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Electrochemical Reduction of α,α'-Dibromo Ketones in Acetic Acid. A Convenient Synthetic Route to Highly Branched α-Acetoxy Ketones

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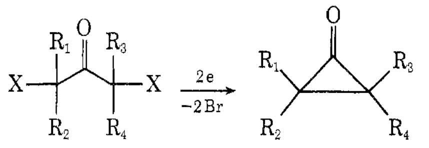
The electrochemical reduction of a number of α,α'-dibromo ketones (1) was carried out in acetic acid containing sodium acetate. From highly branched ketones, e.g., 2,4-dibromo-2,4-dimethyl-3-pentanone (6), the major products were α-acetoxy ketones in good yields and purity. From less highly substituted dibromo ketones, e.g., 4,6-dibromo-5-nonanone (17), the products were simply the parent (dehalogenated) ketones (3). A mechanistic scheme is presented to explain the results. It is believed that the first step is electrochemical reduction of 1 to an α-bromo enolate (33). Protonation of 33 by the solvent affords an enol allylic bromide (34), which can afford either the parent ketone, by ketonization and reduction of the resulting α-bromo ketone, or acetoxy ketone, by ionization to a hydroxyallyl cation and subsequent nucleophilic attack upon this cation by acetate ion. Substituent effects upon these competing processes are discussed.

The chemistry of α,α'-dibromo ketones (1) is as rich and diversified as one would expect for such highly functionalized substances.[2] We became interested in the electrochemical behavior of this class of compounds as an outgrowth of our studies on the electrolytic reductive cyclization of 1,3-dibromoalkanes to cyclopropanes.[3] It was natural to inquire into the feasibility of conversion of dibromo ketones 1 into cyclopropanones 2, i.e.

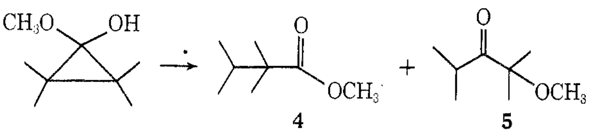


1, X = Br

3, X = H

2

If feasible, we expected that this might prove to be a very general route to cyclopropanones, since a wide variety of substances 1 are available by acid-catalyzed dibromination of the parent ketones (3). Our initial foray into this field showed that 2,4-dibromo-2-methyl-3-pentanone (1, $R_1 = R_2 = CH_3$; $R_3 = R_4 = H$) is indeed converted into the corresponding cyclopropanone when electrolyzed in acetonitrile at room temperature.[4] Because of the instability of cyclopropanones under the electrolysis conditions, it proved more convenient to carry out the electrolyses in methanol, by which means it was possible to trap tetramethylcyclopropanone as its methyl hemiketal by electrolysis of the corresponding dibromide. This hemiketal is itself somewhat thermally labile, however, slowly decomposing to an ester (4) and a ketone (5).



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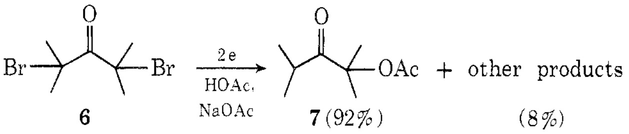
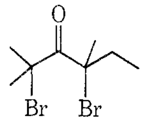
Because this decomposition promised to afford complex mixtures of products from unsymmetrical dibromo ketones, we were interested in an alternate method of intercepting intermediates in the electroreduction of dibromo ketones. We therefore carried out a preliminary electrolysis of 2,4-dibromo-2,4-dimethyl-3-pentanone (6) in acetic acid containing sodium acetate. This reaction afforded 2-acetoxy-2,4-dimethyl-3-pentanone (7) as the major product in quite good yield, along with several minor products. With



6 7 (92%) (8%)

this interesting result in hand, we carried out an extensive study of the electrochemical reduction of 6 and ten other dibromo ketones (8–17) under these conditions. We report



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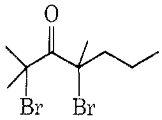

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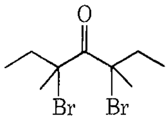

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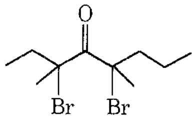

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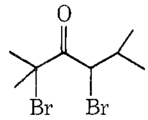

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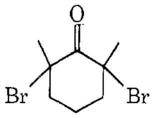

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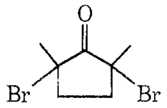

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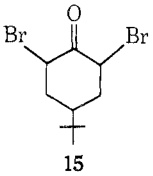

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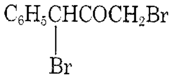
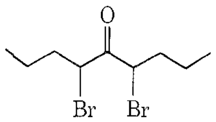


$C_6H_5\underset{\displaystyle Br}{\underset{|}{C}}HCOCH_2Br$

16



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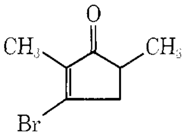
herein the results of that study, which clarify the mechanism of formation of **7** from **6** and demonstrate the scope and synthetic utility of the reaction.

