(3.45 g, 58.4 mmol) at 0 °C under an atmosphere of argon. After the solution had been stirred at this temperature for 20 min, the solvent was removed under reduced pressure. To the residual oil were added 400 mL of ethyl acetate and 50 mL of 5 N hydrochloric acid saturated with sodium chloride. The organic layer was washed three times with 30 mL of brine and dried over anhydrous sodium sulfate. The solvent was evaporated to afford the crude product. Recrystallization from a mixture of 2-propanol and *n*-hexane gave 6.49 g (88 %) of the pure half-amide as colorless crystals: mp 176.5–177 °C dec; IR (KBr) 3330, 2970, 1750, 1635, 1555 cm^{-1}; NMR ($CDCl_3$–Me_2SO-d^6 (20:1 v/v)) δ 1.13 (d, 3 H, *J* = 6.6 Hz), 1.15 (d, 3 H, *J* = 6.0 Hz), 2.11 (s, 3 H), 2.17 (s, 3 H), 3.85–4.24 (m, 1 H), 5.59–5.68 (m, 2 H), 6.67 (br d, 1 H, *J*. = 7.5 Hz, exchangeable with D_2O), 10.12 (br s, 1 H, exchangable with D_2O); MS (chemical ionization), calcd for $C_{11}H_{17}O_7N$ 275, found 276 (MH^+); $[\alpha]^{28}_D$ –21.9° (*c* 1.26, ethanol).

(*R*,*R*)-*N*-(10-Undecenyl)-*N*′-isopropyldiacetyltartramide (3). A mixture of di-*N*-succinimidyl oxalate (1.15 g, 4.05 mmol, Chemiscience Ltd. Tokyo), the half-amide **2** (1.12 g, 4.07 mmol), and pyridine (322 mg, 4.07 mmol) in 50 mL of acetonitrile was stirred at room temperature for 12 h under an atmosphere of argon. The resulting almost clear solution was cooled to 0 °C followed by the addition of a mixture of 10-undecenylamine (678 mg, 4.01 mmol) and triethylamine (406 mg, 4.01 mmol) in 15 mL of acetonitrile. After the mixture was stirred at this temperature for 1.5 h, 700 mL of ethyl acetate and 100 mL of water were added. The layers were separated and the organic layer was washed with water, 1.5 N hydrochloric acid, saturated sodium bicarbonate, and brine, and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the residue was purified by preparative HPLC using 30 g of silica gel and an acetone–*n*-hexane (1:4 v/v) mixture to yield 1.14 g (66%) of the pure diamide as a white solid: mp 148–149 °C; IR (KBr) 3280, 2980, 2930, 2860, 1755, 1650, 1545 cm^{-1}; NMR ($CDCl_3$) δ 1.13 (d, 3 H, *J* = 6.0 Hz), 1.27 (br s, 14 H), 1.92–2.17 (m, 2 H), 2.14 (s, 6 H), 3.12–3.33 (m, 2 H), 3.83–4.22 (m, 1 H), 4.83–5.08 (m, 2 H), 5.55–6.03 (m, 3 H), 6.33–6.73 (br m, 2 H, exchangeable with D_2O); MS (electron impact), calcd for $C_{22}H_{38}O_6N_2$ 426, found 426 (M^+); $[\alpha]^{27}_D$ –13.43° (*c* 2.57, ethanol).

(*R*,*R*)-*N*-(11-(Chlorodimethylsilyl)undecyl)-*N*′-isopropyldiacetyltartramide (4). To a solution of the olefin **3** (877 mg, 2.06 mmol) in 8 mL of chloroform was added 0.1 mL of a 2-propanol solution of chloroplatinic acid (0.13 mol/L) at room temperature. After the mixture was stirred for 4 min, 3 mL of dimethylchlorosilane was added. The mixture was then heated to reflux for 30 min. The solvent and excess silane were removed in vacuo and the residue was coevaporated twice with chloroform to afford the desired silane as a slightly brownish gum. This material was used next stage without purification.

Modified Gel 5. A suspension of 2.0 g of porous silica (Nucleosil 100-5, 5 μm, 100 Å, Marcherey-Nagel, Düren) in 16 mL of benzene was concentrated to ca. 12 mL under an atmosphere of argon. To this azeotropically dried mixture was added a solution of the silane **4** in 6 mL of pyridine at room temperature. After the mixture was gently stirred for 24 h, the modified gel was collected by filtration and washed with chloroform, methanol, acetone, and *n*-hexane, successively: IR (KBr) 2930, 2850, 1760, 1655, 1550 cm^{-1}. Anal. Found: C, 12.33; N, 1.19.

