"19-line" form of the S_2 multiline signal in maximum yield upon subsequent illumination either by a single flash at 0 °C or by continuous illumination at 195 K.

Acknowledgment. This research was supported by the U.S. Department of Energy Soleras Program (Contract DE-FG02-84CH10199), the New Jersey Commission on Science and Technology (Grant 87-240020-7), and the U.S. National Institutes of Health (Grant HL-24644). We thank Drs. Demitri Ghanotakis and Charles Yocum for advice in preparing samples.

Registry No. O_2, 7782-44-7; Mn, 7439-96-5.

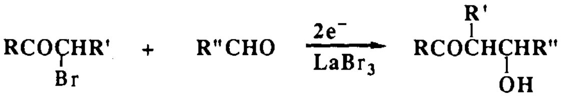
Mechanism of the Lanthanum Bromide Assisted Electrochemical Aldolization of α-Bromo Ketones

Albert J. Fry* and Marko Susla

Contribution from the Department of Chemistry, Wesleyan University, Middletown, Connecticut 06457. *Received July 7, 1988*

Abstract: Linear sweep voltammetry, preparative electrolyses under a variety of experimental conditions, and trapping experiments have been used to explore the mechanism of the formation of the aldol 2-benzoyl-1-phenylpropanol by electrochemical reduction of α-bromopropiophenone in the presence of benzaldehyde and lanthanum bromide. The aldol condensation occurs by reaction of the free (lithio) enolate with a lanthanum bromide–benzaldehyde–tetrahydrofuran complex. Electrochemical reduction of the bromo ketone forms the *Z* enolate highly stereospecifically. The erythro aldol is formed stereoselectively initially, but the condensation is reversible, and the equilibrium mixture of aldols, containing mostly the threo isomer, is isolated from the electrolysis.

We recently described the formation of β-hydroxy ketones (aldols) from the electrochemical reduction of α-bromo ketones (**1**) in the presence of aldehydes (**2**) and lanthanide salts (eq 1).[1]

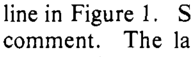


$$\underset{\textbf{1}}{\mathrm{RCO\underset{\displaystyle Br}{C}HR'}} + \underset{\textbf{2}}{\mathrm{R''CHO}} \xrightarrow[\mathrm{LaBr_3}]{2e^-} \underset{\textbf{3}}{\mathrm{RCO\overset{\displaystyle R'}{C}H\underset{\displaystyle OH}{C}HR''}} \qquad (1)$$

Yields of aldol (**3**) were 0–1% in the absence of a lanthanide salt, but were up to 70% or more when such a salt was included in the reaction medium.[1] Relatively little is known concerning the effects of added metal ions on the electrochemical reduction of organic substances,[2,3] although one would expect that such effects ought to be substantial. This reaction represents a convenient system for investigating such effects: (a) the presence of the lanthanide salt is required for successful aldol formation; (b) the reduction potentials of the components of the electrode reaction, i.e., bromo ketones, aldehydes, and lanthanide salts are well separated (vide infra), removing any doubts concerning what the actual electroactive species might be; and (c) solutions of lanthanum halides at moderate concentrations in tetrahydrofuran are homogeneous, making the interpretation of voltammograms easier. We report herein the results of a study of the lanthanide-assisted aldolization of α-bromo ketones, using voltammetric methods, preparative electrolyses, and trapping experiments, which greatly clarifies the mechanism of the electrode reaction, including the complex role played by the metal ion.

Results

Voltammetry. Voltammetric measurements were carried out in tetrahydrofuran (THF) containing 0.5 M $LiClO_4$ (this relatively high supporting electrolyte concentration was employed to minimize uncompensated *iR* effects arising from the high electrical resistance of THF).[4] Linear potential sweep and cyclic voltammetric experiments were carried out at a freshly polished glassy carbon electrode at a sweep rate of 200 mV s^{-1}; potentials were measured relative to a Ag/0.1 M $AgNO_3$ reference electrode.[5] The compounds studied, alone and in various combinations, were α-bromopropiophenone (**4**), benzaldehyde (**5**), propiophenone (**6**),



$\mathrm{C_6H_5CO\underset{\displaystyle Br}{C}HCH_3}$

4

C_6H_5CHO

5

$C_6H_5COCH_2CH_3$

6

and anhydrous $LaBr_3$. The latter substance is insoluble in THF when initially added to the medium, but gradually dissolves as the mixture is stirred over a 15-min interval; a number of recent reports support the presumption that solubilization is associated with the complexation by $LaBr_3$ of at least three and possibly four molecules of THF.[6]

The voltammogram of bromo ketone **4** is shown as the solid line in Figure 1. Several features of this voltammogram require comment. The large peak at ca. −1.5 V corresponds to the electrolytic removal of the bromine atom, with concomitant conversion of **4** to the corresponding enolate (**7**).[7] There is a second, smaller, peak at ca. −2.1 V, close to the corresponding value for propiophenone (**6**) as determined in a separate experiment. More interestingly, there is a pronounced minimum in the voltammetric current at ca. −1.95 V. This is distinctly different behavior from that exhibited by a compound which is reduced in two consecutive steps with no intervening chemical reaction.[8] Instead, the voltammogram of **4** closely resembles that expected for a situation wherein the electroactive substance is reduced to

---

[1] Fry, A. J.; Susla, M.; Weltz, M. *J. Org. Chem.* **1987**, *52*, 2496.

