Electrochemical Reduction of 1-Bromomethyl-2-oxocycloalkane-1-carboxylates at Silver Cathodes in Dimethylformamide: One-Carbon Ring-Expansion Reactions

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Abstract: Free-radical ring-expansion reactions were first explored almost 30 years ago, when Dowd and Choi demonstrated that ethyl cyclodecanone-6-carboxylic acid could be prepared in 71% yield by reduction of ethyl 1-(4-iodobutyl)-2-oxocyclohexane-1-carboxylate in refluxing benzene containing tri-n-butyltin hydride (Bu3SnH) in the presence of 2,2′-azobis(2-methylpropionitrile) (AIBN). Almost simultaneously, Beckwith and co-workers reported the synthesis of methyl cyclononanone-5-carboxylate via treatment of methyl 1-(4-bromomethyl)-2-oxocyclopentanone-1-carboxylate under similar conditions, but with tert-butylbenzene as solvent. Shown in Scheme 1 is a prototypical Dowd-Beckwith ring-expansion reaction.

Soon thereafter, another publication by Dowd and Choi provided additional examples of ring-expansion reactions, along with a discussion of mechanistic aspects of these processes. These early contributions were quickly followed by work that focused on ring-expansion reactions involving heterocyclic compounds, macrocyclic ketones, and cyclobutanones. Other research dealing with ring-expansion reactions has been carried out by Baldwin and co-workers, Boger and Mathivik, and by Wang and co-workers. Since the appearance of these early reports dealing with ring-expansion reactions, there has been an interest in achieving these transformations through the use of methodology that obviates the need for harsh reaction conditions and toxic reagents; Bu3SnH and its by-products have been shown to be harmful to many organisms. In a study by Sugi and Togo, that dealt with the reduction of α-haloalkyl cyclic β-keto esters to afford ring-expanded products, a comparison was made between the effectiveness of Bu3SnH and 1,1,2,2-tetraphenyldisilane (TPDS), each in the presence of AIBN, to promote the desired reactions. It was found that TPDS, which is an environmentally friendly reagent, is generally superior to Bu3SnH in its interactions with a variety of starting compounds. Nevertheless, although all of the foregoing strategies used to carry out ring-expansion reactions can succeed, these approaches almost inevitably involve the use of a radical initiator (AIBN) and another radical-producing reagent (Bu3SnH or TPDS) as well as relatively long reaction times and elevated temperatures.

Electrochemistry has been considered as a viable alternative to purely chemical reactions, and several groups have explored electrochemical reduction of a variety of compounds as an avenue to achieve ring expansions. Shono and co-workers investigated the constant-current reduction of a family of α-(ω-bromoalkyl) β-keto esters at lead cathodes in dimethylformamide (DMF) containing tetrathylammonium tosylate (TEATs) as supporting electrolyte, with trimethylsilyl chloride being added as a promoter; depending on the identity of the starting material, one-carbon ring-expanded products were obtained in yields ranging from 62–76%. Subsequent work involved the use of a pyridine complex of cobaloxime(I), electrified as a mediator at a platinum cathode in a methanol (MeOH) medium, to effect the reductive conversion of 2-(bromomethyl)-2-alkylcyclopentanones to their corresponding ring-expanded products in 51–74% yield. Kawafuchi and Inokuchi employed a zinc cathode in MeOH containing TEATs to carry out the constant-current generation of cobaloxime(I), which served as a catalyst for the electrosynthesis of cyclohexane-1,4-diones via reduction of 2-(bromomethyl)cyclopentane-1,3-diones. In our laboratory, nickel(II) salen, generated at glassy carbon electrodes in DMF containing tetrathylammonium tetrafluoroborate (TMABF4) by means of controlled-potential (bulk) electrolysis, was used to promote reductive three- and four-carbon ring-expansions of several 1-haloalkyl-2-oxocycloalkane-1-carboxylates; unfortunately, the yields of the desired products never exceeded 26%. Although each of the preceding four studies employed a different cathode material, a common feature of all was the need to use a promoter or catalyst to cause reductive cleavage of a carbon–halogen bond that initiates the ring-expansion process.

