Sequenced Reactions with Samarium(II) Iodide. Sequential Intramolecular Barbier Cyclization/Grob Fragmentation for the Synthesis of Medium-Sized Carbocycles

Gary A. Molander,* Yvan Le Huérou, and Giles A. Brown

Roy and Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104-6323

gmolandr@sas.upenn.edu

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Samarium(II) iodide was used to access eight-, nine-, and ten-membered carbocycles via a domino reaction composed of a cyclization/fragmentation process. 2-(Iodoalkyl)-, 2-(iodomethyl)allyl-, and 2-(2-iodomethyl)benzyl-2-methyl-3-(methanesulfonyloxy)cycloalkanones were subjected to Barbier-type reductive coupling conditions. Intermediate cycloalkanedione derivatives were also treated under similar conditions, providing bicyclic hydroxy ketones with complete diastereoselectivity and high yields. This method represents a general and efficient approach to a variety of highly functionalized, stereodefined carbocycles.

Introduction

The formation of medium-sized rings remains challenging because of well-known entropic and enthalpic factors.[1] To circumvent these, numerous methods involving ring expansion or fragmentation have been used to access such frameworks.[2] For example, oxy-Cope rearrangements,[3] Wharton/Grob fragmentations,[4] and samarium(II) iodide sequenced reactions[5] have been successfully applied. Among these methods, the Grob fragmentations possess several attractive features. First, they are stereospecific with regard to the stereochemistry of the leaving group. Consequently, both cis and trans cyclic olefins are accessible from diastereomeric starting materials. Second, the stereochemistry at the alkoxide plays no role in the stereoselectivity of the fragmentation. Finally, the fragmentation proceeds under fairly mild conditions with excellent yields. For these reasons, the reaction has been widely applied to the synthesis of natural products, but the diversity and complexity of the molecules isolated from plants and other organisms dictates the need for further development.[6] This is especially true when it comes to the synthesis of the bicyclic precursor required for the fragmentation.

An elegant way of solving this problem is to perform a domino reaction during which the bicyclic system is first formed and then fragmented to yield a carbocycle. Sequential protocols that are related to this approach have been developed using stannyl radicals to initiate the ring expansion/fragmentation. Unfortunately, the species formed in these cases are often capable of alternative reactions (hydrogen abstraction in particular) that lower the yield of fragmented products.[7] More recently, stannyl anion[8] or indium metal[9] have proven to be useful agents to perform the ring expansion/Grob fragmentation of functionalized cycloalkanones, but they

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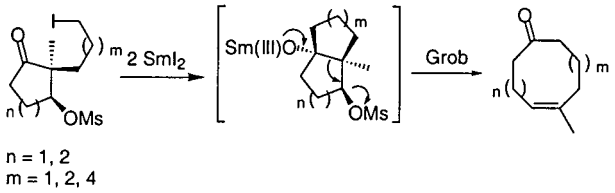
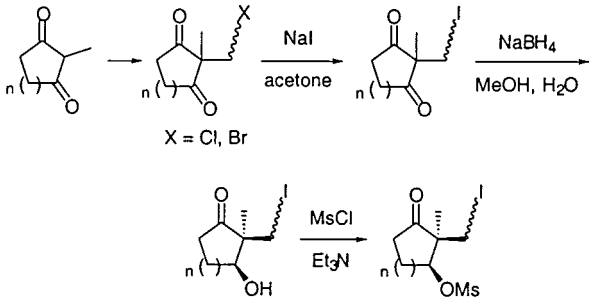
Scheme 1



Scheme 2



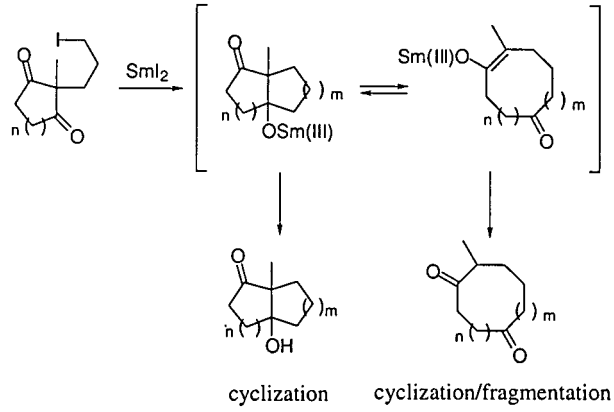
have only been involved in the synthesis of eight-membered rings from cycloalkanone derivatives.