[2] (a) Sopher, D. W.; Utley, J. H. P. *J. Chem. Soc. Perkin Trans. 2* **1984**, 1361. (b) Fournier, F.; Berthelot, J.; Pascal, Y.-L. *Can. J. Chem.* **1983**, *61*, 2121.

[3] (a) There is a very large literature on metal ions as mediators of electrochemical behavior,[3b] but generally in such reactions the metal ion is the electroactive species; we are concerned in the present instance with reactions in which the electroactive species is an organic substrate whose electrochemical behavior is altered by the presence of the metal salt. (b) Torii, S. *Synthesis* **1986**, 873.

[4] Kadish, K. M.; Ding, J. Q.; Malinski, t. *Anal. Chem.* **1984**, *56*, 1741.

[5] The potential of this electrode is +0.35 V versus SCE.

[6] (a) Hazin, P. N.; Huffman, J. C.; Bruno, J. W. *Organometallics* **1987**, *6*, 23. (b) Wengi, C.; Zhongsheng, J.; Yan, X.; Yuguo, F.; Guangdi, Y. *Inorg. Chim. Acta* **1987**, *130*, 125. (c) Brittain, H. G.; Wayda, A. L. *Inorg. Chim. Acta* **1984**, *95*, 21.

[7] Fry, A. J. *Synthetic Organic Electrochemistry*, 2nd ed.; Wiley: New York, in press, Chapter 5.

[8] Demortier, A.; Bard, A. J. *J. Am. Chem. Soc.* **1973**, *95*, 3495.

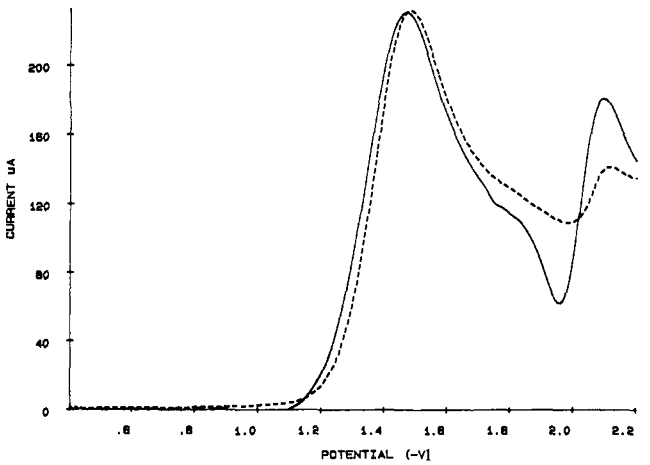


Figure 1. Solid line: voltammogram of α-bromopropiophenone (3.7 mM) at a glassy carbon electrode vs Ag/0.1 M $AgClO_4$, in 0.5 M lithium perchlorate–tetrahydrofuran. Dotted line: diethyl malonate (22 mM) added.

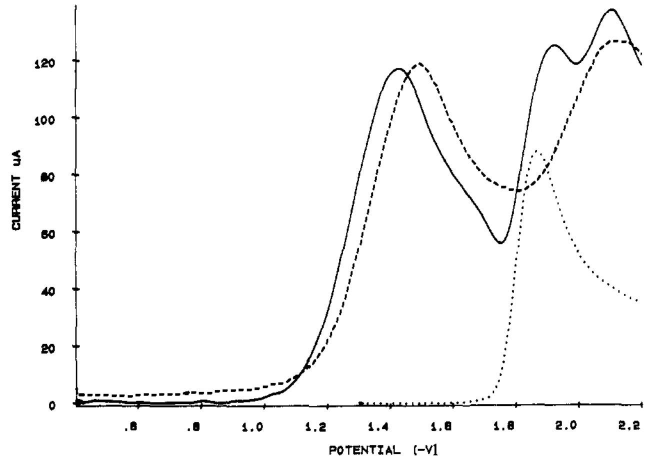
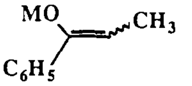


Figure 2. Dotted line: voltammogram of benzaldehyde (3.9 mM) at a glassy carbon electrode vs Ag/0.1 M $AgClO_4$, in 0.5 M lithium perchlorate–tetrahydrofuran. Solid line: Voltammogram of a mixture of α-bromopropiophenone (1.83 mM) and benzaldehyde (1.97 mM). Dashed line: voltammogram of a mixture of α-bromopropiophenone (1.83 mM), benzaldehyde (1.97 mM), and lanthanum bromide (2.00 mM).