In recent years, silver has been found to be a potent electrode for the direct reduction of carbon–halogen bonds, and a great deal of

Scheme 1. An example of the classic Dowd–Beckwith ring-expansion reaction.
research in this area has appeared. A short list of seminal work on this topic is cited at the end of this paper; these references provide additional avenues to the literature. A relatively recent paper from our laboratory includes a reasonably comprehensive bibliography of other contributions in this field. One of the major attributes of silver is its superiority to both carbon and mercury for the electrochemical reduction of halogenated organic compounds. Reductive cleavage of a carbon–halogen bond at a silver electrode can occur at potentials as much as 1 V more positive than the same process at a carbon or mercury cathode.

In the present work, we have employed cyclic voltammetry and controlled-potential (bulk) electrolysis to examine the direct reductions of methyl 1-bromomethyl-2-oxocyclopentane-1-carboxylate (1) and ethyl 1-bromomethyl-2-oxocyclohexane-1-carboxylate (2) at silver cathodes in DMF containing 0.10 M TMABF$_4$ as supporting electrolyte. Ring-expanded products arising from the electrochemical reduction of 1 and 2 have been identified, characterized, and quantitated with the aid of gas chromatography (GC), gas chromatography–mass spectrometry (GC–MS), high-resolution mass spectrometry (HRMS), and $^1$H NMR spectrometry. For each starting compound, we found that four different electrolysis products are formed: (a) the desired ring-expanded product, (b) a dehalogenated product, (c) a dimeric species, and (d) a product, with an extended ester moiety, that has not been previously reported in an electrochemical study. To account for the formation of the four products, a set of pathways has been proposed that involves both radical and carbanion intermediates arising from electroreductive scission of the carbon–bromine bond of each substrate.

**Experimental**

**Reagents.**—Each of the following compounds (with purity indicated in parentheses) was purchased from Aldrich Chemical Company and was used without further purification: methyl 2-oxocyclopentane-1-carboxylate (95%), ethyl 2-oxocyclohexane-1-carboxylate (95%), hexamethylphosphoramide (99%), sodium hydride (60% suspension in mineral oil), diisomethane (99%), tri-n-butyltin hydride (97%), 2,2′-azobis(2-methylpropionitrile) (AIBN, 98%), iodomethane (99.5%), ethyl 2-cyclohexanoneacetate (97%), ethyl 2-(2-oxocyclohexyl)acetate, 5b, ethyl bromoaacetate (98%), n-dodecane (99%), and deuterium oxide (D$_2$O, 99%). Solutions for all electrochemical experiments were prepared with deionized water to remove sodium bicarbonate (and any impurities) and then placed in an oven set at 180°C for 30 min. Then the cathode was rinsed thoroughly in distilled, deionized water to remove sodium bicarbonate; this electrode has a thin layer of silver oxide on the surface. Furthermore, a thin layer of silver oxide may be formed during the use of an electrode, causing it to be partially deactivated; however, in practice, a brief cathodic polarization of the electrode after being introduced into the air-free electrolysis cell can be used to activate the electrode completely.

**Syntheses of methyl 1-bromomethyl-2-oxocyclopentane-1-carboxylate (1) and ethyl 1-bromomethyl-2-oxocyclohexane-1-carboxylate (2).**—We prepared methyl 1-bromomethyl-2-oxocyclopentane-1-carboxylate (1) and ethyl 1-bromomethyl-2-oxocyclohexane-1-carboxylate (2) according to a published procedure by Dowd and Choi, with some modification, that involves the addition of the following reagents: 12.9 g (90 mmol) of methyl 2-oxocyclopentane-1-carboxylate or 15.1 g (90 mmol) of ethyl 2-oxocyclohexane-1-carboxylate in 60 mL of dry tetrahydrofuran slowly to a stirred suspension of 3.8 g (108 mmol) of sodium hydride in 150 mL of dry tetrahydrofuran containing 19.4 g of hexamethylphosphoramidate at room temperature under argon. After each mixture was stirred for 1 h, 52 g (300 mmol) of dibromomethane was added, and the solution was heated at reflux temperature for 10 h. Then the mixture was poured into a separatory funnel containing 600 mL of diethyl ether; the organic layer was washed with five 100-mL portions of water, dried over anhydrous potassium carbonate, filtered, and concentrated. Finally, the residue was vacuum distilled to afford the desired product as a colorless oil; boiling points (0.1 mm) for 1 and 2 were 110–112°C and 117–119°C, respectively. For each of the two compounds, mass and $^1$H NMR spectra were in agreement with previously published data. Our mass spectrometric data for these two substrates are as follows: (a) for 1, $m/z$ (70 eV) 205 [M – OCH$_2$H$_3$]$^+$ (3%); 203 [M – OCH$_3$]$^+$ (3%); 155 [M – Br]$^+$ (100%); 123 [M – Br – CH$_2$OH]$^+$ (53%); 95 [M – Br – CO – CH$_2$OH]$^+$ (53%); HRMS (ESI) m/z: calculated for C$_{10}$H$_{13}$BrO$_2$ [M + H]$^+$ 234.9970, found 234.9967; (b) for 2, $m/z$ (70 eV) 219 [M – OC$_2$H$_5$]$^+$ (8%); 217 [M – OC$_2$H$_4$]$^+$ (8%); 183 [M – Br]$^+$ (100%); 137 [M – Br – C$_2$H$_5$OH]$^+$ (58%); 109 [M – Br – CO – C$_2$H$_5$OH]$^+$ (90%); HRMS (ESI) m/z: calculated for C$_{16}$H$_{23}$BrNaO$_2$ [M + Na]$^+$ 285.0102, found 285.0096.

