2; found: 238.2.

*4.6.12. ethyl-1,4-dimethyl-2-oxocyclohexane-1-carboxylate (**2l**)*

Compound **2l** was prepared from **1l** (39.7 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (2 hours). Purification by flash column chromatography on silica gel (10% $Et_2O$/hexanes) afforded **2l** (17.0 mg, 43%) as a colorless oil. **$R_f$**: 0.41 (20% $Et_2O$/hexanes) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 4.19 (q, *J* = 7.0 Hz, 2H), 2.57–2.51 (m, 1H), 2.39 (ddd, *J* = 13.6, 7.2, 4.0 Hz, 1H), 2.25–2.15 (m, 2H), 1.92–1.84 (m, 1H), 1.73 (ddd, *J* = 13.6, 9.2, 4.0 Hz, 1H), 1.52–1.43 (m, 1H), 1.34 (s, 3H), 1.26 (at, *J* = 7.2 Hz, 3H), 0.98 (d, *J* = 6.4 Hz, 3H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 208.9, 173.3, 61.4, 57.0, 46.8, 33.8, 32.8, 28.9, 20.9, 20.2, 14.2 **IR** ($cm^{-1}$): 2935, 2871, 1735, 1712, 1456, 1377, 1258, 1090, 1026, 860 **GC-MS** (m/z): [M] calc'd for $C_{11}H_{18}O_3$: 198.1; found: 198.2.

*4.6.13. ethyl 1-allyl-4-methyl-2-oxocyclohexane-1-carboxylate (**2m**)*

Compound **2m** was prepared from **1m** (44.9 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (6 hours). Purification by flash column chromatography on silica gel (4% $Et_2O$/hexanes) afforded diastereomers **2ma** (6.5 mg, 14%) and **2mb** (17.5 mg, 39%) as a colorless oil. **2ma**: **$R_f$**: 0.51 (20% $Et_2O$/hexanes) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 5.79–5.68 (m, 1H), 5.12–4.95 (m, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 2.60 (dd, *J* = 14.0, 7.2 Hz, 1H), 2.49–2.39 (m, 2H), 2.29 (dd, *J* = 14.0, 8.0 Hz, 1H), 2.18–2.11 (m, 1H), 1.85–1.70 (m, 2H), 1.45–1.34 (m, 2H), 1.24 (t, *J* = 7.2 Hz, 3H), 0.99 (d, *J* = 6.4 Hz, 3H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 207.1, 171.5, 133.5, 118.4, 61.4, 59.9, 49.5, 39.4, 35.4, 34.9, 31.4, 22.4, 14.3 **IR** ($cm^{-1}$): 2956, 2929, 1713, 1439, 1222, 1196, 1143, 1093, 1027, 918, 608 **GC-MS** (m/z): [M] calc'd for $C_{13}H_{20}O_3$: 224.1; found: 224.2 **2mb**: **$R_f$**: 0.61 (20% $Et_2O$/hexanes) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 5.78–5.67 (m, 1H), 5.08–5.04 (m, 2H), 4.18 (q, *J* = 7.2 Hz, 2H), 2.62 (dd, *J* = 14.0, 6.8 Hz, 1H), 2.55 (dd, *J* = 13.6, 4.4 Hz, 1H), 2.40 (dd, *J* = 14.0, 7.6 Hz, 1H), 2.31 (ddd, *J* = 13.6, 6.4, 4.0 Hz, 1H), 2.26–2.13 (m, 2H), 1.93–1.85 (m, 1H), 1.77 (ddd, *J* = 13.6, 10.0, 4.0 Hz, 1H), 1.52–1.44 (m, 1H), 1.25 (t, *J* = 7.2 Hz, 3H), 0.96 (d, *J* = 6.4 Hz, 3H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 207.8, 171.7, 133.3, 118.6, 61.3, 60.7, 47.4, 38.5, 32.6, 30.7, 28.5, 19.9, 14.3 **IR** ($cm^{-1}$): 2956, 2929, 1713, 1439, 1222, 1196, 1143, 1093, 1027, 918, 608 **GC-MS** (m/z): [M] calc'd for $C_{13}H_{20}O_3$: 224.1; found: 224.2.

