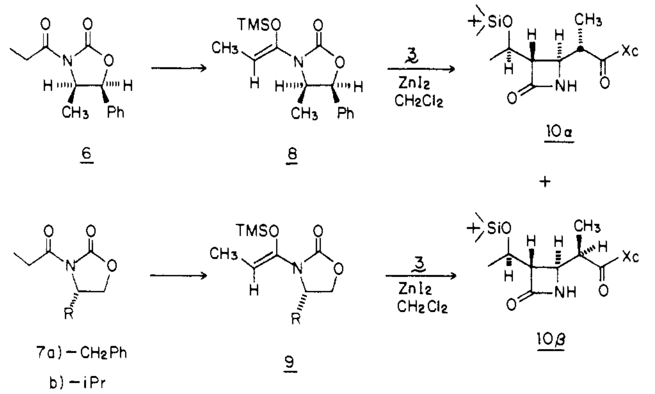
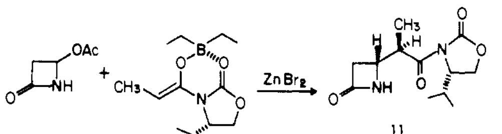
Scheme I



Chiral recognition of tin enolates has been extensively explored by Fujita.[12] The tin enolate was selectively generated by treatment of the propionamide **7b** with Sn(OTf)$_2$[13] and *i*-Pr$_2$NEt (0.3 M in CH$_2$Cl$_2$, −78 °C → room temperature) and to this solution was added the ZnBr$_2$ followed by the azetidinone **3**. Product 80.3%, was obtained in a **10β**:**10α** ratio of 92:8.

The asymmetric induction of the tin enolate with **3** can be rationalized according to a reaction process via a Felkin-type transition state.[14] It is, however, novel that the boron enolate



11

shows the same stereochemical outcome as tin. This boron-mediated reaction parallels the Li and Na enolate alkylations in the chiral carboximides described by Evans[3b] rather than the boron aldol condensation in the same system.[15]

The methodology described herein constitutes a new approach to the construction of chiral carbapenem precursors. Further synthetic and mechanistic studies on this interesting process are under way.

Acknowledgment. We thank Dr. J. P. Springer for X-ray analysis and R. Reamer and L. DiMichele for recording and interpreting ^{1}H and ^{13}C NMR spectra. We are also grateful to Drs. R. Conn and D. Melillo for helpful discussions during this work and Marian Spears for her help in preparing this manuscript.

Supplementary Material Available: Complete physical data for compounds **10β**/**10α** and **2**, Table I, diastereoselective condensation of silyl enol ethers of chiral carboximide (Scheme I), and diastereoselective condensation of diethylboryl enolate of **7b** in the presence of Lewis acids (5 pages). Ordering information is given on any current masthead page.

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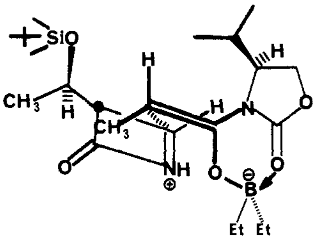
(11) Satisfactory spectral and elemental analyses were obtained. Absolute configuration was confirmed by comparison of the physical data of **2β** and **2α** authentic samples[1a] whose stereochemistry had been confirmed by X-ray analysis.

(12) Nagao, Y.; Yamada, S.; Kumagai, T; Ochiai, M.; Fujita, E. *J. Chem. Soc., Chem. Commun.* **1985**, 1418.

(13) Procedure reported by Batchelor et al. (Batchelor, R. J.; Ruddick, J. N. R.; Sams, J. R.; Aubke, F. *Inorg. Chem.* **1977**, *16*, 1414) was modified. Tin(II) (trifluoromethyl)sulfonate was formed when an excess of CF$_3$SO$_3$H (60 mL Aldrich) was reacted with 10.0 g (52.74 mmol, Aldrich 99.99+%) of anhydrous stannous chloride. The reaction mixture was heated at 80–85 °C for 24 h. After cooling to room temperature, the Sn(OTf)$_2$ was precipitated with 300 mL of anhydrous Et$_2$O, filtered in Schlenk ware, and rinsed with of Et$_2$O (3 × 50 mL). The Sn(OTf)$_2$ was dried in vacuo.