afford a product which then proceeds to destroy more electroactive substance as it diffuses toward the electrode.[9] This suggests that the electrochemically generated enolate **7** reacts with unreacted



7, M = Li

8, M = $LaBr_2$

14, M = $SiMe_3$

4, perhaps by proton interchange between the two; this hypothesis was supported by the disappearance of the current dip at −1.95 V upon addition to the voltammetric solution of excess diethyl malonate (dashed line in Figure 1). Diethyl malonate is an efficient proton donor toward electrochemically generated carbanions.[10] There is also literature precedent for proton exchange between α-halo ketones and enolates generated electrochemically from them.[11] The voltammogram of a solution containing bromo ketone **4** and $LaBr_3$ (3.6 mM each) does not exhibit the current dip associated with the proton exchange process; apparently enolate **7** is trapped by lanthanum bromide to afford a lanthanum enolate (**8**) which is sufficiently nonbasic and otherwise unreactive that it does not react with **4**.

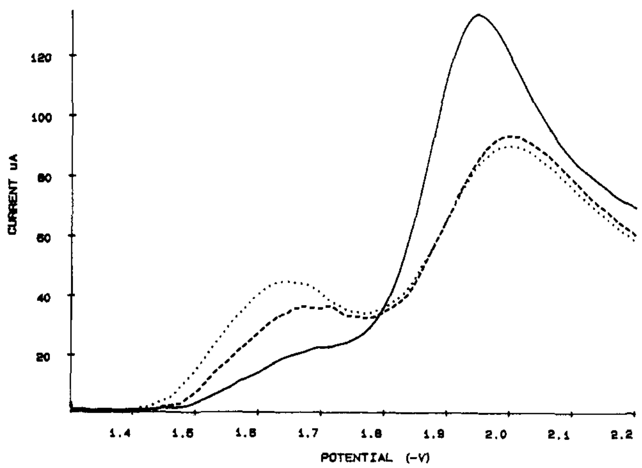


Figure 3. Voltammograms of a mixture of benzaldehyde (3.94 mM), and lanthanum bromide (solid line, 3.98 mM; dashed line, 7.89 mM; dotted line, 11.8 mM) at a glassy carbon electrode vs Ag/0.1 M $AgClO_4$, in 0.5 M lithium perchlorate–tetrahydrofuran.

The voltammogram of benzaldehyde (**5**) is shown as the dotted line in Figure 2; note the fortunate happenstance that the reduction peak of benzaldehyde occurs at ca. −1.9 V, i.e., in the voltammetric "window" created by the current dip in the voltammogram of the bromo ketone. Cyclic voltammetry shows no anodic wave when the direction of potential scan is reversed at −2.0 V. The solid line in Figure 2 represents the voltammogram of an equimolar mixture of **4** and **5**. The peak due to **5** can be easily seen, bracketed by those due to **4**. This voltammogram is identical with a composite "voltammogram" created by digitizing and storing the individual voltammograms of **4** and **5**, summing the currents for **4** and **5** at each potential, and plotting the total currents as a function of potential. The fact that the latter curve is identical with the experimental voltammogram demonstrates that there is no interaction between the two species upon reduction, and is consistent with the results of the preparative electrolysis (vide infra). However, when $LaBr_3$ is added to the medium, *no reduction wave at −1.9 V due to benzaldehyde reduction is observed* (dashed line in Figure 2). We shall return to this significant observation in the Discussion.

Another informative set of experiments involved addition of increasing amounts of $LaBr_3$ (which is reduced at potentials well negative of −2.3 V) to a solution of **5**, such that the molar ratio of **5** to $LaBr_3$ was 1:1, 1:2, and 1:3, respectively (Figure 3). A new wave appears at ca. −1.6 V and increases with increasing concentration of $LaBr_3$. We hypothesized that this wave is associated with a (relatively) long-lived $LaBr_3$–benzaldehyde complex (**9**) (see Discussion) and were interested therefore in the assoication constant for the process (eq 2). This information is

$$\mathbf{5} + LaBr_3 \rightleftharpoons \underset{\mathbf{9}}{C_6H_5CHOLaBr_3} \tag{2}$$

available in principle from the relative heights of the two voltammetric waves, but because of the asymmetry of the LSV peak, the association constant was obtained more easily by measuring the relative heights of the plateaus or symmetrical peaks obtained by semiintegration[12] or semidifferentiation,[13] respectively, of the experimental voltammogram. The voltammograms shown in Figure 3 correspond to values of the equilibrium constant K (eq 2) of 56, 77, and 59, respectively, or an average value of 65 ±

---

(9) Saveant, J. M. *Acc. Chem. Res.* **13**, 323 (1980).