Synthesis and Spectra of Dibromo Ketones. The bromination procedure of Claesson and Thalen[5] (bromine, ketone, aqueous HBr, 60°, no solvent) proved of general utility and was used for the synthesis of most of the dibromo ketones. This procedure failed notably in the case of **14**, which proved to be labile under the conditions of the Claesson–Thalen procedure. It is possible to obtain **14** in 89% yield (after distillation) by bromination in carbon tetrachloride at 0°, but upon standing at room temperature for several hours it decomposes with evolution of hydrogen bromide and bromine to afford a mixture whose principal component is 3-bromo-2,5-dimethylcyclopentenone (**18**). The structure of **18** follows from its mass spectrum [*m/e* 190, 188, 175, 173, and 109 (base peak)], uv spectrum (max 243 nm, log ϵ 4.09, in 95% EtOH), ir spectrum (5.85 and 6.10 μ), and NMR spectrum [d, τ 8.83 (J = 7 Hz); t, τ 8.22 (J = 2 Hz); m, τ 6.6–7.7; relative areas 3:3:3]. The long-range five-bond coupling of the allylic methyl and methylene groups has precedent in other cyclopentenone spectra;[6] coupling constants in such cases are generally ca. 2 Hz. The formation of **18** from **14** presumably involves dehydrobromination, acid-catalyzed debromination, addition of molecular bromine, and final dehydrobromination, i.e.



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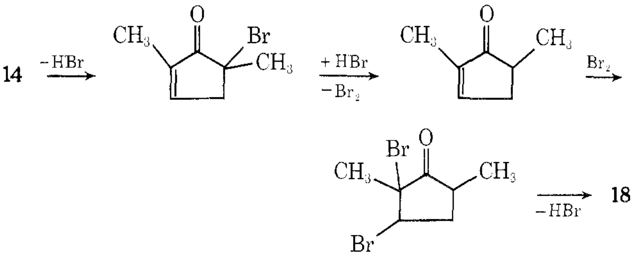
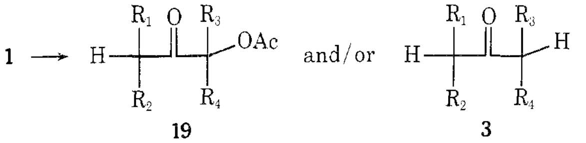


or a variant of this sequence.[7] 2,6-Dibromo-2,6-dimethylcyclohexanone (**13**) is somewhat labile to acid also, and probably undergoes a similar decomposition sequence, but the products of decomposition were not characterized.

The NMR spectra of several of the ketones displayed features worthy of comment here. The spectrum of **10** exhibited two peaks of almost equal height at τ 7.83 and 7.93, one presumably due to the α-methyl groups of the *dl* diastereomer and the other due to the meso diastereomer; the upfield methyl triplets at ca. τ 9 are also doubled. Presumably this indicates a ca. 1:1 mixture of diastereomers. In dibromide **11**, on the other hand, two doublets in ca. 60:40 ratio are observed at τ 7.85 and 7.93, with apparent spacings of 1.2 and 1.0 Hz, respectively. These doublets presumably are associated with the nonequivalent α-methyl groups of the erythro and threo isomers of **11**. A number of the dibromo ketones also exhibit effects associated with diastereotopic methylene and/or methyl groups. Thus, the methylene protons of **16** dxhibit an AB pattern at τ 5.85 and 6.99 (J = 13.0 Hz), and **12** exhibits two pairs of diastereotopic methyl groups: a downfield pair of singlets at τ 7.94 and 8.12 for the *gem*-dimethyl group adjacent to the carbonyl and an upfield pair of doublets (J = 6.5 Hz) at τ 8.80 and 8.96 for the terminal isopropyl group. Other features of the various NMR spectra, including other examples of such effects, are presented in the Experimental Section.

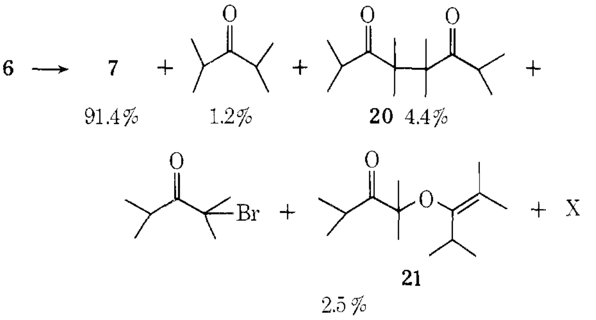
General Characteristics of the Electrochemical Reductions. The electrochemical reductions were carried under standard conditions: acetic acid containing 1.0 M sodium acetate, mercury cathode, 25°C, controlled potential. A few experiments were carried out under other conditions, and will be referred to at the appropriate points in the ensuing discussion. The results of the various electrolyses are summarized in Table I. The major overall reaction may be described in very general terms as



19 **3**

though some side products are formed, usually in low yield (see the column headed "Other" in Table I). The yields of α-acetoxy ketones are generally very good when the starting dibromo ketone is highly branched (**6**, **8**–**12**); reduction to the parent ketone was observed with dibromo ketones **15**–**17**. We will return to this mechanistic dichotomy later, after discussion of the individual electrolyses.

2,4-Dibromo-2,4-dimethyl-3-pentanone (6). Only in the case of **6** were attempts made to identify all of the products of the electrolysis. Except for an unidentified trace product, these attempts were successful; the reaction stoichiometry is shown in eq 1. Acetoxy ketone **7** was identified by comparison with an authentic sample prepared by lead tetraacetate oxidation of diisopropyl ketone.[8,9] The mass spectrum of **7** exhibited features characteristic of all of the acetoxy ketones obtained in our study. Major fragments were observed at *m/e* 172 (parent), 129, 101, 71, 59, and 43 (base). Cleavage of bonds 1 and 2 produces the