Trimethylsilylated Gel 6. To a suspension of 540 mg of modified gel **5** in 18 mL of chloroform was added 2 mL of (trimethylsilyl)imidazole (Tokyo Kasei). After the mixture was refluxed for 12 h under an argon atmosphere, the silica gel was collected by filtration and washed as described above. Anal. Found: C, 14.24; N, 1.19.

Aminolysis of Modified Gel 6. To a suspension of 520 mg of modified gel **6** in 5 mL of methanol was added 10 mL of 0.6 N ammonia in methanol at 0 °C. After the mixture was gently stirred 5 h at the same temperature, the silica was collected by filtration and washed with methanol, acetone, and *n*-hexane: IR (KBr) 2920, 2850, 1650, 1540 cm^{-1}.

Acknowledgment. We thank Mr. Y. Shida and Ms. S. Kaneko for MS measurements and Mr. S. Suzuki for the elemental analyses.

Lanthanide Ion Assisted Electrochemically Initiated Aldol Condensations

Albert J. Fry,* Marko Susla, and Michael Weltz

Department of Chemistry, Wesleyan University, Middletown, Connecticut 06457

Received November 26, 1986

An electrochemical process for effecting directed aldol condensation is described. It is carried out under neutral conditions, can tolerate a wide variety of functional groups, is highly selective for aldehydes over ketones, requires only simple apparatus, and depends for its success upon the efficient mediating effect of trivalent lanthanide ions.

It is well established that electrochemical reduction of alkyl halides generates carbanions.[1] Inasmuch as this electrochemical route to carbanions offers in principle a number of potential advantages over conventional chemical methods (e.g., selectivity[1b] and the possibility of generating carbanions under neutral operating conditions), much useful chemistry would result if one could successfully trap such carbanions with electrophilic reagents. Several reports have described the successful addition of electrochemically generated stabilized carbanions, e.g., those from carbon tetrachloride, ethyl trichloroacetate, and benzylic halides, to a variety of carbonyl acceptors.[2] Attempts in this laboratory and others to effect intermolecular reaction between electrophiles and carbanions generated by the electrochemical reaction of simple alkyl halides have, however, met with little success, apparently because the highly reactive carbanions react with solvent or adventitious proton donors in the medium as fast or faster than they react with the electrophile.

We felt that a solution to this problem might be developed by effecting electrochemical reduction of the alkyl

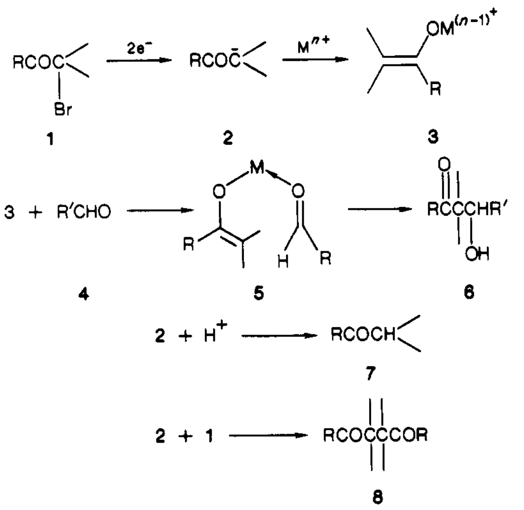
---

[1] (a) Fry, A. J. *Synthetic Organic Electrochemistry*; Harper & Row: New York, 1972. (b) Fry, A. J.; Mitnick, M. A.; Reed, R. G. *J. Org. Chem.* **1970**, *35*, 1232.

[2] (a) Shono, T.; Kise, N.; Masuda, M.; Suzumoto, T. *J. Org. Chem.* **1985**, *50*, 2527. (b) Shono, T.; Kise, N.; Yamazaki, A.; Ohmizu, H. *Tetrahedron Lett.* **1982**, *23*, 1609. (c) Silvestri, G.; Gambino, S.; Filardo, G. G.; Gulotta, A. *Tetrahedron Lett.* **1984**, *25*, 4307. (d) Karrenbrock, F.; Schafer, H. J. *Tetrahedron Lett.* **1978**, *19*, 1521. (e) Steiniger, M.; Schafer, H. J. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 79. (f) Gisselbrecht, J.-P.; Lund, H. *Acta Chem. Scand., Ser. B* **1985**, *39B*, 773, 823.

