# Intramolecular Nucleophilic Acyl Substitution Reactions of Halo-Substituted Esters and Lactones. New Applications of Organosamarium Reagents

Gary A. Molander* and Jeffrey A. McKie

*Department of Chemistry and Biochemistry, University of Colorado, Boulder, Colorado 80309-0215*

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Intramolecular nucleophilic acyl substitution reactions involving a broad range of halo substituted carboxylic acid derivatives have been accomplished in excellent yield employing samarium(II) iodide as the reductive coupling agent. Although particular substrates cyclized most effectively in THF in the presence of tripiperidinophosphine oxide, carboxylic acid esters, the focus of this report, cyclize equally well without such an additive in the presence of a catalytic quantity of iron(III) complexes. Thus a comprehensive series of halo substituted esters were cyclized in excellent yield to the corresponding 4-, 5-, and 6-membered carbocycles. The reaction is extremely mild and selective as demonstrated by experiments wherein alkyl chlorides, acetals, and olefins remain completely intact under the reaction conditions. In addition to introducing a convenient procedure for preparing stereodefined spirocyclic systems, a new ring expansion sequence has been developed that appears extremely general for the preparation of various ring systems.

The development of new annulation methods is among the more challenging and important quests in synthetic organic chemistry. Carbocycles and heterocycles are the essential building blocks of many natural products, and furthermore these systems exhibit ideal topographical features for directing asymmetric syntheses. Transition metal mediated,[1] concerted pericyclic,[2] cationic,[3] and carbanionic[4] approaches to ring synthesis are all commonplace. The intramolecular addition of carbon centered anions to electrophilic functional groups is a classical procedure for the synthesis of various carbocycles, a prevalent subset of cyclic molecules.[5] Although a majority of these existing routes involve vinyl-, aryl-,[6] or heteroatom-stabilized carbanions, the application of nonstabilized organometallic species has received relatively minor attention. The ability to generate an organometallic selectively under mild conditions in the presence of sensitive functional groups is a prerequisite for the success of such a method and a probable reason few satisfactory processes of this type exist.

Previous research from this laboratory provided the first evidence that a carbanionic species is involved in samarium(II) iodide ($SmI_2$) promoted reactions,[7] including intramolecular Barbier reactions.[8] The latter studies on the intramolecular Barbier reaction raised doubts about the previously held conviction that a radical coupling step was involved in the intermolecular version of this reaction.[9] Subsequent to our revelation, several groups reported evidence implicating the existence of $SmI_2$-generated alkylsamariums in related systems.[10]

Samarium(II) iodide has proven to be superior to other reducing agents (e.g., Li, Mg, *t*-BuLi, and *n*-BuLi) typically used in Barbier-type processes.[8,11] The mechanism of the intramolecular $SmI_2$ promoted Barbier reaction, not unlike its more traditional lithium and magnesium counterparts,[12] has proven to be somewhat of an enigma. As mentioned, it is likely that a carbanionic mechanism is operative in many instances, although evidence exists that more than one mechanism may be applicable depending on the particular substrate under consideration. For example, intramolecular Barbier-type reactions of certain isolated ketones incorporating a pendant iodoalkyl side chain proceed through a carbanionic intermediate,[8] but more easily reduced iodoalkyl substituted $\beta$-dicarbonyl substrates proceed through an intermediate that does not involve formation of an organometalllic species.[13] There are virtually no mechanistic details on the cyclization of iodoalkyl substituted $\alpha,\beta$-unsaturated ketones.[14]

In light of our previous findings, we became intrigued by the possibility of generating an alkylsamarium which would take part in intramolecular reactions with electrophiles other than aldehydes and ketones. Prior to this report, $SmI_2$-promoted nucleophilic addition reactions have been limited for the most part to aldehydes and

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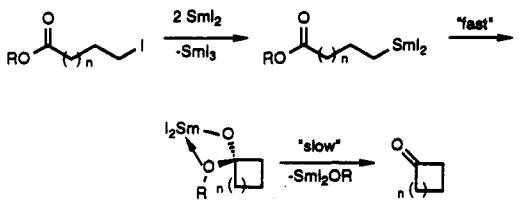
ketones,[15] owing possibly to the tenet that a ketyl intermediate was required for successful coupling. Indeed, Kagan and co-workers have reported that under $SmI_2$-promoted Barbier-type conditions, no nucleophilic acyl substitution occurs between methyl octanoate and methyl iodide.[16] Furthermore, literature precedent indicated that, in general, reactions involving reductive coupling of alkyl halides with carboxylic acid esters in attempts at ketone synthesis suffered from the enhanced reactivity of the ketone relative to the starting ester. Consequently, low yields of the desired ketone were generally obtained for both inter- and intramolecular reactions.[17] Attempted solutions have included the use of acyl derivatives other than carboxylic acid esters,[18] low reaction temperatures,[17b,19] and/or addition of additives to trap the tetrahedral alcoholate intermediate.[17a,20] Despite these developments, modest yields of ketones are realized only when primary alkyl halides are applied to the synthesis of select three- and five-membered rings. Attempts at forming four- and six-membered rings or cyclization of secondary or tertiary alkyl halides has proven to be far less productive.[17,18a,20]

With the aforementioned synthetic challenge in mind, our initial studies of $SmI_2$-promoted intramolecular nucleophilic acyl substitution have focused primarily on the ester functionality as the electrophile because of its ubiquity in organic synthesis, ease of preparation, and the prospect that the oxophilic Sm(III) species generated might stabilize the tetrahedral intermediate, thereby minimizing second addition to the initially formed ketone (eq 1).



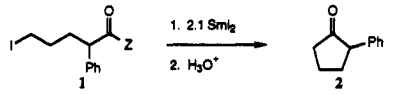

(1)

Herein we detail our studies describing a general, convenient, and exceptionally efficient method for the synthesis of various cycloalkanones and their derivatives, applying a $SmI_2$-promoted intramolecular nucleophilic acyl substitution reaction to a broad range of iodoalkyl-substituted carboxylic acid derivatives.

## Results and Discussion

Preliminary experiments were performed to determine the range of possible acyl derivatives amenable to this substitution reaction. As indicated in Table I, each of the acyl derivatives studied cyclized to some extent under the reaction conditions. Although the carboxylic acid ester and *N*-acyloxazolidinone substrates cyclized efficiently under iron-catalyzed conditions in THF, addition of tripiperidinophosphine oxide [$(C_5H_{10}N)_3PO$] permitted cyclization of all substrates examined with little differentiation in yield.[21] The results displayed in entries 5 and 6 in Table I are particularly noteworthy as potentially convenient approaches to enantiomerically enriched carbocyles from the corresponding sultam[22] or oxazolidinone[23] derivatives. We are currently exploring this interesting possibility.

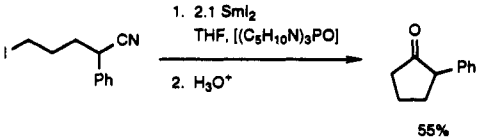
**Table I. Samarium(II) Iodide Promoted Cyclization of Iodoalkyl Acyl Derivatives 1**




| entry | substrate | Z | % isoltd yield 2[a] (condition B)[b] |
|---|---|---|---|
| 1 | 1a | -OEt | 74 (71) |
| 2 | 1b |  | 42 (79) |
| 3 | 1c |  | 40 (81) |
| 4 | 1d | -S-*i*-Pr | 28 (68) |
| 5 | 1e |  | 18 (71) |
| 6 | 1f |  | 64 (69) |

[a] Reactions were run in the presence of 1 mol % iron catalyst [$Fe(DBM)_3$ or $Fe(acac)_3$]. [b] Reactions were run in the presence of 4 equiv of tripiperidinophosphine oxide.

In addition to carboxylic acid derivatives, nitriles also serve as suitable precursors for the reaction. Under appropriate reaction conditions, 2-phenylcyclopentanone can be synthesized in modest yields by reaction of $SmI_2$ with 5-iodo-2-phenylpentanenitrile (eq 2).




(2)

As explained, further studies focused on appropriately functionalized ester substrates (Table II). In an attempt to delineate the synthetic applicability of this reductive cyclization thoroughly, an extensive set of halo esters were synthesized and subjected to the reaction conditions. Optimum conditions involved dropwise addition of the substrate in THF to a 0.15 M solution of $SmI_2$/THF at 0 °C containing a catalytic amount (1 mol %) of iron(III) complex (iron(III) acetylacetonate, [$Fe(acac)_3$], and iron-(III) tris(dibenzoylmethane), [$Fe(DBM)_3$], yield identical results). Reactions were complete within 30 min in most cases. As reported previously for $SmI_2$-promoted intramolecular Barbier-type processes,[8] reactions of alkyl halides were sluggish and yields diminished in the absence of catalyst. In the present case, allylic halides exhibited similar reactivity in the presence or absence of catalyst.

Cyclization to form cyclobutanone, cyclopentanone, and cyclohexanone products occurred in good to excellent yield under the mild reaction conditions. Although the formation of five- and six-membered rings is fairly insensitive to reaction conditions (reactions were typically initiated

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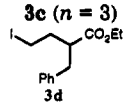
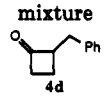
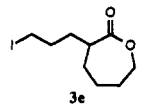
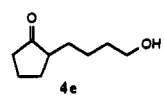
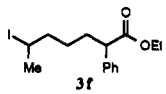
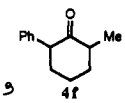
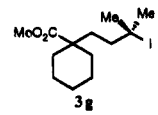
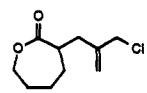
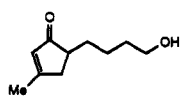
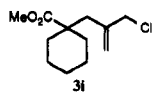
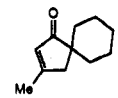
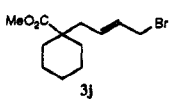
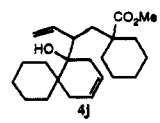
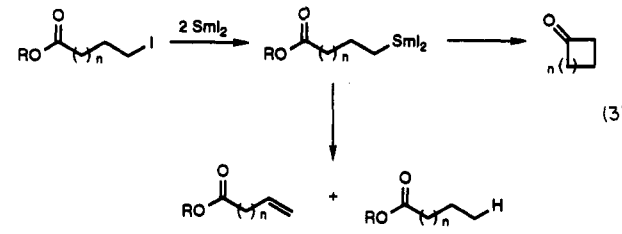
**Table II. Samarium(II) Iodide-Promoted Cyclization of Halo Esters 3**

| entry | substrate | product | % isoltd yield (4) |
|---|---|---|---|
| 1 | **3a** ($n$ = 1) | **4a** | 93 |
| 2 | **3b** ($n$ = 2) | **4b** | 91 |
| 3 | **3c** ($n$ = 3) | mixture | [a] |
| 4 |  **3d** |  **4d** | 74[b] |
| 5 |  **3e** |  **4e** | 91 |
| 6 |  **3f** |  **4f** | 85[c] |
| 7 |  **3g** | mixture | – |
| 8 |  **3h** |  **4h** | 79 |
| 9 |  **3i** |  **4i** | 88 |
| 10 |  **3j** |  **4j** | 90[d] |

[a] A 1:1 mixture of disproportionation products was obtained in 74% yield (see text). [b] The reaction was initiated at −78 °C, then allowed to warm to 0 °C, and quenched immediately following substrate consumption. [c] Cyclization of a 1:1 (cis:trans) mixture of diastereomeric substrates yielded a 1:1 mixture of diastereomeric products. [d] The indicated product was isolated as a single diastereomer of undetermined relative stereochemistry.

at 0 °C), formation of the cyclobutanone derivative (entry 4) required lower reaction temperatures (−30 °C) to minimize product degradation. It was pleasing to discover that four- and six-membered rings could be formed with high efficiency, because attempts at synthesizing such structures via intermediate organolithiums have proven difficult. Furthermore, the ability to cyclize 2° alkyl halides (entry 6) with little diminution in yield attests to the broader applicability of this reaction as compared to methods requiring metal–halogen exchange.[17,18a,20] As illustrated by examples from Table II, both monocarbocyclic and spirocyclic ketones were generated with equal ease utilizing appropriate starting materials.

