to give a brown viscous liquid. The crude product was distilled under reduced pressure in a Kugelrohr apparatus [150 °C (0.05 Torr)] to give a slightly yellow oil, 9,13-dichloro-11-octyl-1,4,7-trioxa-11-azacyclotetradecane (**5a**) (3.34 g, 87%). This compound was used as the starting material of the next step without further purification.

To a stirred suspension of $LiAlH_4$ (0.25 g, 0.0065 mol) in THF (25 mL) was added **5a** (1.00 g, 0.0026 mol) in THF (5 mL) in drops at room temperature, and then the mixture was refluxed for 26 h. After cooling, a small portion of water was added to the mixture. Insoluble matter was removed by filtration and concentrated to give a yellow viscous liquid. The crude product was purified by a Kugelrohr distillation [150 °C (0.08 Torr)] to give a colorless oil (0.59 g, 72%): IR (neat) 2920, 2850, 1460, 1355, 1120 cm^{-1}; NMR ($CDCl_3$) δ 0.88 (t, 3 H), 1.1–1.5 (m, 12 H), 1.6–1.9 (m, 4 H), 2.2–2.6 (m, 6 H), 3.5–3.9 (m, 12 H); MS, *m/e* (relative intensity) 315 (M^+, 9), 216 (100), 158 (14), 128 (22), 58 (50).

Anal. Calcd for $C_{18}H_{37}O_3N$: C, 68.53; H, 11.82; N, 4.44. Found: C, 68.15; H, 11.72; N, 4.51.

11-[2-(Octyloxy)ethyl]-1,4,7-trioxa-11-azacyclotetradecane (2b). The synthetic procedure was almost the same as that used for **2a**. 9,13-Dichloro-11-[2-(octyloxy)ethyl]-1,4,7-trioxa-11-azacyclotetradecane (**5b**) was purified by chromatography over a short alumina column (10:90 dioxane–benzene) (92%). Compound **5b** was used for the next step without further purification: colorless oil; yield 73%; bp 150 °C (0.1 Torr) (Kugelrohr); IR (neat) 2920, 2850, 1460, 1350, 1120 cm^{-1}; NMR ($CDCl_3$) δ 0.84 (t, 3 H), 1.2–1.6 (m, 12 H), 1.6–1.9 (m, 4 H), 2.4–2.6 (t, 4 H), 3.2–3.8 (m, 18 H); MS, *m/e* (relative intensity) 359 (M^+, 1.4), 216 (100), 128 (6), 58 (39), 43 (6).

Anal. Calcd for $C_{20}H_{41}O_4N$: C, 66.81; H, 11.49; N, 3.90. Found: C, 66.80; H, 11.60; N, 3.97.

11-[3-(Octyloxy)propyl]-1,4,7-trioxa-11-azacyclotetradecane (2c). The synthetic procedure was almost the same as that used for **2a**. The intermediate **5c** was purified by chromatography over a short alumina column (5:95 dioxane–benzene) (59%). Compound **5c** was used for the next step without further purification: colorless oil; yield 63%; bp 155 °C (0.06 Torr) (Kugelrohr); IR (neat) 2930, 2860, 1465, 1360, 1120 cm^{-1}; NMR ($CDCl_3$) δ 0.87 (t, 3 H), 1.1–1.6 (m, 12 H), 1.6–1.9 (m, 6 H), 2.2–2.7 (m, 6 H), 3.3–3.9 (m, 16 H); MS, *m/e* (relative intensity) 373 (M^+, 12), 260 (41), 216 (100), 128 (31), 58 (82).

Anal. Calcd for $C_{21}H_{43}O_4N$: C, 67.52; H, 11.60; N, 3.75. Found: C, 67.23; H, 11.55; N, 3.80.