0022-3263/87/1952-2496$01.50/0

Scheme I



halide in the presence of both a metal salt and an electrophile. If properly chosen, the metal ion could be anticipated to play an important dual role in facilitating the aldol reaction: it would stabilize the carbanion by coordinating to it and would also assist the condensation by binding the electrophile as well. To test this general principle, we decided initially to explore the possibility of effecting an electrochemically initiated metal ion assisted directed aldol reaction. A wide variety of methods have been described in the literature for carrying out directed aldol reactions.[3,4] The electrochemical analogue of such processes would involve the electrolytic reduction of an α-bromo ketone in the presence of a metal ion and a carbonyl acceptor (Scheme I).

The question immediately arises as to which metal ion should be used to assist the reaction. A good mediator for this process would form strong metal–oxygen bonds, be more difficult to reduce than the other components of the medium, and afford intermediates that are not strongly basic. We decided to investigate the use of lanthanide salts for this purpose. The putative key intermediate (**5**) in Scheme I contains two metal–oxygen bonds. The unusually short length and associated high strength of the typical lanthanide–oxygen bond can be seen in compilations of X-ray data on metal oxides and hydroxides,[5] and, in fact, much of the recent interest in the use of lanthanides in organic chemistry centers around their highly oxaphilic character.[6] Organolanthanides are also relatively nonbasic,[6] and the trivalent ions are reduced with difficulty electrochemically.[7]

Electrochemical reduction of α-bromo ketones **1** at a carbon cathode in tetrahydrofuran/0.5 M $LiClO_4$ in the presence of aldehydes **4** and lanthanum(III) bromide indeed affords the corresponding aldols **6** (Table I). Cerium trichloride was employed initially but led to production of small amounts of the corresponding α-chloro ketone in addition to the aldol product. The bromide salt was therefore seen to be preferable. However, we found it easier to prepare pure anhydrous lanthanum bromide[8] than cerium bromide; hence, the lanthanum salt has been used exclusively in our recent work, including all of the reactions in Table I.[9] Furthermore, although we have not surveyed a wide variety of metal ions, to this point we have found the lanthanides to be uniquely efficient at assisting these reactions: yields of aldol are less than 3% in the presence of lithium, calcium, and manganese(II) salts and poor to fair in the presence of chromium(III) trichloride. Condensation does not take place or occurs in only low yield in the absence of lanthanide salts (see Table I). Instead, the intermediate lithium enolate undergoes undesirable side reactions, i.e., proton abstraction from other components of the medium, including unreacted bromo ketone, to form the parent ketone **7**, and nucleophilic attack by the enolate upon unreacted bromo ketone to afford dimers **8**, which are formed in quite low (0–2%) yields in the presence of lanthanides. It is not yet clear whether the electroactive species is the free bromo ketone or a complex of this substance with the lanthanide salt. We expect that further mechanistic work now in progress will clarify this point.

Table I. Electrochemically Initiated Aldol Condensations

entry	bromo ketone	carbonyl acceptor	aldol, %[a]	E:T[b]	7, %[a]
1	**9a**	benzaldehyde	80	36:64	18[c]
2	**9a**	isobutyraldehyde	84	35:65	3
3	**9a**	pivalaldehyde	41	55:45	43
4	**9a**	2-naphthaldehyde	50	39:61	50
5	**9b**	benzaldehyde	93	42:58	7
6	**9c**	benzaldehyde	66	0:100	30
7	**9a**	2-phenylpropional	66	*d*	30
8	**10**	benzaldehyde	40		20
9	**9a**	acetophenone	0		90
10	**9b**	benzalacetone	0		90
11	**9a**	benzaldehyde	tr[e,f]		99[f]
12	**9b**	*g*			94[h]
13	**9c**	benzaldehyde[i]	60	43:60	5

[a] Absolute yield (HPLC); average of 2–4 runs; equimolar quantities of bromo ketone, $LaBr_3$, and aldehyde were added except where noted. [b] Erythro:threo ratio (^{1}H NMR).[3a] [c] 0.5% **8** formed. [d] Mixture of diastereomers (9:27:19:45). [e] $LaBr_3$ omitted. [f] 0.7% **8** formed. [g] Aldehyde not added. [h] 6% **8** formed. [i] $CeCl_3$ employed.