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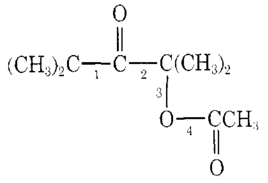


$$(CH_3)_2C\underset{1}{—}\overset{O}{\overset{\|}{C}}\underset{2}{—}C(CH_3)_2\underset{3}{—}O\underset{4}{—}\underset{\overset{\|}{O}}{C}CH_3$$

peaks at *m/e* 129, 101, 71, and 43 (the 43 peak is also formed by cleavage of bond 4). The peak at *m/e* 59 arises by cleavage of bonds 2 and 4 with concomitant hydrogen abstraction to afford a C_3H_7O fragment. This is a characteristic feature of all α-acetoxy ketones isolated (except **30**, which has an alternate decomposition path available), and proved to be very useful in locating the position of the acetoxy group when isomeric acetoxy ketones were isolated. For convenience in subsequent discussions we will refer to

Table I
Electrochemical Reduction of Dibromo Ketones in Acetic Acid–Sodium Acetate[a]

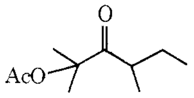
		Relative yields, %					
Dibromide	n[b]	α-Acetoxy ketone (19)	Registry no.	Parent ketone (3)	Registry no.	Other[c]	Total yield, %[d]
6	2.18	91.9	17346-16-6	1.2	21980-75-6	6.9[e]	78
6 (cce)[f]	2.49	94.0		1.0		5.0[g]	83
8	2.21	~98[h]	56829-62-0	~1[h]	56829-69-7	~1[h]	85
9	1.98	90.6	56829-63-1	0.6	56829-70-0	8.8	85
10	2.12	89.6	56829-64-2	4.1	56829-71-1	6.3	82
11	2.07	94.7	56829-65-3	0.2	56829-72-2	5.1	86
12	2.10	76.6	56829-66-4	14.7	56829-73-3	8.7	73
13	2.21	59.1	56829-67-5	2.4	56829-74-4	38.5	68
14	1.48	0	56829-68-6	2.9	1888-57-9	56.0[i]	74
15	[j]	1	52113-92-5	99	98-53-3	0	90
16	[j]	0	54210-98-9	100	103-79-7	0	85
17	[j]	0	3473-24-3	100	502-56-7	0	90

[a] Mercury cathode, 25°C, −1.80 V (vs. Ag/0.1 $AgClO_4$ in HOAc). [b] Number of faradays consumed per mole of starting dibromide. [c] Side products not identified except where noted. [d] Calculated relative to the major product. [e] 4.4% 20, 25% other (see text). [f] Constant current electrolysis. [g] 2.70% 20, 2.3% other. [h] Starting material was a ca. 55:45 mixture of 8 and the corresponding monobromide; the actual yields were 55% acetoxy ketone, 44.7% parent ketone, and 0.3% "other". [i] 43% 32, 13% "other". [j] Not measured.

this fragmentation pattern as "double cleavage". Observation of a metastable peak in this mass spectrum at apparent m/e 39.2 ($M_1 \rightarrow M_2$; $M_1 = 129$, $M_2 = 71$; $M_1 - M_2 = 58$) enables us to assign the sequence of events leading to the peak at 59 as initial cleavage of bond 4, subsequent cleavage of bond 2 to generate a C_3H_6O fragment, and finally hydrogen abstraction by the latter fragment.

Dimer **20** was identified by comparison with an authentic sample prepared by the method of Hoffmann.[10] Structure **21** is tentatively assigned to one of the trace (<1%) products of the electrolysis on the basis of its mass spectrum (m/e 226, 183, 157, 114, 113, 71, 43; calcd for $C_{14}H_{26}O_2$, 226) and NMR spectrum (singlet τ 8.67, multiplets at τ 7.22 and 8.96). It was demonstrated that control of the cathode potential is unnecessary in these electrolyses by carrying out a constant current electrolysis of **6**, which afforded **7** in 83% (crude) yield; distillation afforded **7** of 97% purity (VPC). Thus the electrolysis does not require sophisticated equipment; in fact, the constant current electrolysis was carried out in an open beaker rather than the standard closed electrochemical cell. Temperature control is necessary, however: in an unthermostatted cell the temperature rose to 55° because of current dissipation, and the proportion of **20** in the product rose to over 10%.

2,4-Dibromo-2,4-dimethyl-3-hexanone (8). In this and subsequent electrolyses the products other than acetoxy ketones and parent ketones were not characterized. Reduction of **8** afforded an acetate fraction constituting 98% of the products from **8**, after correction for the presence of ca. 45% monobromo ketone[11] in the dibromo ketone; the monobromo ketone is reduced cleanly to parent ketone.[12] The acetate fraction is an inseparable mixture of 2-acetoxy-2,4-dimethyl-3-hexanone (**22**) and 4-acetoxy-2,4-dimethyl-3-hexanone (**23**); the fact that it is a mixture is demonstrated by its NMR spectrum [two singlets in a ratio of 43:57 at τ 7.93 and 7.95 [$-OCOCH_3$)] and mass spectrum, which exhibited major fragments at 186 (parent), 143, 115, 101*, 85*, 73, 71, 59*, 57*, and 43 (base). (An asterisk next to a mass number denotes a fragment uniquely characteristic of **22**). The peaks at 59* and 73 arise from the "double cleavage" (see above) of **22** and **23**, respectively; the other peaks correspond to cleavage adjacent to carbonyl groups as also observed with **7**.



