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Tetrahedron 63 (2007) 1366–1371
Tetrahedron

The intramolecular reductive cyclization of cyclic enones

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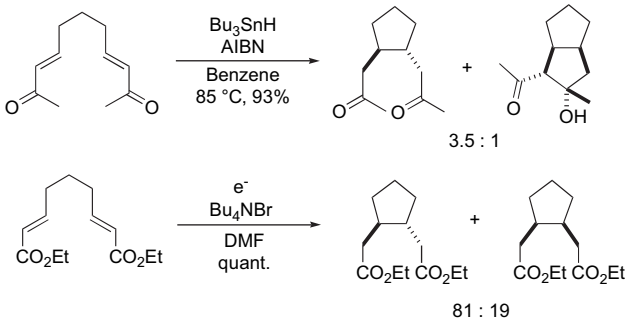
Received 20 October 2006; revised 28 November 2006; accepted 30 November 2006

Abstract—The reductive cyclization (electrohydrocyclization reaction) of tethered cyclic enones has been investigated under electrochemical, metal-mediated, and photochemical conditions. The tricyclic products are generally formed with excellent stereoselectivity, particularly if at least one of the enones is β,β-disubstituted.

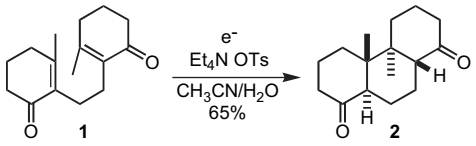
1. Introduction

The hydrodimerization reaction is a highly important reaction, particularly for the preparation of monomers for use in the synthesis of a variety of polymeric compounds.[1] A great deal of research has been conducted on the development of a variety of electrochemical and metal-mediated conditions to effectively conduct these intermolecular reactions. At the same time, relatively little attention has been focused on the development of the intramolecular version of this reaction (the electrohydrocyclization, hereafter called the reductive cyclization).[2] Indeed, the majority of these studies have explored the cyclization of simple tethered acyclic enones or enoates, such as those seen in Scheme 1.[3] While interesting, such focus ignores the vast potential of the reductive cyclization.



Scheme 1. Acyclic enone/enoate cyclizations.[2c,g]

The earliest exception to this trend of using acyclic systems is the reductive cyclization of **1** reported by Mandell and co-workers in 1976 (Scheme 2).[3a] Under controlled potential conditions, this reaction afforded trans/anti/trans tricycle **2** as a single isomer in 65% yield (81% brsm). Thus, four new stereocenters were established with complete stereocontrol. Rather surprisingly, there has been little effort to expand the scope of this transformation in the passing decades. Our efforts to remedy this situation and study the influence of ring size and β-substitution are the focus of this manuscript.[4]



Scheme 2. Mandell's reductive cyclization.

2. Results and discussion

The first challenge was the development of a general and efficient route to a range of cyclization precursors. Mandell's route to **1** featured a Kolbe dimerization of 3-methyl-2-cyclohexen-1-one-2-acetic acid, itself accessible in three steps from ethyl acetoacetate. We felt that a more efficient route would be the dimerization of functionalized allylic halides such as **3** (Scheme 3). The basis for this plan was a report by Chan and Ma that allylic and benzylic halides could be cleanly homo-coupled using a combination of manganese metal and copper(I) chloride.[5] Although it was not clear if such a reaction would work in the presence of a ketone, the fact that allylic acids had been successfully coupled gave this route promise.