(10) Shao, R.-L.; Peters, D. G. *J. Org. Chem.* **1987**, *52*, 652.

(11) Barba, F.; Velasco, M. D.; Guirado, A. *Electrochim.* Acta **1983**, *28*, 259.

(12) Oldham, K. B. *Anal. Chem.* **1972**, *44*, 196.

(13) Dalrymple-Alford, P.; Goto, M.; Oldham, K. B. *J. Electroanal. Chem.* **1977**, *85*, 1.

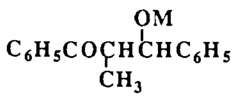
Table I. Electrochemical Reduction of α-Bromopropiophenone[a]

run no.	[**4**], mM	[**5**], mM	[$LaBr_3$], mM[b]	aldol, %[c]	[**14**], %
1	70	70	0	0–1	
2	70	70	18	8	
3	70	70	35	21	
4	70	70	52	55	
5	70	70	70	73	
6	70	70	88	61	
7	70	70	105	45	
8	70	70	140	8	
9	70	70	70	64[e]	
10	70	0	70	12[d]	
11	70	0	0		68[f]
12	70	0	70		5[f]
13	70	70	70[g]	8	

[a] All electrolyses carried out in THF/0.5 M $LiClO_4$. [b] Nominal concentration of $LaBr_3$ at beginning of electrolysis; a saturated solution is 15 mM. [c] Remainder of product is propiophenone, except where noted. [d] Benzaldehyde added after electrolysis was complete. [e] Trimethylchlorosilane added at conclusion of electrolysis; yield given is that of unsilylated aldol. [f] Trimethylchlorosilane (300 mM) added before electrolysis. [g] A second equivalent of $LaBr_3$ was added after electrolysis was complete.

20 M^{-1}. Addition of water (15 mM) to the 1:1 solution of $LaBr_3$ and **5** (3.9 mM in each) had no effect upon the voltammogram, indicating that the new wave is unlikely to arise from the presence of adventitious water. The fact that one can observe discrete voltammetric waves for both aldehyde **5** and the lanthanum complex **9** implies that equilibration between the complex and its individual components is slow on the voltammetric time scale (1–3 s). We presume that this is because formation of **9** involves displacement by benzaldehyde of one of the THF molecules bound to the lanthanum ion. Propiophenone (**6**) exhibits a small voltammetric prewave in the presence of $LaBr_3$, but α-bromopropiophenone (**4**) does not. From the latter fact, it may be estimated that the association constant for the latter with $LaBr_3$ is very small.

Preparative Electrolyses. It was previously reported that electrochemical reduction of a 1:1:1 mixture of **4**, **5**, and $LaBr_3$ in 0.5 M $LiClO_4$ in THF affords in 73% yield a 36:64 mixture of the erythro and threo diastereomers of aldol **10a**, and that **10a**

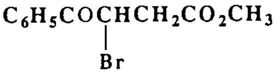


$$C_6H_5CO\underset{CH_3}{C}HC\overset{OM}{H}C_6H_5$$

10a, M = H
b, M = Li
c, M = $LaBr_2$
d, M = $SiMe_3$

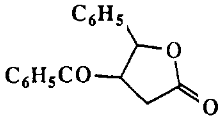
is formed in low (0–1%) yield if $LaBr_3$ is omitted.[1] A number of other experiments were carried out to clarify the role of the metal salt in this reaction (Table I). A series of electrolyses were carried out where the ratio of **4** to **5** was held fixed at 1:1, but the relative amount of $LaBr_3$ was varied (runs 1–8). The data show that the reaction is not catalytic in $LaBr_3$; in fact, a stoichiometric amount of $LaBr_3$ is clearly required. Interestingly, the yield of aldol is markedly lower than when more than 1 equiv of $LaBr_3$ is added to the medium (runs 6–8). This surprising result was checked in a second way (run 13). An electrolysis was carried out in the usual manner with the three components (**4**, **5** and $LaBr_3$) in 1:1:1 ratio, but after the electrolysis was complete, a second equivalent of $LaBr_3$ was added, and the mixture was allowed to stand for 20 min before workup. The yield of **10a** was only 8%. Thus, excess metal salt actually destroys the product aldol (actually the lanthanum aldolate **10c**). HPLC analysis of the product of this experiment, following aqueous acid workup, demonstrated that the aldol had been converted into **5** and **6**; presumably the latter was present in the mixture in the form of its lanthanum enolate before workup. It was also noted (run 10) that the yield of aldol is markedly lower if benzaldehyde is added after electrolysis is complete, rather than at the outset.