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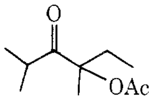

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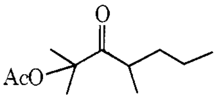
2,4-Dibromo-2,4-dimethyl-3-heptanone (9). The acetoxy ketone fraction from **9** accounted for 90.6% of the total product. This fraction was separable by VPC into a 62:38 mixture of 2-acetoxy-2,4-dimethyl-3-heptanone (**24**) and 4-acetoxy-2,4-dimethyl-3-heptanone (**25**). The mass spectra of **24** and **25** have several peaks in common: m/e 200 (parent), 157, 71, and 43, corresponding to cleavages adjacent to carbonyl groups. In addition, **24** has peaks at m/e 101, 99, and 59, while **25** has peaks at m/e 129 and 87. The peaks at m/e 59 for **24** and 87 for **25** are due to the so-called "double cleavage" and uniquely characterize the point of attachment of the acetoxy group in these compounds.



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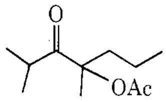

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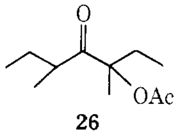
3,5-Dibromo-3,5-dimethyl-4-heptanone (10). The acetate fraction from **10** constituted 89.6% of the total product and was presumably an inseparable mixture of erythro and threo diastereomers of acetoxy ketone **26**. The ratio of the two (assuming both are present) could not be determined by NMR, since the acetyl and downfield α-methyl groups appear as singlets. The mass spectrum of **26** displays major fragments at m/e 200 (parent), 157, 143, 115, 85, 73, 57, and 43. Interpretation is straightforward by analogy with the spectra of the acetoxy ketones already discussed. Note particularly the fragment of m/e 73 corresponding to the "double cleavage" process; a metastable peak was observed at 46.2 ($M_1 \rightarrow M_2$; $M_1 = 157$, $M_2 = 85$, $M_2 - M_1 = 72$) also associated with this process (see the discussion of the mass spectrum of **7**).



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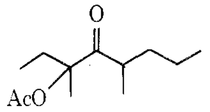
3,5-Dibromo-3,5-dimethyl-4-octanone (11). The acetate fraction from electrolysis of **11** constitutes 94.7% of the total product. It is a 59:41 mixture (separable by VPC) of 3-acetoxy-3,5-dimethyl-4-octanone (**27**) and 5-acetoxy-3,5-dimethyl-4-octanone (**28**). Each acetoxy ketone can



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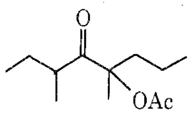

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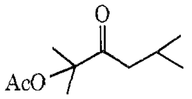
exist as two *dl* diastereomeric pairs, but neither ketone could be resolved into its respective diastereomers by VPC. The mass spectra are unexceptional [**27**, *m/e* 214 (parent)], 171, 115, 99, 73, 71, and 43; **28**, *m/e* 214, 171, 129, 87, 85, 57, and 43). The peaks at 73 and 87 in **27** and **28**, respectively, are due to the "double cleavage" process and permit the assignment of the acetoxyl group in the two isomers.

2,4-Dibromo-2,5-dimethyl-3-hexanone (12). Electrolysis of **12** under the standard conditions afforded an acetate fraction in distinctly lower yield (76.6%) and parent ketone in distinctly higher yield (14%) than with any of the dibromo ketones discussed thus far. We shall return to this significant point later. The acetate fraction consists of an inseparable mixture of 2-acetoxy-2,5-dimethyl-3-hexanone (**29**) and 4-acetoxy-2,5-dimethyl-3-hexanone (**30**). Analysis by NMR indicates an approximately 85:15 ratio of **29** to **30**. The mass spectrum of the mixture displays major fragments at *m/e* 186 (parent), 143, 115, 101*, 85*, 71, 59*, 43 (base), 42, and 41. (The peaks labeled with an asterisk denote fragments characteristic of **29**). The peak at *m/e* 59 and a metastable peak at *m/e* 50.5 are due to the "double cleavage" process of **29**. Interestingly, this process does not occur with **30**, since no major fragment is observed at *m/e* 73; instead, a strong peak is observed at *m/e* 71, i.e., cleavage between bonds 2 and 4 (see the numbering system under the discussion of **7**), followed by *loss*, not gain, of a hydrogen. Presumably the C_4H_8O fragment from **30** loses an α-hydrogen atom to give a carbonyl-containing fragment,[13] a process unavailable to the other acetoxy ketones. The other peaks in the mass spectrum are unexceptional—they arise *from* cleavage adjacent to various carbonyl groups.



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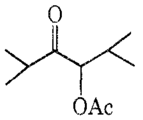

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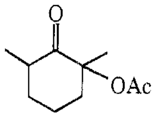
2,6-Dibromo-2,6-dimethylcyclohexanone (13). The acetate fraction from this electrolysis constituted a smaller fraction (59.1%) of the total product than in the case of the dibromo ketones already discussed. Unlike the case of **12**, however, the decrease in yield of acetoxy ketone was not associated with an increased yield of parent ketone (only 2.4%); rather, there were a number of side products in this electrolysis, formed in total yield of almost 40%. The acetate fraction consists of an 87:13 mixture of cis and trans isomers of 2-acetoxy-2,6-dimethylcyclohexanone (**31**), but it was not possible to determine from spectral data which is the major isomer. Major mass spectral peaks for each isomer occur at *m/e* 184 (parent), 141, 113, 71, and 43, and are consistent with mass spectra of cyclic ketones.[13] The side products were not identified (there are at least six in addition to the parent ketone, all with VPC retention times shorter than that of **31**), but our observation of metallic mercury in the trap during attempted preparative VPC suggests that at least one product is a thermolabile organomercurial,[14] and there is probably also some acid-catalyzed decomposition of **13** under the electrolysis as observed with **14** (see below).