The reaction is sensitive to steric factors in both the enolate component and the carbonyl acceptor. As may be seen from Table I, aldehydes condense efficiently with enolates derived from a variety of bromo ketones, yet acetophenone and benzalacetone do not condense (entries 9 and 10). Similarly, the yields of aldol from α-bromopropiophenone (**9a**) and 2-bromo-2,4-dimethyl-3-pentanone (**10**) with benzaldehyde are 80% and 40%, respectively (entries 1 and 8, respectively). A number of the reactions in Table I can produce diastereomeric aldol products. As Table I shows, the reactions are generally not diastereoselective; in fact, the erythro–threo ratios resemble the corresponding equilibrium mixtures.[4] This is unsurprising, given the relatively vigorous conditions (as far as aldol equilibration is concerned)[4] employed in the electrolyses (0 °C, 1–2 h). It is possible that diastereose-

$C_6H_5COCH(R)Br$

9a, R = Me
b, R = Et
c, R = *t*-Bu

$(CH_3)_2CHCOC(CH_3)_2Br$

10

---

(3) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1.

(4) Mukaiyama, T. *Org. React. (N.Y.)* **1982**, *28*, 203.

(5) (a) Sutton, L. E. *Tables of Interatomic Distances and Configurations in Molecules and Ions*; Chemical Society: London, 1958; and Supplement 1956–1959. (b) Kennard, O.; et al. *Molecular Structures and Dimensions*; Oosthock: Utrecht, 1972.

(6) (a) Imamoto, T.; Sugiura, Y.; Takayama, N. *Tetrahedron Lett.* **1984**, *25*, 4233. (b) Imamoto, T.; Kusumoto, T.; Yokoyama, M. *Ibid.* **1983**, *24*, 5233. (c) Luche, J.-L.; Gemal, A. L. *J. Chem. Soc., Chem. Commun.* **1978**, 976.

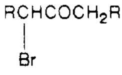
(7) Gritzner, G.; Gutmann, V.; Schober, G. *Monatsh.* **1956**, *96*, 1056.

(8) Taylor, M. D. *Chem. Rev.* **1962**, *62*, 503.

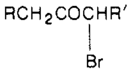
(9) We have also effected successful aldol condensations with cerium bromide and with several lanthanide chlorides (cerium, lanthanum, gadolinium, and ytterbium), but the latter reactions were carried out in dimethylformamide, where yields are not as high as in THF.

lectivity could be improved by operation at lower temperatures and in a different solvent.

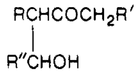
The lack of diastereoselectivity notwithstanding, these reactions have a number of potentially very attractive advantages for effecting directed aldol condensations: (a) the electrolyses are carried out under neutral conditions, and furthermore, the lanthanum enolate intermediates are themselves not very basic;[6] (b) α-bromo ketones are more easily reduced electrochemically than almost any of the common functional groups of organic chemistry;[1,10] (c) enolate formation and hence aldol condensation occur at the point where the bromine atom is attached; (d) the electrolyses can be carried out at constant current with no decrease in yield, which means that they can be carried out more rapidly than at controlled potential, and a very simple power source could be used if desired;[11] (e) the reaction, as noted, is highly selective for aldehydes over ketones. Considerations a–c suggest the possibilities of effecting directed aldol reactions between components bearing a wide range of functional groups, including base-sensitive or other electron-accepting functionalities, and/or the possibility of regioselective aldol condensations, e.g., generation of **13** and **14** from regioisomeric bromo ketones **11** and **12**.


$\mathrm{R}\underset{\mathrm{Br}}{\mathrm{CH}}\mathrm{COCH_2R'}$

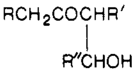
11


$\mathrm{RCH_2CO}\underset{\mathrm{Br}}{\mathrm{CH}}\mathrm{R'}$

12


$\mathrm{R}\underset{\mathrm{R''CHOH}}{\mathrm{CH}}\mathrm{COCH_2R'}$

13


$\mathrm{RCH_2CO}\underset{\mathrm{R''CHOH}}{\mathrm{CH}}\mathrm{R'}$

14

We are exploring some of these synthetic implications, as well as carrying out more detailed mechanistic investigations. Finally, having successfully demonstrated that it is possible to facilitate the reaction between electrochemically generated enolates and aldehydes by added metal ions, we plan to proceed to examine the possibility of trapping more highly basic and therefore more challenging carbanions.

Experimental Section

Lanthanum and cerium chlorides and lithium perchlorate (Alfa Inorganics) were dried at 135 °C in vacuo overnight. THF was distilled from the sodium–benzophenone ketyl.