Another series of electrolyses was carried out with bromo ketoester **11**. Electrochemical reduction of a 1:1:1 mixture of **11**, **5**, and $LaBr_3$ afforded a stereoisomeric mixture of lactones **12**,[14]



$$C_6H_5CO\underset{Br}{C}HCH_2CO_2CH_3$$

11



12

in which *trans*-**12** was observed to predominate over *cis*-**12** by a factor of 6:1. Inclusion of 100% excess $LaBr_3$ in the electrolysis medium does not quench the formation of **12**, though it does reduce the trans–cis ratio to 1:3.

Trimethylchlorosilane Trapping Experiments. Lanthanum enolate **8** and the lanthanum aldolate **10c** turned out to exhibit considerably different reactivity than the "free" (lithio) enolate **7** and aldolate **10b**. Propiophenone (**6**) was treated successively with lithium diisopropylamide and trimethylchlorosilane (**13**) at

$(CH_3)_3SiCl$

13

–78 °C (conditions which should afford the kinetic enolate and its silyl ether)[15] to afford a mixture of the *Z* and *E* enol trimethylsilyl ethers (**14**)[16] in 97.8:2.2 ratio. The major isomer was shown to have the *Z* configuration by nuclear Overhauser enhancement experiments. Electrochemical reduction of **4** in the presence of **13** (without $LaBr_3$ present) afforded the corresponding enol silyl ethers **14** in high yield and with a *Z* to *E* ratio of 99.6:0.4 (run 11). In contrast, the stereoisomeric mixture of ethers **14** was formed in low yield in an identical electrolysis (run 12) to which an equivalent amount of $LaBr_3$ had been added. The major product was **6**; the ratio of **14** to **6** was 1:12. Run 10 in Table I also attests to the relatively low reactivity of the lanthanum enolate **8**. Likewise, addition of **13** to a to a 1:1:1 mixture of **4**, **5**, and $LaBr_3$ after electrolysis was complete did not result in formation of more than a few percent of the silylated aldols **10d** (run 9, Table I). Authentic samples of **14** and **10d** were shown to be stable to the electrolysis conditions; that is, they are not cleaved by $LaBr_3$.

Discussion

The results described above permit us to define the mechanism of the electrochemical aldolization of bromo ketones in considerable detail. They alo explain some of the previously observed[1] characteristics of this reaction. The first question we address is what the actual species in solution are under these conditions. In this connection it is necessary to recall that a chemical reaction has already taken place in this system before any current is passed through the solution. $LaBr_3$ is initially insoluble in THF, but dissolves over a period of 10–15 min. It is clear from recent reports[6] that solubilization is associated with complexation by at least three, and possibly four, molecules of THF by $LaBr_3$. This is important in understanding certain steps in the subsequent reaction sequence (vide infra), because it means that there is considerable steric bulk associated with the metal ion, which bears several solvent and halide ligands.

We rejected the notion that the new voltammetric wave in the voltammogram of **5** upon addition of $LaBr_3$ is due to complex formation between the radical anion of **5** and $LaBr_3$, because this should cause the benzaldehyde reduction wave to simply shift to more positive potentials, rather than splitting into two waves.[17] Rather, we interpret the voltammetry results on the individual components and combinations of them as evidence that benzaldehyde (**5**) forms a complex (**9**) with solvated $LaBr_3$. The

---

[14] Miller, R.; Fickes, G. *J. Org. Chem.* **1985**, *50*, 2374.

[15] House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324.

[16] (a) This reaction has been reported[16b] to yield a single stereoisomer of **14**, whose configuration was not assigned. (b) Rasmussen, J. K.; Hassner, A. *Tetrahedron Lett.* **1973**, *14*, 2783.

[17] Parker, V. D., private communication.

association constant for complex formation is 65 ± 20 M^{-1}. The association constant of bromo ketone **4** with $LaBr_3$ is apparently quite small, because no new wave appears in the voltammogram of **4** when $LaBr_3$ is added to the solution; **4** presumably complexes less well with $LaBr_3$ than does aldehyde **5** because of the steric bulk at the carbonyl group and the electron-withdrawing effect of the bromine atom (recall that the $LaBr_3$ molecule bears several bulky THF ligands). Since lanthanide ions are hard acids, it is quite reasonable that they should complex with carbonyl groups, of which the oxygen atom is a hard base, and indeed there are a number of literature for the existence of such complexes[18] and also for the fact that aldehydes tend to complex with lanthanide(III) ions more strongly than do ketones.[19] At the concentrations employed in the preparative electrolyses[1] (usually 70 mM each in **5**, **6**, and $LaBr_3$), some $LaBr_3$ is undissolved at the outset, although more dissolves as reaction proceeds and the solution is homogeneous at the end of the electrolysis (apparently the aldolate **10c** is soluble in THF). We have measured the solubility of $LaBr_3$ in THF as approximately 15 mM. From this datum and the association constant given above, we can calculate that aldehyde **6** exists in the solution ca. 17% in the form of its $LaBr_3$ complex **9** and 87% as the free aldehyde, while **4** is present as the free bromo ketone. The latter is presumably the actual electroactive species. It must form **7** on electrolysis. The voltammetry and preparative electrolysis results both demonstrate that **7** does not add to benzaldehyde. Yet the benzaldehyde wave is wholly absent when $LaBr_3$ is added to the solution, and the reaction between **7** and **4** is inhibited by the addition of $LaBr_3$ (vide supra). We conclude from this that the aldol condensation actually occurs between enolate **7** and the benzaldehyde–$LaBr_3$ complex **9**. From the time necessary to scan from −1.4 to −1.9 V, and presuming that at least 5% unreacted benzaldehyde could be detected in the voltammogram (dashed line in Figure 2), we estimate the lower limit for the rate constant of the overall process to be 100 M^{-1} s^{-1}.