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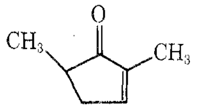
Other Electrolyses. Electrolytic reduction of 2,6-dibromo-4-*tert*-butylcyclohexanone (**15**), α,α'-dibromophenylacetone (**16**), and 4,6-dibromo-5-nonanone (**17**) resulted in clean conversion to the parent ketone in each case (though a trace, ca. 1%, of acetoxy ketone was obtained from **15**). Failure to obtain acetoxy ketones from dibromides **15**–**17** is consistent with the mechanism we believe these reactions to follow (see next section).

Electrolytic reduction of 2,5-dibromo-2,5-dimethylcyclopentanone (**14**) afforded 2,5-dimethylcyclopentenone (**32**) as the major product (43% yield). This product was characterized by NMR, ir, uv, and mass spectroscopy (see Experimental Section) and by its 2,4-dinitrophenylhydrazone, mp 194–195° (lit.[7] mp 194–194.5°). Apparently, under the acidic conditions of the electrolysis **14** is converted into **18**, which is subsequently dehalogenated in straightforward fashion[15] to **32**.



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Mechanistic Discussion. The results described herein are readily understood in terms of the mechanism presented in Scheme I. There is a great deal of evidence[15] that the electrochemical reduction of alkyl halides involves intermediate carbanions; hence the initial intermediate in the reaction sequence must be bromo enolate **33**. Such species have been established by Bordwell and coworkers as intermediates in the base-promoted reactions of bromo ketones.[16] (Indeed, much of Scheme I derives from the extensive studies by Bordwell et al. on the nature of such reactions). Although enolate **33** can be generated either by electrochemical reduction of a dibromo ketone (**1**) or by the action of base upon a monobromo ketone (**36**), the electrochemical reaction has the unique advantage that it may be carried out in acetic acid, where protonation of **33** ought to be rapid.[17] Hence under our conditions the observed chemistry is that of bromo enol **34**, not **33**. Protonation of **33** ought to occur faster on oxygen than on carbon;[18] hence we do not expect monobromo ketone **36** to be formed in any but very minor amounts at this stage. Ionization of the allylic bro-

Scheme I

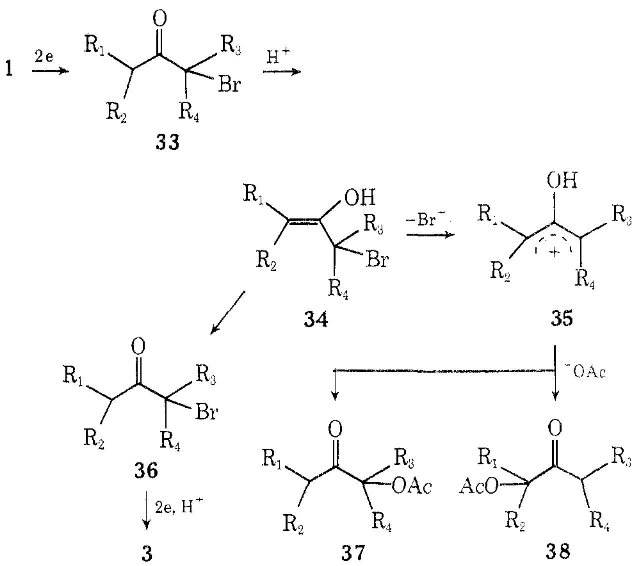


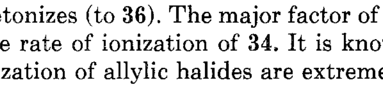
Table II

Compd	Relative solvolysis rate[a]	Compd	Relative solvolysis rate[a]
$CH_2{=}CHCH_2Cl$	1	$(CH_3)_2C{=}CHCH_2Cl$	1.5×10^7
$CH_3CH{=}CHCH_2Cl$	3.6×10^3	$CH_2{=}CHC(CH_3)_2Cl$	8×10^7
$C_6H_5CH{=}CHCH_2Cl$	5×10^5	$(CH_3)_2C{=}CHC(CH_3)_2Cl$	10^{15}[b]

[a] Formic acid. C. A. Vernon, *J. Chem. Soc.*, 423 (1954). [b] Estimated by the method of Vernon.[a]

mine of **34** to afford hydroxyallyl cation **35**, nucleophilic attack by acetate upon the latter,[19] and final ketonization will then afford a mixture of isomeric α-keto acetates **37** and **38**. Actually, it is known that monobromo ketones are reduced electrochemically to the parent ketones (**3**);[12] hence isolation of **3** in only very minor amounts (1–2%) from most of the dibromo ketones (**6**, **8–11**, and **13**) provides confirmation that the major site of protonation of **33** is on oxygen, and, further, that **34** is converted to **35** faster than it can tautomerize to **36**. Recall, however, that several dibromo ketones (**15–17**) are converted cleanly to the parent ketones under the electrolysis conditions, and that another (**12**) afforded a substantial quantity (ca. 15%) of parent ketone. It appears that the route to **3** can become predominant with certain structural types. We do not believe that branching occurs at the point of **33**, i.e., that in such cases protonation occurs on carbon. Rather, we believe that whether parent ketone **3** or acetoxy ketone (**37** and **38**) is formed depends upon the relative rates at which **34** ionizes (to **35**) or ketonizes (to **36**). The major factor of these two is probably the rate of ionization of **34**. It is known that the rates of ionization of allylic halides are extremely sensitive to alkyl substitution.[20] For example, the relative rates of solvolysis of a series of substituted allylic chlorides in formic acid show the effect clearly (Table II). Thus the bromo enols from the tetrasubstituted dibromo ketones **6**, **8–11**, and **13** ought to form far more highly stabilized hydroxyallyl cations than the bromo enols from **15**, **16**, or **17**, favoring therefore the path leading to α substitution.[21] The difference is apparently great enough that ionization of the bromo enols from ketones **15–17** is not competitive with ketonization. The bromo enol from trisubstituted ketone **12** displays intermediate behavior, as expected. The reaction between α,α'-dibromo ketones and zinc–copper couple in methanol[22] displays parallel behavior, in that increasing α-alkyl substitution favors α-substitution, but it is far less sensitive to alkyl substitution than is the electrochemical process.

