Tetrahedron Vol. 47, No. 4/5, pp. 583-592, 1991
Printed in Great Britain

0040-4020/91 $3.00+.00

ANODIC AMIDE OXIDATIONS: FUNDAMENTAL STUDIES CONCERNING THE ANNULATION OF SIX- AND SEVEN-MEMBERED RINGS ONTO AMINES

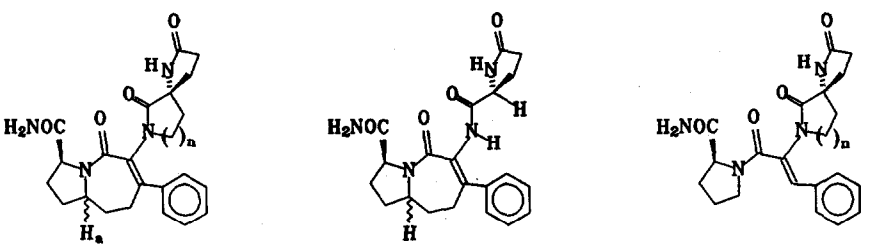
Kevin D. Moeller,* Scott L. Rothfus, and Poh Lee Wong
Department of Chemistry, Washington University, St. Louis, MO 63130

(*Received in USA* 28 *August* 1990)

Abstract: The compatibility of olefinic and acetylenic nucleophiles with an electrochemically based annulation procedure for fusing six- and seven-membered rings onto amines has been examined. Both monosubstituted olefins and acetylenes were found to be good nucleophiles for annulating seven-membered rings onto amines. Disubstituted olefins and acetylenes appear to be good nucleophiles for completing the annulation of six-membered rings onto amines. In addition, the compatibility of several proline derivatives with the annulation procedure was examined.

In 1986,[1] Marshall and Font reported a series of rigid thyrotropin releasing hormone (TRH) analogs (**I** - **III**) that were designed to function as chemical probes for the active analog approach to computer-assisted drug design.[2]

Figure 1



I n=1,2
Both isomers at H_a are desired.

II

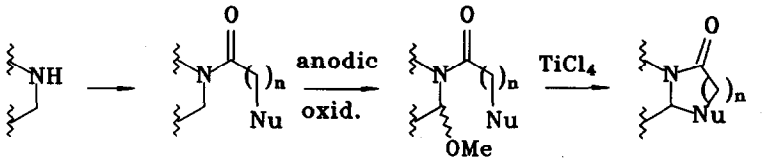
III

Molecular modeling using the Sybyl program[3] predicted that these analogs would occupy the same conformational space as the receptor-bound conformation of TRH. It was reasoned that if the active analog approach is valid, synthesis and testing of the designed analogs should lead to at least one very active analog. Unfortunately, analogs **I** - **III** could not be synthesized for testing.

We became interested in this project when we realized that the electrochemical oxidation of amides[4] might provide an ideal tool for constructing the 1-aza-2-oxobicyclo[5.3.0]decane ring system used to add rigidity to the left-hand side of the rigid TRH analogs. This realization was predicated on the ability of anodic amide oxidations to provide a general means for annulating lactam rings onto amines and amino acid derivatives (Scheme 1).[5] An annulation procedure of this type would appear

useful for the synthesis of rigid peptide analogs because it would allow for the use of amino acid derived starting materials. This would greatly simplify the synthesis because all of the key chiral centers in the analogs would be intact in the initial substrates.

Scheme 1: General Annulation Procedure for Amines



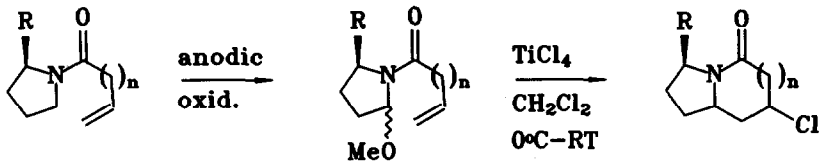
Nu=nucleophile

Unfortunately, relatively few nucleophiles were known to be compatible with the conditions needed for the electrochemical oxidation step. These nucleophiles were limited to an alcohol,[6a] an acid,[6b] a malonate,[6c] a ketone,[5a] a monosubstituted olefin,[6d] and several phenyl rings.[5] Monosubstituted olefins, which would be ideal for the synthesis of the rigid peptide analogs, had not been used in an annulation procedure for making bicyclic lactam ring systems.

With these things in mind, we turned our attention toward determining the scope of the nucleophiles that would be compatible with the proposed annulation procedure. Initially, this work focused on the use of monosubstituted olefins as potential nucleophiles for the formation of six- and seven-membered ring lactams.

As indicated in Table 1, monosubstituted olefins proved to be very useful for constructing seven-membered ring lactams. For example, the constant current electrolysis of **1a** at a carbon anode using a 1*M* tetraethylammonium tosylate in 10% methanol/ acetonitrile electrolyte solution led to the formation of an 82% isolated yield of the methoxylated amide. As in earlier cases,[5b,c,7] the use of acetonitrile as a cosolvent was essential for obtaining good current efficiencies (2-4 F). The reactions could be done using either a carbon or a platinum auxiliary electrode. The methoxylated amide **2a** was cyclized using titanium tetrachloride in methylene chloride (33h, rt, 80% yield) in order to form the bicyclic lactam **3a** and complete the annulation procedure. A mixture of diastereomers was obtained. The anodic oxidation reaction proved to be more problematic when L-prolinol was used as the initial amine (Entry 2). In this case, oxidation afforded a 49% yield of the expected methoxylated product along with a 16% combined yield of two additional methoxylated products. The additional products were derived from the loss of the -CH_2OH substituent on the pyrrolidine ring. Presumably these products formed by the loss of a proton, formaldehyde, and a second electron from the initially formed amide radical cation and then trapping of the subsequent unsubstituted *N*-acyliminium ion. As in case 1, cyclization of the desired methoxylated amide, **2b**, using titanium tetrachloride led to successful completion of the annulation procedure. Again, a mixture of diastereomers was obtained. It is important to note that the formation of a mixture of diastereomeric products is not a concern because the chloride is destined to be removed in the synthesis of the rigid peptide analogs, and because both

Table 1: Annulations Using Monosubstituted Olefins



1 2 3

Entry	Compound	R	n	Cond.	Yield 2 (Rec. 1)	Yield 3
1.	**1a.**	-H	2	A	82%	80%[a]
2.	**1b.**	$-CH_2OH$	2	A	49%[b]	68%[a]
3.	**1c.**	$-CH_2OPivaloyl$	2	A	8%(82%)	N.A.[c]
4.	**1c.**	$-CH_2OPivaloyl$	2	B	40%	90%
5.	**1d.**	$-CH_2OCH_3$	2	A	55%(42%)	77%
6.	**1e.**	$-CO_2Me$	2	A	18%(78%)	N.A.
7.	**1e.**	$-CO_2Me$	2	B	68%(7%)	89%[a]
8.	**1f.**	-H	1	A	73%(22%)	31%[d]
9.	**1g.**	$-CH_2OPivaloyl$	1	A	--[e]	N.A.
10.	**1h.**	$-CO_2Me$	1	A	6%(76%)	N.A.
11.	**1h.**	$-CO_2Me$	1	B	--[f]	N.A.