We mentioned above the intriguing dependence of the yield of **10a** upon the relative amount of $LaBr_3$ in the solution. The yield of aldol is highest when the ratio **4**:**5**:$LaBr_3$ is 1:1:1; that is, it is lower when the $LaBr_3$ proportion is either less than or greater than unity. The reason for the first of these is clear: the reactive carbonyl species is the complex **9**; irrespective of the value K for eq 2, the total amount of **9** available is governed by the amount of $LaBr_3$ present. It is less obvious at first sight why excess $LaBr_3$ should lower the yield of aldol. Run 13, in which the yield of aldol dropped drastically when a second equivalent of $LaBr_3$ was added to the medium after electrolysis was complete, provides an explanation for this effect. It constitutes clear evidence that these aldol condensations are reversible. Lanthanum aldolate **10c** can apparently dissociate, not to **7** to **9**, but rather to the relatively unreactive lanthanum enolate **8** (with this stronger La–O bond) and **5**, and the latter can then complex with the excess $LaBr_3$ to afford **9**. A reviewer advanced an alternative explanation, that the excess $LaBr_3$ could be competing with complex **9** as a trapping agent for lithio enolate **7**, but this is inconsistent with the fact that increasing amounts of $LaBr_3$ actually improve the yield of aldol in runs 1–5.

Scheme I

$$LaBr_3 + nTHF \rightleftharpoons LaBr_3(THF)_n$$

$$n = 3 \text{ or } 4$$

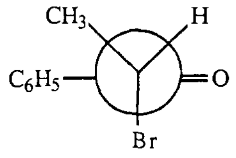
$$LaBr_3(THF)_n + C_6H_5CHO \rightleftharpoons \mathbf{9}$$

$$\mathbf{4} + 2e^- \longrightarrow (Z)\text{-}\mathbf{7}$$

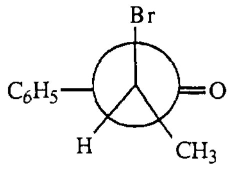
$$\mathbf{7} + \mathbf{9} \longrightarrow \text{erythro-}\mathbf{10c}$$

It is instructive to consider the stereochemical course of the aldol condensation reaction. Two stereoisomeric aldols can be formed in these reactions, *erythro*- and *threo*-**10a**. The stereochemistry of directed aldol condensations has been studied intensely over the last decade.[20] The results may be summarized briefly as follows. Under kinetic conditions (strong, bulky bases; low temperature) a ketone such as **6** affords the Z enolate in substantial excess over the E isomer. Furthermore, the Z enolate reacts with most substrates to form the erythro aldol stereoselectively[20] as the kinetic product when the reactions are conducted for short times at low temperatures. On the other hand, E enolates generally react less stereoselectively and afford mixtures in which the threo aldol predominates. Furthermore, when the aldol condensation is carried out under equilibrating conditions (higher temperatures, longer times), mixtures containing predominantly the threo aldol are also produced. In the latter situations, the threo:erythro ratio is generally not high (frequently it is 1.5-2.5:1). We observed earlier that the lanthanide-assisted electrochemical reactions generally afford mixtures in which the threo:erythro ratio is greater than unity.[1] At that time it was not clear whether this mixture was produced under kinetic or thermodynamic control. Our present results now clearly establish the latter. We base this conclusion upon three facts. (a) The experiments involving 2 equiv of $LaBr_3$ demonstrate unequivocally that equilibrium between products and reactants does occur on the electrolysis time scale. (b) Electrochemical reduction of **4** in the presence of **13** affords almost exclusively the Z isomer of **14**. (c) Electrochemical reduction of bromo ketoester **11** in the presence of $LaBr_3$ affords a mixture of lactones **12** in which the trans:cis ratio is 6:1, whereas the equilibrium mixture of aldols, and therefore lactones, should be near 1:1.[20] To the extent that lactonization occurs, it inhibits reversion to starting materials, and hence the products should more closely approximate the kinetic ratio of aldolates.[21] The trans lactone is derived from the corresponding erythro aldol. The ester group in **11** should not affect the stereochemistry of the condensation step. In general, therefore, these condensations presumably afford an initial erythro-rich mixture (at least 6:1) which equilibrates before workup to a mixture rich in the threo aldol. It will be recalled that this reaction is not quenched by a second equivalent of $LaBr_3$; apparently the second equivalent of $LaBr_3$ is tied up by complexation to the product lactone.