Keywords: Hydrodimerization; Electrohydrocyclization; Electrosynthesis; Samarium diiodide; Cyclization; Stereoselectivity.
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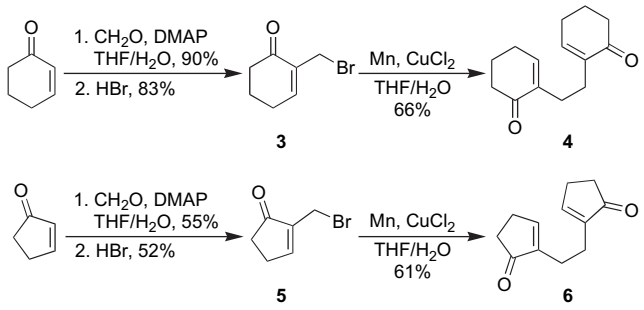
0040–4020/$ - see front matter © 2006 Published by Elsevier Ltd.
doi:10.1016/j.tet.2006.11.084

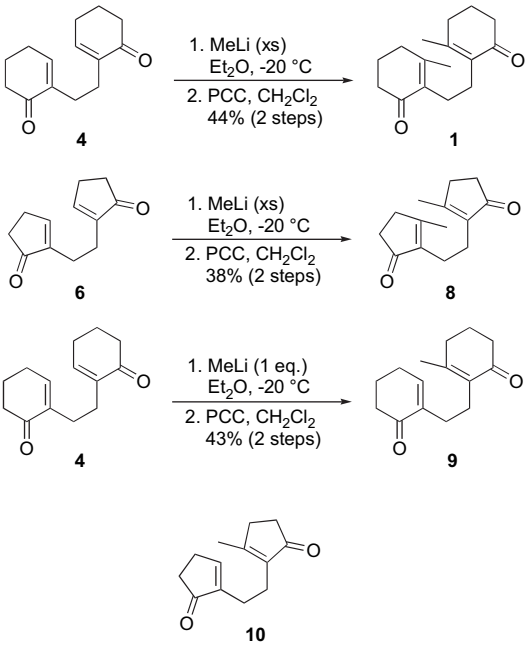


Scheme 3. Preparation of cyclization substrates.

In the event, allylic bromide **3** was prepared from cyclohexenone by a Baylis–Hillman reaction with formaldehyde,[6a] followed by treatment of the allylic alcohol with hydrogen bromide (Scheme 3). With the desired allylic bromide in hand, the homo-coupling proceeded cleanly to afford cyclization substrate **4**. No product was observed from reaction at the ketone, the lower yield being the result of the instability of the allylic bromide, particularly when stored neat. A similar pathway, starting with cyclopentenone, was also effective for the preparation of five-membered ring cyclization precursor **6**. In this case, the lower yields of both steps are likely the result of increased volatility of the products, the very sluggish Baylis–Hillman reaction,[6b] and the even greater sensitivity of bromide **5**.

For methyl-substituted substrates, bis-enones **4** and **6** proved to be satisfactory starting materials (Scheme 4).[7] Thus, treatment with excess methyllithium afforded the corresponding tertiary alcohols, which were subjected to oxidative rearrangement to afford the desired cyclization substrates **1** and **8**. Unsymmetrical substrate **9** was also prepared in this manner by the treatment of **4** with a single equivalent of methyllithium, followed by oxidative rearrangement of the resulting tertiary alcohol. Curiously, attempts to prepare **10** using similar conditions failed, affording only a mixture of **8** and **6**.

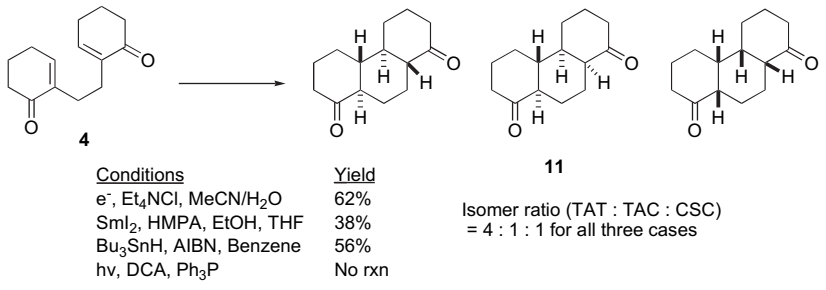
With the desired cyclization substrates in hand, the reductive cyclization could be studied (Scheme 5). Beginning with cyclization substrate **4**, the reductive cyclization was explored under simple electrochemical conditions using a tin cathode and a platinum anode.[4] These conditions resulted in the formation of an inseparable mixture of three isomers of product **11**, the major isomer being trans/anti/trans (TAT). Although the isolated yield of **11** was modest, the reaction itself was quite clean by TLC, showing only