11-[2-[2-(Octyloxy)ethoxy]ethyl]-1,4,7-trioxa-11-azacyclotetradecane (2d). The synthetic procedure was almost the same as that used for **2a**. The intermediate **5d** was purified by chromatography over a short alumina column (10:90 dioxane–benzene) (72%). Compound **5d** was used for the next step without further purification: colorless oil; yield 73%; bp 170 °C (0.06 Torr) (Kugelrohr); IR (neat) 2925, 2860, 1460, 1350, 1290, 1245, 1120, 980, 930 cm^{-1}; NMR ($CDCl_3$) δ 0.94 (t, 3 H), 1.2–1.6 (m, 12 H), 1.6–1.9 (m, 4 H), 2.5–2.8 (m, 4 H), 3.4–3.9 (m, 22 H); MS, *m/e* (relative intensity) 403 (M^+, 1), 284 (1), 230 (3), 217 (15), 216 (100), 186 (4), 158 (4), 128 (11), 58 (26).

Anal. Calcd for $C_{22}H_{45}O_5N$: C, 65.47; H, 11.24; N, 3.47. Found: C, 65.08; H, 11.29; N, 3.53.

Liquid Membrane Transport. Transport experiments were carried out in a U-type cell at 25 °C. The details for transport conditions are summarized in the footnotes of Table I and the caption of Figure 1. In the case of passive transport, the receiving phase was sampled from six different cells after 6, 12, 18, 24, 36, and 48 h and analyzed for cation concentration by using a Nippon Jarrell-Ash AA-8500 atomic absorption spectrometer. The value reported in Table I was the mean of six samples. The deviations from the mean were less than ±10%.

Solvent Extraction.[11] A mixture of an aqueous solution (10 mL) of alkali metal hydroxide (5×10^{-2} M) and picric acid (5×10^{-4} M) and a dichloromethane solution (10 mL) of an appropriate extractant (2.5×10^{-3} M) was shaken at 22 °C for 9 h. The extractability was obtained from the calculation based on the absorption of picrate anion in the aqueous phase at 354 nm in the UV spectrum.

(11) Pedersen, C. J. *Fed. Proc., Fed. Am. Soc. Exp. Biol.* **1968**, *27*, 1305.

Registry No. **1a**, 120547-32-2; **1b**, 120547-33-3; **1c**, 120547-34-4; **2a**, 120547-36-6; **2b**, 120547-41-3; **2c**, 120547-42-4; **2d**, 120547-44-6; **3a**, 15520-05-5; **3b**, 65308-72-7; **3c**, 91374-49-1; **4a**, 117021-77-9; **4b**, 120547-37-7; **4c**, 120547-38-8; **4d**, 120547-43-5; **5a**, 120547-35-5; **5b**, 120547-39-9; **5c**, 120547-40-2; **5d**, 120577-48-2; $TsO(CH_2)_2O(CH_2)_2OTs$, 7460-82-4; Li, 7439-93-2; Na, 7440-23-5; K, 7440-09-7.

A Simplified Synthetic Route to Polyaza Macrocycles

F. Chavez and A. D. Sherry*

Department of Chemistry, University of Texas at Dallas, P.O. Box 830688, Richardson, Texas 75083-0688

Received September 22, 1988

Polyaza macrocycles have received considerable attention in recent years largely because of the cation and anion binding properties of the polyaza cavity.[1-3] Many of the synthetic routes to these systems use high dilution techniques[4] or template syntheses,[5] but the most popular involves the cyclization of the sodium salt of a linear tosylamide with a tosylated diol, as reported by Richman and Atkins.[6] More recently,[7] several large-ring macrocyclic diamines have been synthesized using Cs_2CO_3 to deprotonate the ditosylamide in DMF followed by slow addition of a dibromoalkane. Excellent yields were reported for 17–28-membered rings but low yields and incomplete reactions reported for 11–12-membered rings and for synthesis of the larger rings using Li_2CO_3, Na_2CO_3, or K_2CO_3 for deprotonation.[7] A comparison of yields for the cyclization of a 28-membered diamino macrocycle using cesium carbonate for deprotonation versus preforming the sodium salt, i.e., the Richman–Atkins approach, suggests that a combined ion-pair/template effect may be operative, giving Cs^+ a significant advantage over the smaller Na^+ for this size ring closure. With this background and the knowledge that K_2CO_3 has been used successfully to deprotonate tosylamides in DMF,[8-11] we decided to reinvestigate the use of K_2CO_3 to deprotonate and perhaps aid in the cyclization of 9–15-membered ring polyazamacrocycles. We report here the preparation of a series of previously known tri-, tetra-, and pentaaza macrocycles plus two previously unreported triazabenzo macrocycles.