(14) Houk, K. N. *Pure Appl. Chem.* **1983**, *55*, 277 and references cited therein.

(15) This highly efficient enantioselective alkylation was further extended to provide 3-unsubstituted-4-substituted β-lactams **11** as a major diastereoisomer (≥99:1) in 95% yield. The stereochemistry was confirmed by X-ray analysis (4*R*,5*R*). In contrast, the tin enolate affords at 59:41 ratio of [(4*R*,5*R*)/(4*S*,5*R*)] under the same reaction conditions.



Novel Intramolecular Stereoselective Addition of Electrogenerated Radical Species to the Aromatic Ring[1]

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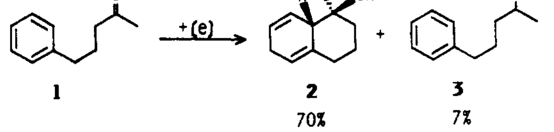
Received March 10, 1986

We have previously reported a novel electroreductive cyclization of nonconjugated olefinic and acetylenic ketones yielding cyclic tertiary alcohols.[2] This cyclization was remarkable in its regio- and stereoselectivities. Recently, we have also found a novel electroreductively induced intramolecular addition of a carbonyl group to an aromatic ring.

A typical reaction is shown in eq 1.[3] This intramolecular



(1)

addition was highly controlled by the material of the cathode, the type of solvents, and the electrolyte. Tin was the best cathode, whereas Cu, Zn, Pb, Al, graphite, Pt, Ni, and Ti did not give satisfactory yield and selectivity. Although *i*-PrOH was a satisfactory solvent, ethanol, DMF, dioxane, and THF gave rather poor results. The effect of the cation of the electrolyte was interesting. Tetraalkylammonium salts such as Et$_4$NOTs and Bu$_4$NBr gave good results, while no cyclized product was obtained when LiClO$_4$ was used as the electrolyte.

The product **2** seemed to be practically a single stereoisomer on the basis of ^{1}H NMR[4] and GLC analyses and could be further purified by recrystallization from carbon tetrachloride.[6] This

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(1) Electroorganic Chemistry. 98.

(2) (a) Shono, T.; Mitani, M. *J. Am. Chem. Soc.* **1971**, *93*, 5284. (b) Shono, T.; Nishiguchi, I.; Ohmizu, H. *Ibid.* **1978**, *100*, 545. (c) Shono, T.; Nishiguchi, I.; Ohmizu, H. *Chem. Lett.* **1976**, 1233.

(3) The electroreduction of 5-phenyl-2-pentanone (**1**) (1.0 g, 6.16 mmol) was carried out by using a Sn cathode (5 × 10 cm^2) and a carbon rod anode at room temperature in isopropyl alcohol (40 mL) containing Et$_4$NOTs (10 g) as a supporting electrolyte. The cathodic and anodic chambers were separated by a ceramic diaphragm and 5*F*/mol of electricity was passed (0.2 A). After usual working up, 1-hydroxy-1-methyl-1,2,3,4,6,9-hexahydronaphthalene (**2**) (70%) and 5-phenyl-2-pentanol (**3**) (7%) were isolated by column chromatography on silica gel.

(4) A trace amount (<1%) of stereoisomer, though not confirmed, seemed to exist. Radical cyclization has been known to proceed with a moderate cis selectivity.[5] The stereoselectivity observed in this cyclization is, however, much higher (cis/trans = ~100) than that (~3.8) reported for the typical radical cyclization. This high stereoselectivity may be well explained by the repulsion between two negatively charged groups as shown in Scheme I.

(5) (a) Beckwith, A. L. J.; Blair, I.; Phillipou, G. *J. Am. Chem. Soc.* **1974**, *96*, 1613. (b) Garst, J. F.; Hines, J. B. *Ibid.* **1984**, *106*, 6443.