**Syntheses of methyl 3-oxocyclohexane-1-carboxylate (3a) and ethyl 3-oxocycloheptane-1-carboxylate (3b).**—Preparation of the title compounds was accomplished via a slightly modified version of the procedure outlined by Dowd and Choi. To begin, we added AIBN (0.042 g, 0.24 mmol) to a stirred mixture of either 1 or 2 (2.6 mmol) in 300 mL of dry benzene containing tri-n-butyltin hydride (0.70, 2.6 mmol), and the resulting solution was refluxed at atmospheric pressure for 24 h. After the mixture was cooled to room temperature, the solvent was removed under reduced pressure to afford the crude product as a yellow oil, which was dissolved in dichloromethane (150 mL) and washed with five 20-mL portions of 10% aqueous potassium fluoride solution. Then the organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure, and the remaining oil was transferred onto a silica-gel column which was eluted with 2:1 hexane–ethyl acetate to afford each of the desired products. Purities of 3a and 3b were checked with the aid of GC and TLC. For each of the two title compounds, mass and $^1$H NMR spectra were in agreement with previously published data. Mass spectral data for the two species are as follows: (a) for 3a, $m/z$ (70 eV) 156 $^{12}$C$_2$H$_7$$^+$ (27%); 125 [M – OCH$_2$H$_3$]$^+$ (10%); 97 [M – CO – OCH$_3$]$^+$ (100%); HRMS (ESI) m/z: calculated for C$_{10}$H$_{15}$O$_2$ [M]$^+$ 156.0786, found 156.0780; (b) for 3b, $m/z$ (70 eV) 184 $^{12}$C$_3$H$_7$$^+$ (47%); 155 [M – C$_2$H$_5$]$^+$ (12%); 139
[M – OC6H5]⁺ (36%); 111 [M – COOC6H5]⁺ (100%); HRMS (ESI) m/z: calcld. for C10H12O3 [M⁺] 184.1099, found 184.1093.

Syntheses of methyl 1-ethyl-2-oxocyclopentane-1-carboxylate (4a) and ethyl 1-ethyl-2-oxocyclohexane-1-carboxylate (4b).— These compounds were prepared according to the same procedure employed for the syntheses of 1 and 2, except that dibromomethane was replaced by iodomethane for 4a and 4b. Identities of these compounds were verified on the basis of mass and ¹H NMR spectral data: (a) for 4a, m/z (70 eV) 156 [M⁺] (3%); 128 [M – C₂H₄]⁺ (100%); 113 [M – C₆H₅O]⁺ (45%); 101 [M – C₃H₃O]⁺ (27%); 69 [M – C₂H₃O]⁺ (50%); ¹H NMR (400 MHz, CDCl₃) δ 1.32 (s, 3H); 1.38–2.90 (m, 6H); 3.71 (s, 3H); HRMS (ESI) m/z: calcld. for C₁₀H₁₆O₃ [M⁺] 184.1099, found 184.1093.