We report in this contribution an intramolecular Barbier-type coupling/fragmentation protocol mediated by samarium(II) iodide (Scheme 1). This mild reductive coupling agent appears especially suited to the desired sequence for the following reasons: several sequential reactions involving SmI_2-promoted coupling followed by elimination or fragmentation have been reported.[5b] The intramolecular Barbier reaction can occur between the iodoalkyl chain and the ketone of the cycloalkanones, generating a bicyclic alkoxide that can then undergo fragmentation. During the latter process, the stereochemistry at the alkoxide center will have no effect on the stereochemistry of the fragmented product because of the characteristics of the Grob fragmentation. As a consequence, even if the annulation is not completely diastereoselective, only one unsaturated isomer will be isolated depending on the configuration of the side chain/leaving group system. We also felt confident that two of the potential problems in such an approach (i.e., reduction or elimination of the leaving group prior to the cyclization) could be avoided. Although SmI_2 reacts with sulfonates under reductive coupling conditions, it does so at rates that are much slower than primary iodides.[10] Finally, SmI_2-promoted processes are essentially neutral so that the leaving group is not expected to be eliminated prior to the reductive cyclization. The major restriction of the method concerns the length of the iodoalkyl chain. All these elements were integrated in our protocol. The following results describe an efficient method for the synthesis of functionalized, stereodefined, eight-, nine-, and ten-membered rings.

Results and Discussion

The substrates were prepared according to the general route shown in Scheme 2. The first step involved the alkylation of 2-methylcycloalkane-1,3-diones with suitable dihalides. Although many methods have been reported for such reactions,[12] 2-methylcycloalkane-1,3-diones are especially prone to *O*-alkylation because of their "W" geometry and steric hindrance at the carbon site.[13] As a consequence, both conditions employed (Cs_2CO_3/DMF and NaH/DMF) yielded mixtures of *C*- and *O*-alkylated products, the *C*-/*O*- ratio depending on the reactivity of the electrophile. From this mixture the desired *C*-alkylated products were isolated.

Scheme 3



Conversion of the resultant *C*-alkylated chloro- or bromo-substituted diones into the corresponding iodides under Finkelstein conditions then provided a series of iodo diones. Only 2-(2-chloroethyl)-2-methylcyclohexane-1,3-dione could not be converted to the corresponding iodide, the latter being too unstable.

At this point, it appeared prudent to submit our intermediate cycloalkanedione derivatives to a SmI_2-promoted intramolecular reductive coupling reaction. This early investigation was undertaken to confirm that the Barbier coupling could be realized and to probe the possibility of fragmentation of the samarium alkoxide intermediates by a retro aldol process (Scheme 3). Thus, diones **1** were added to a solution of SmI_2 containing 2% of NiI_2 as a catalyst at or below 0 °C (Table 1).[14] The first attempt (entry 1) proved to be disappointing because a complex mixture was isolated even when the reaction was carried out under irradiation with visible light.[15] It appeared that none of the conditions used enabled the effective reductive coupling of the chloride to the ketone, and only competitive reduction of the carbonyls or other undesired reactions predominated.[11] Fortunately, the next attempts (entries 2 and 4) were more successful, and 2-(3-iodopropyl)-2-methylcycloalkane-1,3-diones **1b** and **1d** could be effectively transformed to the corresponding bicyclic hydroxy ketones **2b** and **2d** with complete cis diastereoselectivity at the ring junction. As expected, the higher homologues (entries 3, 5, and 6) proved to be more difficult (**1c** and **1e**) or impossible (**1f**) to cyclize owing to entropic considerations. The formation of cyclized products **2c** and **2e** could be observed in 62% and 30%