Attempts at seven-membered ring formation were unsuccessful (entry 3), thereby defining the practical limit of ring size that could be synthesized utilizing this procedure. Interestingly, in the case of entries 3 and 7, a significant quantity of $SmI_2$ remained unreacted following starting material consumption. In addition, the major products isolated (unsaturated esters and dehalogenated alkyl esters) were those expected as a result of radical or organometallic disproportionation (eq 3). In



(3)

the case of entry 3, these esters were isolated in a 1:1 to 1.5:1 ratio depending on the reaction temperature. Disproportionation via a primary radical would expectedly lead to a ca. 10:1 ratio of radical recombination products (dimer) to disproportionation products.[24] However, isolation of the two byproducts in 74–81% yield with no evidence of dimer suggested the products were generated as a result of decomposition of an organometallic intermediate.[24] Significantly, at lower temperatures the proportion of product resulting from β-hydride elimination increased to ca. 1.5 times the amount of saturated material. The major byproducts in the 2° and 3° alkyl halide cyclizations also consisted of varying amounts of the analogous disproportionation products in similar ratios, without evidence of significant dimeric products. Disproportionation of 2° radicals is known to yield a ca. 1:1 ratio of radical combination to disproportionation products, but 3° radicals self react, resulting in a ca. 1:7 ratio of radical combination to disproportionation products.[24] Our current observations, in conjunction with previous results,[8] indicate that a majority of the byproducts we observe in relatively slow cyclizing substrates are a result of intermediate organometallic decomposition. We attribute this phenomenon to an unfavorable combination of the instability of the generated organometallic and slow cyclization rates of the substrates concerned.[25]

As indicated by entries 8 and 9 in Table II, the cyclization of certain allylic substrates also proceeds in excellent yield. The major product isolated in each case was the isomer containing the double bond in conjugation with the ketone. Evidently, isomerization occurred under the reaction conditions, because attempts at quenching the reaction with buffered aqueous solutions also provided the conjugated enone. Interestingly, attempted cyclization of allylic bromide **3j** resulted in isolation of the dimeric structure shown as a single diastereomer in 90% yield. Apparently, cyclization is slow relative to intermolecular addition of the allylsamarium to the intermediate ketone. Notably, in this case the olefin did not isomerize prior to intermolecular addition. Although allylsamariums are known to undergo $\eta^3$ to $\eta^1$ equilibration readily in the presence of donating solvents (e.g., $Et_2O$, THF), isomerization of the allylic anion to the energetically disfavored cis conformer is required for cyclization and is a conceivable factor for the relatively slow cyclization step.[26]

Conversion of substrates **5a** through **5f** to the observed hydroxycycloalkanone products (Table III) represents the final step in a novel and potentially useful multistep ring expansion sequence. Thus, alkylation of a cycloalkanone or its derivative followed by Baeyer–Villiger oxidation

(24) Alternatively, the disproportionation of a dialkyl organometallic would also provide the observed products. Kochi, J. K. *Organometallic Mechanisms and Catalysis*; Academic Press: New York, 1978.

(25) These and previous results are contrary to recent conjecture, suggesting tertiary carbanions are not generated under $SmI_2$ conditions. See refs. 10c and 10d.

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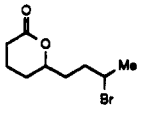
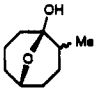
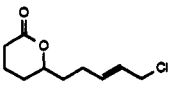
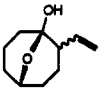
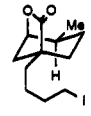
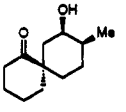
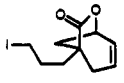
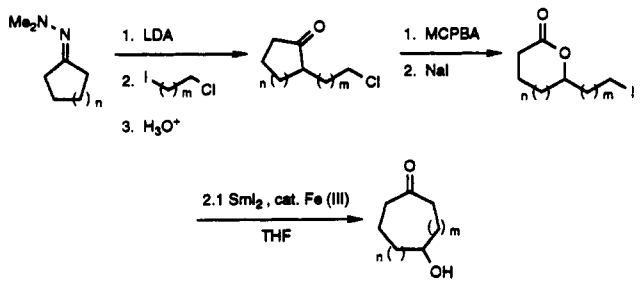
**Table III. Cyclization of Halo Esters 5 To Yield Ring-Expanded Carbocycles or Stereodefined Spirocycles 6**

| entry | substrate | product | % isoltd yield (6) |
|---|---|---|---|
| 1 | **5a** ($n = 1, m = 1$) | **6a** | 93[a] |
| 2 | **5b** ($n = 2, m = 1$) | **6b** | 95[b] |
| 3 | **5c** ($n = 1, m = 2$) | **6c** | 79[c] |
| 4 | **5d** ($n = 2, m = 2$) | **6d** | 82[c] |
| 5 |  **5e** |  **6e** | 76[d] |
| 6 |  **5f** |  **6f** | 82[e] |
| 7 | **5g** ($n = 1$) | **6g** | 91 |
| 8 | **5h** ($n = 2$) | **6h** | 86[f] |
| 9 |  **5i** |  **6i** | 88[g] |
| 10 |  **5j** |  **6j** | 86 |

[a] The crude product was treated with acetic anhydride and triethylamine in $CH_2Cl_2$ to allow isolation of the final product as the keto acetate. [b] The product exists as a 2.3:1 (hemiacetal:hydroxy ketone) mixture. [c] The product exists exclusively as the hemiacetal. [d] The product was isolated as 1.7:1 mixture of hemiacetal diastereomers. [e] The product was isolated as a 1:1 mixture of hemiacetal diastereomers. [f] The product exists as a 4:1 (hydroxy ketone: hemiacetal) mixture. [g] The product was isolated as a 3:1 mixture of diastereomers (the relative stereochemistry of the major diastereomer is shown) employing a 3:1 (endo:exo) diastereomeric mixture of substrates.

**Scheme I**




allows rapid access to a variety of suitably functionalized substrates (Scheme I). The option of preparing these substrates enantiomerically enriched by asymmetric hydrazone alkylation[27] followed by stereospecific Baeyer–Villiger reaction[28] is an additional attractive feature of this method. The overall process appears to be quite general for the preparation of various [$n + 2$] and [$n + 3$] ring expanded products. Again, in contrast to processes employing metal–halogen exchange, 2° halides can be utilized in $SmI_2$-promoted reactions. Cyclization of a 1:1 diastereomeric mixture of 2° bromides **5e** produced a separable 2:1 mixture of the anticipated cyclooctanoid products (**6e**) that exist exclusively as the hemiacetals. The ring expansion reaction also proved to be applicable to allylic systems as indicated by entry 6 in Table III. In this case, six-membered ring formation was accomplished without the complicating double addition side reaction observed for substrate **3j**.

Synthesis of stereodefined spirocyclic systems as exist in certain terpenoids (including the spirovetivane phytoalexins[29]) and which serve as intermediates in various alkaloid syntheses[30] continue to be synthetically challenging. Existing routes to these substituted spiro[4.5]-decane and spiro[5.5]undecane derivatives are typically complicated sequences which engender little hope of achieving high diastereoselectivity or enantioselectivity in the process.[31]

By contrast, selective syntheses of several stereodefined spirocyclic systems have been achieved using the $SmI_2$-promoted protocol by intramolecular nucleophilic acyl substitution reactions. Substrates **5g–5j** in Table III were prepared by related routes involving a Diels–Alder reaction followed by alkylation of the resulting cycloalkanecarboxylic acid, iodolactonization, and removal of the resulting iodide by radical reduction or dehydrohalogenation methods (Scheme II). Reductive cyclization of these substrates using $SmI_2$ allowed efficient synthesis of various stereodefined spirocyclic products.

The ability to perform the $SmI_2$-promoted nucleophilic acyl substitution reaction in the presence of sensitive functional groups (e.g., acetals, entries 1 and 2 in Table IV) confirms the selective nature of this process and in addition makes possible the sequencing of carbon–carbon bond-forming reactions by simple manipulation of the reaction conditions (entries 3–7). For example, the ability to distinguish between halides as in **7c** without halogen exchange in the substrate or product under the reaction conditions permits the selective construction of halo ketones such as **8c** in excellent yield. By a simple modification of the reactions conditions, a sequential process involving either **7c** or **7d** can be accomplished in which initial nucleophilic acyl substitution is followed by an intramolecular Barbier-type carbonyl addition,[8] providing the bridgehead bicyclic alcohol **8d** in each case. Another excellent example of modifying reaction conditions to achieve selectivity in carbon–carbon bond formation is illustrated by reactions of unsaturated ester **7e**. Under simple Fe(III)-catalyzed reaction conditions, **7e** cyclizes to provide **8e** as the exclusive product of the reaction, even though the Sm(III) ketyl of **8e** has a 5-*exo-trig* radical cyclization route open to it (entry 6). Thus,

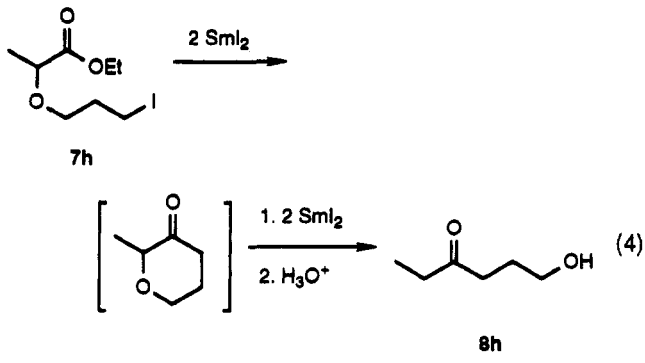
(27) Enders, D.; Kipphardt, H.; Fey. P. *Org. Synth.* **1987**, *65*, 183.
(28) Hassall, C. H. *Org. React.* **1957**, *9*, 73.

(29) (a) Burke, S. D.; Murtishaw, C. W.; Dike, M. S.; Strickland, S. M.; Saunders, J. D. *J. Org. Chem.* **1981**, *46*, 2400. (b) Iwata, C.; Takemoto, Y.; Kubota, H.; Kuroda, T.; Imanishi, T. *Chem. Pharm. Bull.* **1990**, *38*, 361. (c) Ceccherelli, P.; Curini, M.; Marcotullio, M. C.; Rosati, O. *Tetrahedron* **1989**, *45*, 3809. (d) Haack, R. A.; Beck, K. R. *Tetrahedron Lett.* **1989**, *30*, 1605. (e) Nystroem, J. E.; Helquist, P. *J. Org. Chem.* **1989**, *54*, 4695. (f) Pettit, G. R.; Harvey, T. B., III. *Synth. Commun.* **1981**, *11*, 167.
(30) (a) Corey, E. J.; Arnett, J. F.; Widiger, G. N. *J. Am. Chem. Soc.* **1975**, *97*, 430. (b) Corey, E. J.; Petrzilka, M.; Ueda, Y. *Tetrahedron Lett.* **1975**, 4343.
(31) For an exception, see: Hwu, J. R.; Wetzel, J. M. *J. Org. Chem.* **1992**, *27*, 922.

under these reaction conditions a ketyl–olefin reductive cyclization[21] is extremely slow (2 d at room temperature). However, reaction of **7e** in the presence of tripiperidinophosphine oxide and 4 equiv of $SmI_2$ permits a sequential process in which both the nucleophilic acyl substitution and the ensuing ketyl–olefin cyclization proceed effectively to provide a modest yield of tandem cyclized product **8e'** (entry 7).

Other stereodefined bicyclics can also be readily prepared utilizing straightforward synthetic strategies. For example, compounds **7f** and **7g** are easily prepared by Diels–Alder technology. Reaction of such substrates with $SmI_2$, affording linearly fused bicyclic compounds **8f** and **8g**, establishes the ability to generate functionalized, stereodefined ring systems via this protocol. Monitoring the reaction of **7g** in order to ensure a timely quench allows retention of stereochemistry at the readily enolizable stereocenter.

Attempted cyclization of α-heterosubstituted systems proved to be nonproductive in terms of preparation of the desired cyclic systems. Cyclization of the ethyl lactate derivative **7h** resulted in complete consumption of the $SmI_2$. However, 1-hydroxy-4-hexanone[32] was determined to be the major product of the reaction (isolated in 45% yield), and 49% of the starting material was recovered. Rapid reduction of the desired α-alkoxy ketone intermediate is undoubtedly responsible for the observed products (eq 4). Attempts at minimizing the unwanted second reduction proved futile, a result not suprising in light of the facile reductive elimination of analogous α-heterosubstituted carbonyl substrates.[33]



(4)

Proline derivative **7i** proved to react slightly slower than most of the substrates studied without formation of the desired cyclic amine. The major product isolated following starting material consumption was the reduced *N*-*n*-propyl derivative **8i**[34] from apparent protonation of the presumed organosamarium intermediate. An attempt at diminishing this undesired reaction by removal of carbonyl α-hydrogens was not investigated.

## Conclusions

Applying a $SmI_2$-promoted intramolecular reductive cyclization reaction to a series of halo-substituted acyl derivatives has provided the corresponding ketones in excellent yields. The present method appears to be extremely general compared to existing methods and is compatible with various reactive functional groups including acetals, chlorides, and olefins. Allylic, secondary, and primary halides have been cyclized to form a variety of 4- through 6-membered carbocycles with little differentiation in yield. A new ring expansion sequence has been developed that permits the synthesis of hydroxycycloalkanones. A convenient route to stereodefined spirocyclic systems has also been introduced.

## Experimental Section

**Reagents.** Tetrahydrofuran (THF) was distilled immediately prior to use from benzophenone ketyl under Ar. Samarium metal was purchased from Rhône-Poulenc Inc., Phoenix, AZ, and was weighed and stored under an inert atmosphere. $CH_2I_2$ was purchased from Fluka Chemicals and was distilled prior to use. Standard benchtop techniques were employed for handling air-sensitive reagents, and all reactions were carried out under Ar.

**(3-Chloropropyl)phenylacetic Acid.** Phenylacetic acid (3.40 g, 25 mmol) in 20 mL of THF at 0 °C was added slowly to a solution of LDA (58 mmol) in 75 mL of THF and 5 mL of HMPA. After 5 min at 0 °C, the reaction mixture was heated at 50 °C for an additional 2 h and then returned to 0 °C. The electrophile, 1-chloro-3-iodopropane (5.73 g, 28 mmol), was added to the reaction mixture and the resulting suspension was allowed to warm to room temperature and was stirred an additional 3 h. Aqueous workup provided the title compound (4.20 g, 79%). $^1H$ NMR (300 MHz, $CDCl_3$): δ 11.36 (br s, 1H), 7.35–7.21 (m, 5H), 3.77–3.71 (m, 1H), 3.49 (t, $J$ = 6.6 Hz, 2H), 1.97–1.63 (m, 4H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 179.46, 137.90, 128.81, 127.99, 127.68, 50.78, 44.41, 30.24, 30.15.