Synthesis of methyl 2-(2-oxocyclopentyl)acetate (5a).— This compound was prepared according to a procedure outlined by Teixeira and co-workers, and its ¹H NMR spectrum matched that which was previously reported. Mass spectrometric data for this substrate are as follows: m/z (70 eV) 156 [M⁺] (44%); 124 [M – CH₃OH]⁺ (100%); 113 [M – C₆H₅O]⁺ (32%); 97 [M – CO₂CH₃]⁺ (44%); 83 [M – C₆H₅CH₂O]⁺ (46%); HRMS (ESI) m/z: calcld. for C₁₀H₁₄O₂ [M⁺] 157.0865, found 157.0866; (b) for 4b, m/z (70 eV) 184 [M⁺] (99%); 153 [M – OCH₃]⁺ (5%); 142 [M – C₂H₄]⁺ (13%); 110 [M – CH₃CH(OH)CH₂]⁺ (100%); ¹H NMR (400 MHz, CDCl₃) δ 1.28 (s, 3H); 1.42–2.53 (m, 8H); 4.20 (q, J = 7.2 Hz, 2H); HRMS (ESI) m/z: calcld. for C₁₀H₁₆O₃ [M⁺] 184.1099, found 184.1099.

Identifications of dimeric products (6a and 6b).— With the aid of GC–MS and GC–HRMS, the two dimeric species were identified as dimethyl 1,1′-(ethane-1,2-diyl)bis(2-oxocyclopentane-1-carboxylate) (6a) and diethyl 1,1′-(ethane-1,2-diyl)bis(2-oxocyclohexane-1-carboxylate) (6b), which arise from electrochemical reduction of 1 and 2, respectively. Mass spectral data for these two compounds are as follows: (a) for 6a, m/z (70 eV) 310 [M⁺] (trace); 250 [M – 60]⁺ (6%); 190 [M – 120]⁺ (9%); 170 [M – 140]⁺ (12%); 155 [M – 155]⁺ (44%); 138 [M – 172]⁺ (62%); 123 [M – 187]⁺ (100%); 95 [M – 215]⁺ (83%); 67 [M – 243]⁺ (57%); 55 [M – 255]⁺ (30%); HRMS (ESI) m/z: calcld. for C₁₆H₂₆O₄ [M + H⁺] 311.1495, found 311.1486 and (b) for 6b, m/z (70 eV) 366 [M⁺] (1%); 321 [M – 45]⁺ (4%); 293 [M – 73]⁺ (9%); 184 [M – 182]⁺ (80%); 155 [M – 211]⁺ (100%); 109 [M – 257]⁺ (76%); 81 [M – 285]⁺ (81%); 67 [M – 299]⁺ (10%); 55 [M – 311]⁺ (10%); 41 [M – 325]⁺ (6%); HRMS (ESI) m/z: calcld. for C₁₈H₂₈O₄ [M⁺] 366.2042, found 366.2045. Note that the mass spectral fragmentation patterns for 6a and 6b resemble those for dimeric products encountered in our earlier study.18

Separation, identification, and quantitation of electrolysis products.— At the end of each controlled-potential (bulk) electrolysis, the solvent–supporting electrolyte (catholyte) containing the products was partitioned between diethyl ether and water, after which the ether phase was dried over anhydrous sodium sulfate, concentrated under reduced pressure, and analyzed by means of gas chromatography (GC). For the GC measurements, the concentrated ether extracts were injected into an Agilent 7890A gas chromatograph, equipped with a flame-ionization detector and a 30 m × 0.32 mm capillary column (J & W Scientific) with a DB-5 stationary phase equipped with a flame-ionization detector and a 30 m × 0.32 mm capillary column (J & W Scientific) with a DB-5 stationary phase consisting of 5% phenylpolysiloxane and 95% methylpolysiloxane. Peak areas and gas chromatographic response factors for the various products were determined with respect to that of an internal standard (n-dodecane) added in a known amount to the solution prior to the start of each electrolysis; details about the procedure employed to evaluate the yield of each product are available in a previous publication.35 Gas chromatography–mass spectrometry (GC–MS) and gas chromatography–high resolution mass spectrometry (GC–HRMS) were used to confirm the identities of all products; for this work, we employed a capillary column identical to that described above in tandem with an Agilent 5973 inert mass-selective detector operating in electron-ionization mode (70 eV). We carried out GC–HRMS measurements with the aid of a gas chromatograph (Thermo Electron Corporation) equipped with a DB-5 capillary column and coupled to a MAT-95XP magnetic-sector mass spectrometer. To assess deuterium incorporation (from D₂O added to the solvent–supporting electrolyte), the same GC–MS system described above was used to compare mass spectral peak areas for deuterated and nondeuterated compounds (with corrections, as described elsewhere,36 for natural isotope abundance). Identities of synthesized starting materials and products were further confirmed with the aid of a 400-MHz Varian Inova NMR spectrometer.