The formation of diketone **20** as a by-product in the electrolysis of **6** is understandable in terms of Scheme I, by reduction of cation **35** ($R_1 = R_2 = R_3 = R_4 = CH_3$) to a hydroxyallyl radical (**39**), radical coupling to a bis enol, and



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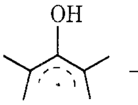
final ketonization to **20**. It is unlikely for steric reasons that **20** arises by coupling of **6** or **36** with **33**; also, were this the case, dimer formation would be more significant with the less substituted dibromo ketones, e.g., **16** or **17**. The other trace product of the electrolysis, tentatively assigned as **21**, is of less obvious origin. It might arise by O to C coupling of **39**, or might involve zwitterion **40**, the conjugate base of **35**.



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In general there seems to be no reason to suspect organomercurials[14] as significant intermediates in these reactions, although they may be minor products (cf. the discussion of by-products in the electrolysis of **13**). Indeed, **7** is still the major product when **6** is electrolyzed using a platinum cathode. Coulometric evidence (Table I) also supports the proposed mechanism: two faradays per mole of **1** are required to generate **33**,[15] and the subsequent reactions leading to acetoxy ketones consume no current.

Conclusions

Electrochemical reduction of highly substituted α,α'-dibromo ketones in acetic acid–sodium acetate affords α-acetoxy ketones in good yields and purity, and does not require sophisticated electrochemical equipment. From our inspection of the literature pertaining to the synthesis of such substances,[23] we believe that it is in fact the synthetic method of choice for highly branched α-acetoxy ketones. For example, preparation of **7** by the lead tetraacetate oxidation of diisopropyl ketone[8] affords in our hands a complex mixture including some bis-acetoxylated material, and less than 50% **7**. On the other hand, the electrochemical conversion of dibromo ketones to α-acetoxy ketones fails with less highly substituted systems, e.g., **15–17**, hence the electrochemical and conventional procedures[23] nicely complement each other. Mixtures of acetoxy ketones are formed from unsymmetrical dibromo ketones, though usually that isomer predominates in which the acetoxy group has entered the less hindered position (but note the predominance of **29** over **30** in the electrolysis of **12**). We plan to explore this point further, but it appears that the reaction will be of most synthetic utility with symmetrical ketones. No attempt was made to maximize yields in our experiments, but we expect that total yields would be higher if the electrolyses were carried out on a larger scale. Finally, we note that the mechanism outlined in Scheme I suggests that a wide variety of nucleophiles could in principle be substituted for acetate ion in this reaction. We plan to explore this possibility.[24,25]

Experimental Section

General. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian A-60A spectrometer in $CDCl_3$ relative to internal tetramethylsilane. Infrared (ir) spectra were recorded as 5.7% solutions (v/v) in CCl_4 on a Perkin-Elmer Model 457 spectrophotometer, and calibrated against a polystyrene reference. Ultraviolet (uv) spectra were recorded on a Perkin-Elmer Model 202 spectrophotometer and calibrated against a holmium oxide glass reference (279.4 nm). Gas chromatographic separations were carried out using a Varian Series 1700 dual column thermal conductivity instrument with temperature programmer. Electrolysis mixtures were analyzed using a 0.25 in. × 8 ft column packed with 5% Carbowax 6000 on Chromosorb G, with the temperature programmed from 100 to 220° at 15°/min. Isomeric acetates were separated on a 0.25 in. × 20 ft column of 5% diethylene glycol succinate (DEGS) on Chromosorb P, in the isothermal mode, at 120°. Mass spectra were recorded (70 eV) on a Perkin-Elmer Hitachi Model RMU-6L spectrometer and were calibrated against perfluorokerosene. Electrochemical experiments were carried out using a Princeton Applied Research Model 170 electrochemistry system.

Materials. Starting ketones were all purchased from the Aldrich Chemical Co. and used without purification. Reagent grade acetic acid was purified by successive treatments with potassium permanganate and triacetyl borate.[26] Reagent grade anhydrous sodium acetate was dried overnight at 150°.

Dibromo Ketones. The method of Claesson and Thalen[5] for dibromination of ketones was used except where noted. Where a literature reference does not appear in the following descriptions, the dibromo ketone is a new compound. Because of their slow decomposition with time, microanalyses were not obtained for such compounds, but their spectral properties, method of synthesis, and chemistry are all completely in accord with the assigned structures. They were distilled in vacuo as clear, colorless liquids before use.

2,4-Dibromo-2,4-dimethyl-3-pentanone (6) was obtained in 61% yield, bp 80° (5 mm) [lit.[5] bp 85–86.5° (10 mm)]; NMR singlet at τ 7.87.

2,4-Dibromo-2,4-dimethyl-3-hexanone (8) was obtained as a ca. 55.45 mixture of 8 and the corresponding isomeric monobromides (5), and was used as such.

2,4-Dibromo-2,4-dimethyl-3-heptanone (9) was obtained in 87% yield, bp 63° (0.6 mm). A distinctive feature of its NMR spectrum is the appearance of three downfield methyl resonances at τ 7.83, 7.87, and 7.93, two of them due to the diastereotopic methyl groups at C-2.