**(3-Chloropropyl)phenylacetyl chloride.** The previously prepared acid (4.2 g, 20 mmol) in 120 mL of benzene was treated with oxalyl chloride (7.62 g, 60 mmol) for 5 min at 0 °C and 3 h at room temperature. The volatiles were removed under vacuum affording the crude acid chloride (4.3 g, 94%) that was used without further purification.

**Ethyl 2-Phenyl-4-pentenoate.** To a solution of LDA (11 mmol) in 15 mL of THF and 2 mL of HMPA at −78 °C was added ethyl phenylacetate (1.64 g, 10 mmol) in 15 mL of THF. The resulting mixture was stirred for 45 min. Allyl bromide (1.45 g, 12 mmol) was added and the reaction was warmed to 0 °C for an additional 30 min. Aqueous workup followed by flash chromatography afforded the title compound (1.80 g, 80%). $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.38–7.18 (m, 5H), 5.75–5.64 (m, 1H), 5.08–4.96 (m, 2H), 4.15–4.02 (m, 2H), 3.6 (dd, $J$ = 8.4, 7.1 Hz, 1H), 2.85–2.75 (m, 1H), 2.53–2.44 (m, 1H), 1.16 (t, $J$ = 7.1 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 173.35, 138.68, 135.28, 128.53, 127.86, 127.20, 116.84, 60.62, 51.42, 37.54, 14.00.

**Ethyl 5-Iodo-2-phenylpentanoate (1a).** To a solution of cyclohexene (0.902 g, 11 mmol) in 20 mL of THF at 0 °C was added $BH_3$-$SMe_2$ (0.522 mL of a 10.5 M solution in $SMe_2$, 5.5 mmol). The reaction mixture was allowed to stir 1.5 h at 0 °C. Ethyl 2-phenyl-4-pentenoate (1.02 g, 5 mmol) in 20 mL of THF was then added, and the resulting reaction mixture was stirred for 1 h at 0 °C and 1 h at room temperature. The reaction was cooled to 0 °C and NaOAc (0.902 g, 11 mmol) in 10 mL of MeOH was added, followed by ICl (1.14 g, 7 mmol) in 10 mL of MeOH. After an additional 1 h at 0 °C, the reaction was quenched (saturated aqueous $NH_4Cl$) and excess ICl was removed by dropwise addition of $NaHSO_3$.[35] Flash chromatography afforded the title compound (1.34 g, 81%). $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.38–7.23 (m, 5H), 4.18–4.05 (m, 2H), 3.53 (t, $J$ = 7.3 Hz, 1H), 3.15 (t, $J$ = 6.6 Hz, 2H), 2.21–2.13 (m, 1H), 1.95–1.71 (m, 3H), 1.20 (t, $J$ = 7.1 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 173.44, 138.58, 128.62, 127.77, 127.30, 60.72, 50.59, 34.13, 31.20, 14.00, 5.73.

***N,N*-Tetramethylene-2-phenyl-4-pentenamide.** To a solution of 2-phenyl-4-pentenoyl chloride (0.973 g, 5 mmol) in 10 mL of $CH_2Cl_2$ at 0 °C were added pyridine (0.553 g, 7 mmol) and

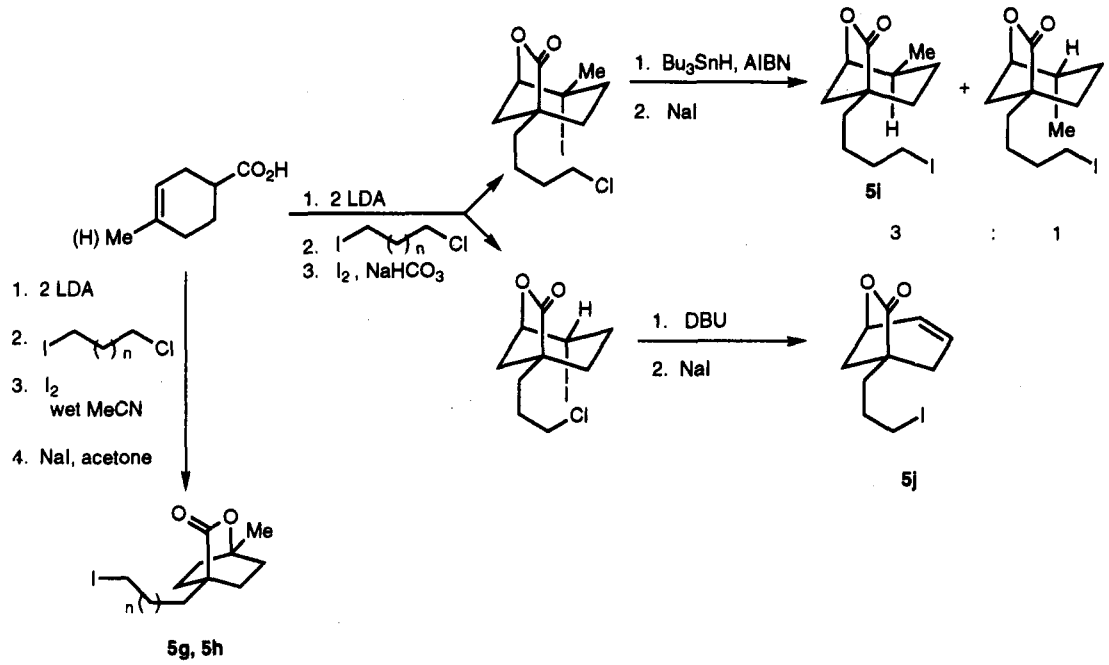
(32) (a) Birkinshaw, S.; Kocienski, P. *Tetrahedron Lett.* **1991**, *32*, 6961. (b) Wallace, P.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2971. (c) Wallace, P.; Warren, S. *Tetrahedron Lett.* **1985**, *26*, 5713.

(33) (a) Molander, G. A.; Hahn, G. *J. Org. Chem.* **1986**, *51*, 1135. (b) White, J. D.; Somers, T. C. *J. Am. Chem. Soc.* **1987**, *109*, 4424. (c) Holton, R. A.; Williams, A. D. *J. Org. Chem.* **1988**, *53*, 5981.

(34) Hoegberg, T.; Raemsby. S.; Stroem, P. *Acta Chem. Scand.* **1989**, *43*, 660.

(35) Gooch, E. E.; Kabalka, G. W. *Synth. Commun.* **1981**, *11*, 521.

**Scheme II**




pyrrolidine (0.426 g, 6 mmol). The resulting solution was allowed to warm to room temperature and stir for 2 h. Aqueous workup followed by flash chromatography afforded the title compound (1.01 g, 88%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.37–7.18 (m, 5H), 5.81–5.65 (m, 1H), 5.04–4.92 (m, 2H), 3.60 (t, $J$ = 7.3 Hz, 1H), 3.44–3.13 (m, 4H), 2.91–2.79 (m, 1H), 2.48–2.37 (m, 1H), 1.90–1.68 (m, 4H). $^{13}$C NMR (300 MHz, $CDCl_3$): $\delta$ 170.80, 139.24, 136.30, 128.42, 127.90, 126.70, 116.06, 50.62, 45.95, 45.68, 38.70, 25.73, 23.87.

***N,N*-Tetramethylene-5-iodo-2-phenylpentanamide (1b).** The title compound was prepared in 71% yield by hydroboration–iodination of *N,N*-tetramethylene-2-phenyl-4-pentenamide as previously described. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.38–7.22 (m, 5H), 3.58–3.10 (m, 7H), 2.21–1.69 (m, 8H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 170.98, 139.44, 128.73, 127.96, 127.00, 49.87, 46.16, 45.92, 35.52, 31.73, 25.91, 24.02, 6.29.

***N*-Methoxy-*N*-methyl 5-chloro-2-phenylpentanamide.** To a solution of 5-chloro-2-phenylpentanoyl chloride (2.31 g, 10 mmol) in 30 mL of $CH_2Cl_2$ at 0 °C were added *N*-methoxy-*N*-methylamine hydrochloride (1.17 g, 12 mmol) and pyridine (1.98 g, 25 mmol). The reaction mixture was allowed to warm to room temperature and was stirred for 2 h. Aqueous workup and flash chromatography yielded the title compound (2.32 g, 91%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.39–7.21 (m, 5H), 4.05-3.96 (m, 1H), 3.58–3.47 (m, 2H), 3.42 (s, 3H), 3.13 (s, 3H), 2.22–1.59 (m, 4H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 174.05, 139.61, 128.54, 127.97, 126.96, 61.120, 46.85, 44.60, 32.09, 31.21, 30.51.

***N*-Methoxy-*N*-methyl-5-iodo-2-phenylpentanamide (1c).** To a solution of *N*-methoxy-*N*-methyl-5-chloro-2-phenylpentanamide (5 mmol, 1.28 g) in 15 mL of acetone was added NaI (3.75 g, 25 mmol). The resulting supension was heated at reflux for 14 h. Aqueous workup and flash chromatography afforded the title compound (1.61 g, 93%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.34–7.21 (m, 5H), 4.03-3.76 (m, 1H), 3.43 (s, 3H), 3.14 (s, 3H), 3.18–3.11 (m, 2H), 2.17–2.03 (m, 1H), 1.89-1.66 (m, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 173.96, 139.57, 128.57, 127.97, 127.00, 61.16, 46.56, 34.75, 32.12, 31.47, 6.05.

**Isopropyl 5-Chloro-2-phenylpentanethioate.** To a solution of 5-chloro-2-phenylpentanoyl chloride (1.16 g, 5 mmol) and pyridine (0.474 g, 6 mmol) in 15 mL of $CH_2Cl_2$ at 0 °C was added isopropylmercaptan (0.532 g, 7 mmol). The resulting solution was allowed to warm to room temperature and was stirred for 3 h. Aqueous workup followed by flash chromatography afforded the title compound (1.24 g, 94%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.38–7.22 (m, 5H), 3.71–3.42 (m, 4H), 2.31–2.18 (m, 1H), 2.01–1.84 (m, 1H), 1.78–1.62 (m, 4H), 1.27 (d, $J$ = 6.8 Hz, 3H), 1.19 (d, $J$ = 6.8 Hz, 3H).

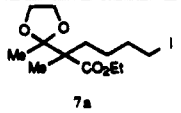
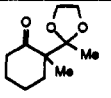
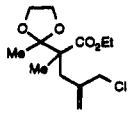
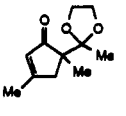
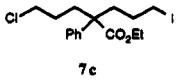
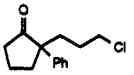
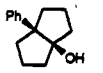
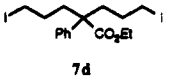
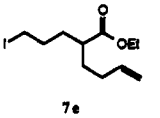
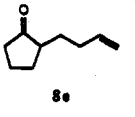
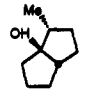
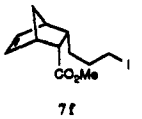
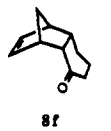
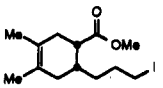
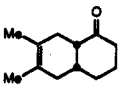
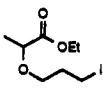
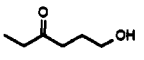
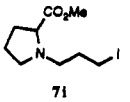
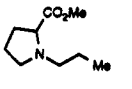
**Isopropyl 5-Iodo-2-phenylpentanethioate (1d).** Finkelstein reaction of isopropyl 5-chloro-2-phenylpentanethioate employing NaI in acetone, as described previously, afforded the title compound in 81% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.37–7.21 (m, 5H), 3.65–3.54 (m, 2H), 3.18–3.08 (m, 2H), 2.24–1.68 (m, 4H), 1.27 (d, $J$ = 7.1 Hz, 3H), 1.18 (d, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 200.06, 138.09, 128.75, 128.12, 127.57, 59.22, 34.88, 33.98, 31.12, 22.87, 22.63, 5.72.

***N*-Butyl-*N*-(5-iodo-2-phenyl-1-oxopentyl)methanesulfonamide (1e).** To a solution of *N*-butylmethanesulfonamide (0.906 g, 6 mmol) in 15 mL of toluene at 0 °C was added NaH (0.168 g, 7 mmol). The resulting suspension was allowed to warm to room temperature and was stirred for 2 h. The reaction mixture was returned to 0 °C and a solution of 5-chloro-2-phenylpentanoyl chloride (1.16 g, 5 mmol) in 10 mL of toluene was added. After 3 h at 0 °C an aqueous workup afforded the crude product. Heating the crude product and NaI (3.75 g, 25 mmol) in 20 mL of acetone at reflux for 12 h afforded the title compound (1.60 g, 60%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.39–7.21 (m, 5H), 4.07 (t, $J$ = 7.1 Hz, 1H), 3.75–3.43 (m, 2H), 3.14–3.06 (m, 2H), 2.96 (s, 3H), 2.21–1.18 (m, 8H), 0.87 (t, $J$ = 7.3 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 173.62, 137.68, 129.27, 127.91, 50.32, 46.24, 42.05, 35.93, 32.12, 31.04, 19.89, 13.51, 5.71.