*4.6.14. 1-allyl-4-methyl-2-oxabicyclo[3.3.1]nonan-6-one (**2n**)*

Compound **2n** was prepared from **1n** (38.9 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (4 hours). Purification by flash column chromatography on silica gel (8% $Et_2O$/hexanes) afforded **2n** (15.9 mg, 41%) as a colorless oil. **$R_f$**: 0.52 (40% $Et_2O$/hexanes) **$^1$H NMR** (500 MHz, $CDCl_3$): δ 5.87 (ddt, *J* = 17.5, 10.5, 7.5 Hz, 1H), 5.13–5.07 (m, 2H), 3.81 (dd, *J* = 12.5, 5.5 Hz, 1H), 3.55 (at, *J* = 12.5 Hz, 1H), 2.57–2.51 (m, 2H), 2.46–2.38 (m, 1H), 2.26 (d, *J* = 7.5 Hz, 2H), 2.14–2.03 (m, 2H), 2.00–1.93 (m, 1H), 1.91–1.87 (m, 2H), 0.81 (d, *J* = 6.5 Hz, 3H) **$^{13}$C NMR** (151 MHz, $CDCl_3$): δ 213.3, 133.6, 118.4, 70.9, 68.0, 49.2, 47.1, 39.1, 36.2, 33.5, 32.1, 14.9 **IR** ($cm^{-1}$): 2926, 1703, 1440, 1104, 1078, 990, 963, 915, 853, 640, 413 **GC-MS** (m/z): [M] calc'd for $C_{12}H_{18}O_2$: 194.1; found: 194.2.

*4.6.15. 5,8-dimethylbicyclo[3.3.1]non-3-en-2-one (**2o**)*

Compound **2o** was prepared from **1o** (32.9 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (4 hours). Purification by flash column chromatography on silica gel (10% $Et_2O$/hexanes) afforded **2o** (14.3 mg, 43%) as a pale-yellow oil. **$R_f$**: 0.32 (10% $Et_2O$/hexanes) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 6.53 (dd, *J* = 10.0, 2.0 Hz, 1H), 6.05 (d, *J* = 10.0 Hz, 1H), 2.36–2.32 (m, 1H), 2.08 (dd, *J* = 12.8, 2.8 Hz, 1H), 1.71–1.53 (m, 3H), 1.45–1.42 (m, 2H), 1.27–1.13 (m, 1H), 1.11 (s, 3H), 0.89 (d, *J* = 6.4 Hz, 3H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 201.7, 157.0, 131.2, 49.5, 42.6, 34.8, 33.8, 33.6, 28.7, 28.1, 19.7 **IR** ($cm^{-1}$): 2956, 2923, 2869, 1670, 1455, 1374, 1218, 1103, 1076, 825, 730, 502 **GC-MS** (m/z): [M] calc'd for $C_{11}H_{16}O$: 164.1; found: 164.2.

*4.6.16. (4aS,7R,8R)-7-methyl-2,3,5,6,7,8-hexahydro-4H-4a,8-methanobenzo[8]annulene-4,9(1H)-dione (**2p**)*

Compound **2p** was prepared from **1p** (43.7 mg, 0.20 mmol, 1.0 equiv) according to the general procedure (4 hours). Purification by flash column chromatography on silica gel (30% $Et_2O$/hexanes) afforded **2p** (32.2 mg, 73%) as a yellow oil. **$R_f$**: 0.25 (40% $Et_2O$/hexanes) **$[\alpha]^{20}_D$**: +64.0° (*c* 1.0, $CHCl_3$) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 6.08 (s, 1H), 2.66–2.48 (m, 4H), 2.46–2.42 (m, 1H), 2.19–2.05 (m, 3H), 1.90–1.83 (m, 1H), 1.81–1.58 (m, 4H), 1.27–1.22 (m, 1H), 0.91 (d, *J* = 6.4 Hz, 3H) **$^{13}$C NMR** (151 MHz, $CDCl_3$): δ 211.5, 200.2, 163.2, 129.3, 51.8, 48.4, 38.3, 35.3, 32.6, 32.5, 31.8, 27.3, 22.4, 19.6 **IR** ($cm^{-1}$): 2926, 2869, 1708, 1659, 1619, 1454, 1249, 1204, 1116, 1032, 621, 519 **GC-MS** (m/z): [M] calc'd for $C_{14}H_{18}O_2$: 218.1; found: 218.2.