Results and Discussion

Cyclic voltammatic behavior of 1-bromomethyl-2-oxocycloalkane-1-carboxylates (1 and 2) at silver cathodes.— Shown in Figure 1 is a cyclic voltammogram recorded at 100 mV s⁻¹ for the direct reduction of a 2.0 mM solution of ethyl 1-bromomethyl-2-oxocyclohexane-1-carboxylate (2) at a freshly polished silver electrode in oxygen-free DMF containing 0.10 M tetramethylammonium tetrafluoroborate (TMABF₄). A well-defined irreversible cathodic peak can be seen at –0.60 V, and a shoulder peak appears at –1.51 V just ahead of the final increase in current that signals reduction of the solvent–supporting electrolyte. We attribute the first cathodic peak to irreversible one-electron reduction of the carboxy–bromine bond and the second cathodic peak to reduction of ethyl 1-methyl-2-oxocyclohexane-1-carboxylate (4b), the latter being the debrominated product arising from reduction of 2.

We found that the cyclic voltammetric behavior of methyl 1-bromomethyl-2-oxocyclopentane-1-carboxylate (1), under conditions identical to those specified in the preceding paragraph, is very similar to that of 2. A pair of irreversible cathodic peaks was seen at –0.47 and –1.52 V that can be assigned, respectively, to one-electron reduction of the carboxy–bromine bond of 1 and then to reduction of methyl 1-methyl-2-oxocyclopentane-1-carboxylate (4a).

To confirm our assignments concerning the second cathodic peak for 1 and 2, we conducted separate cyclic voltammetric studies of the reductions of methyl 2-oxocyclopentane-1-carboxylate and ethyl 1. This result is significant because the 0.10 M solution of ethyl 1-bromomethyl-2-oxocyclohexane-1-carboxylate (2) at a freshly polished silver electrode (area = 0.071 cm²) in oxygen-free DMF containing 0.10 M tetramethylammonium tetrafluoroborate (TMABF₄). Scan goes from 0 to –1.6 to 0 V. Potentials are given with respect to a reference electrode consisting of a cadmium-saturated mercury amalgam, in contact with DMF saturated with both cadmium chloride and sodium chloride; this electrode has a potential of –0.76 V versus an aqueous saturated calomel electrode (SCE) at 25°C.

Figure 1. Cyclic voltammogram recorded at 100 mV s⁻¹ for reduction of 2.0 mM ethyl 1-bromomethyl-2-oxocyclohexane-1-carboxylate (2) at a circular, planar silver cathode (area = 0.071 cm²) in oxygen-free DMF containing 0.10 M TMABF₄. Scan goes from 0 to –1.6 to 0 V. Potentials are given with respect to a reference electrode consisting of a cadmium-saturated mercury amalgam, in contact with DMF saturated with both cadmium chloride and sodium chloride; this electrode has a potential of –0.76 V versus an aqueous saturated calomel electrode (SCE) at 25°C.
2-oxocyclohexane-1-carboxylate (the principal starting materials, respectively, for the synthesis of 1 and 2) at a silver cathode in DMF–0.10 M TMABF₄. For each of these starting materials, a single irreversible cathodic peak was observed that matched the respective second cathodic peaks for 1 and 2.