**3-(5-Iodo-2-phenyl-1-oxobutyl)-2-oxazolidinone (1f).** To a solution of 2-oxazolidinone (0.522 g, 6 mmol) in 15 mL of THF at −30 °C was added MeMgBr (6 mmol, 3 mL of a 2.0 M solution in THF). The mixture was allowed to warm to 0 °C and was stirred for 1 h. 5-Chloro-2-phenylpentanoyl chloride (1.16 g, 5 mmol) in 10 mL of THF was added and the solution was warmed to room temperature. A solution of the crude product, isolated following aqueous workup, and NaI (3.75 g, 25 mmol) in acetone was heated at reflux for 14 h. Aqueous workup and flash chromatography afforded the title compound (1.34 g, 72%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.41–7.22 (m, 5H), 5.00 (t, $J$ = 7.3 Hz, 1H), 4.42–3.84 (m, 4H), 3.14 (t, $J$ = 6.8 Hz, 2H), 2.25–1.62 (m, 4H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 173.58, 153.01, 138.00, 128.68, 128.61, 127.53, 61.68, 47.45, 42.78, 34.64, 31.22, 5.78.

**5-Iodo-2-phenylpentanenitrile (1g).** Phenylacetonitrile (1.17 g, 10 mmol) in 15 mL of THF was added dropwise to a solution of LDA (12 mmol) in 15 mL of THF at −78 °C. The resulting mixture was allowed to stir for 1 h. The electrophile, 1-chloro-3-iodopropane (2.45 g, 12 mmol), in 5 mL of THF was added and the reaction mixture was warmed to 0 °C. After 2 h at 0 °C, an aqueous workup was performed, and the crude product was isolated. This crude product and NaI (4.50 g, 30 mmol) were heated at reflux in acetone for 12 h. Aqueous workup followed by flash chromatography afforded the title compound (1.54 g, 54

**Table IV. Cyclization of Functionalized Halo Esters 7 To Yield Substituted Carbocycles 8**

| entry | substrate | product | % isoltd yield (8) |
|---|---|---|---|
| 1 |  7a |  8a | 80 |
| 2 |  7b |  8b | 78 |
| 3 |  7c |  8c | 83 |
| 4 | 7c |  8d | 79[a] |
| 5 |  7d | 8d | 84 |
| 6 |  7e |  8e | 92 |
| 7 | 7e |  8e' | 61[b] |
| 8 |  7f |  8f | 83 |
| 9 |  7g |  8g | 77[c] |
| 10 |  7h |  8h | 45[d] |
| 11 |  7i |  8i | 81 |

[a] The reaction was run in the presence of 4 equiv of tripiperidinophosphonamide. [b] Conditions as in entry 4 in addition to 2 equiv of *t*-BuOH. [c] The product was isolated in 89% de employing starting material prepared in 95% de. [d] Starting material (49%) was recovered.

%). $^1$H NMR (300 MHz, $CDCl_3$): δ 7.41–7.34 (m, 5H), 3.84 (t, $J$ = 6.6 Hz, 1H), 3.18 (t, $J$ = 6.1 Hz, 2H), 2.12-1.86 (m, 4H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 135.10, 129.11, 128.18, 127.09, 120.25, 36.25, 36.17, 30.09, 4.64.

**Methyl 1-(3-Iodopropyl)cyclohexanecarboxylate (3a).** To a solution of LDA (11 mmol) in 15 mL of THF at −78 °C was added HMPA (1.97 g, 11 mmol). The resulting solution was allowed to stir for 30 min. Ethyl cyclohexanecarboxylate (1.42 g, 10 mmol) was then added at −78 °C. After 45 min, the electrophile, 1-chloro-3-iodopropane (2.45 g, 12 mmol), was added and the reaction mixture was warmed to room temperature and stirred for an additional 1 h. The crude product obtained following aqueous workup was combined with NaI (4.50 g, 30 mmol) and heated at reflux in acetone for 14 h. Aqueous workup followed by flash chromatography afforded the title compound (2.54 g, 82%). $^1$H NMR (300 MHz, $CDCl_3$): δ 3.63 (s, 3H), 3.07 (t, $J$ = 6.6 Hz, 2H), 2.05–1.12 (m, 14H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 176.86, 51.47, 46.41, 40.90, 33.96, 28.24, 25.70, 23.00, 6.79.

**Methyl 1-(4-Iodobutyl)cyclohexanecarboxylate (3b).** Following the general procedure described above, methyl cyclohexanecarboxylate was alkylated with 1-chloro-4-iodobutane. The crude product of this reaction was then subjected to Finkelstein conditions with NaI in acetone to yield the title compound in 86% yield. $^1$H NMR (300 MHz, $CDCl_3$): δ 3.64 (s, 3H), 3.12 (t, $J$ = 7.1 Hz, 2H), 2.08-1.15 (m, 16H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 177.12, 51.44, 46.81, 39.14, 34.03, 33.65, 25.82, 24.97, 23.12, 6.49.

**Methyl 1-(5-Iodopentyl)cyclohexanecarboxylate (3c).** Following the general procedure described above, the title compound was prepared in 82% yield from methyl cyclohexanecarboxylate. $^1$H NMR (300 MHz, $CDCl_3$): δ 3.63 (s, 3H), 3.12 (t, $J$ = 7.1 Hz, 2H), 2.06–1.97 (m, 2H), 1.82–1.07 (m, 16H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 177.28, 51.38, 46.91, 40.24, 34.10, 33.16, 30.80, 25.85, 23.16, 22.94, 6.93.

**Ethyl 2-Benzyl-3-butenoate.** To a solution of LDA (22 mmol) in 30 mL of THF at −78 °C was added 4 mL of HMPA. After 30 min a solution of ethyl crotonate (2.28 g, 20 mmol) in 20 mL of THF was added dropwise over 15 min. Benzyl bromide (4.28 g, 25 mmol) was added after an additional 45 min and the resulting solution was allowed to warm to room temperature. Aqueous workup followed by flash chromatography afforded the title compound (3.43 g, 84%). $^1$H NMR (300 MHz, $CDCl_3$): δ 7.35–7.19 (m, 5H), 5.77–5.63 (m, 1H), 5.08–4.75 (m, 2H), 4.18-4.02 (m, 2H), 3.62–3.57 (m, 1H), 2.84–2.72 (m, 2H), 2.54–2.42 (m, 2H), 1.17 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 173.31, 138.85, 135.38, 128.56, 127.94, 127.21, 116.78, 60.59, 51.60, 37.56, 14.02.

**Ethyl 2-Benzyl-4-iodobutanoate (3d).** Hydroboration and iodination of ethyl 2-benzyl-3-butenoate, as described previously, afforded the title compound in 56% yield. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.32–7.10 (m, 5H), 4.17 (q, $J$ = 7.1 Hz, 2H), 3.20–2.64 (m, 5H), 2.20–1.82 (m, 2H), 1.14 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 174.34, 138.31, 128.84, 128.39, 126.51, 60.51, 48.00, 37.83, 35.25, 14.01, 2.84.

**2-(2-Propenyl)caprolactone.** Alkylation of caprolactone with allyl bromide, in accord with the procedure described previously, afforded the title compound in 77% yield. $^1$H NMR (300 MHz, $CDCl_3$): δ 5.81–5.66 (m, 1H), 5.04-4.92 (m, 2H), 4.23–4.15 (m, 2H), 2.61–2.44 (m, 2H), 2.12–1.25 (m, 7H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 177.06, 135.76, 116.98, 68.25, 42.16, 36.36, 28.84, 28.61, 28.02.

**2-(3-Iodopropyl)caprolactone (3e).** Hydroboration and iodination of 2-(2-propenyl)caprolactone, as described previously, afforded the title compound in 82% yield. $^1$H NMR (300 MHz, $CDCl_3$): δ 4.29–4.14 (m, 2H), 3.21–3.07 (m, 2H), 2.58-2.48 (m, 1H), 1.93–1.42 (m, 10H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 176.97, 68.29, 41.96, 33.70, 31.08, 30.13, 28.60, 28.12, 6.49.

**Ethyl 6-Iodo-2-phenylheptanoate (3f).** Alkylation of ethyl phenylacetate with 1,4-diiodopentane, in accord with the procedure described previously, afforded the title compound as a 1:1 mixture of diastereomers in 52% yield. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.39–7.21 (m, 5H), 4.21–4.06 (m, 3H), 3.54 (t, $J$ = 7.1 Hz, 1H), 2.19–1.22 (m, 6H), 1.89 (d, $J$ = 6.8 Hz, 1.5H), 1.88 (d, $J$ = 6.8 Hz, 1.5H), 1.21 (t, $J$ = 6.9 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 174.20, 174.17, 139.43, 139.36, 129.02, 128.96, 128.90, 128.21, 128.17, 127.58, 61.03, 51.58, 42.82, 42.78, 32.92, 32.84, 30.04, 29.17, 29.16, 28.01, 14.46.

**Methyl 1-(3-Methyl-2-butenyl)cyclohexanecarboxylate.** Alkylation of methyl cyclohexanecarboxylate with 1-bromo-3-methyl-2-butene afforded the title compound in 86% yield. $^1$H NMR (300 MHz, $CDCl_3$): δ 5.05–4.93 (m, 1H), 3.59 (s, 3H), 2.11 (d, $J$ = 7.5 Hz, 2H), 2.10–1.97 (m, 2H), 1.63 (s, 3H), 1.52 (s, 3H), 1.60-1.12 (m, 8H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 177.04, 133.93, 119.11, 51.22, 47.67, 38.64, 33.70, 25.85, 25.79, 23.19, 17.63.

**Methyl 1-(3-Iodo-3-methylbutyl)cyclohexanecarboxylate (3g).** To a solution of methyl 1-(3-methyl-2-butenyl)cyclohexanecarboxylate (0.600 g, 2.86 mmol) in 10 mL of $CH_2Cl_2$ was

added 4 g of $Al_2O_3$ followed by 47% HI (2.2 mL, 12 mmol). After 4 h an additional 2 mL of HI was added and the resulting mixture was allowed to stir overnight. Aqueous workup followed by flash chromatography afforded the title compound (405 mg, 42%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.64 (s, 3H), 2.15–1.93 (m, 2H), 1.84 (s, 6H), 1.73–1.16 (m, 12H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 177.01, 51.73, 51.48, 46.35, 44.32, 38.63, 37.88, 34.00, 25.80, 23.05.

**2-(2-(Chloromethyl)-2-propenyl)caprolactone (3h).** Alkylation of caprolactone with 1-chloro-2-(chloromethyl)-2-propene, as described above, followed by Finkelstein reaction of the resulting chloride provided the title compound in 35% yield. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.20 (s, 1H), 4.85 (s, 1H), 4.32–3.94 (m, 2H), 3.85 (d, $J$ = 9.5 Hz, 1H), 3.80 (d, $J$ = 9.5 Hz, 1H), 2.61–2.24 (m, 3H), 1.74–1.22 (m, 6H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 174.60, 143.60, 115.27, 62.77, 43.68, 36.57, 31.49, 28.02, 23.11, 9.90.

**Methyl 1-(2-(Chloromethyl)-2-propenyl)cyclohexanecarboxylate (3i).** Alkylation of methyl cyclohexanecarboxylate with 1-chloro-2-(chloromethyl)-2-propene, as described previously, afforded the title compound in 70% yield. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.18 (d, $J$ = 1.0 Hz, 1H), 4.88 (d, $J$ = 1.0 Hz, 1H), 3.94 (s, 2H), 3.65 (s, 3H), 2.39 (s, 2H), 2.07–2.02 (m, 2H), 1.62–1.21 (m, 8H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 176.72, 141.53, 118.57, 51.44, 48.87, 47.22, 43.16, 34.51, 25.60, 23.11.

**Methyl *trans*-1-(4-Bromo-2-butenyl)cyclohexanecarboxylate (3j).** Alkylation of methyl cyclohexanecarboxylate with *trans*-1,4-dibromo-2-butene, as described previously, afforded the title compound in 45% yield. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.63–5.57 (m, 2H), 3.87–3.85 (m, 2H), 3.63 (s, 3H), 2.20–2.18 (m, 2H), 2.01–1.97 (m, 2H), 1.59–1.14 (m, 8H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 176.43, 131.09, 129.33, 51.44, 47.42, 42.53, 33.71, 32.60, 25.64, 22.98.

**5-(2-Bromoethyl)-5-pentanolide.** To a solution of 2-(2-bromoethyl)cyclopentanone (1.91 g, 10 mmol) in 30 mL of $CH_2Cl_2$ at room temperature was added 85% MCPBA (5.07 g, 25 mmol). The resulting suspension was allowed to stir overnight. Workup involved addition of 100 mL of pentane followed by filtration through Celite. The filtrate was *carefully* washed with 3 × 30 mL of saturated aqueous $NaHSO_3$, $H_2O$, and brine. Solvent removal followed by flash chromatography afforded the title compound (1.33 g, 64%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.57–4.43 (m, 1H), 3.62–3.48 (m, 2H), 2.64–1.42 (m, 8H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 171.31, 77.73, 38.61, 29.25, 28.50, 27.49, 18.28.