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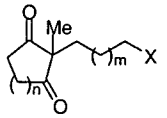
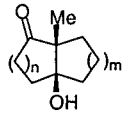
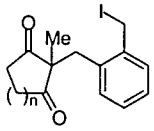
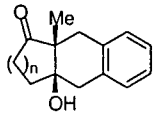
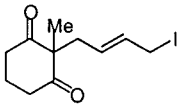
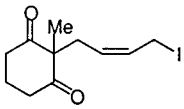
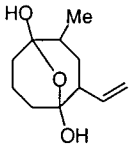
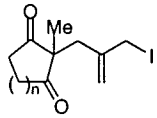
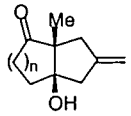
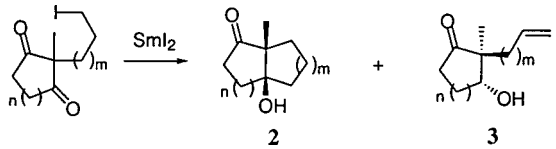
Table 1. Cyclization of Substituted 2-Methylcycloalkane-1,3-diones with SmI_2/Cat. NiI_2

entry	substrate	product	(%) isolated yield
			
1	**1a**, X=Cl, n=2, m=0		--[a]
2	**1b**, X=I, n=1, m=1	**2b**	94
3	**1c**, X=I, n=1, m=2	**2c**	--[b]
4	**1d**, X=I, n=2, m=1	**2d**	87
5	**1e**, X=I, n=2, m=2	**2e**	--[b]
6	**1f**, X=I, n=2, m=4		--[c]
			
7	**4a**, n=1	**5a**	89
8	**4b**, n=2	**5b**	93
9	 **6a**		--[c]
10	 **6b**	 **7**	21
			
11	**8a**, n=1	**9a**	91
12	**8b**, n=2	**9b**	87

[a] Complex mixtures were observed. [b] **2c** and **2e** could be observed by NMR along with **3a** and **3b** but could not be separated. [c] Complex mixture.

Scheme 4



2 **3**

2c, n = 1, m = 2, 62% **3a**, n = 1, m = 2, 33%
2e, n = 2, m = 2, 30% **3b**, n = 2, m = 2, 22%

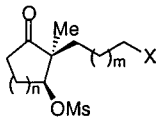
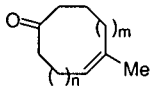
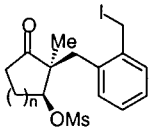
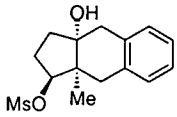
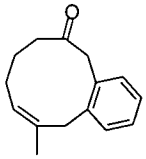
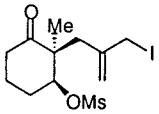
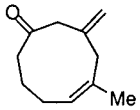
yields; however, these compounds were inseparable from the reduced β-hydroxy ketone products **3a** and **3b** (Scheme 4).[11b] Substrate **1f** gave only a complex mixture of products. At this point it is interesting to note that at room temperature or even under reflux, none of the samarium alkoxide intermediates led to fragmentation.

The highly reactive 2-(2-iodomethyl)benzyl-2-methylcycloalkane-1,3-diones (entries 7 and 8) turned out to be excellent substrates for the cyclization because both **4a** and **4b** were converted to the tricyclic hydroxy ketones **5** without irradiation and in short reaction times. In these two cases the inherent reactivity of the benzylic halide in concert with the conformational bias imposed by the aromatic ring proved to be an excellent combination for the formation of the six-membered ring. Furthermore, the reaction was completely diastereoselective. The cis configuration was assigned on the basis of single-crystal X-ray analysis. As in the preceding examples, none of the conditions tested enabled the fragmentation.