It is of particular interest to compare the above-described cyclic voltammetric behavior of 1 and 2 at a silver cathode to that observed in our previous investigation of the electrochemical reduction of a closely related compound—methyl 1-(4-bromobutyl)-2-oxocyclopentane-1-carboxylate (7)—at a glassy carbon electrode in the same solvent—supporting electrolyte. In our earlier work, the reduction of 7 at a glassy carbon electrode exhibited cathodic peak potentials of −1.58 V (reduction of the carbon–bromine bond) and of −1.90 V (reduction of the keto ester functionality). Thus, the use of silver as a cathode exerts a substantial electrocatalytic effect on the reductive cleavage of the carbon–bromine bonds of both 1 and 2, as reflected by peak potentials of −0.47 and −0.60 V, respectively, for the first stage of reduction of each of these compounds. These observations are fully consistent with our recent studies that reveal the relative ease of reduction of carbon–halogen bonds for numerous substrates at silver cathodes. On the other hand, it is surprising that reduction of the keto ester moieties of 1 and 2 is more facile at silver than at glassy carbon, a finding that does not seem to have been reported previously.

**Controlled-potential (bulk) electrolyses of 1-bromomethyl-2-oxocycloalkane-1-carboxylates (1 and 2) at silver gauze cathodes.** Compiled in Table I are coulometric data and product distributions pertaining to the exhaustive electroreduction of 5.0 and 10.0 mM solutions of compounds 1 and 2 at silver gauze electrodes in DMF containing 0.10 M TMABF₄; all electrolyses were performed at −1.00 V, a potential that ensured the complete reduction of each starting material. Each entry in Table I corresponds to the average of two separate experiments, which were found to be in close agreement. Coulometric n values for reduction of each compound are elevated slightly above 1, which indicates that both radical and carbanion intermediates are involved in the electrochemical reduction of 1 and 2; this point will be discussed further in the next section dealing with mechanism, when results of deuterium-labeling experiments with D₂O are presented. As indicated in Table I, each substrate was completely reduced, and four electrolysis products (identified and quantitated by means of GC and GC–MS) were obtained from each substrate.

From electrolyses of 5.0 mM solutions of 1 and 2, we obtained the desired ring-expanded products—methyl 3-oxocyclohexane-1-carboxylate (3a) and ethyl 3-oxocycloheptane-1-carboxylate (3b)—in yields of 92% and 55%, respectively. Doubling the initial concentrations of 1 and 2 afforded 3a in diminished yield (76%), whereas the yield of 3b was essentially unchanged (52%). Using tri-n-butyltin hydride and AIBN, Dowd and Chori synthesized 3a and 3b chemically in yields of 75% and 73%, respectively. Although the yields of these two compounds obtained in the present investigation seem to be more variable, there appear to be several advantages to the electrochemical methodology. Neither tri-n-butyltin hydride nor AIBN is required, which avoids the need to purify, handle, and dispose of toxic reagents. Other virtues of electrochemistry are shorter reaction times and milder conditions; typically, bulk electrolyses can be completed in no longer than 2 h and can be conducted at room temperature, as opposed to comparatively high temperatures and long reaction times for chemical syntheses.

Three other products arise from electrochemical reductions of 1 and 2 at silver cathodes. As indicated in Table I, dehalogenated compounds (4a and 4b) were found in very small yields (<4%). In some of their earliest work with 1 and 2, Dowd and Chori did not detect any 4a, whereas 4b was obtained in trace amounts. Dehalogenated compounds derived from electrolyses of 1 and 2 are formed in smaller amounts than the analogous products arising from electroreduction of methyl 1-(4-bromobutyl)-2-oxocyclopentane-1-carboxylate or ethyl 1-(3-bromopropyl)-2-oxocyclohexane-1-carboxylate, the latter two compounds giving the debrominated species in 8–14% yield; presumably, longer butyl and propyl radicals have a greater tendency to abstract a hydrogen atom from the solvent (DMF) than to engage in other reactions such as ring-expansion. Products 5a and 5b, formed in trace amounts and in yields ranging from 9–16%, respectively, appear to arise via an unexpected pathway whereby an initially generated alkyl radical attacks the ester moiety instead of the carbonyl site. Although this process has not previously been observed experimentally for either chemical or electrochemical investigations of ring-expansion reactions, a theoretical study by Ardura and Sordo introduces the possibility of this pathway, but concludes that its occurrence is disfavored energetically. Another pair of electrolysis products (6a and 6b) consists of dimeric compounds formed in yields of 9–22% and 24–32%, respectively. These yields are substantially lower than those obtained in our earlier electrochemical work, wherein dimers accounted for 52–83% of the starting material. A conceivable explanation for these differences might lie in how reduction of the various substrates was accomplished. In our previous investigation, nickel(salen) (electrogenerated at a glassy carbon cathode) was employed as a homogeneous-phase catalyst for reductive cleavage of carbon–halogen bonds, whereas the present work involves direct and heterogeneous reduction of a carbon–bromine bond at a silver electrode. Additionally, the size of the alkyl groups of starting materials used in these two studies has been different. Thus, in some future investigation, it might be of interest to carry out a side-by-side comparison in which the behavior of a broader range of substrates is examined by both of our electrochemical strategies.