Koyama and Yoshino[8] have previously reported the synthesis of **2**, **3**, and **4** using K_2CO_3 in DMF under high-

(1) Pedersen, C. J., *J. Am. Chem. Soc.* **1967**, *89*, 7017. Curtis, N. F. *Coord. Chem. Rev.* **1968**, *3*, 3. Cabbiness, D. K.; Margerum, D. W. *J. Am. Chem. Soc.* **1969**, *91*, 6540.

(2) Lynhdoy, L. F. *Chem. Soc. Rev.* **1975**, *4*, 421. Martin, L. Y.; Dehayes, L. J.; Zompa, L. J.; Bush, D. H. *J. Am. Chem. Soc.* **1974**, *96*, 4046. Kimura, E.; Kodama, M. *J. Chem. Soc., Dalton Trans* **1976**, 116. Christensen, J. J.; Eatough, D. J.; Izatt, R. M. *Chem. Rev.* **1974**, *74*, 351. Bradshaw, J. S.; Maas, G. E.; Izatt, R. D.; Christensen, J. J. *Chem. Rev.* **1979**, *79*, 37.

(3) Izatt, R. M.; Christensen, J. J. *Synthetic Multidentate Macrocyclic Compounds*; Academic Press: New York, 1978. Melson, G. A. *Coordination Chemistry of Macrocyclic Compounds*; Plenum Press: New York, 1979.

(4) Rossa, L.; Vogtle, F. *Top. Curr. Chem.* **1983**, *113*, 1.

(5) Laidler, D. A.; Stoddart, J. F. In *The Chemistry of Functional Groups*; Patai, S., Ed.; Wiley: New York, 1980; Suppl. E, Part 1.

(6) Richman, J. E.; Atkins, T. J. *J. Am. Chem. Soc.* **1974**, *96*, 2268.

(7) Vriesema, B. K.; Buter, J.; Kellogg, R. M. *J. Org. Chem.* **1984**, *49*, 110.

(8) Koyama, H.; Yoshino, T. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 481.

(9) Dietrich, B.; Hosseini, M. W.; Lehn, J. M.; Sessions, R. B. *J. Am. Chem. Soc.* **1981**, *103*, 1282.

(10) Hosseini, M. W.; Lehn, J. M. *J. Am. Chem. Soc.* **1982**, *104*, 3525.

(11) Dietrich, B.; Hosseini, M. W.; Lehn, J. M.; Sessions, R. B. *Helv. Chim. Acta* **1983**, *66*, 1262.

0022-3263/89/1954-2990$01.50/0

Scheme I

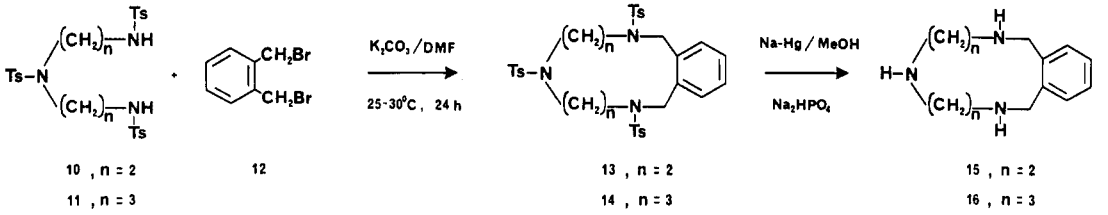
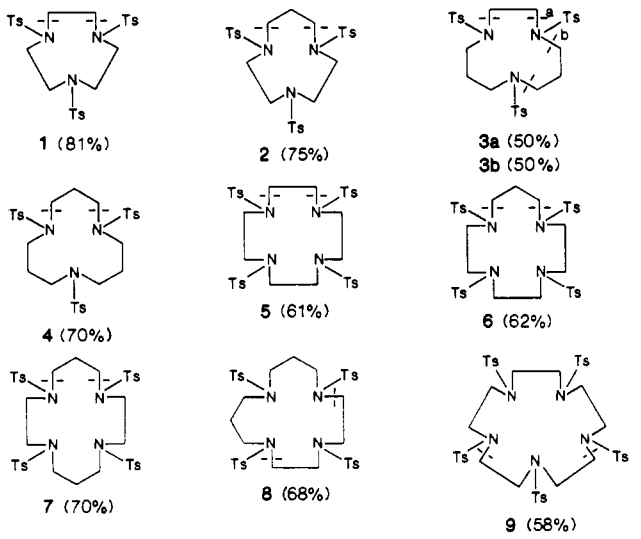