The next reactions involved *trans*- and *cis*-2-(4-iodobut-2-enyl)-2-methylcyclohexane-1,3-diones. Complex mixtures were observed when the trans isomer **6a** was subjected to reductive conditions but the cis isomer **6b** yielded the desired fragmented compound as its hydrated bis-hemiacetal. Unfortunately, none of the conditions tested (irradiation, low temperatures, or exchange to the less reactive bromide) could increase the low yield observed. Substrate **6b** reacts with allylic inversion, generating a strained 6−4 bicyclic ring system that is prone to fragmentation. The 5−5, 5−6, and 6−6 bicyclic systems, formed by substrates **1b-1e**, **4a**, **4b**, **8a**, and **8b**, are too stable to allow the expansion process. These results are consistent with literature precedent.[8,9] Through a similar sequence, Li et al. had previously shown that 4-bromobut-2-enyl-β-keto esters yielded ring-expanded products when treated with indium in water. In that study, both olefin isomers of the substrate allylic halide could be utilized in the process.[9]

Finally, reactive 2-(2-iodomethyl)allyl-2-methylcycloalkane-1,3-diones (entries 11 and 12) were smoothly cyclized, yielding the cis-fused systems **9** with excellent yield and complete diastereoselectivity. The reductive

Table 2. Ring Expansions Mediated by Samarium(II) Iodide

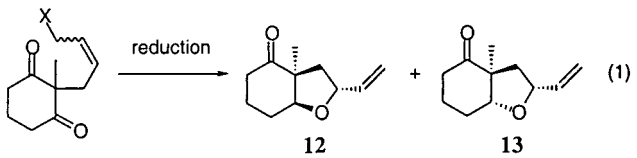
entry	substrate	product	(%) isolated yield
			
1	**14a**, X=Cl, n=2, m=0		--[a]
2	**14b**, X=I, n=1, m=1	**15b**	69
3	**14c**, X=I, n=1, m=2	**15c**	42
4	**14d**, X=I, n=2, m=1	**15d**	86
5	**14e**, X=I, n=2, m=2	**15e**	51
6	**14f**, X=I, n=2, m=4		--[b]
			
7	**16a**, n=1	 **17**	83[c]
8	**16b**, n=2	 **18**	92
9	 **19**	 **20**	91

[a] The mesylate was reduced before the chloride. [b] Complex mixture. [c] The fragmented nine membered ring **21** could be obtained in 88% yield by treating **17** with 1 equiv of NaOMe in methanol heated at reflux (see Scheme 5).

coupling of cyclic diketones bearing iodoalkyl, -allyl, or -benzyl side chains therefore constitutes an effective method to access a variety of diastereomerically pure polycyclic hydroxy ketones affording an alternative to the existing methods.[16]

In light of these results, we felt confident that in the presence of a leaving group, the substrates would undergo fragmentation because the cyclization had occurred with good yields in most of the cases. The requisite 2-substituted-2-methyl-3-(methanesulfonyloxy)cycloalkanones were therefore prepared by reduction of the corresponding cycloalkanediones.

Both chemical and yeast-mediated reduction protocols have been described to access ketols from cyclic diones.[17] We focused on a sodium borohydride reduction, hydrides being known to yield ketols with good diastereoselectivities (Scheme 2). Using $NaBH_4$ in $MeOH/H_2O$, the diones could be reduced with good yields, affording the corresponding ketols with cis/trans selectivities varying from 2/1 to 9/1. The use of $EuCl_3 \cdot 6H_2O$ as a chelating agent proved to increase the diastereoselectivity slightly.[17b,18] In the case of butenyl halides, the reduction of the dione did not yield the expected ketol but rather a mixture of diastereomeric vinyl ethers **12** and **13** resulting from an intramolecular S_N2' displacement of the halide (eq 1).[19] This undesired reaction could not be avoided by using different hydrides (DIBALH, $LiBHEt_3$), exchanging the halogen from iodine to bromine, or by performing the reaction at low temperature.