Scheme 4. Preparation of methyl-substituted substrates.

the formation of **11** and some polymeric by-products at the base of the TLC plate.[8] The stereochemistry of the products was confirmed to be that shown in Scheme 5 by the conversion of bis-ketones **11** into the corresponding perhydrophenanthrenes under Wolff–Kishner conditions.[9] The ^{13}C spectra of these phenanthrenes were then compared with the data for the various isomers reported in the literature.[10] It is worth noting that there could have been epimerization of the stereocenters α to the ketones during the Wolff–Kishner reduction, but this does not appear to have occurred to any significant extent, since the same isomeric ratio is observed both prior to and after the Wolff–Kishner reduction.

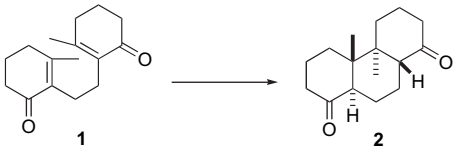
As another avenue of exploration, we were interested in what effect a change in cyclization conditions might have on the outcome of the reaction. In particular, there have been reports using metal-mediated conditions (SmI_2 or Bu_3SnH)[2g,h] and even photochemical conditions.[2d,e,f] For the most part, though, these different reports have examined different substrates, so there was little clear evidence to suggest what, if any, differences in yield and/or selectivity might be observed. To that end, the cyclization of compound **4** was examined under two metal-mediated conditions and Pandey's photochemical conditions (Scheme 5). For the



Scheme 5. Cyclization of substrate **4**.

metal-mediated reactions, the yield of product **11** was similar to or lower than that observed under the electrochemical conditions. Further, the isomeric ratio was identical in all three cases. Rather surprisingly, application of the same photochemical conditions employed by Pandey and co-workers afforded only recovered starting material, even after prolonged reaction times.[2d] At this point, no satisfactory reason for this difference has come to light.

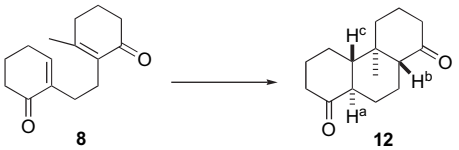
Staying in the cyclohexenone series, dimethyl substrate **1** was studied (Scheme 6). Cyclization under our electrochemical conditions resulted in the formation of a single isomer of **2**, in keeping with Mandell's observations. The yield was definitely lower than that reported by Mandell (50% vs 65% for Mandell), indicating that controlled potential conditions may be an effective means for improving the yield of these cyclizations in general. Samarium diiodide mediated cyclization also afforded only the trans/anti/trans isomer of **2**, but in very modest yield.[11] Finally, neither the tin hydride nor the photochemical conditions afforded any of product **2**, only the starting material was recovered.



Conditions	Yield
e^-, Et_4NCl, $MeCN/H_2O$	50%
SmI_2, HMPA, EtOH, THF	34%
Bu_3SnH, AIBN, Benzene	No rxn
hv, DCA, Ph_3P	No rxn

Scheme 6. Cyclization of substrate **1**.