**5-(2-Iodoethyl)-5-pentanolide (5a).** 5-(2-Bromoethyl)-5-pentanolide (1.24 g, 6 mmol) was treated with NaI (4.50 g, 30 mmol) in 20 mL of acetone heated at reflux for 12 h, as described previously, affording the title compound (1.37 g, 90%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.21–4.16 (m, 1H), 3.09–3.05 (m, 2H), 2.41–1.22 (m, 8H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 170.50, 79.02, 38.62, 28.68, 26.50, 17.60, 0.70.

**6-(2-Iodoethyl)-6-hexanolide (5b).** Baeyer–Villiger reaction of 2-(2-bromoethyl)cyclohexanone followed by Finkelstein reaction, as described previously, afforded the title compound in 70% yield. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.32 (dt, $J$ = 9.0, 3.3 Hz, 1H), 3.25–3.21 (m, 2H), 2.61–2.56 (m, 2H), 2.32–1.43 (m, 8H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 175.07, 79.44, 39.22, 34.57, 33.97, 27.83, 22.68, 2.10.

**5-(3-Iodopropyl)-5-pentanolide (5c).** Baeyer–Villiger reaction of 2-(3-bromopropyl)cyclopentanone followed by Finkelstein reaction, as described previously, afforded the title compound in 42% yield. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.28–4.19 (m, 1H), 3.16–3.07 (m, 2H), 2.58–1.41 (m, 10H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 171.75, 79.22, 36.28, 29.12, 28.48, 27.54, 18.12, 6.23.

**6-(3-Iodopropyl)-6-hexanolide (5d).** Baeyer–Villiger reaction of 2-(3-chloropropyl)cyclohexanone followed by Finkelstein reaction, as described previously, afforded the title compound in 72% yield. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.27–4.20 (m, 1H), 3.16 (t, $J$ = 6.8 Hz, 2H), 2.63–2.55 (m, 2H), 2.04–1.43 (m, 10H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 175.45, 79.28, 37.15, 34.83, 34.60, 29.02, 28.16, 22.87, 6.26.

**5-(4-Bromopentyl)-5-pentanolide (5e).** Baeyer–Villiger reaction on a 1:1 diastereomeric mixture of 2-(3-bromobutyl)-cyclopentanone afforded the title compound as a 1:1 mixture of diastereomers in 82% yield. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.38–4.21 (m, 1H), 4.18–4.03 (m, 1H), 2.63–2.41 (m, 2H), 2.14–1.49 (m, 8H), 1.69 (d, $J$ = 6.6 Hz, 1.5H), 1.68 (d, $J$ = 6.6 Hz, 1.5H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 171.62, 171.50, 80.13, 79.27, 51.53, 50.80, 36.71, 35.74, 34.56, 33.60, 29.32, 29.30, 27.90, 27.78, 26.58, 26.34, 18.41, 18.34.

**3-(2,2-(Ethylenedioxy)cylopentyl)propanal.** To a 100-mL round-bottomed flask fitted with a Dean–Stark trap were added 2-(3-butenyl)cyclopentanone (3.69 g, 15 mmol), ethylene glycol (1.86 g, 30 mmol), TsOH (cat.), and 40 mL of benzene. The resulting solution was heated at reflux for 4 h followed by aqueous workup. Ozonolysis of the crude ethylene ketal followed by flash chromatography afforded the title compound (1.74 g, 63%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 9.96 (t, $J$ = 1.7 Hz, 1H), 3.90–3.81 (m, 4H), 2.42–2.30 (m, 2H), 1.80–1.33 (m, 9H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 202.90, 110.41, 64.53, 64.37, 43.83, 42.10, 28.99, 24.34, 23.49.

**Ethyl *trans*-5-(2,2-(Ethylenedioxy)cyclopentyl)-2-pentenoate.** To a suspension of 60% NaH (0.48 g, 12 mmol) in 80 mL of THF at 0 °C was added triethyl phosphonoacetate (2.92 g, 13 mmol) in 40 mL of THF. The reaction mixture was warmed to room temperature for 2 h and then cooled to 0 °C. 3-(2,2-(Ethylenedioxy)cyclopentyl)propanal (1.84 g, 10 mmol) in 40 mL of THF was added and the solution was allowed to stir overnight. Aqueous workup followed by flash chromatography afforded the title compound (2.34 g, 92%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 6.93 (dt, $J$ = 15.6, 6.8 Hz, 1H), 5.77 (d, $J$ = 15.6 Hz, 1H), 4.14 (q, $J$ = 7.1 Hz, 2H), 3.92–3.79 (m, 4H), 2.28–2.03 (m, 2H), 1.92–1.26 (m, 9H), 1.24 (t, $J$ = 7.1 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 166.74, 149.37, 121.24, 118.01, 64.50, 64.42, 60.04, 45.41, 35.64, 30.72, 29.21, 27.22, 20.52, 14.18.

***trans*-2-(5-Chloro-3-pentenyl)cyclopentanone.** To a solution of ethyl *trans*-5-(2,2-(ethylenedioxy)cyclopentyl)-2-pentenoate (1.40 g, 5.5 mmol) in 60 mL of $Et_2O$ at −40 °C was added DIBAH (2.159 mL, 12.1 mmol) in 30 mL of $Et_2O$. The resulting solution was warmed to −5 °C and stirred overnight and then quenched with 8 g of $NaSO_4 \cdot 12H_2O$. The crude product was dissolved in 50 mL of THF and cooled to 0 °C and 15 mL of 1 M HCL was added dropwise over 5 min. The resulting solution was allowed to warm to room temperature and was stirred for 10 h. Addition of solid $K_2CO_3$ followed by separation of the organic layer and solvent removal afforded the crude keto alcohol. The crude alcohol was dissolved in 20 mL of $CH_2Cl_2$ at 0 °C, and $Et_3N$ (0.71 g, 7 mmol) was added followed by $MeSO_2Cl$ (0.69 g, 6 mmol). After 2 h at 0 °C, an aqueous workup was performed, and the crude methanesulfonate ester was obtained. Displacement of the methanesulfonate with LiCl in DMF afforded the title compound (0.55 g, 59%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.81-5.53 (m, 2H), 3.93 (d, $J$ = 6.1 Hz, 2H), 2.44–1.27 (m, 11H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 223.12, 135.72, 130.65, 53.90, 51.45, 47.48, 32.96, 31.67, 30.21, 21.67.

***trans*-5-(5-Chloro-3-pentenyl)-5-pentanolide (5f).** To a solution of *trans*-2-(5-chloro-3-pentenyl)cyclopentanone (0.47 g, 2.5 mmol) in 20 mL of $CH_2Cl_2$ was added $K_2CO_3$ (0.69 g, 5 mmol) followed by MCPBA (1.03 g, 6 mmol) in several portions over 3 h. After 16 h the usual aqueous workup and flash chromatography afforded the title compound (0.354 g, 35%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.68-5.52 (m, 2H), 4.45–4.31 (m, 1H), 3.94 (d, $J$ = 6.1 Hz, 2H), 2.65–2.34 (m, 4H), 2.10-1.47 (m, 4H).

**1-(3-Chloropropyl)-4-methyl-3-cyclohexenecarboxylic Acid.** Alkylation of 4-methyl-3-cyclohexenecarboxylic acid with 1-chloro-3-iodopropane as described previously afforded the title compound in 95% yield. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.33 (br s, 1H), 3.49 (t, $J$ = 6.6 Hz, 2H), 2.55–1.21 (m, 10H), 1.64 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 183.35, 133.76, 117.97, 44.53, 44.21, 36.19, 32.67, 32.30, 28.48, 26.62, 22.27.

**4-(3-Chloropropyl)-1-methyl-2-oxabicyclo[2.2.2]octan-3-one.** To a solution of 1-(3-chloropropyl)-4-methyl-3-cyclohexenecarboxylic acid (1.08 g, 5 mmol) in 20 mL of $CH_3CN$ was added $I_2$ (2.03 g, 8 mmol) in three portions over 3 h. The resulting solution was allowed to stir overnight. The excess $I_2$ was removed by dropwise addition of $NaHSO_3$ (aq). Routine workup afforded the title compound (0.823 g, 76%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.50 (t, $J$ = 6.6 Hz, 2H), 1.84–1.52 (m, 12H), 1.32 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 177.62, 80.85, 45.36, 39.55, 32.00, 31.46, 28.68, 27.18, 25.18.

**4-(3-Iodopropyl)-1-methyl-2-oxabicyclo[2.2.2]octan-3-one (5g).** 4-(3-Chloropropyl)-1-methyl-2-oxabicyclo[2.2.2]octan-

3-one (0.650 g, 3 mmol) and NaI (2.79 g, 18 mmol) in 20 mL of acetone were heated at reflux for 15 h. Aqueous workup followed by flash chromatography afforded the title compound (0.638 g, 69%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 3.18 (t, $J$ = 7.0 Hz, 2H), 1.82–1.56 (m, 12H), 1.35 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 177.37, 80.39, 39.31, 35.41, 31.28, 28.50, 27.94, 25.07, 7.02.

**1-(4-Chlorobutyl)-4-methyl-3-cyclohexenecarboxylic Acid.** Following the general procedure described previously, 4-methyl-3-cyclohexenecarboxylic acid was alkylated with 4-chloro-1-iodobutane to provide the title compound in 52% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.31 (br s, 1H), 3.50 (t, $J$ = 6.6 Hz, 2H), 2.57-1.24 (m, 12H), 1.62 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 182.96, 133.40, 118.78, 44.60, 44.45, 37.17, 32.95, 32.87, 29.73, 27.35, 23.23, 21.72.

**4-(4-Chlorobutyl)-1-methyl-2-oxabicyclo[2.2.2]octan-3-one.** Lactonization of 1-(4-chlorobutyl)-4-methyl-3-cyclohexenecarboxylic acid as described previously afforded the title compound in 72% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 3.50 (t, $J$ = 6.6 Hz, 2H), 1.74–1.45 (m, 14H), 1.33 (s, 3H).

**4-(4-Iodobutyl)-1-methyl-2-oxabicyclo[2.2.2]octan-3-one (5h).** Following the Finkelstein procedure described previously, the title compound was prepared in 91% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 3.16 (t, $J$ = 6.4 Hz, 2H), 1.82–1.25 (m, 14H), 1.32 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 177.90, 80.47, 39.74, 33.69, 33.22, 31.52, 28.53, 25.26, 24.75, 6.86.

**(1*R**,4*R**,5*R**)-1-(4-Chlorobutyl)-4-iodo-4-methyl-6-oxabicyclo[3.2.1]octan-7-one.** To a solution of 1-(4-chlorobutyl)-4-methyl-3-cyclohexenecarboxylic acid (0.922 g, 4 mmol) and $NaHCO_3$ (0.672 g, 8 mmol) in 20 mL of $CH_3CN$ was added $I_2$ (2.03 g, 8 mmol) in several portions over 1 h. After 3 h at room temperature, aqueous workup afforded the title compound (0.925 g, 65%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 4.56 (d, $J$ = 5.8 Hz, 1H), 3.51 (t, $J$ = 6.3 Hz, 2H), 2.77 (d, $J$ = 12.2 Hz, 1H), 2.35–2.21 (m, 2H), 2.08 (s, 3H), 1.82–1.50 (m, 9H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 178.95, 83.17, 45.68, 45.33, 44.52, 40.92, 39.30, 35.51, 32.81, 32.54, 30.33, 21.47.

**(1*R**,4*R**,5*R**)-1-(4-Chlorobutyl)-4-methyl-6-oxabicyclo[3.2.1]octan-7-one.** To a solution of (1*R**,4*R**,5*R**)-1-(4-chlorobutyl)-4-iodo-4-methyl-6-oxabicyclo[3.2.1]octan-7-one (0.715 g, 2 mmol) in 15 mL of benzene at 75 °C were added separate solutions of $Bu_3SnH$ (0.410 g, 2.5 mmol) in 10 mL of benzene and AIBN (4 mg) in 10 mL of benzene over 20 min. The resulting solution was allowed to stir 3 h. Aqueous workup and flash chromatography provided the title compound as a 3:1 mixture of C-7 epimers (0.415 g, 90%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 4.49 (dd, $J$ = 5.4, 4.6 Hz, 0.33H), 4.40 (d, $J$ = 6.3 Hz, 0.67H), 3.50 (t, $J$ = 6.3 Hz, 2H), 2.24–1.20 (m, 13H), 0.96 (d, $J$ = 6.8 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): (major) $\delta$ 180.20, 80.51, 45.41, 44.67, 40.64, 33.47, 33.09, 32.63, 32.39, 27.19, 21.58, 18.87; (minor) $\delta$ 179.85, 80.11, 46.40, 46.07, 34.53, 33.80, 31.98, 29.32, 29.28, 24.96, 21.53, 15.70.

**(1*R**,4*R**,5*S**)-1-(4-Iodobutyl)-4-methyl-6-oxabicyclo[3.2.1]-octan-7-one (5i).** Following the Finkelstein procedure described previously, the title compound was isolated in 92% yield (as a 3:1 mixture of C-7 epimers). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 4.48 (dd, $J$ = 5.8, 4.4 Hz, 0.33H), 4.39 (d, $J$ = 6.3 Hz, 0.67H), 3.14 (t, $J$ = 6.8 Hz, 2H), 2.34–1.21 (m, 13H), 0.95 (d, $J$ = 6.6 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): (major) $\delta$ 180.12, 80.46, 45.31, 40.62, 33.40, 33.34, 32.63, 32.32, 27.14, 25.12, 18.85, 6.62; (minor) $\delta$ 179.76, 80.06, 45.98, 34.52, 32.98, 29.28, 29.24, 27.10, 25.06, 24.91, 15.68, 6.02.