**Mechanistic features of the reduction of 1-bromomethyl-2-oxocycloalkane-1-carboxylates (1 and 2).** Shown in Scheme 2 is

### Table I. Coulometric data and product distributions for direct reduction of 1-bromomethyl-2-oxocycloalkane-1-carboxylates at silver gauze cathodes held at −1.00 V in DMF containing 0.10 M TMABF₄.

| Compound (mM) | 1 | 2 | 3a | 3b | 4a | 4b | 5a | 5b | 6a | 6b | Total (%) |
|--------------|---|---|----|----|----|----|----|----|----|----|----------|
| 1 (5)        | 1.26 | ND | 92 |   | TR |   | TR | 9  |   |  101 |
| 1 (10)       | 1.26 | 1  | 76 |   | 1  |   | TR | 22 |   |  99 |
| 2 (5)        | 1.12 | ND | 55 |   | 3  |   | 9  | 32 |   |  99 |
| 2 (10)       | 1.18 | 1  | 52 |   | 4  |   | 16 | 24 |   |  97 |

*Yield expressed as the percentage of starting material incorporated into each product; 1 = methyl 1-bromomethyl-2-oxocyclopentane-1-carboxylate; 2 = ethyl 1-bromomethyl-2-oxocyclohexane-1-carboxylate; 3a = methyl 3-oxocyclohexene-1-carboxylate; 3b = ethyl 3-oxocycloheptane-1-carboxylate; 4a = methyl 1-methyl-2-oxocyclopentane-1-carboxylate; 4b = ethyl 1-methyl-2-oxocyclohexane-1-carboxylate; 5a = methyl 2-(2-oxocyclopentyl)acetate; 5b = ethyl 2-(2-oxocyclohexyl)acetate; 6a = dimethyl 1,1′-(ethane-1,2-diyl)bis(2-oxocyclopentane-1-carboxylate); 6b = diethyl 1,1′-(ethane-1,2-diyl)bis(2-oxocyclohexane-1-carboxylate). |
*a* Yield expressed as the percentage of starting material incorporated into each product; 1 = methyl 1-bromomethyl-2-oxocyclopentane-1-carboxylate; 2 = ethyl 1-bromomethyl-2-oxocyclohexane-1-carboxylate; 3a = methyl 3-oxocyclohexene-1-carboxylate; 3b = ethyl 3-oxocycloheptane-1-carboxylate; 4a = methyl 1-methyl-2-oxocyclopentane-1-carboxylate; 4b = ethyl 1-methyl-2-oxocyclohexane-1-carboxylate; 5a = methyl 2-(2-oxocyclopentyl)acetate; 5b = ethyl 2-(2-oxocyclohexyl)acetate; 6a = dimethyl 1,1′-(ethane-1,2-diyl)bis(2-oxocyclopentane-1-carboxylate); 6b = diethyl 1,1′-(ethane-1,2-diyl)bis(2-oxocyclohexane-1-carboxylate).