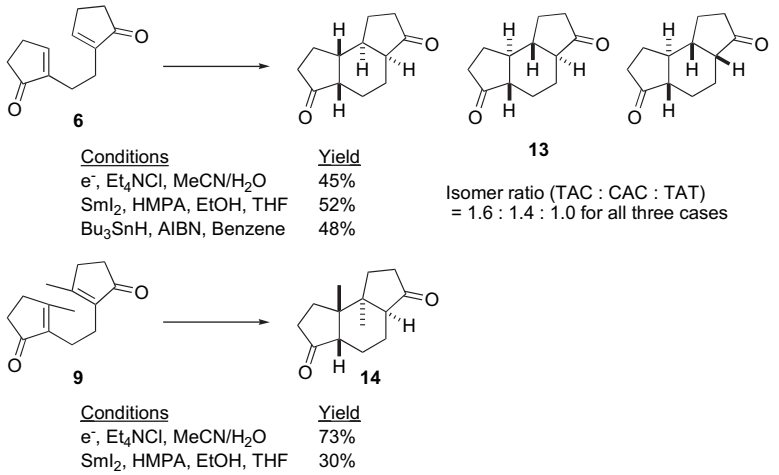
The final substrate in the cyclohexenone series is compound **8**. In light of the complete trans/anti/trans selectivity for the cyclization of **1** (with both enones β,β-disubstituted) compared to the modest (2:1) selectivity for the cyclization of **4** (with neither enone β,β-disubstituted), the cyclization of compound **8** (with one enone β,β-disubstituted) was examined with considerable interest (Scheme 7). Cyclization under the usual electrochemical conditions afforded product **12** as a single isomer (trans/anti/trans) in moderate yield. The samarium diiodide conditions afforded the same product, but in somewhat lower yield. As was the case with substrate **1**, the tin hydride conditions failed to result in any cyclization, affording only recovered **8**. Indeed, it appears that the tin hydride conditions are only applicable to substrates in which there is no β,β-disubstitution of either enone. The stereochemistry of **12** was assigned based on analogy with the results from **2** and **11**. It is further supported by an NOE study, which observed enhancement of the signal for one of the two ring fusion protons α to the ketones (proton a) and no enhancement to the other one (proton b) or to the other ring fusion proton c upon irradiation of the angular methyl group. Thus, the trans/anti/trans isomer is the one most consistent with these observations.



Conditions	Yield
e^-, Et_4NCl, $MeCN/H_2O$	59%
SmI_2, HMPA, EtOH, THF	30%
Bu_3SnH, AIBN, Benzene	No rxn

Scheme 7. Cyclization of substrate **8**.

Finally, the studies of the two cyclopentanone cyclization substrates displayed trends similar to the cyclohexenone series (Scheme 8). Thus, unsubstituted substrate **6** afforded product **13** as a mixture of three isomers. The trans/anti/cis isomer was the major isomer, although the cis/anti/cis isomer was present in nearly equivalent amounts. Again, the stereochemistry of these products was determined by double Wolff–Kischner reduction of the two ketones to afford the perhydroindacene systems, whose spectral data were compared to that reported in the literature.[12] As before, no alteration in the isomer ratio was observed following the Wolff–Kischner reduction, indicating that epimerization is not a significant issue. The cis ring fusion of the [5.6] systems was expected based on the typical preference for the formation of cis-fused [5.6] rings during bridging

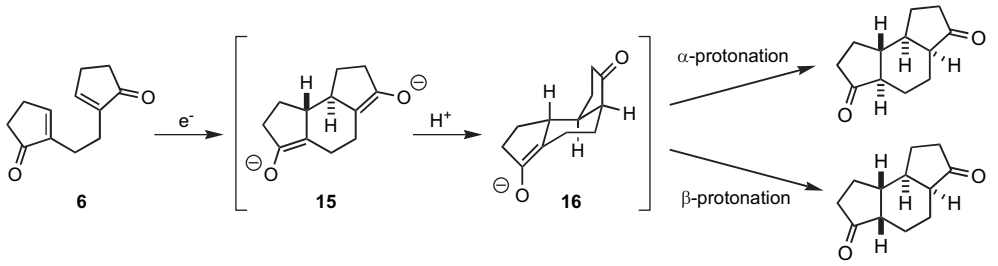


Conditions	Yield
e^-, Et_4NCl, $MeCN/H_2O$	45%
SmI_2, HMPA, EtOH, THF	52%
Bu_3SnH, AIBN, Benzene	48%

Isomer ratio (TAC : CAC : TAT) = 1.6 : 1.4 : 1.0 for all three cases

Conditions	Yield
e^-, Et_4NCl, $MeCN/H_2O$	73%
SmI_2, HMPA, EtOH, THF	30%

Scheme 8. Cyclizations of cyclopentenone substrates.