*4.6.17. 3-(chloromethyl)-5,5,7a-trimethyloctahydro-4H-inden-4-one (**3a**)*

Compound **3a** was prepared from **1d** (38.8 mg, 0.20 mmol, 1.0 equiv) according to the general procedure for carbohalogenation using NCS (106.8 mg, 0.80 mmol, 4.0 equiv) as the halogen source. Purification by flash column chromatography on silica gel (3% $Et_2O$/hexanes) afforded **3a** (27.2 mg, 60%) as a colorless oil. **$R_f$**: 0.56 (10% $Et_2O$/hexanes) **$^1$H NMR** (600 MHz, $CDCl_3$): δ 3.66 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.53 (dd, *J* = 10.8, 6.6 Hz, 1H), 2.86–2.80 (m, 1H), 2.17 (d, *J* = 7.2 Hz, 1H), 1.89 (addt, *J* = 12.6, 7.2, 2.4 Hz, 1H), 1.79 (ddd, *J* = 13.8, 10.8, 3.0 Hz, 1H), 1.68–1.59 (m, 3H), 1.52 (ddd, *J* = 12.6, 6.6, 2.4 Hz, 1H), 1.48–1.43 (m, 2H), 1.15 (s, 3H), 1.11 (s, 3H), 1.10 (s, 3H) **$^{13}$C NMR** (151 MHz, $CDCl_3$): δ 218.2, 59.3, 49.4, 46.0, 44.0, 43.8, 40.4, 35.4, 33.5, 28.6, 26.8, 26.0 **IR** ($cm^{-1}$): 2954, 2869, 1696, 1459, 1384, 1361, 1289, 1105, 1062, 723, 688 **GC-MS** (m/z): [M] calc'd for $C_{13}H_{21}ClO$: 228.1; found: 228.1.

*4.6.19. 8-(chloromethyl)-5-methylbicyclo[3.3.1]non-3-en-2-one (**3b**)*

Compound **3b** was prepared from **1o** (32.6 mg, 0.20 mmol, 1.0 equiv) according to the general procedure for carbohalogenation using NCS (106.8 mg, 0.80 mmol, 4.0 equiv) as the halogen source. Purification by flash column chromatography on silica gel (5% $Et_2O$/hexanes) afforded **3b** (23.9 mg, 60%) as a colorless oil. **$R_f$**: 0.15 (10% $Et_2O$/hexanes) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 6.61 (dd, *J* = 10.0, 2.0 Hz, 1H), 6.10 (dd, *J* = 10.0, 0.8 Hz, 1H), 3.50 (dd, *J* = 11.2, 6.8 Hz, 1H), 3.23 (dd, *J* = 10.8, 7.6 Hz, 1H), 2.71–2.66 (m, 1H), 2.14 (ddd, *J* = 12.8, 3.6, 2.4 Hz, 1H), 1.94–1.84 (m, 2H), 1.59–1.54 (m, 1H), 1.52–1.44 (m, 2H), 1.22–1.11 (m, 1H), 1.16 (s, 3H) **$^{13}$C NMR** (125 MHz, $CDCl_3$): δ 200.5, 157.4, 131.2, 47.6, 45.9, 41.9, 41.6, 34.2, 34.1, 28.5, 24.0 **IR** ($cm^{-1}$): 2926, 2862, 1674, 1456, 828, 731 **GC-MS** (m/z): [M] calc'd for $C_{11}H_{15}ClO$: 198.1; found: 198.1.

*4.6.20. (1R,3S,5S,8aR)-5-(bromomethyl)-2,2,8a-trimethyloctahydro-1,3-methanonaphthalen-4(1H)-one (**3c**)*

Compound **3c** was prepared from **1a** (44.1 mg, 0.20 mmol, 1.0 equiv) according to the general procedure for carbohalogenation using NBS (142.4 mg, 0.80 mmol, 4.0 equiv) as the halogen source. Purification by flash column chromatography on silica gel (10% $Et_2O$/hexanes) afforded **3c** (47.7 mg, 80%) as a white solid. **$R_f$**: 0.45 (10% EtOAc/hexanes) **$[\alpha]^{20}_D$**: –20.0 (*c* 1.0, $CHCl_3$) **$^1$H NMR** (500 MHz, $CDCl_3$): δ 3.89 (dd, *J* = 10.0, 4.0 Hz, 1H), 3.77 (dd, *J* = 10.0, 6.5 Hz, 1H), 2.56 (at, *J* = 5.5 Hz, 1H), 2.51 (adt, *J* =12.5, 6.0 Hz, 1H), 2.18 (d, *J* = 10.0 Hz, 1H), 2.10–2.04 (m, 1H), 1.84 (at, *J* = 4.4 Hz, 1H), 1.81–1.64 (m, 4H), 1.58 (d, *J* = 11.0 Hz, 1H), 1.52–1.48 (m, 1H), 1.36 (s, 3H), 1.24 (s, 3H), 1.10 (s, 3H), 1.07–1.03 (m, 1H) **$^{13}$C NMR** (151 MHz, $CDCl_3$): δ 215.0, 58.9, 55.1, 54.0, 41.7, 40.1, 37.7, 36.0, 32.3, 27.9, 27.6, 26.1, 25.9, 25.9, 16.3 **IR** ($cm^{-1}$): 2948, 2872, 1699, 1465, 1380, 1274, 1240, 1203, 992, 905, 632, 602 **GC-MS** (m/z): [M] calc'd for $C_{15}H_{23}BrO$: 298.1; found: 298.1.