Table I. Summary of the Polyaza Macrocycles Prepared with Use of K_2CO_3 for Deprotonation[a]

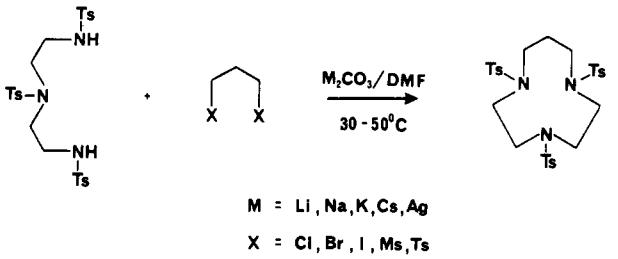


[a] The bonds that are formed during the cyclization are indicated in each structure. For example, structure **3** was prepared two ways, i.e., by reaction of 1,2-dibromoethane (**3a**) or 1,3-dibromopropane (**3b**) with the corresponding linear tritosylamides. *N,N'*-Bis[2-[(*p*-tolylsulfonyl)oxy]ethyl]-*p*-toluenesulfonamide was used as starting materials for **8** and **9**.

dilution conditions and at high temperatures with overall yields of 24, 25, and 8%, respectively. Our conditions gave isolated yields of 50–75% for these same products and 60–80% for the additional macrocycles reported in Table I. All products reported in the table have melting points which agree with literature values, appear as single spots on TLC plates developed in methylene chloride/methanol (95/5), have ^1H and ^{13}C NMR spectra which correspond to the structure indicated, and give C, H, N, O, and S analyses which agree with theoretical values. The synthesis of two new triaza macrocycles, **13** and **14**, are shown in Scheme I to illustrate the general method. A solution of **10** is mixed with finely ground, dry K_2CO_3 in 30 mL of dry DMF. A second concentrated DMF solution containing **12** is added dropwise with stirring over a period of 16–20 h. After a simple workup, 80–85% of **13** is obtained. A small amount (3–5%) of the 2:2 cyclization product detected by TLC in this product is easily separated by silica gel chromatography. The corresponding reaction to form **14** does not yield any detectable 2:2 addition product. The tosyl groups are removed under reductive conditions,[7] and the trihydrochloride salts of **15** and **16** are isolated in greater than 90% yields.

A comparison of leaving group, metal carbonate, and reactant concentration was carried out for the synthesis of **2** (Scheme II). Changing the leaving group, X, had a marked affect upon the rate of cyclization. Bromides and mesylates gave the best results, showing complete, clean reactions in 24 h at 30 °C (70–75%). Chlorides and tosylates reacted more slowly under the same conditions; products of comparable purity but slightly lower yields (60

Scheme II



and 70% respectively) were obtained at 50 °C. Iodides proved to be too reactive, giving mixtures of products which were not separated and purified. Changing the metal carbonate also affected the intramolecular cyclization of **2**, similar to that described elsewhere for other macrocycles.[7,12] For example, isolated yields of **2** using Li_2CO_3, Na_2CO_3, K_2CO_3, Cs_2CO_3, or Ag_2CO_3 were 0, 21, 75, 75, and 0%, respectively. This indicates that K_2CO_3 and Cs_2CO_3 are both excellent bases for deprotonation of tosylamides in DMF. K_2CO_3 is thus the preferred reagent based upon cost considerations. In general, synthesis of each polyaza macrocycle shown in Table I was carried out on a 1-mmol scale of the tosylamide at a final concentration of 0.02 M, after the addition of the dibromide solution. However, cyclizations of **2** were attempted at final concentrations of 0.04, 0.06, and 0.08 M with yields of 65, 69, and 69%, respectively. In addition, compounds **1**, **2**, **5**, and **13** have been prepared on multigram scales with yields of 81, 75, 62, and 90%, respectively, at final concentrations of 0.05 M. It should be noted that those reactions involving 1,2-dibromoethane (**1**, **3a**, and **5**) require an excess of the dibromide (3 equiv) and longer reaction times (72 h) than the corresponding 1,3-dibromopropane reactions.