Conditions: A: Constant current, carbon rod anode, carbon or Pt cathode, and a 1*M* Et_4NOTs in 10% MeOH/ CH_3CN electrolyte solution (see experimental section for details). B: Identical with A except for the use of Bu_4NBF_4 as electrolyte. *a.* The product contained about 5-10% of the unsaturated cyclized product. *b.* A small amount (10%) of **2a** was obtained along with 6% of dimethoxylated **1a**. *c.* N.A. stands for not attempted. *d.* In addition approximately 10% of the uncyclized *N*-α-hydroxylalkyl amide was obtained. *e.* This reaction was typified by a poor mass balance and recovery of a 41% yield of starting material where the double bond had migrated. *f.* This reaction led to a complex mixture of products, as well as double bond migration.

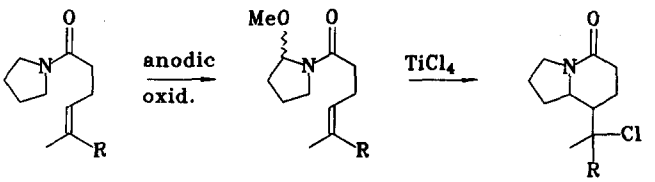
bridgehead isomers of the rigid TRH analogs are required for biological testing. In an effort to circumvent the problems associated with the oxidation of amide **1b**, the alcohol was protected as an ester and the oxidation of amide **1c** examined. The initial conditions using tetraethylammonium tosylate as the electrolyte were not successful. In this instance, anodic oxidation led to the formation of only an 8% yield of the desired methoxylated product even after 2.5F of charge had been passed. An 82% yield of recovered starting material was obtained. When more charge was passed (16.7 F), evidence for loss of the pivaloyl protecting group was obtained. The current efficiency of the reaction could be increased by a change in electrolyte; however, these conditions led to a lower overall mass balance. To this end, constant current electrolysis of **1c** using tetrabutylammonium tetrafluoroborate as the electrolyte led to the formation of the desired methoxylated product in a 40% yield after 3F of charge had been passed. Treatment of the methoxylated amide, **2c**, with titanium tetrachloride led to a

90% yield of a diastereomeric mixture of bicyclic amide products, **3c**. A methyl ether protecting group proved to be more useful. In this case (Entry 5) anodic oxidation led to the formation of the methoxylated amide in a 55% isolated yield along with a 42% yield of recovered starting material after 2.5 F. The methoxylated amide, **2d**, was then cyclized using titanium tetrachloride to form bicyclic amide **3d** in a 77% yield. The anodic oxidation of amide **1e**, derived from proline methyl ester, also showed a dependence on the nature of the electrolyte. Oxidation using tetraethylammonium tosylate as the electrolyte led to the formation of a 18% yield of methoxylated product along with 78% of the recovered starting material. The oxidation of **1e** using tetrabutylammonium tetrafluoroborate led to the formation of a 68% yield of the desired methoxylated amide **2e**. A 7% yield of recovered starting material was obtained. Treatment of the methoxylated amide **2e** with titanium tetrachloride led to the formation of bicyclic amide **3e** in an 89% yield. As in the earlier cyclizations, a mixture of diastereomers was obtained.

Unfortunately, monosubstituted olefins were not useful for the construction of six-membered ring lactams. In the parent case (Entry 8), the anodic oxidation proceeded smoothly to afford a 73% yield of methoxylated product, but the cyclization reaction led to the formation of only a 31% yield of the desired bicyclic amide. After 48 hours at room temperature, the cyclization reaction still afforded material that had not cyclized. Furthermore, the addition of substituents to the amide was deleterious to the oxidation reaction. A satisfactory yield of methoxylated amide could not be obtained for any of the cases attempted. When the oxidation did proceed, the reactions were plagued by migration of the double bond into conjugation with the amide.

Since the use of a monosubstituted olefin was not compatible with an annulation procedure for constructing six-membered ring lactams, we turned our attention toward examining the utility of di- and trisubstituted olefins with the annulation procedure. We hoped that this would allow for the use of olefinic nucleophiles that did not offer the possibility of olefin migration. In order to explore this question, amides **4a** and **4b** were synthesized and then oxidized (Scheme 2).

Scheme 2: Annulations Using Di- and Trisubstituted Olefins



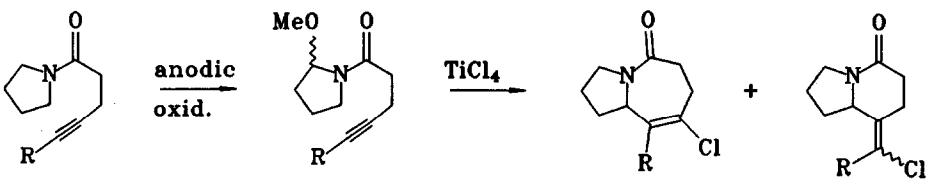
4a. R=H	5a. 62%	6a. 50%
4b. R=CH_3	5b. --	6b. N.A.

The constant current electrolysis of **4a** using a carbon anode and cathode and a 1*M* tetraethylammonium tosylate in 10% methanol/ acetonitrile electrolyte solution led to the formation of a 62% isolated yield of the methoxylated amide **5a**. The cyclization reaction using titanium tetrachloride led to the formation of a complex mixture of products out of which was isolated a 50% yield of the six-

membered ring lactam **6a**. In addition, a 7% yield of material was obtained that has tentatively been assigned as the seven-membered ring lactam. As in the earlier cases, a mixture of diastereomeric products was obtained. The anodic oxidation of amide **4b** turned out to be less successful. In this example, the trisubstituted olefin interfered with the anodic oxidation of the amide. Under no circumstances could a clean methoxylated product be isolated. Clearly, the line that defines when an olefin becomes too electron rich to be compatible with the anodic amide oxidation reaction lies between the di- and trisubstituted olefins.