*4.6.21. 1-(bromomethyl)-3a-methyl-2,3,3a,8a-tetrahydrocyclopenta[a]inden-8(1H)-one (**3d**)*

Compound **3d** was prepared from **1i** (40.1 mg, 0.20 mmol, 1.0 equiv) according to the general procedure for carbohalogenation using NBS (142.4 mg, 0.80 mmol, 4.0 equiv) as the halogen source. Purification by flash column chromatography on silica gel (5% $Et_2O$/hexanes to 10% $Et_2O$/hexanes) afforded diastereomers **3da** (33.6 mg, 60%) and **3db** (18.1 mg, 33%) as white solids. **3da**: **$R_f$**: 0.57 (10% $Et_2O$/hexanes) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.74–7.70 (m, 2H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 4.14 (dd, *J* = 10.4, 3.2 Hz, 1H), 3.33 (at, *J* = 11.2 Hz, 1H), 2.87–2.78 (m, 1H), 2.17 – 2.09 (m, 2H), 1.97 (atd, *J* = 12.8, 6.0 Hz, 1H), 1.62 (s, 3H), 0.90 (ddd, *J* = 26.0, 13.2, 6.4 Hz, 1H) **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 199.7, 159.5, 137.1, 133.7, 128.5, 124.3, 124.2, 75.5, 57.3, 54.9, 40.0, 32.9, 28.9, 27.9 **IR** ($cm^{-1}$): 2965, 2864, 1714, 1604, 1589, 1465, 1214, 764 **GC-MS** (m/z): [M] calc'd for $C_{14}H_{15}BrO$: 278.0; found: 278.0 **3db**: **$R_f$**: 0.23 (10% $Et_2O$/hexanes) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.68–7.62 (m, 2H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 3.70 (dd, *J* = 10.0, 4.8 Hz, 1H), 3.57 (dd, *J* = 10.0, 8.0 Hz, 1H), 2.58–2.50 (m, 2H), 1.98 (ddd, *J* = 14.0, 6.4, 2.0 Hz, 1H), 1.92–1.82 (m, 2H), 1.76–1.67 (m, 1H), 1.54 (s, 3H) **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 207.3, 162.5, 135.8, 135.2, 127.9, 124.2, 123.8, 64.7, 51.0, 46.6, 38.9, 37.5, 31.9, 27.8 **IR** ($cm^{-1}$): 2955, 2865, 1708, 1603, 1463, 1327, 1288, 1241, 763 **GC-MS** (m/z): [M] calc'd for $C_{14}H_{15}BrO$: 278.0; found: 278.0.

*4.6.22. 5-allyl-3-(bromomethyl)-6,6,7a-trimethyloctahydro-4H-inden-4-one (**3e**)*

Compound **3e** was prepared from **1q** (46.9 mg, 0.20 mmol, 1.0 equiv) according to the general procedure for carbohalogenation using NBS (142.4 mg, 0.80 mmol, 4.0 equiv) as the halogen source. Purification by flash column chromatography on silica gel (5% $Et_2O$/hexanes) afforded **3e** (25.1 mg, 40%) as a light yellow oil. **$R_f$**: 0.48 (10% $Et_2O$/hexanes) **$^1$H NMR** (500 MHz, $CDCl_3$): δ 5.81–5.73 (m, 1H), 5.01 (d, *J* = 17.5 Hz, 1H), 4.94 (d, *J* = 10.5 Hz, 1H), 3.47 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.34 (dd, *J* = 10.0, 7.5 Hz, 1H), 2.79–2.72 (m, 1H), 2.47–2.38 (m, 2H), 2.12–2.05 (m, 3H), 1.76–1.43 (m, 7H), 1.17 (s, 3H), 1.05 (s, 3H), 0.87 (s, 3H) **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 213.9, 137.7, 115.6, 64.4, 56.6, 49.3, 47.8, 46.5, 43.1, 39.8, 38.4, 31.5, 30.1, 29.9, 28.4, 24.5 **IR** ($cm^{-1}$): 2954, 2871, 1699, 1464, 1381, 1369, 1350, 1263, 1230, 1192, 999, 911 **GC-MS** (m/z): [M] calc'd for $C_{16}H_{25}BrO$: 312.1; found: 312.1.