It is entirely reasonable that the Z enolate should be formed preferentially upon reduction of bromo ketones such as **4** at an electrode surface. Reduction of α-bromo ketones is known to occur from a conformation in which the carbon–bromine bond is perpendicular to the plane of the carbonyl group.[22] There are two such conformations (**15** and **16**, written as Newman projections along the bond connecting the carbonyl and alpha carbon atoms) available to **4** and other acyclic bromo ketones. Reduction of **15** requires that the methyl and phenyl groups rotate toward each



15



16

---

(18) Fukuzawa, S.; Tsuruta, T.; Fujinami, T.; Sakai, S. *J. Chem. Soc. Perkin Trans. 1* **1987**, 1473. (b) Natale, N. R. *Org. Prep. Proced. Int.* **1983**, *15*, 387.

(19) (a) Luche, J.-L.; Gemal, A. L. *Chem. Commun.* **1978**, 976. (b) Luche, J.-L; Gemal, A. L. *J. Am. Chem. Soc.* **1979**, *101*, 5848. (c) Gemal, A. L.; Luche, J.-L. *Tetrahedron Lett.* **1981**, *22*, 4077.

(20) (a) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1. (b) Mukaiyama, T. *Org. React.* **1982**, *28*, 203.

(21) A referee suggested that the product lactones can equilibrate under the "strongly" conditions of the electrolysis; we consider this unlikely, inasmuch as methoxide ion is undoubtedly strongly bound to the oxaphilic lanthanum(III) ion, thus greatly diminishing its basicity. The low nucleophilicity of such species has already been demonstrated herein.

(22) (a) Wilson, A. M.; Allinger, N. L. *J. Am. Chem. Soc.* **1961**, *83*, 1999. (b) Kabasakalian, P.; McGlotten, J. *Anal. Chem.* **1962**, *34*, 1440.

other as the enolate is formed. No such problem exists with **16**; hence this should be the preferred conformation for reduction, generating the *Z* enolate.

Our electrolysis and voltammetric results enable us to conclude that aldol formation does not arise by reaction either (a) the free enolate and uncomplexed benzaldehyde (run 1), (b) the lanthanum enolate and free benzaldehyde (run 10), or (c) the lanthanum enolate and the complexed aldehyde (run 13). We conclude that aldol formation involves the remaining alternative, condensation between the free enolate **7** and the lanthanum–complexed aldehyde **9**. It is possible at this point to summarize the sequence of events leading to aldol formation (Scheme I). Lanthanum bromide dissolves in THF, accompanied by complexation with three or four THF molecules. Solvated $LaBr_3$ is in equilibrium with free benzaldehyde and complex **9**. The (uncomplexed) bromo ketone **4** is reduced stereospecifically to its *Z*-enolate **7**, which then reacts rapidly with **9** to afford erythro lanthanum aldolate **10c** stereoselectively. The latter reaction is reversible, and ultimately an equilibrium mixture of erythro and threo aldols is produced.

The lanthanum enolate **8** and aldolate **10c** formed in these reactions are quite unreactive. Lithium enolate **7**, prepared either by treatment of **6** with LDA at −78 °C or by electrochemical reduction of **4**, readily forms the enol silyl ether **14**. The yield of **14** is greatly reduced, however, if $LaBr_3$ is present in the medium (run 12). Apparently $LaBr_3$ can trap the enolate faster than can trimethylchlorosilane. Similarly, the stereoisomeric mixture of aldols **10a** can be converted to the corresponding silyl ethers **10b** by reaction with **13**, but addition of **13** to a 1:1:1 mixture of **4**, **5**, and $LaBr_3$ after electrolysis is complete does not result in formation of the silylated aldols (run 9). The low reactivity of **8** and **10c** toward electrophiles such as **5** and **13** is presumably associated with the strength of the lanthanum–oxygen bond and concomitant diminished nucleophilicity of the enolate oxygen; this is why the reactions are not catalytic in $LaBr_3$. The mechanism shown in Scheme I also explains why yields of aldol adduct are lower when the bromo ketone and/or aldehyde is sterically congested, and why ketones are poor carbonyl acceptors in these reactions.[1] The reactive species toward the enolate is not the carbonyl compound itself, but rather a carbonyl compound–lanthanide complex, in which the metal ion is also coordinated to several solvent molecules. This should cause substantial steric hindrance in reactions in which the enolate ion bears a bulky group; the complex itself should be weaker when the carbonyl compound bears a bulky substituent.