Although the annulation procedure utilizing a disubsitituted olefin as the nucleophile did lead to the formation of the desired six-membered ring lactam, the reaction was disconcerting for a couple of reasons. First, the yield of the titanium tetrachloride cyclization was rather low, and second, the annulation procedure afforded a product that contained an undesired 1-chloroethyl substituent. A multistep procedure, that might be difficult in the context of a complex rigid peptide analog, would be needed to remove these extra carbons. Recently, Speckamp and coworkers have reported that acetylenes can function as effective nucleophiles for accomplishing the intramolecular trapping of *N*-acyliminium ions.[8] The reactions were shown to be capable of leading to both six- and seven-membered ring formation depending on the nature of the acetylene. In an effort to see if acetylenic nucleophiles would be compatible with the current annulation procedure, amides **7a** and **7b** were

Scheme 3: Annulations Using Acetylenes



7a. R=H	8a. 73% (23% S.M.)	9a. 70%	10a. --
7b. R=CH_3	8b. 70% (19% S.M.)	9b. --	10b. 82%

synthesized. Constant current electolysis of **7a** in a divided cell using a carbon anode and a 1*M* tetraethylammonium tosylate in 10% methanol/ acetonitrile electrolyte solution led to the formation of a 73% isolated yield of the methoxylated amide **8a**. The use of a divided cell was required in order to protect the acetylene from reduction. Cyclization of the methoxylated amide with titanium tetrachloride in methylene chloride led to the formation of the unsaturated seven-membered ring lactam **9a** in a 70% isolated yield. Formation of the seven-membered ring in this case was consistent with the observations reported by Speckamp.[8] In a similar fashion, constant current electrolysis of **7b** led to the formation of methoxylated amide **8b** in a 70% isolated yield along with 19% of the recovered starting material. Titanium tetrachloride cyclization of methoxylated amide **8b** led to the formation of the six-membered ring lactam in an 82% isolated yield. Formation of the six-membered ring in this case was again consistent with the observations reported by Speckamp.[8] This cyclization

proceeded in a fashion that was much cleaner than the cyclization originating from methoxylated amide **5a**. In addition, it seems apparent that the exocyclic carbons in this case can be readily removed with the use of an ozonolysis reaction.

In conclusion, the anodic oxidation of amides can provide a means for annulating six- and seven-membered rings onto amines and amino acid derivatives using simple olefinic and acetylenic nucleophiles. It is hoped that this annulation procedure will provide a convenient method for constructing a series of rigid peptide analogs. Efforts along these lines are currently underway.

Experimental Section[9]

General Procedure for the Anodic Oxidation of Amides in the Presence of Olefins: *N*-α-Methoxy-*N*-(4-pentenoyl)pyrrolidine (2a): An oven-dried vial was fitted with a two-holed rubber stopper equipped with a carbon rod anode and a platinum wire cathode. A syringe needle was pushed through the rubber stopper and used as a nitrogen inlet. The vial was charged with 0.458 g (3 mmol) of *N*-4-pentenoylpyrrolidine and 15 mL of a 1 *M* tetraethylammonium tosylate in 10% methanol/ acetonitrile electrolyte solution. The mixture was degassed with a stream of nitrogen for 5 min. The reaction was then electrolyzed at a constant current of 26.7 mA and monitored by TLC. After 3 F of charge had been passed, the reaction was transferred to a round bottom flask and concentrated *in vacuo* until a viscous liquid was formed. The liquid was immediately chromatographed through silica gel using ether as the eluant to afford 0.449 g (82%) of the methoxylated product. An additional 4% of the hydroxylated material was obtained. The spectral data for the mixture of amide rotomers were as follows: TLC R_f = 0.41 using ether; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.96-5.82 (m, 1H), 5.46 (d, 0.5H, J = 4.9 Hz), 5.10 (d, 0.5 Hz, J = 1.6 Hz), 5.04-4.98 (m, 2H), 3.68-3.55 (m, 2H), 3.39, 3.30 (two s, 3H), 2.57-2.38 (m, 4H), 2.22-1.63 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.4, 173.2, 138.2, 138.0, 115.6, 115.5, 89.1, 87.4, 56.7, 54.2, 46.3, 45.7, 34.1, 33.5, 31.6, 31.1, 29.2, 28.7, 23.0, 21.1; GCMS (35 eV) m/e (rel. intensity) 169 (M-14, 0.6), 168 (M-15, 6), 151 (8), 138 (1), 128 (3), 86 (12), 85 (9), 70 (100), 69 (97), 68 (66); HRMS (EI) m/e: Calcd. for $C_{10}H_{17}NO_2$, 183.1259; Found, 183.1247.

***N*-α-Methoxy-2-hydroxymethyl-*N*-(4-pentenoyl)pyrrolidine (2b):** The data are reported for the mixture of diastereomers and amide rotomers. TLC R_f = 0.24 using ether; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.94-5.80 (m, 1H), 5.63 (d, 0.25H, J = 5.3 Hz), 5.11 (d, 0.75H, J = 1.5 Hz), 5.10-4.94 (m, 2H), 4.70-4.67 (br s, 1H), 4.22-4.15 (m, 1H), 3.79-3.53 (m, 2H), 3.32, 3.29 (two s, 3H), 2.62-2.38 (m, 4H), 2.11-1.68 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2, 174.9, 137.9, 137.6, 116.0, 115.9, 90.4, 87.9, 67.5, 65.5, 61.6, 59.1, 54.6, 54.5, 33.8, 33.4, 30.8, 30.1, 29.2, 29.1, 25.6, 25.0; IR (neat, NaCl) 3630-3310 br, 3077, 2978, 2941, 2829, 1641, 1428, 1360, 1199, 1088, 999, 914 cm^{-1}; GCMS (70eV) m/e (rel. intensity) 213 (M^+, 0.2), 212 (M-1, 0.2), 182 (M-31, 9), 181 (1), 150 (2), 130 (2), 101 (11), 100 (100), 99 (18), 83 (13), 82 (14), 781 (12), 69 (27), 68 (95); HRMS (EI) m/e: Calcd. for $C_{11}H_{19}NO_3$, 213.1365; Found, 213.1370.