*4.6.23. (1S,3aR,4R,6S)-1-(iodomethyl)-3a,5,5-trimethyloctahydro*

*-7H-4,6-methanoinden-7-one (3f)*

Compound **3f** was prepared from **1b** (41.3 mg, 0.20 mmol. 1.0 equiv) according to the general procedure for carbohalogenation using NIS (180.0 mg, 0.80 mmol, 4.0 equiv) as the halogen source. Purification by flash column chromatography on silica gel (10% $Et_2O$/hexanes) afforded **3f** (60.9 mg, 92%) as a yellow oil. $\mathbf{R_f}$: 0.46 (20% $Et_2O$/hexanes) $[\alpha]^{20}_D$: +1.7° (*c* 1.0, $CHCl_3$) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 3.78 (dd, *J* = 9.6, 2.8 Hz, 1H), 3.40 (dd, *J* = 9.6, 7.6 Hz, 1H), 2.54 (at, *J* = 5.2 Hz, 1H), 2.51–2.45 (m, 1H), 2.02 (at, *J* = 6.4 Hz, 1H), 2.00–1.84 (m, 3H), 1.78–1.70 (m, 1H), 1.59 (d, *J* = 11.2 Hz, 1H), 1.52–1.44 (m, 2H), 1.37 (s, 3H), 1.25 (s, 3H), 1.00 (s, 3H) **$^{13}$C NMR** (151 MHz, $CDCl_3$): δ 215.5, 60.2, 58.5, 52.3, 50.3, 45.3, 42.5, 39.9, 33.3, 28.6, 27.4, 26.0, 25.3, 15.2 **IR** ($cm^{-1}$): 2950, 1701, 1461, 1378, 1250, 1201, 981, 831, 801, 586, 520. **GC-MS** (m/z): [M] calc'd for $C_{14}H_{21}IO$: 332.1; found: 332.1.

*4.6.24. (1R,3S,4aR,5S,8aR)-5-(iodomethyl)-2,2,8a-trimethyloctahydro-1,3-methanonaphthalen-4(1H)-one (3g)*

Compound **3g** was prepared from **1a** (440 mg, 2.0 mmol. 1.0 equiv) according to the general procedure for carbohalogenation using $I_2$ (2.0 g, 8.0 mmol, 4.0 equiv) as the halogen source. Purification by flash column chromatography (15% $Et_2O$/hexanes) afforded **3g** (602 mg, 87%) as a yellow solid. $\mathbf{R_f}$: 0.38 (10% $Et_2O$/hexanes) $[\alpha]^{20}_D$: –8.2° (*c* 1.0, $CHCl_3$) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 3.74 (dd, *J* = 9.6, 3.6 Hz, 1H), 3.60 (dd, *J* = 9.6, 6.4 Hz, 1H), 2.55 (at, *J* = 5.6 Hz, 1H), 2.50 (adt, *J* = 10.8, 6.0 Hz, 1H), 2.06 (d, *J* = 9.6 Hz, 1H), 1.83 (at, *J* = 5.6 Hz, 1H), 1.77–1.61 (m, 5H), 1.57 (d, *J* = 10.8 Hz, 1H), 1.47–1.39 (m, 1H), 1.35 (s, 3H), 1.23 (s, 3H), 1.10 (s, 3H), 1.08–1.03 (m, 1H) **$^{13}$C NMR** (101 MHz, $CDCl_3$): δ 214.9, 58.9, 55.6, 55.0, 40.1, 37.3, 36.1, 32.3, 28.2, 27.8, 27.6, 25.9, 19.4, 16.3 **IR** ($cm^{-1}$): 2947, 2871, 1694, 1464, 1389, 1203, 906, 727, 647, 571, 513, 431 **GC-MS** (m/z): [M] calc'd for $C_{15}H_{23}IO$: 346.1; found: 346.1.

*4.6.25. (2S,4R,4aR,10S)-10-(iodomethyl)-3,3,4a-trimethyl-3,4,4a,9,10,10a-hexahydro-2,4-methanophenanthren-1(2H)-one (3h)*

Compound **3h** was prepared from **1g** (53.7 mg, 0.20 mmol. 1.0 equiv) according to the general procedure for carbohalogenation using NIS (180.0 mg, 0.80 mmol, 4.0 equiv) as the halogen source. Purification by flash column chromatography on silica gel (5% $Et_2O$/hexanes) afforded **3h** (63.9 mg, 81%) as a white solid. $\mathbf{R_f}$: 0.41 (10% $Et_2O$/hexanes) $[\alpha]^{20}_D$: –37.3° (*c* 1.0, $CHCl_3$) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.23–7.19 (m, 2H), 7.14–7.06 (m, 2H), 3.41 (dd, *J* = 9.6, 7.6 Hz, 1H), 3.32 (dd, *J* = 9.2, 6.4 Hz, 1H), 2.91–2.81 (m, 3H), 2.72–2.65 (m, 2H), 2.47 (at, *J* = 5.6 Hz, 1H), 2.32 (adt, *J* = 11.2, 6.0 Hz, 1H), 1.58 (s, 3H), 1.41 (s, 3H), 1.25 (s, 3H), 0.94 (d, *J* = 10.8 Hz, 1H) **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 212.7, 143.9, 134.0, 129.4, 127.3, 126.3, 126.2, 58.2, 55.6, 55.5, 40.7, 39.2, 37.4, 33.3, 30.8, 27.7, 26.4, 25.3, 14.6 **IR** ($cm^{-1}$): 2973, 2956, 2924, 1694, 1444, 1236, 1180, 986, 920, 763, 728, 592, 494, 436 **GC-MS** (m/z): [M] calc'd for $C_{19}H_{23}IO$: 394.1; found: 394.1.