(6) **2**: mp 102–103 °C; UV (hexane) λ_{max} 210 nm (ε 2043); IR (KBr) 3350, 1660, 1650, 1270, 1180, 1165, 1118, 1112, 1099, 958, 920, 908, 865, 785, 680 cm^{-1}; ^{1}H NMR (CCl$_4$) δ 0.99 (s, 3 H), 1.12–2.30 (m, 7 H), 2.52–2.68 (br s, 3 H), 5.32–5.45 (br s, 1 H), 5.61–5.95 (m, 2 H); ^{13}C NMR (CDCl$_3$) 21.78 (q), 24.15 (t), 26.76 (t), 34.89 (t), 41.98 (d), 48.88 (t), 74.43 (s), 118.27 (d), 124.07 (d), 125.71 (d), 135.96 (s) ppm; mass spectrum, *m/e* 164 (M$^+$).

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Scheme I

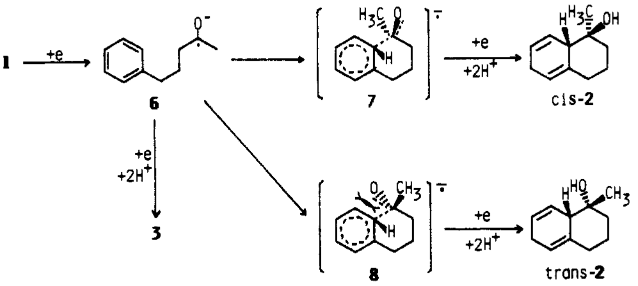
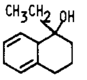
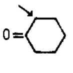
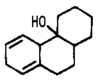
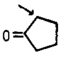
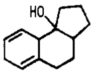
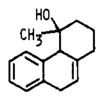
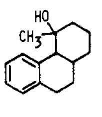
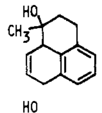
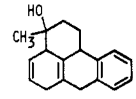
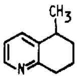
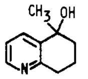
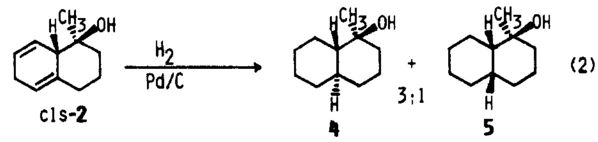


Table I. Electroreduction of β- or γ-Aryl Ketones

starting material ArCH$_2$CH$_2$Y		product[a] and yield, %[b]			
Ar	Y				
C$_6$H$_5$	CH$_2$COC$_2$H$_5$		55		19[c]
C$_6$H$_5$			45[d]		37[c]
C$_6$H$_5$			21		36[c]
β-Naph	CH$_2$COCH$_3$		26		27[e]
α-Naph	COCH$_3$		74[f]		
9-Anth[g]	COCH$_3$		54[h]		
α-Py	CH$_2$COCH$_3$		14[i]		6[i,j]

[a] Satisfactory spectroscopic and elemental analyses were obtained for all compounds. [b] Isolated yield. [c] Yield of noncyclized alcohol. [d] mp 111-112 °C. [e] mp 131-132 °C. [f] mp 104-105 °C. [g] 9-Anthranyl. [h] mp 141-142 °C. [i] See ref 14. [j] mp 99-101 °C.

product **2** was assigned to be the cis isomer, in which a hydroxy group and a hydrogen on C-9 are located on the same side, by analyzing ^{13}C NMR spectra[7] of the hydrogenated products **4**[8] and **5**[9] (eq 2). Similar stereoselectivity has been observed in our

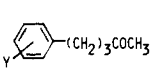
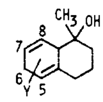
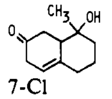
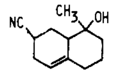
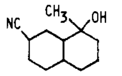
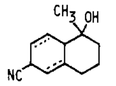
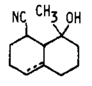
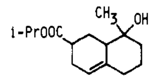
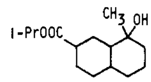


(2)

previously reported electroreductive cyclization of nonconjugated olefinic ketones.[2a,b]

The most plausible mechanism of cyclization is shown in Scheme I. The anion radical **6**[10] generated by one-electron transfer to the carbonyl group attacks the aromatic ring to give the cis intermediate **7** rather than trans **8**, since oxygen atom and phenyl group repel each other owing to their negative charge.