Scheme 9. Enolate protonation sequence.

protonation or alkylation.[13] The reduction in selectivity between the CAC and TAC isomers, compared to that observed in the cyclization of **4**, is likely due to the effects encountered in the protonation of the presumed bis-enolate intermediate **15** (Scheme 9). Assuming that protonation of both enolates is not simultaneous, then protonation of one enolate will result in cup-shaped mono-enolate **16**. Now protonation of the other enolate would be expected to occur from the convex or β face, thereby affording the trans [5.6] ring fusion. As expected, both metal-mediated conditions also afforded the same isomeric mixture of product **13**, and in relatively similar yields.

Finally, substrate **9** does undergo cyclization under the electrochemical conditions with good efficiency to afford product **14** as a single isomer. The stereochemistry is assigned as being cis/anti/cis. This is supported by the stereochemical outcomes of the previous reactions as well as the observation that product **14** must be one of the symmetry-containing isomers, since only six carbon signals are observed in the ^{13}C NMR spectrum.

3. Conclusion

In conclusion, these efforts have shown that the reductive cyclization of tethered bis-enones does have considerable scope. In the presence of β,β-disubstitution, the reaction is also quite stereoselective, affording single isomers of the cyclized products. This control, coupled with the concise route to these compounds, should enable ready application to a variety of natural and non-natural terpenoid products. These efforts are underway and will be reported in due course.

4. Experimental

4.1. General

Proton (^1H) and carbon (^{13}C) nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AM-360 MHz or AM-300 MHz spectrometer as a solution in deuterochloroform. Chemical shifts are reported in parts per million relative to tetramethylsilane. Infrared (IR) spectra were recorded on a Perkin–Elmer Spectrum Bx spectrophotometer. Reactions were monitored by thin-layer chromatography (TLC) with precoated silica gel plates. Silica gel (100–200 mesh) was used for all chromatography. All solvents were reagent grade unless stated otherwise. All non-aqueous reactions were performed under an atmosphere of argon. Samarium(II) iodide was freshly prepared prior to use from samarium metal and 1,2-diiodoethane.[14]

4.2. 2-[2-(6-Oxocyclohex-1-enyl)ethyl]cyclohex-2-enone [4]

Aqueous 48% HBr (4 mL) was added to 0.500 g (3.96 mmol) of 2-hydroxymethylcyclohex-2-enone[6a] and the reaction mixture was stirred for 1 h. The reaction was then quenched with water (4 mL) and extracted with methylene chloride (3×10 mL). The combined organic extracts were dried with anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford 0.72 g (96%) of **3** as a yellow oil. To a solution of 0.340 g (1.78 mmol) of bromide **3** in a THF/water mixture (2 mL, 1:1 v/v) were added 24.0 mg (0.178 mmol) of copper(II) chloride and 0.29 g (5.33 mmol) of manganese powder. The mixture was stirred overnight under an atmosphere of argon. The reaction was then quenched with 1 N HCl and extracted with ether (3×10 mL). The combined organic layers were dried with magnesium sulfate, filtered, and concentrated in vacuo. The resulting oil was purified by flash chromatography using ethyl acetate/hexanes (1:3) as eluant to afford 0.26 g (66%) of **4** as a yellow oil. IR ($CDCl_3$) 2929, 2859, 1670, 1632; ^1H NMR (360 MHz, $CDCl_3$) δ 6.61–6.59 (t, J=3.6 Hz, 2H), 2.33–2.22 (m, 8H), 2.18 (s, 4H), 1.91–1.84 (m, 4H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 199.2, 145.5, 138.9, 38.4, 28.4, 25.9, 23.0. HRMS (EI) calcd for $C_{14}H_{18}O_2$: 218.1454, found: 218.1452.