*4.6.26. 1-(hydroxymethyl)-3a,5,5-trimethyloctahydro-7H-4,6-methanoinden-7-one (3i) and (1S,3aR,4R,6S)-3a,5,5-trimethyl-7-oxooctahydro-1H-4,6-methanoindene-1-carbaldehyde (3j)*

Compound **3i** and **3j** was prepared from **1b** (41.3 mg, 0.20 mmol, 1.0 equiv) according to the general procedure for anionic cyclization, followed bubbling $O_2$ for 10 minutes and stirring at room temperature for 24 hours under an oxygen atmosphere (balloon). Purification by flash column chromatography on silica gel (40% $Et_2O$/hexanes) afforded **3i** (10 mg, 23%) and **3j** (12.1 mg, 27%) as colorless oils. **3i**: $\mathbf{R_f}$: 0.08 (40% $Et_2O$/hexanes) $[\alpha]^{20}_D$: –29.5° (*c* 0.3, $CHCl_3$) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 3.83 (dd, *J* = 10.4, 4.0 Hz, 1H), 3.51 (dd, *J* = 10.4, 9.6 Hz, 1H), 2.65 (at, *J* = 5.2 Hz, 1H), 2.50 (adt, *J* = 11.2, 6.4 Hz, 1H), 2.21 (d, *J* = 9.2 Hz, 1H), 2.14–2.03 (m, 2H), 1.83–1.68 (m, 2H), 1.56 (d, *J* = 11.6 Hz, 1H), 1.48–1.41 (m, 2H), 1.39 (s, 3H), 1.24 (s, 3H), 1.03 (s, 3H) **$^{13}$C NMR** (151 MHz, $CDCl_3$): δ 219.0, 68.2, 61.4, 58.5, 51.8, 50.3, 45.0, 42.3, 40.2, 28.8, 28.4, 27.3, 26.1, 25.1 **IR** ($cm^{-1}$): 3425, 2950, 2873, 1686, 1473, 1378, 1273, 1239, 1069, 1027, 521 **GC-MS** (m/z): [M] calc'd for $C_{14}H_{22}O_2$: 222.2; found: 222.2 **3j**: $\mathbf{R_f}$: 0.27 (40% $Et_2O$/hexanes) $[\alpha]^{20}_D$: –6.1° (*c* 0.7, $CHCl_3$) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 11.55 (s, 1H), 4.34 (dd, *J* = 12.8, 4.8 Hz, 1H), 3.70 (dd, *J* = 12.8, 9.6 Hz, 1H), 2.69 (at, *J* = 5.6 Hz, 1H), 2.58–2.48 (m, 2H), 2.46 (d, *J* = 7.6 Hz, 1H), 2.09 (at, *J* = 5.6 Hz, 1H), 1.90–1.71 (m, 2H), 1.53 (d, *J* = 11.6 Hz, 1H), 1.49–1.41 (m, 1H), 1.40 (s, 3H), 1.24 (s, 3H), 1.08 (s, 3H) **$^{13}$C NMR** (151 MHz, $CDCl_3$): δ 220.0, 81.7, 59.3, 59.0, 51.9, 45.7, 45.6, 41.7, 39.7, 28.5, 28.4, 27.3, 26.1, 26.0 **IR** ($cm^{-1}$): 2951, 2877, 2361, 2338, 1701, 1459, 1388, 1272, 1245, 1041, 985, 668 **GC-MS** (m/z): [M] calc'd for $C_{14}H_{20}O_2$: 220.1; found: 220.2.