***N*-α-Methoxy-2-pivaloyloxymethyl-*N*-(4-pentenoyl)pyrrolidine (2c):** The data are reported for the mixture of diastereomers and amide rotomers (4 compounds). TLC R_f = 0.60 using ether; ^{1}H NMR (300 MHz, $CDCl_3$) 5.92-5.78 (m, 1H), 5.63 (d, 0.25H, J = 4.7 Hz), 5.10-4.95 (m, 2H), 4.92 (d, 0.25H, J = 1.8 Hz), 4.46-4.26 (m, 2H), 4.21 (d, 1H, J = 7.5 Hz), 3.31, 3.29 (two s, 3H), 2.61-2.34 (m, 4H), 2.18-1.72 (m, 4H), 1.19 (br s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 173.0, 138.1, 137.9, 115.8, 115.5, 90.0, 89.8, 88.2, 67.6, 65.2, 63.7, 56.2, 56.1, 55.8, 54.4, 39.0, 33.8, 33.3, 30.8, 29.3, 29.2, 29.1, 29.0, 27.3, 27.2, 25.3, 24.5; IR (neat, NaCl) 3078, 2976, 2827, 1727, 1659, 1460, 1409, 1366, 1315, 1284, 1160, 1071, 1036, 986, 911 cm^{-1}; GCMS (35 eV) m/e (rel. intensity) 297 (M^+, 0.3), 282 (m-15, 0.1), 196 (2), 184 (26), 182 (12), 114 (9), 101 (28), 100 (100), 99 (12), 98 (17), 83 (17), 82 (35), 81 (29), 80 (18), 71 (13), 69(14), 68 (98); HRMS (EI) m/e: Calcd. for $C_{16}H_{27}NO_4$, 297.1940; Found, 297.1929.

***N*-α-Methoxy-2-methoxymethyl-*N*-(4-pentenoyl)pyrrolidine (2d):** The date are reported for the mixture of diastereomers and amide rotomers (4 compounds). TLC R_f = 0.57 using ether; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.93-5.79 (m, 1H), 5.62 (d, 0.25H, J = 4.7 Hz), 5.10-4.94 (m, 2H), 4.90 (d, 0.75H, J = 1.9 Hz), 4.33-4.16 (m, 2H), 4.09 (br s, 1H), 3.38, 3.33, 3.30, and 3.26 (four s, 6H), 2.55-2.34 (m, 4H), 2.15-1.78 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 172.8, 138.3, 138.0, 115.6, 115.3, 90.1, 88.1, 77.7, 74.4, 72.4, 59.2, 57.1, 57.0, 56.6, 55.9, 54.2, 33.8, 33.2, 30.9, 30.7, 29.2, 29.1, 27.2, 25.9, 24.7; IR (neat/

NaCl) 3077, 2927, 2952, 2898, 2827, 1666, 1425, 1360, 1290, 1196, 1121, 1086, 986, 911 cm^{-1}; GCMS (30 eV) m/e (rel. intensity) 227 (M^+, 0.6), 196 (M-OCH_3, 2), 195 (M-$HOCH_3$, 6), 183 (4), 182 (34), 150 (5), 114 (15), 101 (6), 100 (100), 68 (54); HRMS (EI) m/e: Calcd. for $C_{12}H_{21}NO_3$, 227.1521; Found, 227.1519.

Methyl *N*-α-methoxy-*N*-(4-pentenoyl)proline (2e): The data are reported for the mixture of diastereomers and amide rotomers (4 compounds). TLC R_f = 0.40 using ether; ^1H NMR (300 MHz, $CDCl_3$) δ 5.95-5.78 (m, 1H), 5.68 (d, 0.25H, J = 4.7 Hz), 5.16-5.10 (m, 2H), 5.05-5.00 (dd, 0.5H, J = 1.8, 9.9 Hz), 4.99-4.98 (dd, 0.25H, J = 1.5, 8.7 Hz), 4.57 (d, 0.5H, J = 9.3 Hz), 4.43 (t, 0.5 H, J = 8.5 Hz), 3.79, 3.76 (two s, 0.4H) 3.75, 3.71 (two s, 2.6H), 3.42, 3.41 (two s, 0.4H), 3.39, 3.31 (two s, 2.6H), 2.66-1.66 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.4, 173.2, 172.9, 172.8, 138.0, 137.8, 115.7, 115.5, 89.6, 89.2, 88.8, 87.7, 59.6, 59.2, 59.1, 59.0, 54.4, 54.3, 52.8, 52.4, 33.3, 33.2, 31.5, 29.6, 29.4, 29.2, 29.0, 28.9, 28.7, 28.6, 26.4, 26.1; IR (neat, NaCl) 3077, 2982, 2952, 2829, 1750, 1665, 1415, 1369, 1198, 1179, 1087, 1069, 1003, 913 cm^{-1}; GCMS (70 eV) m/e (rel. intensity) 241 (M^+, 0.01), 226 (M-CH_3, 0.4), 211 (M-CH_2O, 0.5), 182 (14), 128 (22), 100 (100), 68 (31); HRMS (EI) m/e: Calcd. for $C_{12}H_{19}NO_4$, 241.1314; Found, 241.1315.

***N*-α-Methoxy-*N*-(3-butenoyl)pyrrolidine (2f):** The data are reported for the mixture of amide rotomers. TLC R_f= 0.44 using ethyl acetate; ^1H NMR (300 MHz, $CDCl_3$) δ 6.08-5.93 (m, 1H), 5.45 (d, 0.5 H, J - 4.9 Hz), 5.21-5.11 (m, 2H), 5.02 (d, 0.5 H, J = 4.1 Hz), 3.67-3.57 (m, 1H), 3.45-3.33 (m, 1H), 3.39, 3.1 (two s, 3H), 3.17 (dd, 2H, J = 6.7, 1.5 Hz), 2.22-1.62 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 171.5, 132.3, 131.7, 118.4, 118.1, 89.1, 87.5, 56.8, 54.1, 46.3, 45.9, 40.1, 39.5, 31.6, 31.1, 23.1, 21.1; IR (neat, NaCl) 3079, 2980, 2941, 2889, 2828, 1660, 1411, 1365, 1270, 1177, 1084, 994, 918 cm^{-1}; GCMS (70 eV) m/e (rel. intensity) 154 (M-CH_3, 2), 139 (M-CH_2O, 22), 138 (11), 137 (19), 128 (30), 85 (46), 70 (67), 69 (98), 68 (100); HRMS (EI) m/e: Calcd. for $C_9H_{15}NO_2$, 169.1103; Found, 169.1115.