**1-(3-Chloropropyl)-3-cyclohexenecarboxylic Acid.** Alkylation of 3-cyclohexenecarboxylic acid with 1-chloro-3-iodopropane, as described previously, provided the title compound in 78% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 11.98 (br s, 1H), 5.83–5.63 (m, 2H), 3.50 (t, $J$ = 6.3 Hz, 2H), 2.54–1.48 (m, 10H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 183.17, 126.68, 124.84, 45.32, 44.60, 35.57, 32.92, 29.62, 27.89, 22.70.

**(1*R**,4*R**,5*R**)-1-(3-Chloropropyl)-4-iodo-6-oxabicyclo-[3.2.1]octan-7-one.** Following the iodolactonization procedure described above, the title compound was isolated in 81% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 4.76 (dd, $J$ = 6.1, 4.4 Hz, 1H), 4.47 (dd, $J$ = 5.2, 4.4 Hz, 1H), 3.58–3.50 (m, 2H), 2.70 (d, $J$ = 12.2 Hz, 1H), 2.44–1.51 (m, 9H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 178.62, 78.22, 45.82, 44.75, 37.79, 31.55, 29.93, 29.29, 27.39, 23.20.

**(1*R**,5*R**)-1-(3-Chloropropyl)-6-oxabicyclo[3.2.1]oct-3-en-7-one.** To a solution of (1*R**,4*R**,5*R**)-1-(3-chloropropyl)-4-iodo-6-oxabicyclo[3.2.1]octan-7-one (0.657 g, 2.0 mmol) in 20 mL of THF was added DBU (0.334 g, 2.2 mmol). The resulting solution was heated at reflux for 10 h. Aqueous workup followed by flash chromatography provided the title compound (0.368 g, 92% yield). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 6.26–6.19 (m, 1H), 5.92–5.81 (m, 1H), 4.74–4.63 (m, 1H), 3.59-3.42 (m, 2H), 2.35–2.21 (m, 3H), 1.98–1.72 (m, 5H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 179.98, 131.12, 129.17, 71.60, 45.03, 44.90, 38.18, 35.34, 31.98, 27.19.

**(1*R**,5*R**)-1-(3-Iodopropyl)-6-oxabicyclo[3.2.1]oct-3-en-7-one (5j).** Following the Finkelstein procedure described previously, the title compound was prepared in 89% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 6.23–6.18 (m, 1H), 5.89-5.83 (m, 1H), 4.73–4.69 (m, 1H), 3.20–3.13 (m, 2H), 2.35–2.27 (m, 3H), 2.00–1.71 (m, 5H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 179.94, 131.07, 129.13, 71.58, 44.88, 38.19, 38.15, 35.52, 35.29, 28.08, 5.96.

**Ethyl 3,3-(Ethylenedioxy)-2-(4-iodobutyl)-2-methylbutanoate (7a).** The title compound was prepared in 93% yield from ethyl 2-(4-iodobutyl)-2-methyl-3-oxobutanoate[11a] by treatment with ethylene glycol in benzene as described previously. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 4.12 (q, $J$ = 7.1 Hz, 2H), 3.95–3.82 (m, 4H), 3.13 (t, $J$ = 7.0 Hz, 2H), 1.28 (s, 3H), 1.23 (t, $J$ = 7.1 Hz, 3H), 1.98–1.20 (m, 6H), 1.16 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 174.20, 111.73, 65.18, 64.86, 60.58, 54.71, 33.94, 32.60, 25.80, 20.62, 16.98, 14.14, 6.56.

**Ethyl 2-(2-(Chloromethyl)-2-propenyl)-3,3-(ethylenedioxy)-2-methylbutanoate (7b).** The title compound was prepared in 89% yield from the ethyl 2-(2-(chloromethyl)-2-propenyl)-2-methyl-3-oxobutanoate[11a] as described previously. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.20 (s, 1H), 4.92 (s, 1H), 4.21–3.84 (m, 8H), 3.01 (d, $J$ = 14.1 Hz, 1H), 2.23 (d, $J$ = 14.1 Hz, 1H), 1.31 (s, 3H), 1.24 (t, $J$ = 7.1 Hz, 3H), 1.14 (s, 3H). $^{13}$C (75 MHz, $CDCl_3$): $\delta$ 174.15, 141.78, 118.62, 111.64, 65.30, 64.92, 60.85, 54.28, 48.79, 36.52, 20.57, 17.01, 13.92.

**Ethyl 2-(3-Chloropropyl)-2-phenyl-4-pentenoate.** Ethyl 2-phenyl-4-pentenoate was alkylated with 1-chloro-3-iodopropane, as described previously, to afford the title compound in 85% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.38–7.20 (m, 5H), 5.64–5.53 (m, 1H), 5.18–5.04 (m, 2H), 4.14 (q, $J$ = 7.1 Hz, 2H), 3.48 (t, $J$ = 6.6 Hz, 2H), 2.90–2.72 (m, 2H), 2.17–2.08 (m, 2H), 1.66–1.57 (m, 2H), 1.19 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 174.90, 141.80, 133.28, 128.34, 126.81, 126.32, 118.44, 60.75, 53.13, 45.05, 39.31, 32.13, 27.38, 13.95.

**Ethyl 5-Chloro-2-(3-iodopropyl)-2-phenylpentanoate (7c).** Hydroboration and iodination of ethyl 2-(3-chloropropyl)-2-phenyl-4-pentenoate, as described previously, afforded the title compound in 81% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.35–7.18 (m, 5H), 4.10 (q, $J$ = 7.1 Hz, 2H), 3.45 (t, $J$ = 6.4 Hz, 2H), 3.10 (t, $J$ = 6.5 Hz, 2H), 2.11–2.03 (m, 4H), 1.60–1.54 (m, 4H), 1.14 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 175.06, 141.74, 128.47, 126.95, 126.27, 60.93, 53.94, 45.13, 35.95, 32.48, 28.21, 27.48, 14.02, 6.62.

**Ethyl 2,2-Bis(3-iodopropyl)-2-phenylpentanoate (7d).** Subjecting 7c to the Finkelstein conditions, as described previously, afforded the title compound in 89% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.37–7.20 (m, 5H), 4.13 (q, $J$ = 7.1 Hz, 2H), 3.13 (t, $J$ = 6.6 Hz, 4H), 2.21–2.02 (m, 4H), 1.75–1.56 (m, 4H), 1.18 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 175.36, 142.09, 128.84, 127.33, 61.30, 53.17, 36.32, 28.56, 14.44, 7.11.

**Ethyl 2-(3-Chloropropyl)-4-pentenoate.** Following the general procedure described previously, ethyl 4-pentenoate was alkylated with 1-chloro-3-iodopropane to provide the title compound in 68% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.82–5.69 (m, 1H), 5.08–4.92 (m, 2H), 4.12 (q, $J$ = 7.1 Hz, 2H), 3.5 (t, $J$ = 6.3 Hz, 2H), 2.41–1.48 (m, 9H), 1.24 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 175.72, 137.72, 115.25, 60.26, 44.63, 44.21, 31.48, 31.39, 30.23, 29.41, 14.26.

**Ethyl 2-(3-Iodopropyl)-4-pentenoate (7e).** Following the general Finkelstein procedure described previously, the title compound was prepared in 85% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.81–5.68 (m, 1H), 5.08–4.84 (m, 2H), 4.11 (q, $J$ = 7.1 Hz, 2H), 3.14 (t, $J$ = 6.6 Hz, 2H), 2.40–2.20 (m, 1H), 2.08–1.97 (m, 2H), 1.81–1.45 (m, 6H), 1.23 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 175.63, 137.66, 115.24, 60.24, 43.90, 32.45, 31.42, 31.36, 31.05, 14.25, 6.09.

**Methyl 6-Chloro-2-hexynoate.** To a solution of 5-chloro-1-hexyne (7.52 g, 73 mmol) in 120 mL of THF at −78 °C was added *n*-BuLi (80 mmol, 50 mL, 1.6 M in hexanes) over 15 min. The resulting solution was allowed to stir 30 min. Methyl chloroformate (7.56 g, 80 mmol) was added and the resulting solution was warmed to room temperature. Aqueous workup followed by distillation provided the title compound (9.58 g, 82 %): $^1$H NMR (300 MHz, $CDCl_3$): δ 3.70 (s, 3H), 3.59 (t, $J$ = 6.3 Hz, 2H), 2.49 (t, $J$ = 6.9 Hz, 2H), 2.10–1.92 (m, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 153.60, 87.36, 76.58, 52.48, 43.04, 30.07, 15.90.

**Methyl *cis*-6-Chloro-2-hexenoate.** To a suspension of 17 mmol of dicyclohexylborane in 20 mL of THF at 0 °C was added a solution of methyl 6-chloro-2-hexynoate (2.41 g, 15 mmol) in 15 mL of THF over 15 min. The reaction mixture was stirred for 1 h at 0 °C, and the reaction was then quenched with AcOH (1.02 g, 17 mmol). Flash chromatography followed by distillation afforded the title compound (1.41 g, 61%) as a single isomer. $^1$H NMR (300 MHz, $CDCl_3$): δ 6.20 (dt, $J$ = 11.50, 7.6 Hz, 1H), 5.81 (d, $J$ = 11.50 Hz, 1H), 3.69 (s, 3H), 3.53 (t, $J$ = 6.6 Hz, 2H), 2.81–2.77 (m, 2H), 1.94–1.80 (m, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 166.64, 148.34, 120.54, 51.09, 44.24, 31.84, 26.38.

**Methyl 5-(3-Iodopropyl)bicyclo[2.2.1]hept-2-ene-6-carboxylate (7f).** To a solution of methyl *cis*-6-chloro-2-hexenoate (0.34 g, 2.26 mmol) in 10 mL of toluene at 0 °C was added $Et_2AlCl$ (0.336 g, 2.7 mmol) followed by excess cyclopentadiene. The resulting solution was heated at 50 °C overnight. Aqueous workup afforded the crude bicyclic chloride that was combined with NaI (1.50 g, 10 mmol) in acetone and heated at reflux for 12 h. Aqueous workup and flash chromatography afforded the title compound (0.47 g, 65%). $^1$H NMR (300 MHz, $CDCl_3$): δ 6.30 (dd, $J$ = 5.7, 2.8 Hz, 1H), 6.02 (dd, $J$ = 5.7, 2.8 Hz, 1H), 3.57 (s, 3H), 3.16–2.94 (m, 4H), 2.80-2.76 (m, 1H), 2.44–2.35 (m, 1H), 1.88–1.67 (m, 2H), 1.45–1.21 (m, 3H), 0.98–0.83 (m, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 174.06, 136.82, 132.91, 51.01, 48.60, 47.89, 45.68, 45.42, 43.01, 32.55, 31.12, 6.38.

**(1*R**,2*S**)-Methyl 4,5-Dimethyl-2-(3-iodopropyl)-4-cyclohexenecarboxylate (7g).** Following the general procedures described previously, 2,3-dimethyl-1,3-butadiene was condensed with methyl *cis*-6-chloro-2-hexenoate. The crude product was subjected to Finkelstein conditions to provide the title compound in 62% yield as a 40:1 mixture of diastereomers. $^1$H NMR (300 MHz, $CDCl_3$): δ 3.62 (s, 3H), 3.13–3.07 (m, 2H), 2.65–2.59 (m, 1H), 2.17–1.71 (m, 7H), 1.58–1.53 (m, 6H), 1.33–1.24 (m, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 74.91, 123.56, 123.26, 51.33, 42.77, 35.49, 33.84, 31.80, 30.68, 18.97, 18.68, 6.59.

**Ethyl 2-(3-Iodopropoxy)propionate (7h).** To a solution of ethyl lactate (1.18 g, 10 mmol) in 15 mL of allyl bromide was added $CaSO_4$ (5 g) followed by $Ag_2O$ (4.17 g, 18 mmol) in three portions over 30 min. The resulting suspension was allowed to stir overnight and was then filtered through Celite. The solvent was removed under vacuum. The crude material was subjected to the hydroboration–iodination procedure described previously to afford the title compound (2.12 g, 74%). $^1$H NMR (300 MHz, $CDCl_3$): δ 4.22–4.14 (m, 2H), 3.92 (q, $J$ = 6.8 Hz, 1H), 3.64–3.57 (m, 1H), 3.45–3.38 (m, 1H), 3.30–3.24 (m, 2H), 2.10–2.02 (m, 2H), 1.36 (d, $J$ = 6.8 Hz, 3H), 1.26 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 173.22, 75.16, 69.37, 60.82, 33.41, 18.53, 14.17, 3.23.