3,5-Dibromo-3,5-dimethyl-4-heptanone (10) was obtained in 62% yield, bp 68° (0.6 mm). For NMR spectrum see Discussion.

3,5-Dibromo-3,5-dimethyl-4-octanone (11) was obtained in 91% yield, bp 68° (0.3 mm). For NMR spectrum see Discussion.

2,4-Dibromo-2,5-dimethyl-3-hexanone (12) was obtained in 84% yield, bp 45° (0.3 mm) [lit.[27] 41° (1 mm)]. For NMR spectrum see Discussion.

2,6-Dibromo-2,6-dimethylcyclohexanone (13) was obtained in 72% yield, bp 64° (0.3 mm); it solidified in the refrigerator. Corey et al.[28] report mp 27–28° for the cis isomer. Singlets in the NMR at τ 7.98 and 8.08, ratio 85:15, suggest that our sample is a mixture of isomers.

2,5-Dibromo-2,5-dimethylcyclopentanone (14). To a solution of 0.54 g of 2,5-dimethylcyclopentanone in 10 ml of CCl_4 under nitrogen at 0° was added dropwise a solution of 0.5 ml of bromine in 10 ml of CCl_4. The orange color of the solution was discharged within 5 min after addition was complete. The solution was diluted with CCl_4, washed with saturated aqueous $NaHCO_3$, dried over magnesium sulfate, and evaporated at aspirator pressure to yield 1.16 g (89%) of a colorless oil, unstable at room temperature. Its NMR spectrum consisted of two broadened singlets at τ 7.6 and 8.0, relative areas 2:3. If this dibromide is allowed to stand overnight at room temperature, it decomposes, evolving both Br_2 and HBr. After extraction with ether, washing with sodium bisulfite and sodium bicarbonate, drying, and removal of solvent, a yellow oil was obtained. Analysis by VPC indicated a mixture of products. The major product was isolated by preparative VPC and was shown to be 3-bromo-2,5-dimethylcyclopentenone (18) (see Discussion).

Anal. Calcd for C_7M_9BrO: C, 44.47; H, 4.80. Found: C, 44.34; H, 4.79.

2,6-Dibromo-4-*tert*-butylcyclohexanone (15) was prepared by the method of Bordwell and Wellman.[29] The sample used was a mixture of stereoisomers.

1,3-Dibromo-1-phenylacetone (16)[30] was prepared by bromination of phenylacetone in acetic acid, bp 138° (1.8 mm). Its NMR spectrum consists of singlets at τ 2.63 and 4.20, and an AB quartet at τ 5.85 and 5.99 (J = 13.0 Hz), relative areas 5:1:2, respectively.

4,6-Dibromo-5-nonanone (17) was prepared by the method of Claesson and Thalen,[5] bp 70–75° (1 mm) [lit.[2c] 132–135° (20 mm)]. The NMR spectrum of this (presumably) *dl*-meso mixture exhibited a broad triplet (J = 7 Hz) near τ 5.2, in addition to the upfield alkyl absorptions.

Electrolysis of Dibromo Ketones. The electrolysis cell was of standard design.[31] The anode compartment and cell divider was a 25 × 150 mm unfired Vycor test tube immersed in the catholyte. The electrochemical cell was immersed in a Varian Model 9661-00 ultrasonic cleaner (which provided efficient stirring), filled with water and containing a copper coil and thermoregulator, both connected to a Haake Model F constant-temperature water circulator, and set to maintain the electrolysis cell at 25 ± 1°. The anolyte and catholyte solutions were both 1.0 M solutions of sodium acetate in acetic acid. The anode was a platinum gauze; the cathode was a mercury pool (ca. 10 ml of mercury). The reference electrode, constructed from heavy wall 5 m o.d. Teflon tubing closed on one end by a 3 mm o.d. plug of unfired Vycor, consisted of a silver wire immersed in a 0.1 M solution of $AgClO_4$ in acetic acid. Electrolyses of 10 mmol of dibromide were carried out at −1.8 V relative to this reference. (At this potential reduction of acetic acid is negligible). The electrolysis was terminated when the current had decayed to a constant value (ca. 2 mA). The catholyte was then separated from mercury and sodium bromide by filtration. Water (100 ml) was added, and the resulting solution was extracted with three 25-ml portions of CCl_4. The extracts were combined, washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, and evaporated at aspirator pressure to yield the crude product, which was then investigated by VPC. Spectral data were measured on samples purified by preparative VPC. [Satisfactory microanalyses (±0.4%) for all acetoxy ketones were submitted for review. Ed.]

Constant Current Electrolysis of 6. One electrolysis was carried out in an open beaker containing a mercury pool, 250 ml of NaOAc–HOAc solution, and the above-mentioned anode compartment. The solution was stirred magnetically and purged with nitrogen during the reduction. Temperature was not regulated, and rose as high as 55°C at one point. A constant current of 0.50 A was passed for 400 min for the electrolysis of 50 mmol of dibromo ketone. (This amount of current represents a 25% excess over the theoretical). The results of this experiment are described in the Discussion (cf. Table I).

Acknowledgments. Financial support was supplied by the National Science Foundation. Mr. Donald Albert measured the mass spectra. Undergraduates Jerry Segal and Joel Dixon examined the electrochemical behavior of **15** and **17**, respectively. We wish to acknowledge the prior work of Dirlam, Eberson, and Casanova in this area (ref 9b), although our ideas were developed independently.

Registry No.—**18,** 56829-75-5; **21,** 56829-76-6; **22,** 56829-77-7; **24,** 56829-78-8; **27,** 56829-79-9; **29,** 56829-80-2; *cis*-**31,** 56829-81-3; *trans*-**31,** 56829-82-4; **32,** 4041-11-6.