***N*-α-Methoxy-*N*-(4-hexenoyl)pyrrolidine (5a):** The data is reported for the mixture of amide rotomers. TLC R_f = 0.52 using 50% dichloromethane/ ether; ^1H NMR (300 MHz, $CDCl_3$) δ 5.52 (d, 0.5H, J = 4.8 Hz), 4.99 (d, 0.5 H, J = 4.4 Hz), 3.69-3.53 (m, 1H), 3.43-3.30 (m, 1H), 3.39, 3.30 (two s, 3H), 2.51-2.30 (m, 4H), 2.20-1.68 (m, 4H), 1.65 (d, 3H, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 172.9, 130.3, 125.9, 125.8, 88.8, 87.0, 56.4, 53.9, 45.9, 45.3, 34.5, 33.9, 31.2, 30.8, 27.9, 27.3, 22.9, 22.7, 20.8, 17.6; IR (neat, NaCl) 3000, 2937, 2887, 2861, 1652, 1419, 1073, 1069 cm^{-1}; GCMS (70 eV) m/e (rel. intensity) 197 (M^+, 0.6), 182 (M-CH_3, 2), 165 (M-CH_3OH, 4), 86 (15), 70 (100), 69 (37), 55 (26); HRMS (EI) m/e: Calcd. for $C_{11}H_{19}NO_2$, 197.1415; Found, 197.1395.

General Procedure for the Anodic Oxidation of Amides in the Presence of Acetylenes: *N*-α-Methoxy-*N*-(4-hexynoyl)pyrrolidine (8b): A 1 *M* solution of tetraethylammonium tosylate in 10% methanol/ acetonitrile was prepared and degassed (nitrogen was bubbled through the solution for 5 min). A portion of the solution (7.5 mL) was transferred by syringe to the cathodic chamber of a standard H-cell. To the anodic chamber were added 0.345 g (2.1 mmol) of *N*-4-hexynoylpyrrolidine, 2.89 g (20.9 mmol) of anhydrous potassium carbonate as an acid scavanger, and 7.5 mL of the electrolyte solution. The anodic and cathodic chambers were equipped with a carbon rod electrode. The reaction was electrolyzed at a constant current of 28 mA and monitored by TLC. After 4 F of charge had been passed, the reaction was filtered, concentrated *in vacuo*, and then immediately chromatographed through silica gel using 30% ether/ dichloromethane as eluant. The reaction led to the formation of 0.287 g (70%) of the methoxylated product along with 66.6 mg (19%) of the recovered starting material. The spectral data is reported for the mixture of amide rotomers. TLC R_f = 0.42 using 30% ether/ dichloromethane; ^1H NMR (300 MHz, $CDCl_3$) δ 5.45 (d, 0.5 H, J = 4.8 Hz), 5.04 (d, 0.5 H, J = 4.3 Hz), 3.67-3.55 (m, 1H), 3.44-3.34 (m, 1H), 3.38, 3.32 (two s, 3H), 2.64-2.48 (m, 4H), 2.20-1.80 (m, 4H), 1.77 (t, 3H, J = 2.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0, 171.7, 88.6, 87.0, 78.1, 77.9, 75.8, 75.7, 56.3, 53.9, 45.9, 45.3, 39.9, 33.4, 31.2, 30.7, 22.6, 20.7, 14.3, 13.9, 3.2; IR (neat, NaCl) 2922, 2888, 2830, 1651, 1419, 1339, 1246, 1178, 1082 cm^{-1}; GCMS (70 eV) m/e (rel. intensity) 180 (M-CH_3, 20), 164 (m-OCH_3, 11), 100 (7), 95 (7), 85 (12), 70 (100), 53 (22); HRMS (EI) m/e: Calcd. for $C_{11}H_{17}NO_2$, 195.1259; Found, 195.1253.

***N*-α-Methoxy-*N*-(4-pentynoyl)pyrrolidine (8a):** The data are reported for the mixture of amide rotomers. TLC R_f = 0.45 using 40% ether/ dichloromethane; ^1H NMR (300 MHz, $CDCl_3$) δ 5.45 (d, 0.5 H, J = 4.9 Hz), 5.02 (d, 0.5 H, J = 4.1 Hz), 3.69-3.55 (m, 1H), 3.43-3.34 (m, 1H), 3.39, 3.32 (two s, 3H), 2.71-2.52 (m, 4H), 2.15 (m, 1H), 2.03-1.78 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 171.2,

88.7, 87.1, 83.6, 83.4, 68.5, 56.4, 53.9, 46.9, 45.4, 33.5, 32.8, 31.2, 30.6, 22.6, 20.7, 13.9, 13.6; IR (neat, NaCl) 3293, 2931, 2883, 2840, 2116, 1653, 1420, 1177, 1082 cm^{-1}; GCMS (70 eV) m/e (rel. intensity) 181 (M^+, 0.4), 166 (M-CH_3, 20), 150 (M-OCH_3, 38), 86 (27), 85 (22), 84 (23), 81 (21), 71 (45), 70 (100), 53 (89); HRMS (EI) m/e: Calcd. for $C_{10}H_{15}NO_2$, 181.1103; Found 181.1099.

General Procedure for the $TiCl_4$-Catalyzed Cyclizations: 1-Aza-5-chloro-2-oxobicyclo[5.3.0]decane (3a): To an oven-dried 50 mL round-bottom flask was added 0.387 g (2.11 mmol) of the methoxylated amide along with 20 mL of dry dichloromethane. The reaction mixture was cooled to -78°C and then 5.3 mL (5.3 mmol) of a 1*M* titanium tetrachloride in dichloromethane solution (Aldrich) was added. The solution turned deep red (colors have ranged from bright yellow to black with no apparent effect on the yield of the reaction). The temperature was maintained at -78°C for 30 min and then the dry ice/ acetone bath removed. After 33 h the reaction was poured into a separatory funnel containing dichloromethane and a 30% (w/w) aqueous sodium potassium tartrate solution. The aqueous layer was extracted twelve times with dichloromethane. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to obtain an *ca.* 1:1 mixture of diastereomers. The crude product was chromatographed through silica gel using 5% methanol/ ether as the eluant to afford 0.319 g (80%) of the cyclized products. A partial separation of diastereomers was obtained. In addition, the material contained about 5% of an unsaturated cyclized material. ^1H NMR data suggested that isomer 1 had a trans relationship about the seven-membered ring between C_8 and the chloride (psuedoaxial orientation). Isomer two was assigned as having a cis relationship between C_8 and the chloride (psuedoequatorial chloride). The spectral data for the partially separated mixture of diastereomers were as follows (NMR ratio of isomer 2/ isomer 1 = 77/23): TLC R_f = 0.38 using 5% methanol/ ether; ^1H NMR (300 MHz, $CDCl_3$) δ 4.62 (p, 0.23H, J = 3.3 Hz), 4.28-4.20 (m, 0.23H), 4.02 (tt, 0.77H, J = 11.8, 4.1 Hz), 3.71 (m, 1.77H), 3.40 (m, 1H), 3.05 (app. ddd, 0.23H, J *ca.* 14.5, 11.9, 2.5 Hz), 2.62-2.05 (m, 5H), 1.95-1.68 (m, 4.77H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.7, 111.8, 60.5, 60.0, 56.4, 52.0, 47.1, 46.0, 43.2, 35.4, 34.8, 34.3, 33.7, 31.4, 23.5; IR (neat, NaCl) 2950, 2874, 1643, 1449, 1350, 1236, 1192, 762 cm^{-1}; GCMS (PCI) m/e (rel. intensity) 190 (M+3, 33), 188 (M+1, 100), 187 (M^+, 6), 152 (M-Cl, 67), 151 (M-HCl, 1.5), 110 (9), 70 (18), 55 (10); HRMS (EI) m/e: Calcd. for $C_9H_{14}ClNO$, 187.0764; Found, 187.0761.