**Methyl 1-(2-Propenyl)pyrrolidine-2-carboxylate.** To a solution of proline·HCl methyl ester (1.51 g, 10 mmol) in 20 mL of DMF were added $K_2CO_3$ (4.42 g, 25 mmol) and allyl bromide (1.33 g, 11 mmol). The resulting suspension was allowed to stir overnight. Aqueous workup followed by Kugelrohr distillation afforded the title compound (1.45 g, 86%). $^1$H NMR (300 MHz, $CDCl_3$): δ 5.92-5.81 (m, 1H), 5.16–5.02 (m, 2H), 3.65 (s, 3H), 3.24 (dd, $J$ = 12.7, 6.7 Hz, 1H), 3.12-3.03 (m, 3H), 2.38–1.67 (m, 5H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 174.60, 135.16, 117.49, 65.17, 57.68, 53.42, 51.72, 29.42, 22.96.

**Methyl 1-(3-Iodopropyl)pyrrolidine-2-carboxylate (7i).** Following the general hydroboration–iodination procedure described above, the title compound was prepared from methyl 1-(2-propenyl)pyrrolidine-2-carboxylate in 62% yield. $^1$H NMR (300 MHz, $CDCl_3$): δ 3.66 (s, 3H), 3.21–3.05 (m, 4H), 2.76–2.67 (m, 1H), 2.49–2.40 (m, 1H), 2.35–2.27 (m, 1H), 2.08–1.72 (m, 6H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 174.53, 65.89, 54.93, 53.38, 51.76, 32.30, 29.16, 23.15, 4.14.

**Preparation of $SmI_2$ Solution.** Samarium metal (0.301 g, 2.00 mmol) was added under a flow of Ar to an oven-dried round bottomed flask containing a magnetic stirring bar and septum inlet. To the samarium was added 12 mL of THF followed by $CH_2I_2$ (0.492 g, 1.84 mmol). The mixture was allowed to stir at room temperature for 2 h. The resulting deep blue solution was used directly to effect the following reductive cyclizations.

**General Procedure for Cyclization of Iodoalkyl Substituted Acyl Derivatives.** To the $SmI_2$ (1.84 mmol) in THF was added $Fe(DBM)_3$ (13 mg, 0.018 mmol) in 2 mL of THF. The resulting solution was cooled to −30 °C. For conditions B in Table I, 4 equiv (2.0 g, 7.4 mmol) of tripiperidinophosphine oxide was added in place of the iron(III) catalyst. A solution of the iodoalkyl acyl derivative (0.83 mmol) in 15 mL of THF was added via cannula and the resulting solution was allowed to warm to room temperature. Following complete reaction (<30 min) and aqueous workup, the desired product was isolated by flash chromatography (hexanes:ethyl acetate) and/or Kugelrohr distillation.

**2-Phenylcyclopentan-1-one (2)**[36] **(1a,** 0.292 g, 0.88 mmol): yield 0.104 g (74%). $^1$H NMR (300 MHz, $CDCl_3$): δ 7.39–7.17 (m, 5H), 3.33 (dd, $J$ = 10.7, 8.8 Hz, 1H), 2.58–1.85 (m, 6H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 218.00, 138.38, 128.48, 128.05, 126.77, 55.16, 38.27, 31.58, 20.68. IR ($CCl_4$): 3042, 2953, 1745 cm$^{-1}$. LRMS (EI) m/e: 160 (47), 117 (12), 104 (100), 91 (13). Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.22; H, 7.61. Conditions B: (**1a,** 0.286 g, 0.86 mmol), yield 0.098 g (71%).

**1b:** 0.179 g, 0.50 mmol; yield 0.034 g (42%). Conditions B: 0.207 g, 0.58 mmol; yield 0.073 g (79%).

**1c:** 0.163 g, 0.47 mmol; yield 0.030 g (40%). Conditions B: 0.191 g, 0.55 mmol; yield 0.071 g (81%).

**1d:** 0.229 g, 0.63 mmol; yield 0.028 g (28%). Conditions B: 0.188 g, 0.52 mmol; yield 0.057 g (68%).

**1e:** 0.192 g, 0.44 mmol; yield 0.013 g (18%). Conditions B: 0.288 g, 0.66 mmol; yield 0.075 g (71%).

**1f:** 0.205 g, 0.55 mmol; yield 0.056 g (64%). Conditions B: 0.217 g, 0.58 mmol; yield 0.064 g (69%).

**1g:** 0.142 g, 0.50 mmol; yield 0.017 g ( 21%). Conditions B: 0.117 g, 0.41 mmol; yield 0.036 g (55%).

**Spiro[4.5]decan-1-one (4a)**[37] **(3a,** 0.310 g, 1.00 mmol): yield 0.142 g (93%). $^1$H NMR (300 MHz, $CDCl_3$): δ 2.24–2.18 (m, 2H), 1.84–1.78 (m, 4H), 1.64–1.57 (m, 3H), 1.41–1.24 (m, 7H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 223.81, 49.38, 37.70, 33.86, 31.95, 25.64, 22.08, 18.83. IR ($CCl_4$): 2932, 2857, 1729, 1446 cm$^{-1}$. HRMS: calcd for $C_{10}H_{16}O$: 152.1201, found 152.1230. LRMS (EI) *m/e*: 152 (69), 97 (100), 81 (98), 67 (43).

**Spiro[5.5]undecan-1-one (4b)**[37a,38] **(3b,** 0.231 g, 0.71 mmol): yield 0.108 g (91%), mp 39–40 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ 2.33 (t, $J$ = 6.7 Hz, 2H), 1.85–1.61 (m, 8H), 1.46–1.24 (m, 8H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 216.92, 48.86, 38.50, 33.59, 28.10, 26.18, 21.91, 20.49. IR ($CCl_4$): 2932, 2857, 1702, 1446 cm$^{-1}$. LRMS (EI) *m/e*: 166 (41), 111 (100), 81 (68), 67 (90). Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.51; H, 10.84.

**2-Benzylcyclobutan-1-one (4d)**[39] **(3d,** 0.332 g, 1.00 mmol): yield 0.118 g (74%). $^1$H NMR (300 MHz, $CDCl_3$): δ 7.35–7.16 (m, 5H), 3.64–3.57 (m, 1H), 3.14–2.77 (m, 4H), 2.20–2.08 (m, 1H), 1.79–1.67 (m, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 211.00, 138.81,

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128.68, 128.52, 128.44, 126.26, 61.06, 44.35, 35.03, 16.47. IR ($CCl_4$): 3027, 2921, 1782 $cm^{-1}$. LRMS (EI) *m/e*: 160 (36), 131 (32), 117 (100), 104 (29), 91 (38). Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.25; H, 7.28.

**2-(4-Hydroxybutyl)cyclopentan-1-one (4e)**[40] (**3e**, 0.282 g, 0.88 mmol): yield 0.125 g (91%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.58 (t, $J$ = 6.6 Hz, 2H), 2.30-1.19 (m, 14H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 221.83, 62.42, 49.04, 38.06, 32.48, 29.40, 29.22, 23.61, 20.59. IR ($CCl_4$): 3430, 2931, 1734 $cm^{-1}$. LRMS (EI) *m/e*: 156 (4), 138 (3), 97 (13), 84 (100). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.27; H, 10.41.

**1-Methyl-6-phenylcyclohexan-1-one (4f)**[36e,41] (**3f**, 0.407 g, 1.13 mmol): yield 0.181 g (85%) as a 1:1 mixture of diastereomers (cis:trans). Heating the isolated mixture in EtOH/EtONa at reflux for 48 h resulted in a 10:1 (cis:trans) mixture of diastereomers. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.39–7.16 (m, 5H), 3.82 (t, $J$ = 5.8 Hz, 0.5H, trans), 3.64 (dd, $J$ = 12.0, 5.2 Hz, 0.5H, cis), 2.68–1.49 (m, 7H), 1.13 (d, $J$ = 6.8 Hz, 1.5H, trans), 1.08 (d, $J$ = 6.3 Hz, 1.5H, cis). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ cis, 211.29, 138.82, 128.68, 128.14, 126.74, 57.60, 45.74, 37.07, 36.28, 25.69, 14.62: trans; 213.97, 138.34, 128.61, 127.52, 126.67, 53.79, 42.99, 35.20, 31.77, 20.93, 15.48. IR ($CDCl_3$): 3049, 2931, 1713, 1449 $cm^{-1}$. LRMS (EI) *m/e*: 188 (29), 130 (100), 117 (37), 104 (78), 91 (36). Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.56. Found: C, 82.71; H, 8.63.

**5-(4-Hydroxybutyl)-3-methyl-2-cyclopenten-1-one (4h)** (**3h**, 0.273 g, 0.93 mmol): yield 0.123 g (79%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.82 (s, 1H), 3.56 (t, $J$ = 6.5 Hz, 2H), 2.68 (dd, $J$ = 18.4, 6.5 Hz, 1H), 2.34–2.29 (m, 2H), 2.21 (d, $J$ = 18.4 Hz, 1H), 2.06 (s, 3H), 1.76–1.28 (m, 6H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 212.36, 177.71, 129.83, 62.28, 46.52, 39.62, 32.44, 30.93, 23.27, 19.28. IR ($CCl_4$): 3433, 2921, 2856, 1692, 1622 $cm^{-1}$. HRMS: calcd for $C_{10}H_{16}O_2$ 168.1150, found 168.1155. LRMS (EI) *m/e*: 168 (4), 109 (28), 96 (100).

**3-Methylspiro[4.5]-2-decen-1-one (4i)**[42] (**3i**, 0.189 g, 0.82 mmol): yield 0.118 g (88%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.80 (s, 1H), 2.39 (s, 2H), 2.06 (s, 3H), 1.70–1.61 (m, 5H), 1.52–1.21 (m, 5H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 214.47, 175.94, 128.40, 49.72, 46.01, 33.16, 25.16, 22.97, 19.34. IR ($CCl_4$): 2921, 2856, 1698, 1627, 1447, 1425 $cm^{-1}$. HRMS: calcd for $C_{11}H_{16}O$ 164.1201, found 164.1189. LRMS (EI) *m/e*: 164 (57), 149 (36), 109 (100), 96 (37).

**Methyl 1-[2-(2-Hydroxyspiro[5.5]-3-undecenyl)-3-butenyl]cyclohexanecarboxylate (4j)** (**3j**, 0.281 g, 1.02 mmol): yield 0.165 g (90%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.89 (ddd, $J$ = 17.2, 10.5, 7.3 Hz, 1H), 5.41 (dd, $J$ = 15.1, 6.7 Hz, 1H), 5.31 (dd, $J$ = 15.1, 6.4 Hz, 1H), 5.06 (dd, $J$ = 10.5, 1.0 Hz, 1H), 4.98 (dd, $J$ = 17.2, 1.0 Hz, 1H), 3.62 (s, 3H), 2.70 (q, $J$ = 8.1 Hz, 1H, tertiary allylic CH), 2.24–1.04 (m, 27H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 176.56, 137.87, 129.64, 127.96, 115.92, 79.08, 51.34, 47.58, 44.22, 43.70, 43.37, 39.98, 33.73, 33.65, 32.92, 31.89, 31.79, 26.00, 25.61, 23.00, 22.69, 22.16. IR ($CCl_4$): 3542, 2921, 2845, 1725, 1442, 1197, 1127, 995, 968, 908 $cm^{-1}$. HRMS: calcd for $C_{23}H_{36}O_3$ 360.2664, found 360.2622. LRMS (EI) *m/e*: 360 (1), 165 (16), 137 (100), 95 (50), 81 (89).

**Cycloheptan-4-one Acetate (6a)** (**5a**, 0.269 g, 1.06 mmol): yield 0.168 g (93%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.94–4.92 (m, 1H), 2.60–2.34 (m, 4H), 2.00 (s, 3H), 1.91–1.76 (m, 6H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 213.39, 170.15, 73.13, 43.34, 37.61, 34.67, 28.72, 21.15, 18.77. IR ($CCl_4$): 2931, 1729, 1697, 1237, 1024 $cm^{-1}$. HRMS: calcd for $C_9H_{14}O_3$ 170.0943, found 170.0938. LRMS (EI) *m/e*: 170 (0.1), 110 (100), 82 (56), 43 (77).

**1-Hydroxy-9-oxabicyclo[4.2.1]nonane (6b)**[43] (**5b**, 0.271 g, 1.01 mmol): yield 0.136 g (95%), as a 2.3:1 mixture of hemiacetal: hydroxy ketone). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.51 (tt, $J$ = 7.7, 2.0 Hz, 0.7H), 3.88–3.79 (m, 0.3H), 3.07 (s, 0.7H), 2.59–1.24 (m, 12.3H). $^{13}C$ NMR (75 MHz, $CDCl_3$): (hemiacetal) $\delta$ 108.16, 75.68, 41.36, 36.80, 36.08, 30.94, 23.52, 23.06; (hydroxy ketone) $\delta$ 217.62, 70.40, 39.92, 39.30, 33.20, 30.16, 28.48, 21.59. IR ($CCl_4$): 3390, 2932, 2856, 1703, 1452 $cm^{-1}$. HRMS: calcd for $C_8H_{14}O_2$ 142.0994, found 142.1001. LRMS (EI) *m/e*: 142 (7), 124 (25), 113 (54), 83 (90), 55 (100).

**1-Hydroxy-9-oxabicyclo[3.3.1]nonane (6c)**[43c,44] (**5c**, 0.260 g, 0.97 mmol): yield 0.109 g (79%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.31 (t, $J$ = 5.7 Hz, 1H), 2.61 (br s, 1H), 2.14–1.83 (m, 6H), 1.75–1.57 (m, 4H), 1.49 (dd, $J$ = 13.9, 5.8 Hz, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 93.79, 72.35, 36.07, 28.10, 20.41. IR ($CCl_4$): 3368, 2932, 1152 $cm^{-1}$. HRMS: calcd for $C_8H_{14}O_2$ 142.0994, found 142.0992. LRMS (EI) *m/e*: 142 (88), 124 (40), 114 (100), 96 (78), 68 (79), 60 (81), 55 (88).