In summary, our results demonstrate that the present method offers a practical and versatile alternative to the widely used Richman–Atkins procedure for synthesis of small- to medium-sized polyaza macrocycles. The reactions may be carried out in a single reaction vessel at or near room temperature, and a variety of leaving groups may be selected, depending upon the availability of starting materials.

Experimental Section

Melting points were determined with a Thomas-Hoover melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were acquired on a JEOL JNM-FX 200 spectrometer with chemical shifts reported in ppm from tetramethylsilane. Elemental analyses were performed by Galbraith Laboratories, Inc., and mass spectral results were obtained from ICR Research Associates, Inc. Aldrich precoated silica gel on polyester plates were used for thin-layer chromatography. All reagents were analytical grade and used as received, except where noted. Dimethylformamide (DMF) was dried over KOH and distilled, and potassium carbonate was ground and dried at 100 °C under vacuum for 24 h prior to use. The linear amines were purchased from Aldrich and N-*p*-toluenesulfonylation of the linear amines

(12) Buter, J.; Kellogg, R. M. *J. Chem. Soc., Chem. Commun.* **1980**, 466.

was performed via the procedure described by Koyama-Yoshino.[8]

9,10-Benzo-1,4,7-tris(*p*-tolylsulfonyl)-1,4,7-triazacycloundecane (13). *N,N',N''*-Tris(*p*-tolylsulfonyl)diethylenetriamine (15 g, 26 mmol) was dissolved in DMF (430 mL) containing finely ground, anhydrous K_2CO_3 (8.6 g, 62 mmol) and stirred for 1 h at 30 °C. A solution of α,α'-dibromo-*o*-xylene (8.4 g, 32 mmol) in DMF (220 mL) was added dropwise over a period of 16–20 h. The reaction progress was monitored by TLC (small aliquots were removed, evaporated to dryness under vacuum, and redissolved in CH_2Cl_2 for spotting on plates; the chromatograms were developed in 95/5 v/v CH_2Cl_2/MeOH). After 16–20 h, the volume was reduced to 65 mL, and excess ice–water was added. The resulting white solid was collected by filtration and washed with water to neutral pH. The wet solid was suspended in ethanol (100 mL) and gradually heated to reflux. After 1 h, the solid was filtered off while hot and dried at 50 °C under vacuum for 12 h. A minor product (5%) likely corresponding to the 2:2 addition product was separated by silica gel column chromatography (99/1 CH_2Cl_2/MeOH), yielding 15 g of **13** (85% yield): mp 208–210 °C; ^{1}H NMR ($CDCl_3$) δ 2.38 (s, 3 H), 2.46 (s, 6 H), 2.95 (t, 4 H), 3.38 (s, 4 H), 4.40 (br, 4 H), 7.24–7.75 (m, 16 H); ^{13}C NMR δ 21.56, 49.68, 52.09, 52.78, 127.48, 128.90, 129.56, 130.00, 132.12, 143.91. Anal. Calcd for $C_{33}H_{37}N_3S_3O_6$: C, 59.35; H, 5.58; N, 6.29; O, 14.38. Found: C, 58.93; H, 5.60; N, 6.25; O, 14.36.