4.3. 2-[2-(6-Oxocyclopent-1-enyl)ethyl]cyclopent-2-enone [6]

Aqueous 48% HBr (4 mL) was added to 0.500 g (3.96 mmol) of 2-hydroxymethylcyclopent-2-enone[6b] and the reaction mixture was stirred for 1 h. The reaction was then quenched with water (4 mL) and extracted with methylene chloride (3×10 mL). The combined organic extracts were dried with anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford 0.244 g (55%) of **5** as a yellow oil. To a solution of 0.065 g (0.37 mmol) of bromide **5** in a THF/water mixture (2 mL, 1:1 v/v) were added 4.9 mg (0.037 mmol) of copper(II) chloride and 0.061 g (1.11 mmol) of manganese powder. The mixture was stirred overnight under an atmosphere of argon. The reaction was then quenched with 1 N HCl and extracted with ether (3×10 mL). The combined organic layers were dried with magnesium sulfate, filtered, and concentrated in vacuo. The resulting oil was purified by flash chromatography using ethyl acetate/hexanes (1:3) as eluant to afford 0.043 g (61%) of **6** as a yellow oil. IR ($CDCl_3$) 2918, 1696, 1629; ^1H NMR (360 MHz, $CDCl_3$) δ 7.33–7.32 (t, J=3.6 Hz, 2H), 2.55–2.54 (m, 4H), 2.41–2.37 (m, 4H), 2.37 (s, 4H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 210, 157.8, 145.3, 34.5, 26.5, 22.8. HRMS (EI) calcd for $C_{12}H_{14}O_2$: 190.1107, found: 109.1108.

4.4. 3-Methyl-2-[2-(2-methyl-6-oxocyclohex-1-enyl)-ethyl]cyclohex-2-enone [1]

A solution of 0.12 g (0.55 mmol) of enone **4** in anhydrous ether (1 mL) was added dropwise to 0.86 mL (1.4 mmol) of a 1.6 M solution of methyllithium in ether at −20 °C. The reaction mixture was stirred at this temperature for 4 h, and then quenched by the addition of saturated aqueous ammonium chloride and warmed to room temperature. The mixture was extracted with methylene chloride (3×10 mL) and the combined organic layers were dried with magnesium sulfate, filtered, and concentrated in vacuo. This crude alcohol was then dissolved in methylene chloride (1.2 mL) and added to a stirred suspension of 0.18 g (0.83 mmol) of PCC in methylene chloride (1.2 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stir for 5 h. The reaction mixture was then concentrated in vacuo and purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluant to afford 0.060 g (44%) of **1** as white crystals. Mp=68 °C; IR ($CDCl_3$) 2954, 2892, 1657, 1627, 1381; ^1H NMR (360 MHz, $CDCl_3$) δ 2.34–2.28 (m, 8H), 2.23 (s, 4H), 1.98 (s, 6H), 1.89–1.87 (m, 4H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 198.8, 156.1, 135.0, 37.7, 32.7, 24.5, 22.2, 21.2. HRMS (EI) calcd for $C_{16}H_{22}O_2$: 246.1801, found: 246.1799.

4.5. 3-Methyl-2-[2-(2-methyl-5-oxocyclopent-1-enyl)-ethyl]cyclopent-2-enone [9]