**1-Hydroxy-10-oxabicyclo[4.3.1]decane (6d)** (**5d**, 0.282 g, 1.00 mmol): yield 0.128 g (82%). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.14–4.05 (m, 1H), 2.42 (br s, 1H), 2.10–1.28 (m, 14H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 97.78, 72.43, 36.49, 35.68, 30.03, 27.53, 21.13, 19.79, 17.48. IR ($CCl_4$): 3386, 2932, 1079 $cm^{-1}$. HRMS: calcd for $C_9H_{16}O_2$ 156.1150, found 156.1151. LRMS (EI) *m/e*: 156 (17), 113 (64), 110 (66), 97 (81), 71 (63), 69 (84), 68 (97), 55 (100).

**1-Hydroxy-2-methyl-9-oxabicyclo[3.3.1]nonane (6e)** (**5e**, 0.237 g, 1.01 mmol). High $R_f$ diastereomer: yield 0.076 g (48%), mp 86–88 °C. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.24–4.20 (m, 1H), 2.73 (br s, 1H), 2.26–1.42 (m, 11H), 1.06 (d, $J$ = 7.1 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 94.56, 72.15, 37.16, 35.99, 28.50, 27.57, 24.04, 20.63, 14.44. IR ($CCl_4$): 3391, 2931, 1013 $cm^{-1}$. LRMS (EI) *m/e*: 156 (48), 114 (100), 96 (55), 74 (91), 68 (74). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.47; H, 10.28. Low $R_f$ diastereomer: yield 0.044 g (28%), mp 59–61 °C. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.23–4.21 (m, 1H), 3.25 (br s, 1H), 2.06–1.40 (m, 11H), 0.97 (d, $J$ = 5.9 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 96.31, 72.43, 40.64, 31.28, 29.46, 29.43, 28.13, 20.29, 16.94. IR ($CCl_4$): 3370, 2931, 1146, 1018 $cm^{-1}$. LRMS (EI) *m/e*: 156 (52), 114 (100), 96 (57), 74 (51), 68 (52). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 68.64; H, 10.19.

**2-Ethenyl-1-hydroxy-9-oxabicyclo[3.3.1]nonane (6f)** (**5f**, 0.185 g, 0.91 mmol): yield 0.126 g (82%), as a 1:1 mixture of diastereomers. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 6.22–6.13 (m, 0.5H), 6.10–5.90 (m, 0.5H), 5.29–5.21 (m, 1H), 5.16–5.08 (m, 1H), 4.32–4.30 (m, 1H), 3.10 (br s, 1H), 2.59 (br s, 1H), 2.42–1.40 (m, 11H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 138.58, 137.25, 119.15, 115.60, 95.23, 92.76, 72.25, 72.18, 49.49, 48.17, 34.98, 32.40, 28.70, 28.35, 27.94, 26.17, 25.59, 24.27, 20.55, 20.12. IR ($CCl_4$): 3380, 2932 $cm^{-1}$. LRMS (EI) *m/e*: 168 (4), 150 (9), 108 (29), 81 (27), 54 (100). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.54; H, 9.23.

***cis*-7-Hydroxy-7-methylspiro[4.5]decan-1-one (6g)** (**5g**, 0.280 g, 0.91 mmol): yield 0.152 g (92%), mp 85–86 °C. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 2.31-2.20 (m, 2H), 1.95–1.22 (m, 13H), 1.20 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 223.51, 68.04, 48.51, 37.45, 34.51, 32.63, 30.61, 27.39, 18.69. IR ($CCl_4$): 3466, 2932, 1729 $cm^{-1}$. LRMS (EI) *m/e*: 164 (M-18, 12), 96 (100). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.56; H, 10.13.

***cis*-8-Hydroxy-8-methylspiro[5.5]undecan-1-one (6h)** (**5h**, 0.348 g, 1.08 mmol): yield 0.181 g (86%), as a 4:1 mixture of hydroxy ketone:hemiacetal, mp 94–98 °C. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 2.36 (t, $J$ = 6.8 Hz, 1.6H), 1.99–1.33 (m, 15.4H), 1.17 (s, 2.4H), 1.08 (s, 0.6H). $^{13}C$ NMR (75 MHz, $CDCl_3$): (hydroxy ketone) $\delta$ 216.21, 69.22, 47.70, 38.29, 34.59, 32.92, 32.02, 28.79, 27.65, 20.68; (hemiacetal) $\delta$ 99.22, 71.14, 35.59, 35.49, 34.00, 33.58, 32.87, 31.96, 28.55, 26.55, 22.81, 21.00. IR ($CCl_4$): 3391, 2932, 2857, 1745, 1702 $cm^{-1}$. LRMS (EI) *m/e*: 178 (M - 18, 17), 110 (100), 95 (26). Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.72. Found: C, 73.49; H, 10.73.

**(7*R**,8*S**,11*R**)-7-Hydroxy-8-methylspiro[5.5]undecan-1-one (6i)** (**5i**, 0.322 g, 1.00 mmol): yield 0.173 g (88%), as 3:1 mixture of C-8 epimers. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.53 (s,

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0.33H), 4.18 (d, $J$ = 6.8 Hz, 0.67H), 3.72–3.68 (m, 1H), 2.60–1.07 (m, 15H), 0.91 (d, $J$ = 6.8 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): (major) $\delta$ 219.67, 68.89, 43.07, 40.70, 38.22, 37.06, 34.93, 28.00, 24.55, 20.42, 17.44; (minor) $\delta$ 219.94, 68.05, 50.33, 46.39, 43.86, 39.42, 38.36, 34.78, 31.63, 28.21, 20.38, 18.35. IR ($CCl_4$): 3423, 2932, 2868, 1691 cm$^{-1}$. LRMS (EI) $m/e$: (major) 178 (M − 18, 16), 110 (100), 95 (22); (minor) 178 (M − 18, 33), 110 (100), 95 (32). Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.15; H, 10.31.

**(6*R**,10*R**)-6-Hydroxyspiro[4.5]-7-decen-1-one (6j)** (**5j**, 0.333 g, 1.14 mmol): yield 0.163 g (86%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.86–5.80 (m, 1H), 5.70–5.64 (m, 1H), 4.18 (br s, 1H), 3.01 (d, $J$ = 9.5 Hz, 1H), 2.42–2.21 (m, 3H), 2.01-1.68 (m, 8H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 222.50, 130.35, 125.18, 64.26, 47.79, 36.89, 36.85, 36.06, 31.72, 18.49. IR ($CCl_4$): 3436, 2919, 1730 cm$^{-1}$. LRMS (EI) $m/e$: 148 (M − 18, 7), 104 (84), 91 (100). Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.02; H, 8.67.

**2-Methyl-2-(1,1-(ethylenedioxy)ethyl)cyclohexan-1-one (8a)** (**7a**, 0.396 g, 1.07 mmol), yield 0.170 g (80%), bp 85 °C/0.02 mmHg. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 4.92–3.81 (m, 4H), 2.54–2.43 (m, 1H), 2.38–2.29 (m, 1H), 2.09–1.99 (m, 1H), 1.86–1.45 (m, 5H), 1.22 (s, 3H), 1.11 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 213.97, 112.15, 64.60, 64.36, 55.86, 40.55, 34.48, 26.41, 21.26, 20.50, 20.34. IR ($CCl_4$): 2942, 2878, 1702, 1040 cm$^{-1}$. LRMS (EI) $m/e$: 183 (M − 15, 5), 87 (100). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.68; H, 9.37.

**3,5-Dimethyl-5-(1,1-(ethylenedioxy)ethyl)-2-cyclopenten-1-one (8b)** (**7b**, 0.270 g, 0.98 mmol): yield 0.150 g (78%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.79 (s, 1H), 3.92–3.85 (m, 4H), 2.75 (d, $J$ = 18.8 Hz, 1H), 2.17 (d, $J$ = 18.8 Hz, 1H), 2.04 (d, $J$ = 0.7 Hz, 3H), 1.26 (s, 3H), 1.15 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 210.29, 176.39, 129.22, 111.43, 64.74, 64.71, 55.14, 45.30, 20.31, 19.53, 19.21. IR ($CCl_4$): 2932, 1702, 1622, 1040 cm$^{-1}$. LRMS (EI) $m/e$: 181 (M − 15, 5), 87 (100). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 66.98; H, 8.40.

**2-(3-Chloropropyl)-2-phenylcyclopentan-1-one (8c)** (**7c**, 0.449 g, 1.10 mmol): yield 0.216 g (83%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.38–7.18 (m, 5H), 3.38 (t, $J$ = 6.6 Hz, 2H), 2.62–2.59 (m, 1H), 2.25–2.20 (m, 2H), 2.02–1.45 (m, 7H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 219.22, 138.85, 128.64, 126.94, 126.74, 56.11, 45.04, 37.28, 36.13, 34.03, 27.97, 18.50. IR ($CCl_4$): 3060, 2953, 1734 cm$^{-1}$. LRMS (EI) $m/e$: 236 (4), 160 (44), 131 (35), 118 (100), 91 (20). Anal. Calcd for $C_{14}H_{17}ClO$: C, 71.03; H, 7.24. Found: C, 70.56; H, 7.29.

***cis*-5-Phenylbicyclo[3.3.0]octan-1-ol (8d)** (**7d**, 0.280 g, 0.56 mmol): yield 0.095 g (84%), mp 38–39 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.45–7.20 (m, 5H), 2.43–2.32 (m, 2H), 1.96–1.72 (m, 10H), 1.09 (br s, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 144.68, 128.31, 127.38, 126.16, 90.75, 58.92, 41.24, 39.64, 22.67. IR ($CCl_4$): 3551, 3444, 3038, 2942, 2868 cm$^{-1}$. LRMS (EI) $m/e$: 202 (55), 174 (35), 160 (100), 131 (77), 117 (67), 91 (61). Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.28; H, 8.85.

**2-(3-Butenyl)cyclopentan-1-one (8e)**[45] (**7e**, 0.322 g, 1.04 mmol): yield 0.133 g (92%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.79–5.63 (m, 1H), 5.01–4.86 (m, 2H), 2.30–1.63 (m, 9H), 1.51–1.40 (m, 1H), 1.35–1.22 (m, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 221.32, 137.99, 114.98, 48.33, 38.02, 31.49, 29.41, 28.69, 20.58. IR ($CCl_4$): 2931, 1734 cm$^{-1}$. LRMS (EI) $m/e$: 138 (13), 84 (100), 41 (26). Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.26; H, 10.44.

**(1*R**,2*S**,6*S**)-2-Methylbicyclo[3.3.0]octan-1-ol (8e′)**[45a,b,d,46] (**7e**, 0.206 g, 0.66 mmol): yield 0.056 g (61%), mp 58–59 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 2.15–2.02 (m, 2H), 1.87–1.42 (m, 8H), 1.22–0.99 (m, 3H), 0.94 (d, $J$ = 6.8 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 92.83, 51.52, 45.45, 36.06, 34.96, 32.43, 29.87, 25.76, 13.27. IR ($CCl_4$): 3607, 3363, 2942 cm$^{-1}$. LRMS (EI) $m/e$: 140 (12), 111 (35), 97 (100), 84 (69). Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 76.98; H, 11.67.

***endo*-Tricyclo[6.2.1.0$^{2,7}$]-8-undecen-2-one (8f)**[47] (**7f**, 0.298 g, 0.93 mmol): yield 0.125 g (83%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 6.12 (dd, $J$ = 5.6, 2.9 Hz, 1H), 5.95 (dd, $J$ = 5.8, 3.2 Hz, 1H), 3.21 (br s, 1H), 2.82 (br s, 1H), 2.70–2.56 (m, 2H), 2.32–2.21 (m, 1H), 1.98–1.60 (m, 4H), 1.42–1.22 (m, 2H), 0.78–0.64 (m, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 215.42, 137.62, 134.90, 51.57, 48.26, 46.45, 45.11, 41.31, 39.28, 27.90, 21.70. IR ($CCl_4$): 2942, 2868, 1702 cm$^{-1}$. LRMS (EI) $m/e$: 162 (6), 97 (82), 66 (100). Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.25; H, 8.84.

**(1*R**,6*S**)-8,9-Dimethylbicyclo[4.4.0]-8-decen-2-one (8g)**[48] (**7g**, 0.339 g, 1.01 mmol): yield 0.139 g (77%), as a 17:1 mixture of cis:trans isomers. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 2.64–2.60 (m, 1H), 2.41–1.62 (m, 11H), 1.58 (s, 3H), 1.53 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 213.02, 123.37, 122.69, 49.02, 39.69, 36.31, 33.81, 30.00, 28.16, 23.96, 19.08, 18.60. IR ($CCl_4$): 2899, 1707 cm$^{-1}$. LRMS (EI) $m/e$: 178 (100), 163 (65), 145 (58), 119 (58). Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.17. Found: C, 80.45; H, 10.03.

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**Supplementary Material Available:** Copies of $^1$H and $^{13}$C NMR spectra of compounds for which no elemental analysis was obtained (86 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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