12 **13**

cis X = Br, **10a**; X = I, **6a**
trans X = Br, **11a**; X = I, **6b**

After mesylation under standard conditions (MsCl, Et_3N, CH_2Cl_2, −78 °C, 3 h), the diastereomers were

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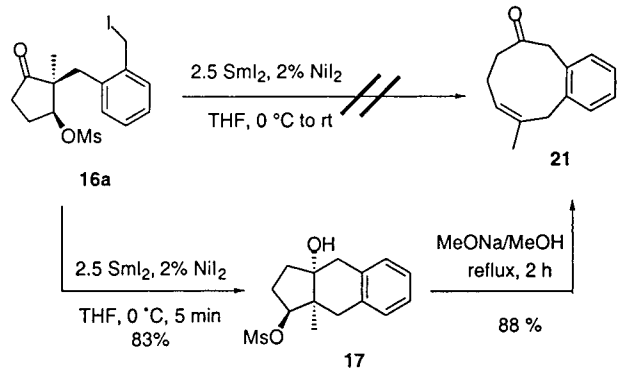
Scheme 5



separated by recrystallization, and their configuration was confirmed by NOE experiments. Only the cis isomers could be isolated diastereomerically pure. The cis keto mesylates were treated with samarium(II) iodide in THF in the presence of 2% NiI_2. The reactivity of these substrates proved to be consistent with the reactivity of the parent diones. Furthermore, the intermediate organosamarium species underwent fragmentation at room temperature (Table 2). Finally, the isolated yields were similar to those observed for the previous cyclizations (Table 1), suggesting that the fragmentations are quantitative and irreversible. The ring expansion also proved to be stereoselective because the isolated olefins showed the expected cis geometry. The configurations were assigned on the basis of NOE experiments and by comparison with literature data.[4f] As observed during the preliminary study, the chloroalkyl substrate **14a** (entry 1) did not yield the desired eight-membered ring. However, eight-, nine-, and ten-membered cycloenones could be readily generated from substrates **14b**, **14c**, and **14d**, respectively (entries 2−5).

Surprisingly, **16a** (entry 7) could not be fragmented under standard conditions. The only isolated product was the intermediate hydroxy mesylate **17**. Heating the reaction mixture at reflux yielded degraded products. Use of either LiBr or HMPA as alternative additives for the SmI_2 reaction also failed to induce fragmentation. However, **17** was easily fragmented to **21** by treatment with sodium methoxide in methanol heated at reflux (Scheme 5). At this point, it is not clear why the samarium alkoxide of **16** did not fragment. Even if it does not easily satisfy the antiperiplanar orientation required for synchronous fragmentation because of conformational factors, this barrier should also apply to several of the other intermediates in the study that do undergo fragmentation at room temperature. The nature of the alkoxide-metal species must play an important role as demonstrated by the results displayed in Scheme 5. The bond between the oxophilic samarium(III) and the alkoxide appears to be too strong to allow further reaction compared to the more ionic bond engaged between sodium and oxygen. However, even if the nine-membered ring cannot be directly accessed during the sequential process, it can still be obtained in two steps with an overall yield of 73%. The homolog, **16b**, cyclizes and readily fragments to provide cyclodecenone **18** in excellent yield (entry 8).

Finally, substrate **19** can be smoothly converted to cyclononadienone **20** in exceptional yield (entry 9). Of particular note here is the fact that no isomerization of the exomethylidene to the conjugated endocyclic isomer was observed. This result attests to the mild nature of these cyclization/fragmentation processes, which apparently occur under near-neutral reaction conditions.

Conclusion

A samarium(II) iodide-promoted sequential cyclization/fragmentation protocol was developed that provides an efficient approach to the synthesis of functionalized, stereodefined medium-sized carbocycles. This method involves the reduction under Barbier-type conditions of substituted keto mesylates bearing iodoalkyl, -allyl, or -benzyl side chains. The reaction proceeds in a stereoselective manner with high yields under mild conditions. The cyclization of cycloalkanediones under similar conditions was also observed, yielding functionalized polycyclic hydroxy ketones in high yields with complete diastereoselectivity.