A solution of 0.048 g (0.24 mmol) of enone **6** in anhydrous ether (1 mL) was added dropwise to 0.34 mL (0.54 mmol) of a 1.6 M solution of methyllithium in ether at −20 °C. The reaction mixture was stirred at this temperature for 4 h, and then quenched by the addition of saturated aqueous ammonium chloride and warmed to room temperature. The mixture was extracted with methylene chloride (3×10 mL) and the combined organic layers were dried with magnesium sulfate, filtered, and concentrated in vacuo. This crude alcohol was then dissolved in methylene chloride (1.2 mL) and added to a stirred suspension of 0.090 g (0.41 mmol) of PCC in methylene chloride (1.2 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and then stirred for 5 h. The reaction mixture was then concentrated in vacuo and purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluant to afford 0.020 g (38%) of **9** as a yellow oil. IR ($CDCl_3$) 2917, 1693, 1644; ^1H NMR (360 MHz, $CDCl_3$) δ 2.45–2.42 (t, J=3.6 Hz, 4H), 2.37–2.33 (t, J=3.6 Hz, 4H), 2.03 (s, 4H), 1.99 (s, 6H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 209.4, 170.9, 158.0, 34.2, 31.5, 21.4, 17.1. HRMS (EI) calcd for $C_{14}H_{18}O_2$: 218.1454, found: 218.1453.

4.6. 3-Methyl-2-[2-(6-oxocyclohex-1-enyl)ethyl]-cyclohex-2-enone [8]

A solution of 0.11 g (0.50 mmol) of enone **4** in anhydrous THF (1 mL) was added dropwise to 0.21 mL (0.34 mmol) of a 1.6 M solution of methyllithium in ether at −20 °C. The reaction mixture was stirred at this temperature for 4 h, and then quenched by the addition of saturated aqueous ammonium chloride and warmed to room temperature. The mixture was extracted with methylene chloride (3×10 mL) and the combined organic layers were dried with magnesium sulfate, filtered, and concentrated in vacuo. This crude alcohol was then dissolved in methylene chloride (2.8 mL) and added to a stirred suspension of 0.091 g (0.42 mmol) of PCC in methylene chloride (2.8 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and then stirred for 5 h. The reaction mixture was then concentrated in vacuo and purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluant to afford 0.050 g (43%) of **8** as a yellow oil and 0.010 g (8%) of recovered **4**. IR ($CDCl_3$) 2928, 2866, 1707, 1669, 1628; ^1H NMR (360 MHz, $CDCl_3$) δ 6.68 (t, J=3.6 Hz, 1H), 2.41–2.25 (m, 8H), 2.03 (s, 4H), 1.96 (s, 3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 198.9, 156.2, 145.5, 135.0, 385, 37.8, 32.7, 28.5, 26.0, 24.5, 23.0, 22.2, 21.2. HRMS (EI) calcd for $C_{15}H_{20}O_2$: 232.1627, found: 232.1624.

4.7. General procedure for the reductive cyclization under electrochemical conditions

A solution of 2.75 g (16.6 mmol) of tetraethylammonium chloride in a mixture of acetonitrile and water (35 mL, 4:1 v/v) was added to a solution of 0.095 g (0.44 mmol) of **4** in acetonitrile (28 mL) in a beaker fitted with a rubber stopper with holes for the two electrode leads and an argon purge line. The solution was degassed by bubbling argon through for 45 min. A constant current of 0.18 amp was applied for 2 h using tin foil (2 cm square) as the sacrificial anode and platinum (2 cm square) as the cathode. The reaction mixture was then concentrated in vacuo and the residue was dissolved in 5% aqueous sodium chloride solution (60 mL). The aqueous layer was extracted with ether (3×30 mL). The combined organic layers were dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography using ethyl acetate/hexanes (1:3) as eluant to afford 0.060 g (62%) of **11** as a white crystalline solid.

4.8. General procedure for the reductive cyclization under samarium diiodide conditions

A solution of 9 mL (0.9 mmol) of samarium diiodide in THF was added dropwise to a mixture of 0.050 g (0.21 mmol) of **6**, 0.3 mL (1.68 mmol) of HMPA, and 0.1 mL of ethanol in 1 mL of THF. Following the completion of the addition, the reaction was quenched with 0.1 N HCl and extracted with ether (3×10 mL). The combined ether layers were dried with magnesium sulfate, filtered, and concentrated in vacuo. The resulting crude material was purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluant to afford 0.026 g (52%) of **13** as a white solid.