Lanthanum Bromide. Lanthanum oxide (Alfa) was dissolved in concentrated HBr containing excess ammonium bromide (to repress hydrolysis to insoluble LaOBr[8]) and heated on the steam bath to drive off most of the water; residual water and ammonium bromide were then removed in vacuo while (12–18 h) the temperature was slowly raised to 350 °C. Material prepared by this procedure is completely soluble in water, indicating the absence of LaOBr. Cerium bromide was prepared by a similar procedure, but its purity was variable from run to run.

Sample Electrolysis Procedure. Benzaldehyde (0.5 g, 4.7 mmol), bromo ketone **9a** (1.0 g, 4.7 mmol), 1.78 g of lanthanum bromide (4.7 mmol), and 100 mL of a 0.5 M solution of $LiClO_4$ in dry THF were added to a magnetically stirred divided cell; the anode compartment was a ceramic cup (Coors Porcelain Co. #60494) filled with the same $LiClO_4$/THF solution. The cathode was a carbon cloth electrode (Union Carbide Corp. No. X2014 WCA graphite cloth).[12] The cell was chilled in an ice bath and purged with N_2 for 3–5 min, and a constant current of 0.2 A was then passed for 110% of the calculated time for a two-electron reduction. Concentrated HCl (3 mL) in 10 mL of H_2O was added, and stirring was continued for 3 min. The THF was removed by rotary evaporation, 150 mL of CH_2Cl_2 was added, and the latter was separated, washed successively with 100-mL portions of H_2O and dilute aqueous Na_2SO_4, and dried over $MgSO_4$. The products were analyzed by quantitative HPLC (column, 5 × 250 mm, packed with a C_{18} reversed phase on 5-μm silica gel support; eluent, 60–70% methanol in water at 1.5 mL/min; detection at 240 nm). Pure samples of aldols for calibration of the HPLC procedure were isolated by chromatography over silica gel with elution by 85:15 hexane/ethyl acetate.

Acknowledgment. Financial support by the National Science Foundation (Grant #85-02078 to A.J.F.) is gratefully acknowledged, as is a grant from the same agency to Wesleyan University in partial support of the 400-MHz NMR spectrometer used in this work. Joseph Sokol and Jonathan Haber carried out a number of preliminary electrolyses.

---

[10] Voltammetry at a glassy carbon microelectrode established the reduction potential of α-bromopropiophenone to be −1.5 V vs. Ag/0.1 M $AgNO_3$ in THF/0.5 M $LiClO_4$; this potential is unaffected by the addition of $LaBr_3$. Benzaldehyde is reduced at −1.9 V under these conditions, and $LaBr_3$ is reduced at an even more negative potential. We will report full details of the voltammetry later when a mechanistic study presently in progress is complete.

[11] Fry, A. J.; O'Dea, J. J. *J. Org. Chem.* **1975**, *40*, 3625. See, specifically pp 3627 and 3630 of this reference.

[12] Hand, R.; Carpenter, A. K.; O'Brien, C. J.; Nelson, R. F. *J. Electrochem. Soc.* **1972**, *119*, 74.

Electrochemical Reduction of (1-Bromo-2,2-dimethylpropyl)benzene in Dimethylformamide on Carbon Electrodes

Albert J. Fry* and Thomas A. Powers

Department of Chemistry, Wesleyan University, Middletown, Connecticut 06457

Received December 23, 1986

Products from the electrochemical reduction of (1-bromo-2,2-dimethylpropyl)benzene (**4a**) on carbon electrodes in dimethylformamide containing lithium perchlorate were found to depend upon the electrolysis potential. At relatively positive potentials the products are derived primarily from the coupling of two benzylic radicals, whereas at more negative potentials the products are derived from the corresponding carbanions. This establishes for the first time the mechanism of bibenzyl formation in the electrochemical reduction of benzyl bromides at nonmetallic electrodes. It has also been found that the *meso*–*dl* ratios of the 1,2-di-*tert*-butyl-1,2-diphenylethane products are dependent upon electrolysis potential and that head-to-head coupling of 1-phenyl-2,2-dimethylpropyl radicals is sterically restricted.

Many studies have been made into the mechanism of the electrochemical reduction of alkyl halides.[1,2] The general outlines of the electrode process are known (Scheme I). The initial, and potential-determining, step

0022-3263/87/1952-2498$01.50/0