Experimental Section

General Procedures. ^1H and ^{13}C NMR were recorded at 500 and 125 MHz for proton and carbon, respectively. $CDCl_3$ was employed as the solvent unless stated otherwise, and residual $CHCl_3$ was applied as an internal standard ($\delta = 7.24$ ppm) for ^1H spectra while the $CDCl_3$ signal served as internal standard ($\delta = 77.0$ ppm) for ^{13}C spectra. Standard flash chromatography procedures were followed using 32−63 μm silica gel.[20] Tetrahydrofuran (THF) was distilled immediately prior to use from sodium benzophenone ketyl under Ar. Samarium metal was purchased from Aldrich (99.9%, 40 mesh). CH_2I_2 was purchased from Aldrich, distilled under Ar, and stored over copper granules. NiI_2 powder was purchased from Aldrich (99.999%). Standard benchtop techniques were employed for handling air-sensitive reagents,[21] and all air-sensitive reactions were carried out under N_2.

General Procedure for the Alkylation of 2-Methylcycloalkane-1,3-diones with Dihaloalkanes. 2-(2-Chloroethyl)-2-methylcyclohexane-1,3-dione (1a). To a solution of 2-methylcyclohexane-1,3-dione (12.6 g, 100 mmol) in 150 mL of dry DMF was added anhydrous Cs_2CO_3 (35.8 g, 110 mmol) at room temperature. The suspension was stirred for 10 min, and 1-bromo-2-chloroethane (43 g, 300 mmol) was added at once. The resulting yellow suspension was stirred for 14 h at room temperature and then quenched with 150 mL of brine. The mixture was extracted several times with EtOAc, and the organic extracts were washed with water and dried with $MgSO_4$. Flash chromatography (50% EtOAc/petroleum ether) yielded 1.72 g (9%) of the title compound and 9 g (48%) of 3-(2-chloroethoxy)-2-methylcyclohex-2-enone as colorless oils. **1a**: ^1H NMR ($CDCl_3$, 500 MHz) δ 3.36 (t, $J = 7.3$ Hz, 2H), 2.65−2.55 (m, 4H), 2.27 (t, $J = 7.4$ Hz, 2H), 1.98−1.87 (m, 2H), 1.08 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 209.5, 63.2, 40.3, 37.7, 37.3, 23.1, 17.5; IR (film) ν_{max} 1726, 1697, 1457, 1317 cm^{-1}; HRMS (CI^+) calc for $(M - H)^+$ $C_9H_{12}ClO_2$ 187.0525, found 187.0527. **3-(2-Chloroethoxy)-2-methylcyclohex-2-enone**: ^1H NMR ($CDCl_3$, 500 MHz) δ 4.17 (t, $J = 5.6$ Hz, 2H), 3.67 (t, $J = 5.6$ Hz, 2H), 2.50−2.45 (m, 2H), 2.27 (t, $J = 6.8$ Hz, 2H), 1.95−1.88 (m, 2H), 1.64 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 198.7, 169.9, 116.0, 67.3, 42.2, 36.1, 25.4, 20.8, 7.3; IR (film) ν_{max} 2949, 1620, 1355, 1234 cm^{-1}; HRMS (CI^+) calc for $(M)^+$ $C_9H_{13}ClO_2$ 188.0604, found 188.0594.

General Procedure for Alkylation of 2-Methylcycloalkane-1,3-diones with Bis(benzylic) and Bis(allylic) Dihalides. 2-(2-Bromomethyl)benzyl-2-methylcyclopentane-1,3-dione. To a suspension of hexanes washed NaH (1.76 g, 66 mmol) in 70 mL of anhydrous DMF at 0 °C was slowly added a solution of 2-methyl-1,3-cylopentanedione (4.5 g, 40 mmol) in 70 mL of anhydrous DMF. The resulting solution