4.9. General procedure for the reductive cyclization under tributyltin hydride conditions

To 0.089 g (0.41 mmol) of **4** in a dry flask under argon were added 6.7 mg (0.041 mmol) of AIBN, 0.33 mL (1.2 mmol) of tributyltin hydride, and 4.1 mL of freshly distilled benzene. The resulting solution was degassed by bubbling argon through the solution for 20 min. The reaction mixture was then heated to reflux for 5 h. After cooling to room temperature, the reaction mixture was concentrated in vacuo. The resulting crude material was purified by flash chromatography using ethyl acetate/hexanes (1:3) as eluant to afford 0.050 g (56%) of **11** as a white solid.

4.9.1. Dodecahydrophenanthrene-1,8-dione [11]. White crystalline solid, mp=125 °C. IR ($CDCl_3$) 2928, 2859, 1698; ^1H NMR (360 MHz, $CDCl_3$) δ 2.37–1.25 (m, 20H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 211.9, 211.5, 211.2, 54.2, 53.8, 49.8, 49.6, 45.6, 42.8, 41.7, 41.3, 41.2, 39.2, 29.2, 28.4, 27.2, 26.1, 25.8, 23.7, 22.7, 22.1, 21.3, 21.1. HRMS (EI) calcd for $C_{14}H_{18}O_2$: 218.1454, found: 218.1457. Note that data are for the mixture of three stereoisomers.

4.9.2. 4a-Methyldodecahydrophenanthrene-1,8-dione [12]. Yellow oil. IR ($CDCl_3$) 2936, 2859, 1704; ^1H NMR (360 MHz, $CDCl_3$) δ 2.34–1.23 (m, 19H), 0.92 (s, 3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 215.0, 213.2, 60.3, 55.5, 52.3, 41.0, 35.8, 31.2, 29.6, 26.1, 24.3, 22.2, 21.1, 21.0, 19.8, 18.6, 15.5, 15.4, 14.1. HRMS (EI) calcd for $C_{15}H_{20}O_2$: 232.1627, found: 232.1630.

4.9.3. Dodecahydro-*as*-indacene-3,6-dione [13]. White crystalline solid, mp=65 °C. IR ($CDCl_3$) 2929, 1735; ^1H NMR (360 MHz, $CDCl_3$) δ 2.37–1.26 (m, 16H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 219.0, 218.2, 217.2, 53.1, 50.3, 47.8, 43.5, 42.8, 37.1, 35.1, 34.0, 26.2, 25.3, 23.4, 22.7, 22.2, 21.9, 18.9. HRMS (EI) calcd for $C_{12}H_{14}O_2$: 190.1107, found: 190.1109. Note that data are for the mixture of three isomers.

4.9.4. 8a,8b-Dimethyldecahydro-*as*-indacene-3,6-dione [14]. White crystalline solid, mp=105 °C. IR ($CDCl_3$) 2949, 2922, 2854, 1735; ^1H NMR (360 MHz, $CDCl_3$) δ 2.35–2.28 (m, 2H), 2.03–1.92 (m, 2H), 1.74–1.70 (m, 2H), 1.69 (s, 4H), 1.27–1.22 (m, 2H), 0.94 (s, 3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 219.7, 54.3, 42.4, 33.4, 29.3, 22.8, 20.3. HRMS (EI) calcd for $C_{14}H_{18}O_2$: 218.1454, found: 218.1454.

Acknowledgements

We thank the State University of New York at Binghamton and the Research Foundation for financial support of this work.

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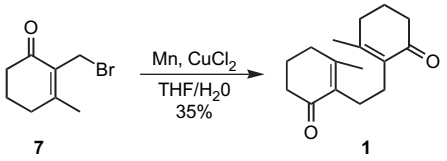

8. These reaction conditions have not been optimized and, given the appearance of polymerized material, a reduction in the reaction concentration may lead to improved isolated yields. At the same time, the use of other cathodes (Zn, Sn, Ni, Pb, Cu, glassy C) has been briefly explored and it either fails to afford any cyclization product or affords only trace amounts of the anticipated products.
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