*4.7. Experimental Procedures and Characterization Data for Mechanistic Studies*

*4.7.1. (1R,3S,4aR,5S,8aR)-2,2,8a-trimethyl-5-(methyl-d)octahydro-1,3-methanonaphthalen-4(1H)-one (2a-$d_1$)*

To a flame-dried, 10 mL microwave vial equipped with a magnetic stir bar was added $Zn(OTf)_2$ (109.1 mg, 0.30 mmol, 1.5 equiv). The vial was capped, evacuated flame-dried under vacuum for 10 seconds (this process was repeated 3 times). The reaction vessel was backfilled with $N_2$ before 1,2-dimethoxyethane (2 mL, 0.1 M) was added. To the stirred mixture was added ketone **1a** (44.0 mg, 0.20 mmol, 1.0 equiv) and $Zn(TMP)_2$ (0.48 mL, 0.5 M in toluene, 0.24 mmol, 1.2 equiv). The reaction vessel was sealed with parafilm, and placed in an 80 °C preheated oil bath and stirred for four hours.

The reaction vessel was removed from the oil bath and $D_2O$ (2 mL, 110.8 mmol, 554.2 equiv) was added to the reaction mixture. The mixture was stirred at ambient temperature for 30 miuntes before sat. aq. $NH_4Cl$ (1 mL) and $Et_2O$ (1 mL) were added. The organic phase was separated and the aqueous phase was extracted with $Et_2O$ (2 x 1 mL). The combined organic extracts were filtered over a small pad of dry silica gel and concentrated under reduced pressure by rotary evaporation. Purification by flash column chromatography over silica gel (5% $Et_2O$/hexanes) afforded **2a-*$d_1$*** (30.0 mg, 68%, 60% D) as a colorless oil. $\mathbf{R_f}$: 0.46 (10% $Et_2O$/hexanes) $[\alpha]^{20}_D$: –49.0° (*c* 1.0, $CHCl_3$) **$^1$H NMR** (400 MHz, $CDCl_3$): δ 2.51 (t, *J* = 5.2 Hz, 1H), 2.44 (adt, *J* = 10.8, 6.4 Hz, 1H), 1.88–1.78 (m, 2H), 1.72–1.55 (m, 6H), 1.34 (s, 3H), 1.29–1.21 (m, 1H), 1.19 (s, 3H), 1.12–1.08 (m, 2.4H), 1.04 (s, 3H), 0.99–0.96 (m, 1H) **$^{13}$C NMR** (151 MHz, $CDCl_3$): δ 215.7, 59.3, 59.3, 58.8, 55.0, 40.6, 35.9, 32.3, 31.5, 31.4, 30.5, 30.5, 28.0, 27.7, 25.8, 25.3, 22.4, 22.1 (t, *J* = 19.3 Hz), 16.7 **IR** ($cm^{-1}$): 2929, 2871, 1700, 1464, 1379, 1274, 1240, 1202, 787, 516 **GC-MS** (m/z): [M] calc'd for $C_{19}H_{23}DO$: 221.2; found: 221.2.

*4.7.2. (1S,4S,5S)-4,6,6-trimethyl-4-(pent-4-en-1-yl)bicyclo-[3.1.1]heptan-2-one-3,3-$d_2$ (1a-$d_2$)*

To a 10 mL microwave vial was added $K_2CO_3$ (332 mg, 2.4 mmol, 3.0 equiv), **1a** (176 mg, 0.8 mmol, 1.0 equiv) and $D_2O$ (0.6 mL, 1.33 M). The reaction vessel capped, placed into a preheated 120 °C oil bath, and stirred for 4 days. To the reaction mixture was added $H_2O$ (2 mL) and $Et_2O$ (2 mL) and the organic phase was separated. The aqueous phase was extracted with $Et_2O$ (2 x 2 mL) and the combined organic extracts were filtered over a small pad of dry silica gel and concentrated under reduced

pressure by rotary evaporation. The crude mixture was resubjected to the above reaction conditions (4 days) and workup procedure without further purification to afford **1a-*d*$_2$** (169 mg, 95%) as a colorless oil. **R$_f$**: 0.45 (10% EtOAc/hexanes) **[$\alpha$]$^{20}_D$**: –16.2° (*c* 1.0, $CHCl_3$) **$^1$H NMR** (400 MHz, $CDCl_3$): 5.79 (ddt, *J* = 17.2, 10.4, 6.8 Hz, 1H), 5.00 (dd, *J* = 17.2, 1.2 Hz, 1H), 4.95 (d, *J* = 10.0 Hz, 1H), 2.53 (adt, *J* = 5.2 Hz, 1H), 2.47 (adt, *J* = 10.8, 6.0 Hz, 1H), 2.04–1.96 (m, 3H), 1.63 (d, *J* = 10.8 Hz, 1H), 1.40–1.30 (m, 4H), 1.36 (s, 3H), 1.14 (s, 3H), 1.02 (s, 3H) **$^{13}$C NMR** (151 MHz, $CDCl_3$): δ 214.9, 138.8, 114.8, 58.3, 51.7, 43.6, 41.1, 34.5, 34.3, 27.6, 26.0, 25.6, 24.9, 23.1 **IR** (cm$^{-1}$): 2933, 1708, 1641, 1473, 1388, 1242, 1204, 991, 909, 733, 640, 503 **GC-MS** (m/z): [M] calc'd for $C_{15}H_{22}D_2O$: 222.2; found: 222.2.