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was stirred for 1 h at room temperature and then added over 2 h to a solution of α,α′-dibromo-*o*-xylene in 70 mL of anhydrous DMF. The reaction mixture was stirred for an additional 48 h and then cooled to 0 °C before being hydrolyzed with 200 mL of ice. The organic materials were extracted with Et_2O, and the organic phase was washed with brine and dried over $MgSO_4$. Flash chromatography (50% EtOAc/petroleum ether) yielded 2.3 g (19%) of the title compound and 1.3 g (11%) of 3-(2-bromomethylbenzyloxy)-2-methylcyclohex-2-enone as colorless crystals. **2-(2-Bromomethyl)benzyl-2-methylcyclopentane-1,3-dione**: mp 86−88 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.35−7.30 (m, 1H), 7.25−7.19 (m, 2H), 7.10−7.05 (m, 1H), 4.68 (s, 0.6H), 4.60 (s, 1.4H), 3.19 (m, 2H), 2.69−2.57 (m, 2H), 2.23−2.14 (m, 2H), 1.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 217.3, 136.5, 136.3, 135.0, 131.1, 130.9, 130.4, 130.2, 129.92, 128.88, 127.9, 127.8, 58.1, 28.0, 44.2, 37.7, 37.5, 35.7, 31.9, 21.0, 20.8; IR (film) ν_{max} 2969, 1762, 1722, 1449 cm^{-1}; HRMS (CI$^+$) calc for (MH)$^+$ $C_{14}H_{16}BrO_2$ 295.0333, found 295.0329. **3-(2-Bromomethyl)benzyloxy-2-methylcyclohex-2-enone**: mp 94 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.41−7.32 (m, 4H), 5.37 (s, 2H), 4.66 (s, 2H), 2.71−2.67 (m, 2H), 2.46−2.40 (m, 2H), 1.65 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 205.2, 183.1, 135.3, 134.5, 130.6, 129.3, 129.2, 128.7, 117.1, 68.4, 43.6, 33.5, 25.2, 6.1; IR (film) ν_{max} 2920, 1632, 1339 cm^{-1}; HRMS (CI$^+$) calcd for (MH)$^+$ $C_{14}H_{16}BrO_2$ 295.0333, found 295.0344.

General Procedure for the Finkelstein Reaction. 2-(3-Iodopropyl)-2-methylcyclohexane-1,3-dione (1d). To the chloride precursor (4 g, 20 mmol) in 150 mL of acetone was added 30 g (0.2 mol) of NaI. The solution was heated at reflux for 12 h and cooled to room temperature, and 200 mL of water was added. The aqueous phase was extracted with Et_2O, and the combined organic phases were washed with 10% aqueous $Na_2S_2O_3$ and brine and dried over $MgSO_4$. Purification by flash chromatography (50% EtOAc/petroleum ether) afforded 5.2 g (88%) of **1d** as a yellow oil:^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.07 (dd, J = 1.3, 6.7 Hz, 2H), 2.65−2.51 (m, 4H), 1.98−1.82 (m, 4H), 1.62−1.57 (m, 2H), 1.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 209.7, 64.9, 37.8, 37.1, 28.6, 20.2, 17.6, 5.8; IR (film) ν_{max} 1725, 1693, 1456 cm^{-1}; HRMS (CI$^+$) calcd for (MH)$^+$ $C_{10}H_{15}ClO_2$ 295.0195, found 295.0187.

General Procedure for Reduction and Mesylation of the 1,3-Diones. Methanesulfonic Acid, (*Z*)-(2*R,3*R**)-2-(2-Chloroethyl)-2-methyl-3-oxocyclohexyl Ester (14a).** To the dione **1a** in 30 mL of THF at room temperature was added dropwise 2.5 mL of a 0.5 M solution of aqueous $NaBH_4$. The solution was stirred for 1 h at room temperature, 60 mL of water were added, and the pH was adjusted to 2 with a 0.5 M aqueous HCl solution. The aqueous phase was extracted with Et_2O, and the combined organic phases were washed with brine and dried over $MgSO_4$. The crude mixture (60/40 cis/trans) was purified by flash chromatography (30% EtOAc/petroleum ether) to yield 756 mg (79%) of the alcohol as a colorless liquid. To 1.65 g (8.7 mmol) of the alcohol in 140 mL of CH_2Cl_2 and 1.8 g (18 mmol) of Et_3N at −78 °C were added 1.5 g (13 mmol) of MsCl. The solution was stirred for 2 h at the same temperature and hydrolyzed with 150 mL of brine. The aqueous phase was extracted with Et_2O, and the combined organic phases were washed with brine and dried over $MgSO_4$. Purification by flash chromatography (30% EtOAc/petroleum ether) and recrystallization (Et_2O/EtOAc/petroleum ether) yielded 1.70 g (73%) of **14a** as colorless crystals: mp 84−86 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.71 (t, J = 4.8 Hz, 1H), 3.55−3.47 (m, 1H), 3.44−3.38 (m, 1H), 3.02 (s, 3H), 2.49−2.38 (m, 2H), 2.33−2.25 (m, 1H), 2.22−2.17 (m, 2H), 2.08−1.95 (m, 2H), 1.76−1.70 (m, 1H), 1.23 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 209.8, 85.9, 52.8, 39.6, 38.9, 37.1, 35.7, 27.0, 19.9, 19.3; IR (film) ν_{max} 1712, 1350, 1174 cm^{-1}; HRMS (CI$^+$) calc for (MH)$^+$ $C_{10}H_{18}ClO_4S$ 269.0614, found 269.0627.