Experimental Section

General. Lanthanum bromide was prepared as previously described.[1] Lithium perchlorate was dried in an Abderhalden apparatus at 111 °C overnight over P_2O_5. Tetrahydrofuran (THF) was distilled from benzophenone sodium ketyl immediately before use, and injected directly into the sealed dried cell. Voltammograms were measured in 25 mL of tetrahydrofuran in a commercial (Brinkmann) cell containing 0.5 M $LiClO_4$ and the electroactive substance (ca. 4 mM). Linear sweep and cyclic voltammograms were carried out using a PAR Model 170 electrochemistry system at a sweep rate of 200 mV/s relative to a $Ag/AgNO_3$ reference electrode.[5] The working electrode for voltammetry, a glassy carbon electrode (Bioanalytical Systems), was freshly polished prior to each measurement, using Sargent–Welch polishing alumina No. 2. Linear sweep voltammetric data were recorded on a Datalabs DL901 transient recorder and transferred to an AT&T 6300 computer for storage, data processing, and plotting on a Hewlett–Packard digital plotter. Semiintegrals were computed using a standard algorithm.[23] Semiderivatives were obtained by differentiating the semiintegral curve using the differentiation option in the Hyperplot© (Columbus, Ohio) data processing–plotting package.

Methyl 3-Bromo-3-benzoylpropionate (11). A solution of Br_2 (7.4 g, 46 mmol) in 25 mL of acetic acid was added slowly to a solution of methyl 3-benzoylpropionate[24] (8.9 g, 46 mmol) in 25 mL of acetic acid over a 1-h interval. After addition was complete, the solution was stirred overnight, at which point it was pale yellow. The solution was poured into 75 mL of dilute $NaHCO_3$ and then extracted with 100 mL of CH_2Cl_2. After washing with water, the organic extract was dried over Na_2SO_4 and the solvent removed by rotary evaporation. Distillation afforded methyl 3-bromo-3-benzoylpropionate (**11**) as a pale yellow liquid, 9.98 g (80%), bp 144–147 °C (0.2 mm): NMR (Silanor) δ 7.9–8.1 (m, 2 H), 7.3–7.7 (m, 3 H), 3.7 (s, 3 H), 5.1 (dd, 1 H, J_{AX} = 8.4 Hz, J_{BX} = 5.7 Hz), 3.50 (dd, 1 H, J_{AB} = 17.4 Hz, J_{AX} = 8.4 Hz), 3.12 (dd, 1 H, J_{AB} = 17.4 Hz, J_{BX} = 5.7 Hz).

Preparative Electrolyses. Preparative electrolyses were carried out in a magnetically stirred divided cell in which the anode compartment was a Coors porcelain cup No. 60494 containing a platinum anode immersed in 40 mL of 0.5 M $LiClO_4$. The cathode was a carbon cloth[25] electrode (Union Carbide Corp. No. X2014 WCA graphite cloth). The cell was chilled in ice and purged with nitrogen, after which a constant current of 200 mA was passed for 100% of the calculated time for a two-electron reduction of the bromo ketone. The electrolyses were worked up as previously described, except for runs 9, 11, and 12. In the latter experiments, the reaction mixture was poured into saturated $NaHCO_3$ and extracted with hexane. The organic layer was then washed once with dilute $NaHCO_3$, dried over $MgSO_4$, and filtered; the filtrate was then evaporated on a rotary evaporator. Product analyses were carried out by quantitative HPLC as previously described.[1] Mixtures containing silylated products were analyzed using an eluent consisting of 60:40 methanol–water.

Acknowledgment. Financial support by the National Science Foundation in the form of Grant No. 85-02078 to A.J.F. and a grant for partial support of the 400-MHz NMR spectrometer used in this work are gratefully acknowledged. Michael Weltz carried out the experiments on bromo ketoester **11** as part of his senior honors thesis research.

Registry No. **4**, 2114-00-3; **5**, 100-52-7; **6**, 93-55-0; *erythro*-**10a**, 71908-02-6; *threo*-**10a**, 71908-03-7; **11**, 26551-48-4; *trans*-**12**, 95891-68-2; **13**, 75-77-4; (*Z*)-**14**, 66323-99-7; (*E*)-**14**, 71268-59-2; *cis*-**12**, 95891-69-3; $LaBr_3$, 13536-79-3; lithium diisopropylamide, 4111-54-0.

---

(23) Whitson, P. E.; Vanden Born, H. W.; Evans, D. H. *Anal. Chem.* **1975**, *45*, 1298.

(24) Kugel, M. *Justus Liebigs Ann. Chem.* **1898**, *299*, 50.

(25) Hand, R.; Carpenter, A. K.; O'Brien, C. J.; Nelson, R. F. *J. Electrochem. Soc.* **1972**, *119*, 74.