1-Aza-5-chloro-10-hydroxymethyl-2-oxobicyclo[5.3.0]decane (3b): The data for the mixture of two main isomers are reported. The material contained about 5% of the unsaturated product. The NMR ratio of the isomers was *ca.* 60/40. TLC R_f = 0.25 using 5% methanol/ ether; ^1H NMR (300 MHz, $CDCl_3$) δ 4.95-4.70 (br hump, 0.6H), 4.64-4.60 (m, 0.6 H), 4.48-4.40 (m, 0.4H), 4.34-4.21 (m, 1H), 4.05 (tt, 0.6H, J = 11.7, 4.2 Hz), 3.90-3.80 (m, 0.4H), 3.67-3.60 (m, 2H), 3.12 (ddd, 0.6H, J = 14.3, 12.1, 2.2 Hz), 2.62-1.60 (m, 9.4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.7, 174.4, 66.2, 65.9, 61.8, 61.7, 60.0, 59.1, 57.4, 53.2, 45.6, 42.7, 35.2, 32.9, 32.2, 31.7, 31.4, 30.7, 26.4, 26.2; IR (neat, NaCl) 3300 br, 2950, 2881, 1620, 1452, 1353, 1234, 1180, 1052, 914 cm^{-1}; GCMS (PCI) m/e (rel. intensity) 220 (M+3, 33), 218 (M+1, 100), 182 (M-Cl, 41), 140 (11); HRMS (EI) m/e: Calcd. for $C_{10}H_{16}NO_2Cl$, 217.0869; Found, 217.0865.

1-Aza-5-chloro-2-oxo-10-pivaloyloxymethylbicyclo[5.3.0]decane (3c): The data for the mixture of diastereomers are reported. The material contained about 5% of the unsaturated product. TLC R_f = 0.66 using 10% methanol/ ether; ^1H NMR (300 MHz, $CDCl_3$) δ 4.63 (p, 0.5H, J = 3.4 Hz), 4.47-4.36 (m, 1.5H), 4.15, 4.14, 4.13, 4.11 (four s, 1.5H), 4.10-3.99 (tt partially buried, 0.5H, J = 11.7, 4.2 Hz), 3.82 (t, 0.5H, J = 9.6 Hz), 3.06 (ddd, 0.5H, J = 14.3, 11.9, 2.3 Hz), 2.60-1.60 (m, 10H), 1.23, 1.22, 1.21, 1.20 (four s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.9, 173.9, 172.8, 63.3, 60.7, 59.8, 57.1, 57.0, 56.9, 52.6, 46.3, 43.3, 38.9, 35.6, 33.5, 32.4, 31.9, 31.4, 29.8, 27.3, 25.8, 25.6; IR (neat, NaCl) 2968, 2932, 2883, 1726, 1638, 1447, 1365, 1284, 1162, 1033, 977 cm^{-1}; GCMS (70 eV) m/e (rel. intensity) 218 (2), 216 (M-85), 201 (6), 199 (16), 189 (4), 188 (35), 187 (11), 186 (100), 150 (22), 122 (14), 82 (29), 68 (26); HRMS (EI) m/e: Calcd. for $C_{15}H_{24}ClNO_3$-C_5H_9O, 216.0791; Found, 216.0792.

1-Aza-5-chloro-10-methoxymethyl-2-oxobicyclo[5.3.0]decane (3d): The data for the mixture of diastereomers are reported. The material contained about 10% of the unsaturated cyclized product. TLC R_f = 0.60 using 10% methanol/ ether; ^1H NMR (300 MHz, $CDCl_3$) δ 5.57 (m, 2H, vinyl protons for the minor cyclized impurity), 4.64-4.57 (m, 0.5H), 4.36-4.25 (m, 1H), 4.22-4.38 (m, 0.5H), 3.98 (tt with a small tt underneath, 0.5H, J = 12.1, 4.2 Hz), 3.80 (t, 0.2H, J = 9.9 Hz), 3.60 (m, 0.3H), 3.55-3.41 (m, 2H), 3.36, 3.35, 3.33, 3.32 (four s, 3H), 3.12-3.00 (m, 0.5H), 2.62-2.48 (m, 0.5H), 2.42-2.28 (m, 2.5H), 2.20-2.05 (m, 2H), 2.00-1.76 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.4, 173.1, 130.0, 129.9,

128.9, 121.0, 73.2, 73.0, 72.3, 72.2, 72.0, 61.0, 60.5, 60.0, 59.2, 58.4, 58.3, 58.2, 58.0, 57.9, 57.7, 57.1, 57.0, 56.2, 56.1, 52.8, 52.6, 46.3, 46.1, 43.3, 43.3, 37.0, 36.9, 35.8, 35.7, 34.8, 33.6, 33.0, 32.9, 32.6, 32.0, 31.9, 31.8, 31.4, 31.2, 26.8, 26.6, 25.9, 25.7, 25.0; IR (neat, NaCl) 2967, 2952, 2891, 2828, 1658, 1642, 1441, 1351, 1232, 1173, 1117, 1078, 1004, 974, 856, 755 cm^{-1}; GCMS for the olefinic compound (35 eV) m/e (rel intensity) 195 (M^+, 3), 163 (8), 151 (10), 150 (100), 122 (12), 80 (11), 79 (33), 68 (32); GCMS for the chlorinated compound (35 eV) m/e (rel intensity) 233 (M+2, 0.3), 231 (M^+, 0.9), 216 (M-15, 1), 199 (M-32, 6), 188 (33), 187 (11), 186 (100), 150 (20), 122 (21), 82 (10), 79 (11), 68 (27); HRMS (EI) m/e: Calcd. for $C_{11}H_{18}ClNO_2$, 231.1026; Found, 231.1025.