General Procedure for the Sequenced Reactions Using Samarium(II) Iodide. Samarium metal (420 mg, 2.8 mmol) was added under a flow of N_2 to an oven-dried flask. 20 mL of THF were added, the suspension was cooled between −10 °C and 0 °C, and CH_2I_2 (699 mg, 2.6 mmol) was added. The mixture was stirred at room temperature for 2 h, and NiI_2 (2% mol) was added. After stirring 5 min, the deep-blue solution was cooled to the requisite temperature, and the substrate (1 mmol) in 10 mL of THF was added over 5 min. The reaction was irradiated or not with visible light (250 W krypton lamp) while keeping the temperature at the previously mentioned level. After the starting material was consumed (TLC or GC analysis), the reaction mixture was warmed to room temperature and stirred for 1 h. The resultant solution was quenched with a saturated aqueous solution of Rochelle's salt and extracted several times with Et_2O. The organic extracts were washed with brine and dried over $MgSO_4$. The products were purified by flash chromatography unless stated otherwise.

3α-Hydroxy-6α-methylhexahydropentalen-1-one (2b).[16b] Prepared from **1b** (279 mg, 1 mmol) according to the general procedure described above (under irradiation, −30 °C for 3 h) to afford, after flash chromatography (50% EtOAc/petroleum ether), **2b** (144 mg, 94%) as a colorless gel:^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.51−2.42 (m, 1H), 2.34−2.24 (m, 1H), 2.13−2.04 (m, 1H), 1.98−1.72 (m, 5H), 1.63−1.42 (m, 3H), 1.10 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 222.0, 87.4, 58.6, 40.1, 36.2, 35.9, 32.8, 22.2, 16.3; IR (film) ν_{max} 3452, 1731 cm^{-1}; HRMS (CI$^+$) calc for (MH)$^+$ $C_9H_{15}O_2$ 155.1072, found 155.1073.

(*Z*)-10-Methyl-5,7,8,11-tetrahydrobenzocyclononen-6-one (21). 17 (60 mg, 0.2 mmol) was added to a solution of NaOMe (11 mg, 0.2 mmol) in 3 mL of MeOH and heated to reflux for 1 h. The MeOH was evaporated, and 3 mL of water were added. The aqueous phase was extracted with EtOAc, and the combined organic phases were washed with brine and dried over $MgSO_4$. After evaporation of the solvent, the resulting solid was recrystallized (Et_2O/petroleum ether) to yield **21** (34 mg, 88%) as colorless crystals: mp 118−120 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.19−7.11 (m, 4H), 5.23 (t, J = 8.5 Hz, 1H), 3.76 (s, 2H), 3.39 (s, 2H), 2.76−2.67 (m, 2H), 2.62−2.55 (m, 2H), 1.57 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 210.0, 138.2, 136.5, 134.0, 132.5, 130.8, 127.0, 126.9, 122.6, 45.8, 44.0, 37.0, 24.1, 22.9; IR (film) ν_{max} 2959, 1704, 1470 cm^{-1}; HRMS (CI$^+$) calcd for (M)$^+$ $C_{14}H_{16}O$ 200.120115, found 200.120287.

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Supporting Information Available: Full experimental details, ^{1}H and ^{13}C NMR spectra for all compounds, and X-ray structural data for **5a** and **5b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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