11,12-Benzo-1,5,9-tris(*p*-tolylsulfonyl)-1,5,9-triazacyclotridecane (14) was prepared as described above from *N,N',N''*-tris(*p*-tolylsulfonyl)dipropylenetriamine and α,α'-dibromo-*o*-xylene in 87% yield. Analytical sample recrystallized from CH_2Cl_2/MeOH: mp 259–263 °C; ^{1}H NMR ($CDCl_3$) δ 1.43 (m, 4 H), 2.41 (s, 3 H), 2.44 (s, 6 H), 2.90 (t, 4 H), 3.18 (t, 4 H), 4.45 (s, 4 H), 7.23–7.76 (m, 16 H); ^{13}C NMR δ 21.52, 28.24, 46.00, 46.50, 49.43, 127.18, 128.68, 129.67, 129.81, 129.96, 134.31, 143.70. Anal. Calcd for $C_{35}H_{41}N_3S_3O_6$: C, 60.40; H, 5.94; N, 6.04; O, 13.80. Found: C, 60.69; H, 6.03; N, 6.10; O, 13.59.

9,10-Benzo-1,4,7-triazacycloundecane (15). To a suspension of compound **13** (4.0 g, 6 mmol) in 48 mL of dry methanol was added dibasic sodium phosphate (4.3 g) and 3% sodium amalgam (56 g). The mixture was gently refluxed overnight, and second equal portions of dibasic sodium phosphate (4.3 g) and sodium amalgam (56 g) were added. After the mixture was refluxed for an additional 12 h, water (300 mL) was added, and the solution was extracted with 4 × 100-mL portions of chloroform. The extracts were dried over anhydrous sodium sulfate, and the solvent was removed under vacuum to give **15** as a light yellow oil in 90% yield: ^{1}H NMR ($CDCl_3$) δ 2.76 (s, 8 H), 3.63 (s, 4 H), 7.18–7.20 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 43.36, 47.92, 51.89, 127.75, 130.55, 139.20. The trihydrochloride salt was prepared by dissolving **15** in 50 mL of absolute ethanol, and, after the solution was cooled in an ice–acetone bath, 15 mL of concentrated (37%) HCl was added to give a white solid. This was filtered, washed with absolute ethanol, and dried under vacuum to afford the trihydrochloride salt in 94% yield: mp 262–267 °C; ^{1}H NMR (D_2O) δ 3.32–3.35 (m, 8 H), 4.25 (s, 4 H), 7.53 (s, 4 H); ^{13}C NMR (D_2O) δ 44.05, 47.84, 130.83, 132.59, 133.34; MS *m/e* 315 (M^+, 5.2) 214 (100). Anal. Calcd for $C_{12}H_{22}N_3Cl_3$: C, 45.80; H, 7.05; N, 13.35. Found: C, 46.03; H, 7.39; N, 13.42.

11,12-Benzo-1,5,9-triazacyclotridecane (16) was prepared in 65% yield as described above except the detosylation reaction was carried out in a 1:1 mixture of methanol/acetonitrile to improve solubility: ^{1}H NMR ($CDCl_3$) δ 1.62 (p, 4 H), 2.60–2.68 (m, 8 H), 3.00 (s, 3 H), 3.68 (s, 4 H), 7.14 (s, 4 H); ^{13}C NMR δ 27.73, 47.86, 53.52, 127.40, 130.95, 139.09. The trihydrochloride salt was prepared in 91% yield as described above: mp 274–283 °C; ^{1}H NMR (D_2O) δ 2.25 (s, 4 H), 3.34 (s, 8 H), 4.41 (s, 4 H), 7.57 (s, 4 H); ^{13}C NMR δ 22.60, 44.88, 45.21, 48.13, 133.30; MS *m/e* 308 (M^+ - 36, 1.3), 234 (100). Anal. Calcd for $C_{14}H_{26}N_3Cl_3$: C, 49.06; H, 7.65; N, 12.26. Found: C, 49.28; H, 7.73; N, 11.66.

Acknowledgment. This work was supported by research grants from The Robert A. Welch Foundation (AT-584) and Mallinckrodt, Inc.