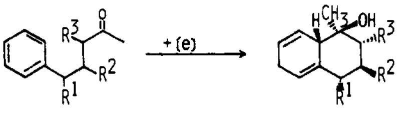
Table II. Electroreduction of Ar-Substituted 5-Phenyl-2-pentanones

starting material		product[a] and yield, %[b]			
					
p-CH$_3$	7-CH$_3$	56[c]			12[d]
m-CH$_3$	6-CH$_3$	19	8-CH$_3$	18[e]	36[d]
o-CH$_3$	5-CH$_3$	29[f]			46[d]
p-OCH$_3$	7-OCH$_3$	73			5[d]
m-OCH$_3$	8-OCH$_3$	17	6-OCH$_3$	~0[g]	39[d]
p-N(CH$_3$)$_2$		19[h]			25[d]
p-Cl	7-Cl	63[i]			3[d]
p-CN		32[j]		24[j]	
m-CN				~62[k]	
p-CO$_2$CH$_3$		13[j]		34[j]	6[d]

[a] Satisfactory spectroscopic and elemental analyses were obtained for all compounds. [b] Isolated yield. [c] mp 64-65 °C. [d] Yield of noncyclized alcohol. [e] mp 74-76 °C. [f] 95-96 °C. [g] A trace amount of 6-methoxy isomer, which could not be identified, seemed to exist from ^{1}H NMR. [h] mp 64-65 °C. [i] mp 68-71 °C. [j] Obtained as a mixture of two stereoisomers. [k] Cyclized products were obtained as a mixture of several olefinic and saturated compounds.

Another mechanism in which the phenyl ring is reduced to an anion radical which reacts with the carbonyl group may be unlikely, since the phenyl ring in butylbenzene was completely inert under the same reaction conditions.

It was remarkable that a methyl group located between the phenyl and carbonyl groups did not inhibit the cyclization and also that the product was stereochemically a single isomer (eq 3).[11]



(3)

9a R^1=CH$_3$, R^2,R^3=H 60%
9b R^1,R^3=H, R^2=CH$_3$ 68%
9c R^1,R^2=H, R^3=CH$_3$ 60%

Other starting materials and products obtained under the same reaction conditions are summarized in Tables I and II.[12] Although the stereoconfigurations of the cyclized products were not determined, ^{1}H and ^{13}C NMR spectra showed that each of them was almost a single stereoisomer. It is not always completely clear, but a m-substituted[13] electron donating group (CH$_3$O-) hindered the cyclization considerably, whereas an electron withdrawing one (CN-) favored the reaction. These results suggest that the active species attacking the aromatic ring has an anionic character.

This cyclization was limited to six-membered ring formation.

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(7) Ayer, W. A.; Browne, L. M.; Fung, S.; Stothers, J. B. S. *Org. Magn. Reson.* **1978**, *11*, 73.

(8) ^{13}C NMR (CDCl$_3$) 21.24 (q), 23.35 (t), 25.53 (t), 26.39 (t), 26.66 (t), 34.13 (t), 34.59 (t), 39.42 (d), 42.86 (t), 53.17 (d), 72.71 (s) ppm.

(9) ^{13}C NMR (CDCl$_3$) 20.77 (q), 21.77 (t), 23.40 (t), 24.67 (t), 26.88 (t), 29.08 (d), 31.60 (t), 32.13 (t), 33.97 (t), 47.81 (d), 72.71 (s) ppm.

(10) The anion radical is not a free anion radical but is partially neutralized with the cation of the supporting electrolyte.

(11) The stereoconfigurations, though not always confirmed certainly, were estimated as shown in eq 3 by ^{13}C NMR. mp: **9b**, 44-46 °C; **9c**, 79-81 °C.

(12) Benzonitrile, methyl benzoate, and pyridine were also inert under our reaction conditions. However, when the aromatic ring is a polynuclear hydrocarbon, the possibility that the reduction of the aromatic ring is the initial step may not be excluded.

(13) Since the active species attacks the ortho or para position of the meta substituent, the meta substituent would show a more remarkable effect on the reaction than ortho and para substituents.

(14) Although the mechanism is not always clear, elimination of the hydroxy group and/or aromatization of the initially formed coupling product took place under the condition of electroreduction.