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(24) (a) We have recently found that **6** is converted to **7** cleanly and in high yield by the action of metallic mercury in acetic acid containing sodium acetate; the reaction is considerably slower than the electrode reaction, but affords **7** in purer form. We are exploring the scope and synthetic utility of this reaction. (b) Daniel Herr, unpublished research.

(25) A referee has suggested that those compounds affording parent ketones as product (**15–17**) might exhibit different *i–E* curves than those (e.g., **6**) affording acetoxy ketones. This is not the case: all dibromo ketones examined by us exhibit a single drawn-out *i–E* curve.[9b]

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Stereochemistry and Mechanism of Electrophilic Additions to Tricyclo[4.2.2.$0^{2,5}$]deca-3,7-diene Derivatives

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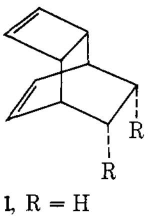
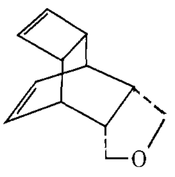
Electrophilic addition of iodine azide, mercuric acetate, nitrosyl chloride, and diborane to tricyclo[4.2.2.$0^{2,5}$]deca-3,7-diene derivatives **2**, **4**, and **5** is described. Reaction of iodine azide with diester **2** furnishes a syn azido iodide **6**. On the other hand, IN_3 addition to **4** and **5** in acetonitrile solvent results in transannular solvent participation and tetrazoles **8** and **10** are formed via Hassner–Ritter reaction. In methylene chloride solvent dienes **4** and **5** furnish the tetracyclic azido iodides **8** and **10**. Oxymercuration of **2**, **4**, and **5** with mercuric acetate yields the corresponding syn oxymercurials in high yield. The exclusive syn addition of IN_3 and $Hg(OAc)_2$ to the cyclobutene double bond of tricyclo[4.2.2.$0^{2,5}$]deca-3,7-dienes is interpreted in terms of the dominant role of twist strain theory. The long-range effects of substituents at C_9 and C_{10} on the reaction rates and product formation is also discussed.

Neighboring group participation by a distant double bond in carbocation reactions is now a well-established phenomenon.[2] The chemical reactivity of rigid molecules containing two isolated π bonds in favorable spatial orientation for transannular interaction provides a convenient and interesting route for generating a variety of polycyclic molecules of current interest. The addition of various electrophiles to several olefinic substrates, e.g., norbornadiene,[3] cyclic C_8,[4] C_9,[5] and C_{10}[6] 1,5-dienes, norbornadiene–cyclopentadiene adducts[7] and their chlorinated analogs (Isodrin–Aldrin series[8]), hexamethyl(Dewar benzene),[9] and 9,10-benzotricyclo[4.2.2.$2^{2,5}$]dodeca-3,7,9-triene,[10] has been investigated to elicit information about the nature of carbocation intermediates, proximity effects, transannular reactions, and ^1H NMR perturbations. Many of these reactions have found useful synthetic applications.[11,12] The tricyclo[4.2.2.$0^{2,5}$]deca-3,7-diene ring system 1 (R = H), readily available[13] from cyclooctatetraene via the diene synthesis, is endowed with a unique geometrical disposition of a strained cyclobutene double bond and a sterically shielded cyclohexene moiety, ideally suited for the study of transannular cyclizations and electrophilic additions. Furthermore, the variation of substituents at C_9 and C_{10} without altering the geometrical disposition of the double bonds provides an interesting variant for the study of long-range electronic effects. The addition of electrophiles to the dimethyl maleate adduct **2** of COT and its congeners has been studied by Reppe,[13] Nenitzescu,[14] and others[15,16] but no unambiguous structural assignments to the products were made. In a recent study, we[17] as well as others[18] have described the addition of halogens and pseudohalogens to **2** leading to the formation of tetracyclic lactones like **3** via a novel cross-type transannular cyclization. In continuation of these studies, we wish to describe here some interesting results of addition of iodine azide, mercuric acetate, diborane, and nitrosyl chloride to some derivatives of **1**. The additions of iodine azide and mercuric acetate have been found to be highly regio- and stereospecific syn additions and highlight the role of twist strain theory in electrophilic additions to strained olefins. The substrates selected for these studies were the diester **2**, ether **4**, and the dimethyl compound **5** in which the geometrical disposition of the double bonds and reacting site remains the same, while the availability of π electrons for participation by the C_7–C_8 double bond is altered owing to the presence of electron-withdrawing and -donating groups at C_9 and C_{10} endo position. The effect of this variation is distantly located substituents on the reaction rates and product formation is also discussed. The diolefinic substrates were prepared via a slight modification of literature procedures[14] and are described in the Experimental Section.



1, R = H
2, R = $\underset{\substack{\| \\ \mathrm{O}}}{\mathrm{C}}\mathrm{OCH_3}$
5, R = CH_3



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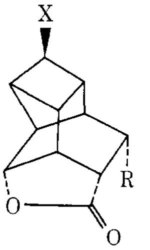

3, X = Cl, Br, etc.;
R = $\underset{\substack{\| \\ \mathrm{O}}}{\mathrm{C}}\mathrm{OCH_3}$

Iodine Azide Additions.[19] The reaction of diester **2** with IN_3 solution prepared in situ from excess of sodium azide and iodine monochloride in acetonitrile (−5°) according to the procedure of Fowler, Hassner, and Levy[20] afforded a crystalline azido iodide **6**, mp 137°, in near-quantitative