1-Aza-10-carbomethoxy-5-chloro-2-oxobicyclo[5.3.0]decane (3e): The diastereomers were partially separated into two sets of two isomers by column chromatography. The spectral data for the first pair of isomers off the column were as follows: TLC R_f = 0.58 using 10% methanol/ ether; ^1H NMR (300 MHz, $CDCl_3$) δ 4.68-4.66 (m, 1H), 4.57 (dd, 0.5H, J = 8.4, 2.7 Hz), 4.36-4.27 (m, 0.5H), 4.08 (tt, 0.5H, J = 11.7, 4.1 Hz), 3.99 (m, 0.5 H), 3.74, 3.72 (two s, 3H), 3.11-3.01 (m, 0.5H), 2.58-2.52 (m, 1H), 2.42-1.85 (m, 7.5H), 1.84-1.69 (m, 1H; ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 173.0, 172.9, 60.6, 60.3, 60.0, 59.8, 56.7, 52.8, 52.5, 45.9, 42.6, 35.1, 33.5, 32.7, 32.5, 30.9, 28.1, 27.5 cm^{-1}; IR (neat, NaCl) 3055, 2954, 2929, 2885, 2853, 1744, 1641, 1436, 1366, 1274, 1200, 1177, 1071, 1004, 964, 921, 850, 801, 736 cm^{-1}; GCMS (70eV) m/e (rel. intensity) 247 (M+2, 1.6), 245 (M^+, 4.6), 188 (33), 187 (11), 186 (100), 150 (26), 122 (25), 80 (14), 79 (18), 69 (15), 68 (54), 67 (11); HRMS (EI) m/e: Calcd. for $C_{11}H_{16}{}^{35}ClNO_3$, 245.0819; Found, 245.0811. The spectral data for the second pair of isomers off the column were as follows: TLC R_f = 0.47 using 10% methanol/ ether; ^1H NMR (300 MHz, $CDCl_3$) δ 4.68-4.49 (m, 1.5H), 4.08-3.98 (tt, 0.5H, J = 11.8, 3.9 Hz), 3.85-3.77 (m, 0.5H), 3.76, 3.73 (two s, 3H), 3.15 (ddd, 0.5H, J = 14.5, 12.1, 2.4 Hz), 2.62-1.63 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1, 173.2, 173.0, 172.6, 129.1, 120.5, 60.5, 60.3, 60.2, 59.9, 57.2, 52.6, 52.5, 45.2, 43.2, 35.1, 33.2, 33.0, 32.1, 31.3, 31.2, 28.0, 27.6; IR (neat, NaCl) 2957, 2953, 1730, 1642, 1422, 1365, 1322, 1283, 1265, 1220, 1189, 1167, 1119, 1069, 1023, 1007, 974 cm^{-1}; GCMS (70 eV) m/e (rel. intensity) 247 (M+2, 1.3), 245 (M^+, 3.9), 189 (4), 188 (33), 187 (11), 186 (100), 150 (23), 128 (11), 122 (23), 80 (12), 79 (16), 69 (14), 68 (52); HRMS (EI) m/e: Calcd. for $C_{11}H_{16}ClNO_3$, 245.0819; Found, 245.0815.

1-Aza-4-chloro-2-oxobicyclo[4.3.0]nonane (3f): The reaction led to the formation of two isomers. The spectral data for isomer one were as follows: TLC R_f = 0.39 using 10% methanol/ ether; ^1H NMR (300 MHz, $CDCl_3$) δ 4.21-4.10 (m, 1H), 3.65-3.55 (m, 1H), 3.44 (m, 2H), 3.03 (dd, 1H, J = 17.6, 6.2 Hz), 2.63-2.54 (m, 2H), 2.15 (p, 1H, J = 5.8 Hz), 2.06-1.97 (m, 1H), 1.90-1.64 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 168.0, 57.0, 51.4, 44.4, 41.7, 39.5, 32.7, 21.9; IR (neat, NaCl) 2946, 2873, 1634, 1464, 1412, 1333 cm^{-1}; GCMS (70 eV) m/e (rel. intensity) 175 (M+2), 16), 173 (M^+, 50), 138 (M-Cl, 76), 110 (8), 82 (23), 70 (100); HRMS (EI) m/e: Calcd. for $C_8H_{12}ClNO$, 173.0607; Found, 173.0635. The spectral data for isomer two were as follows: TLC R_f = 0.33 using 10% methanol/ ether; ^1H NMR (300 MHz, $CDCl_3$) δ 4.65-4.60 (m, 1H), 3.98-3.88 (m, 1H), 3.69-3.47 (m, 2H), 2.81 (m, 2H), 2.43-2.37 (m, 1H), 2.17 (p, 1H, J = 5.8 Hz), 2.07-1.97 (m, 1H), 1.91-1.43 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7, 53.9, 53.5, 44.7, 40.2, 36.2, 32.6, 21.8; IR (neat, NaCl) 2965, 2913, 2872, 1628, 1464, 1404, 1338, 951 cm^{-1}; GCMS (70 eV) m/e (rel. intensity) 173 (M^+, 4), 138 (M-Cl, 13), 137 (13), 82 (16), 70 (100), 53 (7); HRMS (EI) m/e: Calcd. for $C_8H_{12}ClNO$, 173.0607; Found, 173.0630.

1-Aza-4-(1-chloroethyl)-2-oxobicyclo[4.3.0]nonane (6a): Two isomers were isolated and separated by column chromatography. The spectral data for the major data (36% Yield) were as follows: TLC R_f = 0.33 using 10% methanol/ ether; ^1H NMR (300 MHz, $CDCl_3$) δ 4.19 (app. p, 1H, J = 6.3 Hz), 3.71 (m, 1H), 3.64-3.42 (m, 2H), 2.55 (dt, 1H, J_d = 17.2 Hz, J_t = 6.71 Hz), 2.38-2.21 (m, 2H), 2.04-1.74 (m, 6H), 1.59 (t, 3H, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 59.8, 56.7, 43.9, 40.8, 30.3, 27.5, 24.2, 22.4, 21.6; IR (neat, NaCl) 2957, 2921, 2881, 1619, 1460, 1416, 1382, 1326, 1243 cm^{-1}; GCMS (70 eV) m/e (rel. intensity) 166 (M-Cl, 2), 150 (87), 122 (52), 108 (37), 94 (67), 80 (44), 70 (100), 53 (47); HRMS (EI) m/e: Calcd. for $C_{10}H_{16}NOCl$, 201.0920; Found, 201.0926. The spectral data for the minor isomer (14% yield) were as follows: TLC R_f = 0.50 using 10% methanol/ ether; ^1H NMR (300 MHz, $CDCl_3$) δ 4.03 (dq, 1H, J_d = 8.9 Hz, J_q = 6.7 Hz), 3.81-3.70 (m, 2H), 3.38-3.30 (m, 1H), 2.37 (m, 3H), 2.10-1.90 (m, 2H), 1.88-1.68 (m, 4H), 1.59 (d, 3H, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 60.6, 57.4, 43.9, 43.3, 30.5, 27.8, 23.3, 22.3, 21.6; IR (neat, NaCl) 2957, 2928, 2888, 1623, 1458, 1420, 1378, 1325, 1237 cm^{-1}; GCMS (70 eV) m/e (rel. intensity) 203 (M+2, 4), 201 (M^+, 12), 166 (M-Cl, 27), 138 (8), 110 (30), 83 (17), 70(100); HRMS (EI) m/e: Calcd. for $C_{10}H_{16}NOCl$, 201.0920; Found,

201.0926.

1-Aza-5-chloro-2-oxo-5-bicyclo[5.3.0]decene (9a): TLC R_f = 0.32 using 5% methanol/ ether; ^1H NMR (300 MHz, $CDCl_3$) δ 5.81 (m, 1H), 4.52 (m, 1H), 3.69-3.61 (m, 1H), 3.52-3.44 (m, 1H), 2.97-2.46 (m, 4H), 2.35-2.28 (m, 1H), 1.93-1.72 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 135.6, 128.0, 54.5, 46.7, 34.6, 33.6, 32.2, 22.9; IR (neat, NaCl) 2974, 2939, 2877, 1645, 1455, 1343, 1305, 1226, 1160, 1015, 915, 766 cm^{-1}; GCMS (70 eV) m/e (rel. intensity) 150 (M-Cl, 100), 122 (38), 108 (9), 94 (13), 80 (16), 53 (17); HRMS (EI) m/e: Calcd. for $C_9H_{12}NO^{35}Cl$, 185.0607; Found, 185.0608.

1-Aza-5-(1-chloroethylidene)-2-oxobicyclo[4.3.0]nonane (10b): The data is reported for the mixture of products. TLC R_f = 0.32 using 5% methanol/ ether; ^1H NMR (300 MHz, $CDCl_3$) δ 4.19 (dd, 1H, J = 11.3, 5.2 Hz), 3.79 (dt, 1H, J_d = 12.1 Hz, J_t = 8.7 Hz), 3.38-3.30 (m, 1H), 3.16-3.05 (m, 1H), 2.56-2.46 (m, 2H), 2.29-2.12 (m, 2H), 2.19, 2.15 (two s, 3H), 2.04-1.82 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 130.1, 125.2, 59.1, 43.3, 32.0, 31.6, 25.0, 22.5, 21.5; IR (neat, NaCl) 2958, 2923, 1648, 1457, 1380, 1261, 1189, 1080 cm^{-1}; GCMS (70 eV) m/e (rel. intensity) 201 (M+2, 0.3), 199 (M^+, 1), 164 (M-Cl, 67), 143 (M-C_3H_4O, 30), 136 (35), 128 (32), 108 (100) 93 (23), 80 (19), 77 (20), 70 (37); HRMS (EI) m/e: Calcd. for $C_{10}H_{14}NOCl$, 199.0764; Found, 199.0760.

Acknowledgments: This work was supported by Washington University, the donors of the Petroleum Research Fund, administered by the American Chemical Society, and by the Biomedical Research Support Program, Division of Research Resources, National Institutes of Health. We also gratefully acknowledge the Washington University High Resolution NMR Facility, partially supported by NIH 1S10R02004 and the Washington University Mass Spectrometry Resource Center, partially supported by NIHRR00954 for their assistance.

References and Notes

1. Font, J. Ph. D. Thesis, Washington University in St. Louis, 1986.
2. For reviews see a) Marshall, G. R.; Barry, C. D.; Bosshard, H. E.; Dammkoehler, R. A.; Dunn, D. A. In *Computer-Assisted Drug Design*, Olson, E. C.; Christoffersen, R. E. Eds.; American Chemical Society, Washington D. C., 1979, pg. 205, b) Marshall, G. R. *Ann. Rev. Pharmacol. Toxicol.* **1987**, *27*, 193, c) Marshall, G. R. and Motoc, I. In *Molecular Graphics and Drug Design*, Burgen, A. S. V.; Roberts, G. C. K.; Tute, M. S. Eds.; Elsevier, Amsterdam, 1986, 115.
3. Tripos Associates 1699 South Hanley Road, St. Louis, MO 63144. For examples see reference 2.
4. For reviews see a) Shono, T. *Tetrahedron* **1984**, *40*, 811, b) Shono, T.; Matsumura, Y.; Tsubata, K. In *Organic Synthesis* vol. 63, Saucy, G. Ed.; Organic Synthesis Inc., 1984, pg. 206 and references therein, and c) Shono, T. In *Topics in Current Chemistry* vol. 148, Steckhan, E. Ed., Springer-Verlag, Berlin Heidelberg New York, 1988, 131.
5. a) Shono, T.; Matsumura, Y.;Tsubata, K. *J. Am. Chem. Soc.* **1981**, *103*, 1172, b) Moeller, K. D.; Tarazi, S.; Marzabadi, M. R. *Tetrahedron Lett.* **1989**, *30*, 1213, c) Moeller, K. D.; Wang, P. W.; Tarazi, S.; Marzabadi, M. R.;Wong, P. L. *J. Org. Chem.*, submitted.
6. a) Okita, M.; Wakamatsu, T.; Mori, M.; Ban, Y. *Heterocycles* **1980**, *14*, 1089, b) Irie, K.; Ban, Y. *Heterocycles* **1981**, *15*, 201, c) Okita, M.; Wakamatsu, T.; Ban, Y. *Heterocycles* **1983**, *20*, 401, d) Shono, T.; Matsumura, Y.; Uchida, K.; Tagami, K. *Chem. Lett.* **1987**, 919.
7. Hanzlik, R. P.; Hall, L. R.; Iwamoto, R. T. *J. Org. Chem.* **1989**, *54* 2446.
8. Schoemaker, H. E.; Boer-Terpstra, TJ.; Dijkink, J.; Speckamp, W. N. *Tetrahedron* **1980**, *36*, 143.
9. General experimental conditions will be reported elsewhere (ref. 5c). Preparative electrolyses were conducted using a model 630 coulometer, a model 410 potentiostatic controller, and a model 420A power supply purchased from The Electrosynthesis Company, Inc. Carbon rod (Cat. No. GR-12) and platinum wire (Cat. No. C-500) were also purchased from The Electrosynthesis Company, Inc. Tetraethylammonium tosylate and tetrabutylammonium tetrafluoroborate were purchased from Aldrich and used without purification. Anhydrous methanol was purchased from Aldrich in Sure/Seal bottles and used without purification.