Registry No. **1**, 52667-89-7; **2**, 35980-65-5; **3**, 35980-66-6; **4**, 35980-67-7; **5**, 52667-88-6; **6**, 71089-73-1; **7**, 71089-74-2; **8**, 52601-79-3; **9**, 52601-74-8; **10**, 56187-04-3; **11**, 35980-64-4; **12**, 91-13-4; **13**, 120637-12-9; **14**, 120637-13-0; **15**, 120637-14-1; **15**·3HCl, 120637-16-3; **16**, 120637-15-2; **16**·3HCl, 120637-17-4; 1,4,8-triazaoctane tritosylate, 35980-63-3; 1,4,7,10-tetraazadecane tetratosylate, 55442-07-4; 1,4,8,11-tetraazaundecane tetratosylate, 111514-29-5; *N,N'*-bis[2-[(*p*-toluenesulfonyl)oxy]ethyl]-*p*-toluenesulfonamide, 16695-22-0; 1,2-dibromoethane, 106-93-4; 1,3-dibromopropane, 109-64-8.

Syntheses and Rearrangements of Spiro-Fused Dihydroisoquinolones[1]

Jahangir,*[,2] Lawrence E. Fisher,* Robin D. Clark, and Joseph M. Muchowski

Syntex Research, 3401 Hillview Avenue, P.O. Box 10850, Palo Alto, California 94304

Received November 7, 1988

We have shown that the addition of lithiated *N,N*-diethyl-*o*-toluamides to benzaldimines and subsequent electrophilic trapping of 4-lithio-3-aryl-3,4-dihydro-1(2*H*)-isoquinolones is a viable route to *trans*-3-aryl-4-substituted-3,4-dihydro-1(2*H*)-isoquinolones and to a number of benzo[*c*]phenanthridines and other natural products.[3] We wished to ascertain if this lithiated toluamide strategy could be used to construct spiro annelated isoquinolones of structure **1** by addition of lithiated *N,N*-diethyl-*o*-toluamide **2** to ketimines of general structure **3**. We reasoned that these spiro compounds might undergo rearrangement to fused isoquinolones such as **4** (n = 1) whose ring system is found in a large number of amaryllidaceae alkaloids[4] (Scheme I).

We now report the results of a study on the generality of spiroisoquinolone synthesis by two routes: An annelation–trapping sequence and a carboxylate dianion addition/hydrolysis route. We also present our results from the study of the cationic rearrangement of these spiroisoquinolones.

Discussion

N,N-Diethyl-*o*-toluamide (**5**) was deprotonated with LDA in THF at −70 °C and treated with *n*-butyl-, cyclobutyl-, cyclopentyl-, cyclohexyl-, cycloheptyl-, cyclooctyl-, and 4-*tert*-butylcyclohexylketimines **3a–f**.[5] Only in the cases of the ketimines corresponding to cyclohexanone, cycloheptanone, or 4-*tert*-butylcyclohexanone, (**3c**, **3d**, **3f**) were the expected spiro-fused isoquinolones (**6a–c**) obtained (Scheme II). In each of the other cases, the starting toluamide (**5**) and the corresponding ketones were recovered after acidic hydrolysis. These results indicated that deprotonation of the ketimine by the strongly basic lithiated species **2** might be much faster than the desired nucleophilic addition/annelation.

Attempts to mediate the basicity of lithio species **2** through the use of anhydrous cerium chloride or zinc chloride failed to produce the desired cycloadducts. Instead, only starting toluamide **5** and the ketones resulting

(1) Contribution No. 776 from the Syntex Institute of Organic Chemistry.

(2) Syntex Postdoctoral Fellow, 1987–1988.

(3) (a) Clark, R. D.; Jahangir *J. Org. Chem.* **1987**, *52*, 5378. (b) Clark, R. D.; Jahangir *Heterocycles* **1988**, *27*, 871. (c) Clark, R. D.; Jahangir *J. Org. Chem.* **1988**, *53*, 2378.

(4) For examples, see: Fuganti, C. *The Alkaloids*; Manske, R. H. F., Ed.; Academic: New York, 1975; Vol. XV, p 83.

(5) Each *n*-butylcycloalkylimine was prepared from its corresponding ketone in benzene by azeotropic removal of water. *n*-Butyl was chosen for ease of preparation.

0022-3263/89/1954-2992$01.50/0