*Species was not detected.*

*A trace (≤1%) of the species was detected.*
a set of mechanistic pathways for the reduction of 1 and 2 that can account for the various electrolysis products. In the first step, irreversible one-electron reductive cleavage of the carbon–bromine bond of each compound results in the formation of radical intermediate 8 [Reaction 1]. Since the coulometric $n$ value is relatively close to 1 (Table 1), we conclude that this process dominates the electrochemistry of 1 and 2. As 8 is produced, it can engage in several follow-up reactions. Most importantly, 8 can undergo the desired reaction which entails radical attack on the carbonyl moiety to form a transient cyclopropyl alkoxy radical species that quickly opens to give the ring-expanded intermediate 9, which subsequently gains a hydrogen atom from the solvent (DMF) to yield $3a$ or $3b$ [Reaction 2]. Alternatively, before occurrence of the ring-expansion reaction, 8 can accept a hydrogen atom from the solvent to give $4a$ or $4b$ [Reaction 3], or 8 can be further reduced to a carbanion that is protonated by residual water ($\sim 40$ mM) in the solvent–supporting electrolyte to form $4a$ or $4b$ [Reaction 4]; however, in view of the results listed in Table 1, neither of these processes is significant. It is conceivable that 9 could be further reduced and protonated to yield $3a$ or $3b$ [Reaction 5]; however, we regard this process as no more important than reduction of 8. To account for the appearance of relatively small amounts of $5a$ and $5b$, we propose that primary alkyl radical 8 attacks the ester moiety (instead of the carbonyl site) to give a different cycloalkyl alkoxy radical intermediate that rapidly reopens to form 10 which leads (after hydrogen-atom abstraction from the solvent) to $5a$ or $5b$ [Reaction 6]. Self-coupling of 8 leads to a dimeric product ($6a$ or $6b$) [Reaction 7]. Finally, radical 10 could undergo one-electron reduction, followed by protonation, to form $5a$ or $5b$ [Reaction 8]; again this event is unlikely.
Table II. Deuterium ion incorporation into various products formed from direct electrolysis of 5.0 mM solutions of methyl 1-bromomethyl-2-oxocyclopentane-1-carboxylate (1) or ethyl 1-bromomethyl-2-oxocyclohexane-1-carboxylate (2) at a silver gauze cathode held at −1.00 V in DMF containing 0.10 M TMABF4 and 50 mM D2O.

| Product                                      | Deuterium incorporation (%) |
|----------------------------------------------|----------------------------|
| methyl 3-oxocyclohexane-1-carboxylate (3a)   | 20                         |
| ethyl 3-oxocycloheptane-1-carboxylate (3b)   | 15                         |
| ethyl 1-methyl-2-oxocyclohexane-1-carboxylate (4b) | 14                  |
| ethyl 2-(2-oxocyclohexyl)acetate (5b)       | 10                         |

Reactions 4, 5, and 8 involve the one-electron reduction of a radical intermediate (8, 9, and 10, respectively) to generate a carbanion that is subsequently protonated by adventitious water in the system. Evidence for the minor participation of carbanion intermediates in forming the various electrolysis products was obtained from a series of experiments involving electrochemical reduction of 5.0 mM solutions of 1 or 2 at silver gauze cathodes held at −1.00 V in DMF containing 0.10 M TMABF4 and 50 mM D2O. Listed in Table II are the percentages of deuterium incorporation (determined with the aid of GC–MS experiments) in products 3a, 3b, 4b, and 5b. In general, the percentage of deuterium found in these four products ranged from 10–20%. These results are in remarkable accord with the coulometric values and product distributions compiled in Table I. For example, consider the first entry in Table I, for which the average yields of 3a and 6a were 92% and 9%, respectively; if 20% of the 3a resulted from a two-electron process, the predicted coulometric n value should have been 1.09, whereas the tabulated n value is 1.26. Similarly, for the third entry in Table I, the predicted n value should have been 1.09, whereas the tabulated n value is 1.12.

Conclusions

In this work, we have investigated the direct electrochemical reductions of methyl 1-bromomethyl-2-oxocyclopentane-1-carboxylate (1) and ethyl 1-bromomethyl-2-oxocyclohexane-1-carboxylate (2) at silver cathodes in dimethylformamide (DMF) containing 0.10 M tetramethylammonium tetrafluoroborate (TMABF4). Our goal was to cleave electrolytically the carbon–bromine bond of each compound via a one-electron process to form a radical intermediate that undergoes a ring-expansion reaction to afford methyl 3-oxocyclohexane-1-carboxylate (3a) and ethyl 3-oxocycloheptane-1-carboxylate (3b), respectively. Using initial concentrations of 1 and 2 at the 5.0 mM level, we obtained 3a and 3b in respective yields of 92% and 55%. Our approach avoids the use of (a) classic reagents (tri-n-butyltin hydride and AIBN) at elevated temperatures for extended times, (b) a so-called promoter compound (trimethylsilyl chloride), or (c) electrogenerated electron-transfer mediators (cobaloxime(I) or nickel(I) salen). Moreover, the electrochemical strategy described in this study can be accomplished within 2 h at room temperature.

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