*4.7.3. (1R,3S,5S,8aR)-2,2,8a-trimethyl-5-(methyl-d)octahydro-1,3-methanonaphthalen-4(1H)-one-4a-d (**2a-*d*$_2$**)*

Compound **2a-*d*$_2$** was prepared from **1a-*d*$_2$** (22.2 mg, 0.1 mmol, 1.0 equiv) according to the general procedure for anionic cyclization. Compound **2a-*d*$_2$** (20.0 mg, 90%) was isolated by preparatory thin layer chromatography (8% EtOAc/hexanes) and determined to have 0% deuterium incorporation at the methyl group. **R$_f$**: 0.67 (10% EtOAc/hexanes) **[$\alpha$]$^{20}_D$**: –38.8° (*c* 1.0, $CHCl_3$) **$^1$H NMR** (500 MHz, $CDCl_3$): 2.51 (at, *J* = 5.5 Hz, 1H), 2.44 (adt, *J* = 10.5, 6.5 Hz, 1H), 1.87–1.82 (m, 1H), 1.80 (at, *J* = 6.0 Hz, 1H), 1.72–1.54 (m, 5H), 1.34 (s, 3H), 1.25–1.20 (m, 1H), 1.19 (s, 3H), 1.11 (d, *J* = 6.5 Hz, 3H), 1.04 (s, 3H), 0.98–0.95 (m, 1H) **$^{13}$C NMR** (151 MHz, $CDCl_3$) δ 215.6, 59.3, 58.8, 55.0, 40.7, 35.9, 35.8, 32.3, 31.5, 31.4, 30.5, 30.5, 28.0, 27.9, 27.7, 25.8, 25.8, 25.3, 25.3, 22.4, 22.3, 16.7 **IR** (cm$^{-1}$): 2925, 2870, 1701, 1463, 1378, 1240, 1204, 1030, 978, 910, 639, 514 **GC-MS** (m/z): [M] calc'd for $C_{15}H_{22}D_2O$: 221.2; found: 221.2.

*4.7.4. Preparation of Negishi Reagent*

To a flame-dried 10 mL microwave vial equipped with a magnetic stir bar was added Zn dust (26.2 mg, 0.40 mmol, 2.0 equiv) and LiCl (17.0 mg, 0.40 mmol, 2.0 equiv). The vial was capped, evacuated, and flame-dried for 10 seconds under reduced pressure (this process was repeated 3 times). The reaction vessel was backfilled with $N_2$ and THF (1.0 mL) and 1,2-dibromoethane (6.4 µL, 0.074 mmol, 37 mol %) were added to the reaction mixture. The reaction vessel was placed into a 70 °C preheated oil bath and stirred for 30 minutes. The reaction vessel was removed from the oil bath cooled to ambient temperature before a solution of $I_2$ (5.1 mg, 0.02 mmol, 10 mol %) and TMSCl (7.6 µL, 0.06 mmol, 30 mol %) in THF (0.5 mL) was added. The reaction vessel was placed in a 70 °C preheated oil bath and stirred for 30 minutes. The reaction vessel was removed from the oil bath and cooled to ambient temperature before a solution of **3g** (69.3 mg, 0.20 mmol, 1.0 equiv) in THF (0.5 mL) was added to the reaction mixture to give a solution with a final concentration of 0.1 M. The reaction vessel was placed in a 70 °C preheated oil bath and stirred for 6 hours.

The reaction vessel was removed from the oil bath and cooled to ambient temperature before $D_2O$ (0.5 mL, 25 mmol, 125 equiv) was added to the reaction mixture and the reaction mixture was stirred for 3 hours at ambient temperature. To the reaction mixture was added sat. aq. $NH_4Cl$ (2 mL) and $Et_2O$ (1 mL). The organic phase was separated and aqueous phase was extracted with $Et_2O$ (2 x 2 mL). The combined organic extracts were filtered over a small pad of dry silica gel and concentrated under reduced pressure by rotary evaporation. The $^1$H-NMR yield of **2a-*d*$_1$** (22%, 47% deuterium incorporation) and **1a** (54%, 48% deuterium incorporation) was determined using 1,3,5-trimethoxybenzene as an internal standard. The amount of deuterium incorporation of each product was determined after isolation by preparatory thin layer chromatography (20% $Et_2O$/hexanes).

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**Appendix A. Supplementary data**

Supplementary data related to this article could be found at:

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**Declaration of interests**

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: