

REACTIONS OF 3-ETHYL- AND 3-PHENYL-1-AZABICYCLO-[1.1.0]BUTANES WITH TOSYL CHLORIDE AND TOSYL AZIDE

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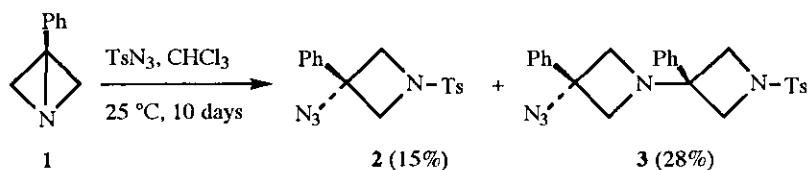
Abstract- Reactions of 3-ethyl-1-azabicyclo[1.1.0]butane (**4**) with TsCl and with TsN₃ have been studied in aqueous THF solution and in the presence of a variety of nucleophilic trapping agents. Thus, reaction of **4** with TsCl-Na₂CO₃ afforded *N-p*-toluenesulfonyl-3-chloro-3-ethylazetidene (**6**, 34%), *N*-(*N'*-*p*-toluenesulfonyl-3'-ethyl-3'-azetidyl)-3-chloro-3-ethylazetidene (**7**, 3.4%), and *N-p*-toluenesulfonyl-3-ethyl-3-hydroxyazetidene (**8**, 31%). When this reaction was repeated in the presence of a tenfold molar excess of NaCl, the yield of **6** increased to 80%, primarily at the expense of **8**, which was isolated in only 4.3% yield. When this reaction was performed in the presence of a tenfold molar excess of NaN₃, the predominant reaction products were TsN₃ (32%) and an inseparable mixture of **6** and *N-p*-toluenesulfonyl-3-azido-3-ethylazetidene (**9**; product ratio **6**:**9** = 1:1). Finally, **4** reacted with TsN₃ under four different sets of reaction conditions. In every case, **9** was the major product isolated from these reactions (32-74%). Similar results were obtained for the corresponding reactions of 3-phenyl-1-azabicyclo[1.1.0]butane (**1**) with TsCl. All of the results reported herein are consistent with expectations based upon a mechanism that involves nucleophilic trapping of a putative tertiary carbocationic intermediate.

INTRODUCTION

3-Substituted 1-azabicyclo[1.1.0]butanes were first synthesized in the late 1960s.^{1,2} Despite their unusual and highly strained bicyclic structures, little initial interest was shown in pursuing studies of their chemical properties and behavior. However, the current decade has witnessed a renaissance of interest in 1-azabicyclo[1.1.0]butane chemistry.³ Thus, reactions of carbenes⁴ and a variety of other electrophiles^{5,6} with 3-substituted 1-azabicyclo[1.1.0]butanes have been reported. In addition, the use of compounds of this type as intermediates in the synthesis of energetic materials, particularly 1,3,3-trinitroazetidene ("TNAZ"), has been reported.⁷

As part of a continuing study of additions of biparticulate electrophiles to 3-substituted 1-azabicyclo[1.1.0]butanes,^{3-6,7a} we reported recently that 3-phenyl-1-azabicyclo[1.1.0]butane (**1**) reacts only very slowly at ambient temperature with *p*-toluenesulfonyl azide ("tosyl azide", TsN₃) in CHCl₃ solution.^{6c} After this reaction had proceeded for ten days, two products (**2** and **3**) could be isolated in low yield (Scheme 1).^{6c} We now report the results of corresponding studies of reactions of **1** and of 3-ethyl-1-azabicyclo[1.1.0]butane (**4**) with TsCl and with TsN₃ that have been performed in aqueous THF and/or aqueous acetone solution and in the presence of a variety of nucleophilic trapping agents.

Scheme 1



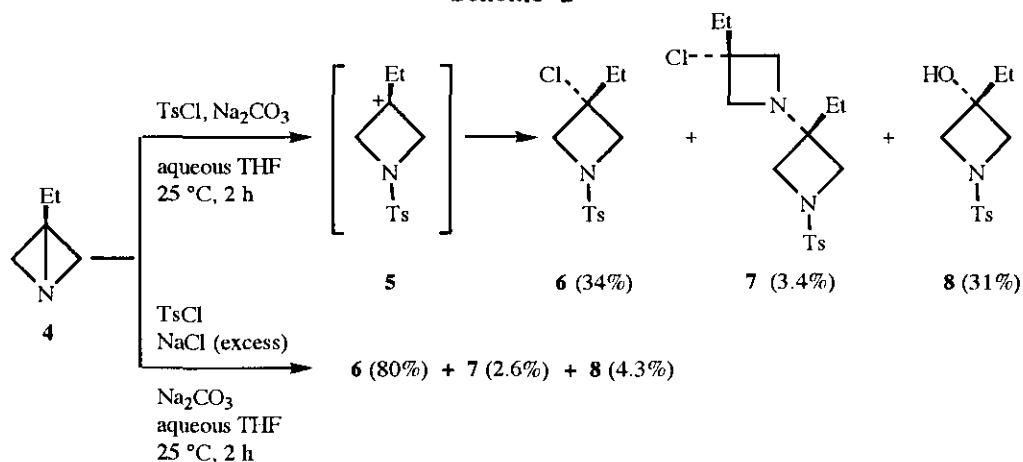
RESULTS AND DISCUSSION

A. Reaction of 3-Ethyl-1-azabicyclo[1.1.0]butane (4) with TsCl. This reaction was performed in aqueous tetrahydrofuran (THF) in the presence of Na_2CO_3 at ambient temperature for 2 h. Workup of the reaction mixture followed by column chromatographic purification of the crude material thereby obtained afforded three products (**6-8**) (Scheme 2), which were formed in 34, 3.4, and 31% yields, respectively. When this reaction was repeated in the presence of a large excess of NaCl (10 equivalents), the yield of **6** increased to 80%, while that of **7** and **8** dropped to 2.6 and 4.3%, respectively.

It seems likely that electrophilic addition of TsCl to **4** proceeds *via* formation of a tertiary carbocationic intermediate, i.e., **5** (Scheme 2). When the reaction is performed in the presence of a tenfold excess of NaCl, the yield of **6** increases, primarily at the expense of the corresponding yield of **8**. This result clearly indicates that under the reaction conditions employed, Cl^- is capable of functioning as an efficient nucleophilic trapping agent for **5**.

Interestingly, somewhat divergent results were obtained when this reaction was performed in the presence of a large excess of NaN_3 (10 equivalents). Under these conditions, the major product isolated *via* column chromatographic purification of the crude reaction product was TsN_3 (32% yield), which was followed sequentially by an inseparable 1:1 mixture of **6** and *N-p*-toluenesulfonyl-3-azido-3-ethylazetidene (**9**, combined yield of **6** + **9** = 85%), **7** (4.2%), and, finally **8** (4.4%; see Scheme 3). The fact that a considerable

Scheme 2



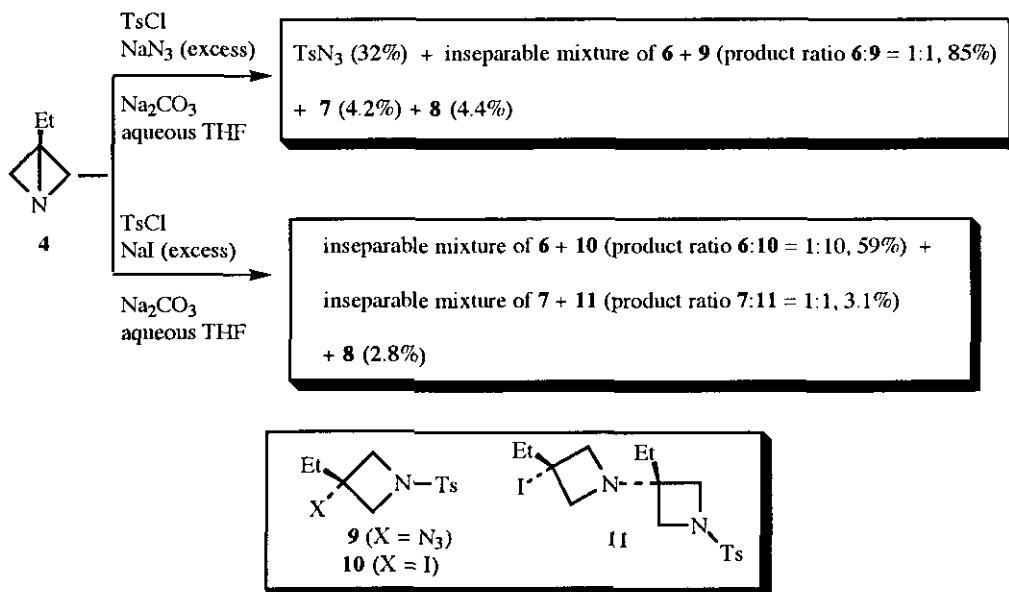
quantity of TsN_3 , formed *in situ* *via* reaction of TsCl with NaN_3 , is isolated among the reaction products leads us to conclude that TsN_3 is considerably less reactive toward **4** than is TsCl under the reaction conditions employed herein.

Finally, the reaction of **4** with TsCl was performed in the presence of a large excess of NaI (10 equivalents). The results obtained *via* column chromatographic purification of the crude product of this reaction are shown in Scheme 3. A total of five reaction products were obtained, two as inseparable mixtures [i.e., (**6** + **10**) and (**7** + **11**)] and one pure compound (**8**). Compound (**10**) was identified as one component of the mixture of (**6** + **10**) *via* careful analysis of the ^1H and ^{13}C NMR spectra of this product mixture. For purposes of spectral comparison, authentic **10** was prepared separately *via* sequential reaction of **4** with NaI-HCl followed by Na_2CO_3 and, finally, TsCl (see the EXPERIMENTAL Section).

The data displayed in Scheme 3 indicate that **10** is by far the predominant reaction product of the reaction of **4** with TsCl performed in the presence of a large excess of NaI. The formation of **10** is accompanied by only small amounts of dimeric products, i.e., **7** and **11**. We conclude that I^- functions as an effective nucleophilic trap for carbocationic intermediate (**5**) in this reaction.

B. Reaction of 3-Ethyl-1-azabicyclo[1.1.0]butane (4**) with TsN_3 .** This reaction was performed in aqueous tetrahydrofuran (THF) in the presence of Na_2CO_3 at ambient temperature for 7 days by using a total of four different sets of reaction conditions. The results thereby obtained are summarized in Scheme 4. In each case, the major reaction product was found to be *N-p*-toluenesulfonyl-3-azido-3-ethylazetidene (**9**); isolated yields of **9** varied between 32-74%. The most dramatic depressing effect of added nucleophiles on the yield of **9** was observed when the reaction of **4** with NaN_3 was performed in the presence of excess NaI. Small but significant amounts of dimeric products [i.e., **11** and **12** (obtained as an inseparable mixture) and **13**] accompanied the formation of **9** when the reaction of **4** with NaN_3 was performed in the presence of excess NaI. Surprisingly, **10** was *not* one of the products formed when the reaction of **4** with TsN_3 was performed in the presence of excess NaI. The reasons for the apparent inability of NaI to effectively trap the putative carbocationic intermediate (**5**) are not apparent to us. Additional experiments that are designed to clarify this apparent anomaly currently are underway in our laboratory.

Scheme 3



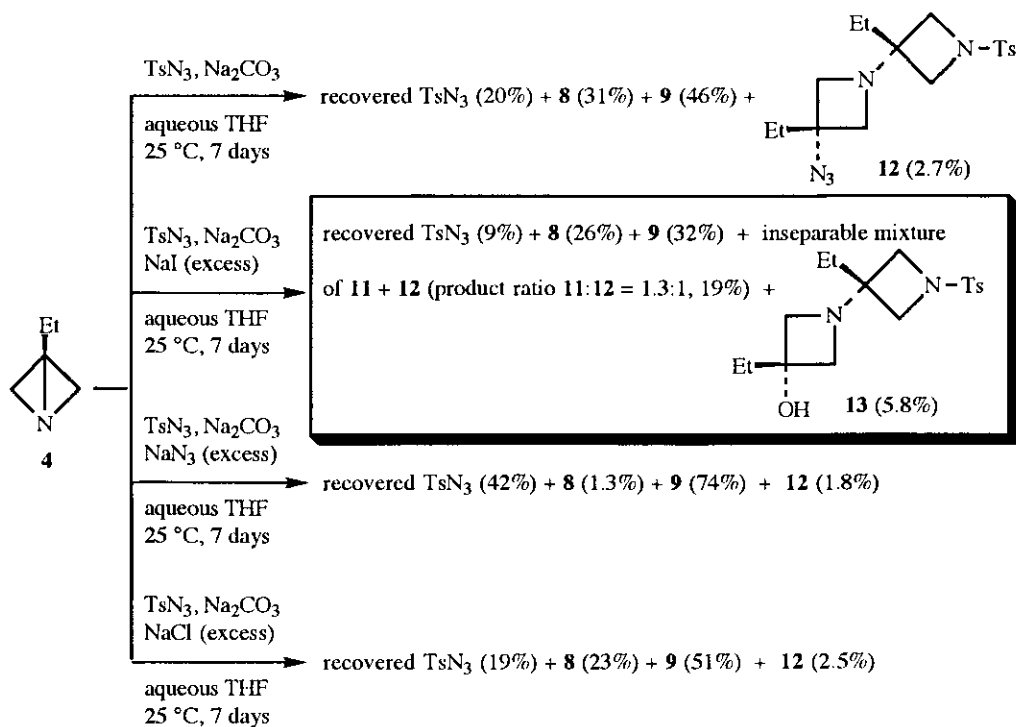
We note that the yield of **9** increased from 46% to 74% when the reaction of **4** with TsN_3 was performed in the presence of a tenfold molar excess of NaN_3 . Interestingly, addition of a tenfold molar excess of NaCl had a nearly imperceptible effect course of the reaction of **4** with TsN_3 . We conclude from this result that Cl^- functions only as a relatively ineffective nucleophilic trap in this reaction.

C. Reaction of 3-Phenyl-1-azabicyclo[1.1.0]butane (1) with TsCl . This reaction was performed in aqueous acetone instead of aqueous THF due to limited solubility of both **1** and TsCl in the latter solvent. The fully homogenous reaction mixture was maintained at ambient temperature for 18 h. After workup, the crude reaction product was analyzed *via* careful integration of its ^1H NMR spectrum. Subsequently, this product was purified *via* column chromatography.

Reaction of **1** with TsCl , when performed in the presence of Na_2CO_3 (to prevent polymerization), afforded *N-p*-toluenesulfonyl-3-chloro-3-phenylazetidene (**14**, 60% yield) along with *N-p*-toluenesulfonyl-3-hydroxy-3-phenylazetidene (**15**, 30% yield). Contrary to the results obtained for similar experiments performed in aqueous THF (*vide supra*), we find that excess TsCl hydrolyzed almost completely when aqueous acetone was employed as the reaction medium. Interestingly, no evidence for the formation of dimeric products was gleaned *via* analysis of the ^1H NMR spectrum of the crude product, nor were any dimeric products isolated *via* column chromatographic purification.

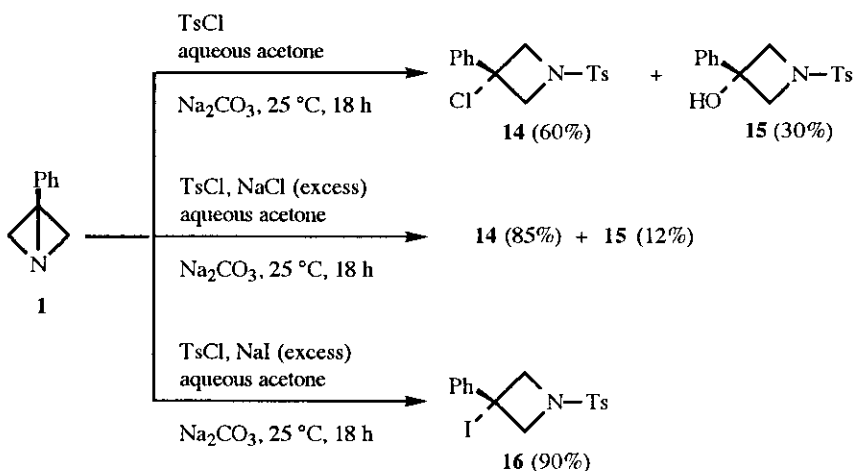
When this reaction was repeated in the presence of a tenfold molar excess of NaCl , the yield of **14** increased to 85%, while that of **15** dropped to 12% (see Scheme 5). This result is consistent with expectations based upon a mechanism that involves nucleophilic trapping (by Cl^- vs. HO^-) of a putative tertiary carbocationic intermediate.

Scheme 4



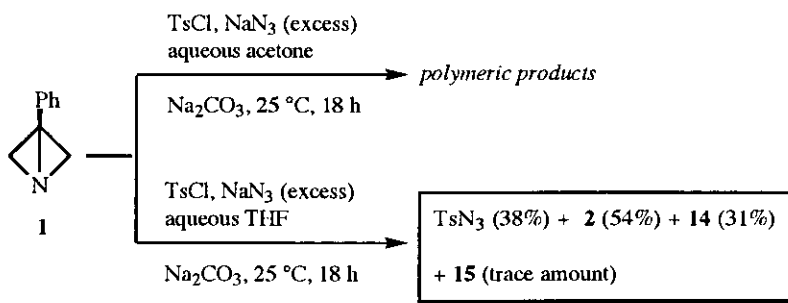
The corresponding reaction of **1** with TsCl performed in the presence of a tenfold molar excess of NaI resulted in the formation of a highly unstable product. Preliminary attempts to isolate this material from the crude reaction product resulted only in our obtaining **15** accompanied by polymeric material and free I₂. Eventually, we succeeded in isolating the primary reaction product, *N-p*-toluenesulfonyl-3-iodo-3-phenylazetididine (**16**) in high yield (90%) by first concentrating the reaction mixture *in vacuo* to remove most of the acetone (solvent) followed immediately by rapid filtration of the resulting concentrate. Compound (**16**) forms pale yellow crystals (from methanol) which decompose very slowly with evolution of free I₂ when stored at ambient temperature.

Scheme 5



Finally, the reaction of **1** with TsCl was performed in aqueous acetone solution (homogeneous) in the presence of a tenfold molar excess of NaN₃. Unexpectedly, the only products that could be isolated from this reaction included TsN₃ accompanied by diacetone alcohol and an unidentified polymeric material. Careful analysis of the ¹H NMR spectrum of the crude product revealed the presence of only traces of **2** and **14**. When this reaction was repeated by using aqueous THF as solvent (heterogeneous), the following products were obtained: *N-p*-toluenesulfonyl-3-azido-3-phenylazetididine (**2**, 54% yield), *N-p*-toluenesulfonyl-3-chloro-3-phenylazetididine (**14**, 31% yield), TsN₃ (38% yield), and **15** (trace amount; see Scheme 6.) We expect that similar results would be obtained by allowing **1** to react with a mixture of TsCl and TsN₃ in dry THF.

Scheme 6



For comparison, reactions of **1** with TsCl and with mixtures of TsCl-TsN₃ were performed in nonaqueous medium (CDCl₃ solution). In every case, **14** was the only adduct that resulted from these reactions. In particular, there was no evidence for the formation of **2** in any of these reactions, a result which indicates that TsCl is much more highly reactive toward **1** than is TsN₃ (*vide infra*).

SUMMARY AND CONCLUSIONS

3-Ethyl-1-azabicyclo[1.1.0]butane (**4**) reacts with TsCl-Na₂CO₃ to produce **6** (34%), **7** (3.4%), and **8** (31%). When this reaction was repeated in the presence of a tenfold molar excess of NaCl, the yield of **6** increased to 80%, primarily at the expense of **8**, which was isolated in only 4.3% yield. When this reaction was performed in the presence of a tenfold molar excess of NaN₃, the predominant reaction products were TsN₃ (32%) and an inseparable mixture of **6** and *N-p*-toluenesulfonyl-3-azido-3-ethylazetidide (**9**; product ratio **6:9** = 1:1). Finally, **4** reacted with TsN₃ under four different sets of reaction conditions. In every case, **9** was the major product isolated from these reactions (32-74% yield). In general, the results of these experiments can be explained in terms of nucleophilic trapping of a putative carbocationic intermediate, i.e., **5**. However, the fact that **10** was not formed when the reaction of **4** with TsN₃ was performed in the presence of a tenfold molar excess NaI is an anomalous result that merits further investigation.

A similar series of reactions with TsX was studied by using 3-phenyl-1-azabicyclo[1.1.0]butane (**1**) as substrate. The results thereby obtained are consistent with our conclusion that additions of TsX across the highly strained N-C(3) σ -bond proceed *via* formation of a tertiary carbocationic intermediate which is trapped subsequently by a nucleophile.

In virtually all of the reactions studied herein, the ratio of reaction products obtained for a given reaction between 3-phenyl- or 3-ethyl-1-azabicyclo[1.1.0]butane (**1** or **4**) and TsX was strikingly dependent upon the reaction medium employed. It seems likely that a series of complex reactions occurs subsequent to carbocation formation that involves interactions of the various species present in solution with the solvent medium.

Reactions of either **1** or **4** with TsN₃ proceeded considerably more slowly than the corresponding reactions with the other *p*-toluenesulfonyl derivatives employed in this study. It seems likely that this result reflects the stabilizing resonance interaction between the azide group and the adjacent sulfonyl group in TsN₃ which serves to reduce the electrophilicity of sulfur in TsN₃ *vis-à-vis* that of the sulfur atom in the other *p*-toluenesulfonyl derivatives studied.

EXPERIMENTAL

Melting points are uncorrected. Elemental microanalytical data were obtained by personnel at M-H-W Laboratories, Inc., Phoenix, AZ and at the Microanalytical Laboratory of the Polish Academy of Sciences, Lodz, Poland.

Reaction of 3-Ethyl-1-azabicyclo[1.1.0]butane (4**) with TsCl.** A solution of Na₂CO₃ (22 mg, 0.20 mmol) in H₂O (6 mL) was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution were added sequentially with stirring **4**¹ (82 mg, 0.98 mmol) followed by solution of TsCl (370 mg, 1.96 mmol) in THF (2 mL). After the addition of reagents had been completed, the external cold bath was removed, and the reaction mixture was allowed to warm gradually to the ambient temperature with stirring during 2 h. Ice (5 g) was added to the reaction mixture, and the resulting aqueous suspension was ex-

tracted with CH_2Cl_2 (2 x 20 mL). The organic layer was washed with ice-cold water (15 mL), dried (MgSO_4), and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by using a 10-30% EtOAc-hexane gradient elution scheme.

Workup of the first chromatography fraction afforded *N-p*-toluenesulfonyl-3-chloro-3-ethylazetidene^{1b} (**6**, 91 mg, 34 %) as a colorless oil that slowly solidified upon standing several weeks at ambient temperature. The resulting solid material displayed mp 67-68 °C (lit.,^{1b} mp 66 °C); IR (film) 2974 (m), 2947 (w), 2885 (w), 1463 (m), 1366 (s), 1169 (vs), 685 cm^{-1} (vs); ^1H NMR (CDCl_3) δ 0.91 (t, $J = 7.2$ Hz, 3 H), 83 (q, $J = 7.2$ Hz, 2 H), 2.43 (s, 3 H), 3.90 (s, 4 H), 7.35 (AB, $J_{\text{AB}} = 8.6$ Hz, 2 H), 7.70 (AB, $J_{\text{AB}} = 8.6$ Hz, 2 H); ^{13}C NMR (CDCl_3) δ 8.5 (q), 21.6 (q), 33.9 (t), 61.9 (s), 64.3 (t), 128.3 (d), 129.8 (d), 131.4 (s), 144.4 (s). Anal. Calcd for $\text{C}_{12}\text{H}_{16}\text{NO}_2\text{ClS}$: C, 52.65; H, 5.89. Found: C, 52.39; H, 5.66.

Continued elution of the chromatography column afforded a second fraction that contained *N-(N'-p*-toluenesulfonyl-3'-ethyl-3'-azetidiny)-3-chloro-3-ethylazetidene (**7**, 6.0 mg, 3.4%) as a colorless oil that slowly solidified upon standing at ambient temperature. The resulting solid material displayed mp 79-80 °C; IR (film) 2978 (m), 2936 (m), 2884 (w), 1464 (m), 1350 (s), 1168 (s), 690 cm^{-1} (vs); ^1H NMR (CDCl_3) δ 0.73 (t, $J = 7.3$ Hz, 3 H), 0.93 (t, $J = 7.2$ Hz, 3 H), 1.37 (q, $J = 7.3$ Hz, 2 H), 1.87 (q, $J = 7.2$ Hz, 2 H), 2.44 (s, 3 H), 3.07 (AB, $J_{\text{AB}} = 8.0$ Hz, 2 H), 3.12 (AB, $J_{\text{AB}} = 8.0$ Hz, 2 H), 3.41 (AB, $J_{\text{AB}} = 8.7$ Hz, 2 H), 3.63 (AB, $J_{\text{AB}} = 8.7$ Hz, 2 H), 7.38 (AB, $J_{\text{AB}} = 8.1$ Hz, 2 H), 7.73 (AB, $J_{\text{AB}} = 8.1$ Hz, 2 H); ^{13}C NMR (CDCl_3) δ 7.6 (q), 8.7 (q), 21.6 (q), 28.5 (t), 34.2 (t), 54.8 (t), 57.7 (s), 61.4 (t), 63.2 (s), 128.3 (d), 129.9 (d), 131.4 (s), 144.2 (s). Anal. Calcd for $\text{C}_{17}\text{H}_{25}\text{N}_2\text{O}_2\text{ClS}$: C, 57.21; H, 7.06. Found: C, 57.35; H, 7.24.

The third chromatography fraction, when concentrated *in vacuo*, afforded pure *N-p*-toluenesulfonyl-3-ethyl-3-hydroxyazetidene (**8**, 80 mg, 31%), as a colorless oil that slowly solidified upon standing at ambient temperature. The resulting solid material displayed mp 72-73 °C; IR (film) 3493 (s), 3038 (m), 2980 (m), 2945 (m), 2886 (m), 1314 (s), 1171 (vs), 764 cm^{-1} (vs); ^1H NMR (CDCl_3) δ 0.83 (t, $J = 7.4$ Hz, 3 H), 1.61 (q, $J = 7.4$ Hz, 2 H), 2.41 (s, 3 H), 2.47 (s, 1 H, OH), 3.54 (AB, $J_{\text{AB}} = 8.6$ Hz, 2 H), 3.65 (AB, $J_{\text{AB}} = 8.6$ Hz, 2 H), 7.34 (AB, $J_{\text{AB}} = 8.0$ Hz, 2 H), 7.69 (AB, $J_{\text{AB}} = 8.0$ Hz, 2 H); ^{13}C NMR (CDCl_3) δ 8.19 (q), 21.5 (q), 31.0 (t), 62.5 (t), 69.8 (s), 128.3 (d), 129.7 (d), 131.4 (s), 144.2 (s). Anal. Calcd for $\text{C}_{12}\text{H}_{17}\text{NO}_3\text{S}$: C, 56.45; H, 6.71. Found: C, 56.58; H, 6.60.

Reaction of 3-Ethyl-1-azabicyclo[1.1.0]butane (4**) with TsCl in the Presence of Excess NaCl (10 equivalents).** A solution of Na_2CO_3 (22 mg, 0.21 mmol) and NaCl (625 mg, 10.7 mmol) in H_2O (6 mL) was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution were added sequentially with stirring **4**¹ (89 mg, 1.07 mmol) followed by solution of TsCl (305 mg, 1.60 mmol) in THF (2 mL). After the addition of reagents had been completed, the external cold bath was removed, and the reaction mixture was allowed to warm gradually to the ambient temperature with stirring during 2 h. Ice (5 g) was added to the reaction mixture, and the resulting aqueous suspension was extracted with CH_2Cl_2 (2 x 20 mL). The organic layer was washed with ice-cold water (15 mL), dried (MgSO_4), and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by using a 10-30% EtOAc-hexane gradient elution scheme.

Workup of the first chromatography fraction afforded **6**^{1b} (238 mg, 80%) as a colorless oil that solidified upon standing at ambient temperature for several weeks. The solid material thereby obtained displayed mp

79-80 °C; The IR, ¹H NMR and ¹³C NMR spectra of this material are identical in all respects with the corresponding spectra obtained previously for authentic **6** (*vide supra*).

Continued elution of the chromatography column afforded a second fraction that contained **7** (5.0 mg, 2.6%) as a colorless oil that slowly solidified upon standing at ambient temperature. The resulting solid material displayed mp 79-80 °C; The IR, ¹H NMR and ¹³C NMR spectra of this material are identical in all respects with the corresponding spectra obtained previously for authentic **7** (*vide supra*).

The third chromatography fraction, when concentrated *in vacuo*, afforded pure **8** (12 mg, 4.3%), as a colorless oil that slowly solidified upon standing at ambient temperature. The resulting solid material displayed mp 72-73 °C. The IR, ¹H NMR and ¹³C NMR spectra of this material are identical in all respects with the corresponding spectra obtained previously for authentic **8** (*vide supra*).

Reaction of 3-Ethyl-1-azabicyclo[1.1.0]butane (4) with TsCl in the Presence of Excess NaN₃ (10 equivalents). A solution of Na₂CO₃ (11 mg, 0.11 mmol) and NaN₃ (344 mg, 5.30 mmol) in H₂O (3 mL) was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution were added sequentially with stirring **4**¹ (44 mg, 0.53 mmol) followed by a solution of TsCl (151 mg, 0.79 mmol) in THF (1 mL). After the addition of reagents had been completed, the external cold bath was removed, and reaction mixture was allowed to warm gradually to ambient temperature with stirring during 2 h. Ice (5 g) was added to the reaction mixture, and the resulting aqueous suspension was extracted with CH₂Cl₂ (2 x 15 mL). The organic layer was washed with ice-cold water (10 mL), dried (MgSO₄), and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by using a 10-30% EtOAc-hexane gradient elution scheme.

Workup of the first chromatography fraction afforded TsN₃ (50 mg, 32% yield based on TsCl.). Continued elution of the chromatography column afforded a second fraction that contained a mixture of **6** and *N*-*p*-toluenesulfonyl-3-azido-3-ethylazetidene (**9**)^{6c} (125 mg, 85%; product ratio 1 : 1, as determined by careful integration of the ¹H NMR spectrum of the product mixture). Despite several attempts, this mixture could not be separated *via* column chromatography on silica gel. Our conclusion that this mixture consists solely of an inseparable mixture of **6** and **9** is supported by analysis of the IR, ¹H NMR and ¹³C NMR spectra of the mixture and comparison of these spectra with the corresponding spectra obtained previously for authentic **6** (*vide supra*) and **9**^{6c}.

The third chromatography fraction was concentrated *in vacuo*, thereby affording pure **7** (4.0 mg, 4.2%) as a colorless oil that slowly solidified upon standing at ambient temperature. The resulting solid material displayed mp 79-80 °C. The IR, ¹H NMR and ¹³C NMR spectra of this material are identical in all respects with the corresponding spectra obtained previously for authentic **7** (*vide supra*).

The fourth chromatography fraction, when concentrated *in vacuo*, afforded pure **8** (6.0 mg, 4.4%), as a colorless oil that slowly solidified upon standing at ambient temperature. The resulting solid material displayed mp 72-73 °C. The IR, ¹H NMR and ¹³C NMR spectra of this material are identical in all respects with the corresponding spectra obtained previously for authentic **8** (*vide supra*).

Reaction of 3-Ethyl-1-azabicyclo[1.1.0]butane (4) with TsCl in the Presence of Excess NaI (10 equivalents). A solution of Na₂CO₃ (17 mg, 0.16 mmol) and NaI (1.20 g, 8.10 mmol) in H₂O (5 mL) was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution were added

sequentially **4**¹ (67 mg, 0.81 mmol) followed by a solution of TsCl (231 mg, 1.2 mmol) in THF (1.6 mL). After the addition of reagents had been completed, the external cold bath was removed, and reaction mixture was allowed to warm gradually to ambient temperature with stirring during 2 h. Ice (5 g) was added to the reaction mixture, and the resulting aqueous suspension was extracted with CH₂Cl₂ (2 x 20 mL). The organic layer was washed with ice-cold water (15 mL), dried (MgSO₄), and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by using a 10-30% EtOAc-hexane gradient elution scheme.

Workup of the first chromatography fraction afforded an inseparable mixture of **6** and *N*-*p*-toluenesulfonyl-3-iodo-3-ethylazetidene (**10**) (169 mg, 59%; product ratio 1 : 10, as determined by careful integration of the ¹H NMR spectrum of the product mixture). Despite several attempts this mixture could be separated *via* column chromatography on silica gel. Our conclusion that this mixture consists solely of an inseparable mixture of **6** and **10** is supported by analysis of the IR, ¹H NMR and ¹³C NMR spectra of the mixture and by comparison of these spectra with the corresponding spectra obtained previously for authentic **6** (*vide supra*) and **10** (*vide infra*)

Continued elution of the chromatography column afforded a second fraction that contained an inseparable mixture of **7** and *N*-(*N*'-*p*-toluenesulfonyl-3'-ethyl-3'-azetidiny)-3-iodo-3-ethylazetidene (**11**, 5.0 mg, 3.1%; product ratio 1:1, as determined by careful integration of the ¹H NMR spectrum of the product mixture). Despite several attempts this mixture could not be separated *via* column chromatography on silica gel. ¹H and ¹³C NMR data for **11** were arrived at by subtracting the resonance signals that correspond to **7** (*vide supra*) from the corresponding NMR spectra of the inseparable mixture of **7** and **11**. In this way, the following NMR data were obtained for **11**: ¹H NMR (CDCl₃) δ 0.73 (t, *J* = 7.3 Hz, 3 H), 0.90 (t, *J* = 7.1 Hz, 3 H), 1.36 (q, *J* = 7.3 Hz, 2 H), 1.76 (q, *J* = 7.1 Hz, 2 H), 2.44 (s, 3 H), 3.18 (AB, *J*_{AB} = 8.3 Hz, 2 H), 3.40 (two overlapping AB patterns, *J*_{AB} = 8.8 Hz, 4 H), 3.57 (AB, *J*_{AB} = 8.8 Hz, 2 H), 7.38 (AB, *J*_{AB} = 8.2 Hz, 2 H), 7.73 (AB, *J*_{AB} = 8.2 Hz, 2 H); ¹³C NMR (CDCl₃) δ 7.5 (q), 12.7 (q), 21.6 (q), 28.5 (t), 36.3 (s), 38.5 (t), 55.0 (t), 57.26 (s), 65.1(t), 128.3 (d), 129.9 (d), 131.2 (s), 144.2 (s).

Workup of the third chromatography fraction, afforded pure **8** (6.0 mg, 2.8%) as a colorless oil that slowly solidified upon standing on ambient temperature. The resulting solid displayed mp 72-73 °C. The IR, ¹H NMR and ¹³C NMR spectra of this material are identical in all respects with the corresponding spectra obtained previously for authentic **8** (*vide supra*).

***N*-*p*-Toluenesulfonyl-3-ethyl-3-iodoazetidene (**10**)**. A solution of **4** (100 mg, 1.2 mmol) and NaI (2.16 g, 14.4 mmol) in water (5 mL) was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution was added dropwise with stirring concentrated aqueous HCl (1 mL, excess), and the resulting mixture was stirred at 0 °C for 0.5 h. Solid Na₂CO₃ (1.59 g, 14.4 mmol) then was added portionwise, and the resulting mixture was stirred at 0 °C for 10 min. To this mixture was added THF (5 mL) followed by portionwise addition of TsCl (680 mg, 3.6 mmol) with stirring during 15 minutes. After the addition of TsCl had been completed, the resulting mixture was stirred for 2 h at 0 °C. The reaction mixture was poured into ice-water (25 mL), and the resulting aqueous suspension was extracted with CH₂Cl₂ (40 mL). The organic layer was washed with ice-cold 6 M aqueous HCl (3 x 15 mL), dried (MgSO₄), and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on

silica gel by eluting with 10% EtOAc-hexane. Pure **10** (219 mg, 50%) was thereby obtained as a colorless microcrystalline solid. Recrystallization of this material from EtOAc-hexane afforded analytically pure **10** as a colorless microcrystalline solid: mp 88-89 °C; IR (KBr) 2962 (w), 1454 (m), 1342 (vs), 1174 (vs), 818 (m), 669 (vs), 623 (m), 559 cm⁻¹ (s); ¹H NMR (CDCl₃) δ 0.89 (t, *J* = 7.1 Hz, 3 H), 1.70 (q, *J* = 7.1 Hz, 2 H), 2.44 (s, 3 H), 4.06 (AB, *J*_{AB} = 9.3 Hz, 2 H), 4.23 (AB, *J*_{AB} = 9.3 Hz, 2 H), 7.36 (AB, *J*_{AB} = 8.1 Hz, 2 H), 7.70 (AB, *J*_{AB} = 8.1 Hz, 2 H); ¹³C NMR (CDCl₃) δ 12.7 (q), 21.6 (q), 31.5 (s), 38 (t), 67.8 (t), 128.3 (d), 129.82 (d), 131.4 (s), 144.5 (s). Anal. Calcd for C₁₂H₁₆NO₂IS: C, 39.46; H, 4.42; Found: C, 39.48; H, 4.46.

Reaction of 3-Ethyl-1-azabicyclo[1.1.0]butane (1) with TsN₃. A solution of Na₂CO₃ (20 mg, 0.19 mmol) in H₂O (6 mL) was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution were added sequentially **4**¹ (84 mg, 1.01 mmol) followed by a solution of TsN₃ (219 mg, 1.11 mmol) in THF (2.0 mL). After the addition of reagents had been completed, the external cold bath was removed, and reaction mixture was allowed to warm gradually to ambient temperature and then stirred at that temperature for 7 days. The reaction mixture was extracted with CH₂Cl₂ (2 x 20 mL). The organic layer was washed with water (15 mL), dried (MgSO₄), and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by using a 10-30% EtOAc-hexane gradient elution scheme.

Workup of the first chromatography fraction afforded recovered TsN₃ (42 mg, 20%). Continued elution of the chromatography column afforded a second fraction that contained **5**. When this fraction was concentrated *in vacuo*, pure **9** (130 mg, 46%) was obtained as a colorless microcrystalline solid: mp 81-82 °C (lit.,^{6c} mp 81-82 °C). The IR, ¹H NMR and ¹³C NMR spectra of this material are identical in all respects with the corresponding spectra reported previously for authentic **9**.^{6c}

Continued elution of the chromatography column afforded a third fraction that contained *N*-(*N*-*p*-toluenesulfonyl-3'-ethyl-3'-azetidynyl)-3-azido-3-ethylazetididine (**12**). When this fraction was concentrated *in vacuo*, pure **12** (5.0 mg, 2.7%), was obtained as a colorless, viscous oil: IR (neat) 2976 (vs), 2876 (s), 2104 (vs), 1595 (m), 1456 (s), 1384 (vs), 1255 (s), 1149 (vs), 1084 (s), 912 (m), 812 (m), 729 (s), 678 cm⁻¹ (vs); ¹H NMR (CDCl₃) δ 0.74 (t, *J* = 7.3 Hz, 3 H), 0.84 (t, *J* = 7.3 Hz, 3 H), 1.44 (q, *J* = 7.3 Hz, 2 H), 1.64 (q, *J* = 7.3 Hz, 2 H), 2.44 (s, 3 H), 2.87 (s, 4 H), 3.40 (AB, *J*_{AB} = 8.7 Hz, 2 H), 3.62 (AB, *J*_{AB} = 8.7 Hz, 2 H), 7.38 (AB, *J*_{AB} = 8.3 Hz, 2 H), 7.74 (AB, *J*_{AB} = 8.3 Hz, 2 H); ¹³C NMR (CDCl₃) δ 7.6 (q), 8.0 (q), 21.6 (q), 28.5 (t), 29.8 (t), 54.5 (t), 56.1 (t), 57.7 (s), 59.5 (s), 128.4 (d), 129.8 (d), 131.3 (s), 144.2 (s). Anal. Calcd for C₁₇H₂₅N₅O₂S: C, 56.18; H, 6.93; Found: C, 55.99; H, 7.07.

The third chromatography fraction, when concentrated *in vacuo*, afforded pure **8** (80 mg, 31%), as a colorless oil that slowly solidified upon standing at ambient temperature. The resulting solid material displayed mp 72-73 °C. The IR, ¹H NMR and ¹³C NMR spectra of this material are identical in all respects with the corresponding spectra obtained previously for authentic **8** (*vide supra*).

Reaction of 3-Ethyl-1-azabicyclo[1.1.0]butane (1) with TsN₃ in the Presence of Excess NaI (10 equivalents). A solution of Na₂CO₃ (16 mg, 0.17 mmol) and NaI (1.17 g, 7.8 mmol) in H₂O (4.7 mL) was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution were added sequentially **4**¹ (65 mg, 0.78 mmol) followed by a solution of TsN₃ (231 mg, 1.17 mmol) in THF

(1.6 mL). After the addition of reagents had been completed, the external cold bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature and then was stirred at that temperature for 7 days. The reaction mixture was extracted with CH_2Cl_2 (2 x 20 mL). The organic layer was washed with water (15 mL), dried (MgSO_4), and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by using a 10-30% EtOAc-hexane gradient elution scheme.

Workup of the first chromatography fraction afforded recovered TsN_3 (21 mg, 9%). Continued elution of the chromatography column afforded a second fraction that contained **9**. When this fraction was concentrated *in vacuo*, pure **9** (69 mg, 32%) was obtained as a colorless microcrystalline solid: mp 81-82 °C (lit.,^{6c} mp 81-82 °C). The IR, ^1H NMR and ^{13}C NMR spectra of this material are identical in all respects with the corresponding spectra reported previously for authentic **9**.^{6c}

Continued elution of the chromatography column afforded a third fraction that contained an inseparable mixture of **11** and **12** (31 mg, 19%; product ratio **11** : **12** = 1.3 : 1, as determined *via* analysis and careful integration of the ^1H NMR spectrum of the product mixture). Despite several attempts this mixture could be separated *via* column chromatography on silica gel. ^1H NMR and ^{13}C NMR data for **11** were arrived at by subtracting the resonance signals that correspond to **12** (*vide supra*) in the corresponding NMR spectra of the inseparable mixture of **11** and **12**. It should be noted that the resonance signals obtained in this way for **11** are identical to those that had been obtained previously for this compound by subtracting the resonance signals that correspond to **7** in the corresponding NMR spectra of an inseparable mixture of **7** and **11** (*vide supra*).

Continued elution of the chromatography column afforded a fourth fraction that contained *N-p*-toluenesulfonyl-3-ethyl-3-hydroxyazetidide (**8**, 52 mg, 26%) as a colorless oil that slowly solidified upon standing at ambient temperature. The solid material thereby obtained displayed mp 72-73 °C. The IR, ^1H NMR and ^{13}C NMR spectra of this material are identical in all respects with the corresponding spectra obtained previously for authentic **8** (*vide supra*).

Finally, a fifth chromatography fraction was collected, which, when concentrated *in vacuo*, afforded pure *N*-(*N-p*-toluenesulfonyl-3'-ethyl-3'-azetidyl)-3-hydroxy-3-ethylazetidide (**13**, 9.0 mg, 6.8%) as a colorless oil; IR (film) 3509 (s), 2970 (s), 2915 (s), 2846 (s), 1595 (m), 1457 (s), 1397 (s), 1160 (s), 814 cm^{-1} (m); ^1H NMR (CDCl_3) δ 0.73 (t, $J = 7.4$ Hz, 3 H), 0.86 (t, $J = 7.4$ Hz, 3 H), 1.38 (q, $J = 7.4$ Hz, 2 H), 1.63 (q, $J = 7.4$ Hz, 2 H), 1.90 (br s, 1 H), 2.44 (s, 3 H), 2.77 (AB, $J_{\text{AB}} = 8.0$ Hz, 2 H), 2.94 (AB, $J_{\text{AB}} = 8.0$ Hz, 2 H), 3.39 (AB, $J_{\text{AB}} = 8.6$ Hz, 2 H), 3.67 (AB, $J_{\text{AB}} = 8.6$ Hz, 2 H), 7.37 (AB, $J_{\text{AB}} = 8.3$ Hz, 2 H), 7.73 (AB, $J_{\text{AB}} = 8.3$ Hz, 2 H); ^{13}C NMR (CDCl_3) δ 7.5 (q), 7.6 (q), 21.6 (q), 28.5 (t), 31.3 (t), 54.6 (t), 57.7 (s), 59.4 (t), 70.4 (s), 128.3 (d), 129.7 (d), 131.7 (s), 144.1 (s). Anal. Calcd for $\text{C}_{17}\text{H}_{26}\text{N}_2\text{O}_3\text{S}$: C, 60.33; H, 7.74. Found: C, 60.09; H, 7.63.

Reaction of 3-Ethyl-1-azabicyclo[1.1.0]butane (4) with TsN_3 in the Presence of Excess NaN_3 (10 equivalents). A solution of Na_2CO_3 (19 mg, 0.18 mmol) and NaN_3 (570 mg, 8.9 mmol) in H_2O (5.4 mL) was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution were added sequentially **4**¹ (74 mg, 0.89 mmol) followed by a solution of TsN_3 (263 mg, 1.34 mmol) in THF (1.8 mL). After the addition of reagents had been completed, the external cold bath was removed, and the

reaction mixture was allowed to warm gradually to ambient temperature and then was stirred at that temperature for 7 days. The reaction mixture was extracted with CH_2Cl_2 (2 x 20 mL). The organic layer was washed with water (15 mL), dried (MgSO_4), and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by using a 10-30% EtOAc-hexane gradient elution scheme.

The first chromatography fraction contained recovered TsN_3 (111 mg, 42%). Continued elution of the chromatography column afforded a second fraction that contained **9**.^{6c} Pure **9** (198 mg, 79%) was isolated from this chromatography fraction as a colorless microcrystalline solid: mp 81-82 °C (lit.,^{6c} mp 81-82 °C). The IR, ^1H NMR and ^{13}C NMR spectra of this material are identical in all respects with the corresponding spectra reported previously for authentic **9**.^{6c}

Continued elution of the chromatography column afforded a second fraction that contained **12** (3.0 mg, 1.8%), which was isolated from this chromatography fraction as a colorless oil. The IR, ^1H NMR and ^{13}C NMR spectra of this material are identical in all respects with the corresponding spectra obtained previously for authentic **12** (*vide supra*).

The third chromatography fraction, when concentrated *in vacuo*, afforded pure **8** (3.0 mg, 1.3%), which was isolated from this chromatography fraction as a colorless oil that slowly solidified upon standing at ambient temperature. The solid material thereby obtained displayed mp 72-73 °C. The IR, ^1H NMR and ^{13}C NMR spectra of this material are identical in all respects with the corresponding spectra obtained previously for authentic **8** (*vide supra*).

Reaction of 3-Ethyl-1-azabicyclo[1.1.0]butane (4) with TsN_3 in the Presence of Excess NaCl (10 equivalents). A solution of Na_2CO_3 (9 mg, 0.09 mmol) and NaCl (257 mg, 4.4 mmol) in H_2O (3 mL) was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution were added sequentially **4**¹ (37 mg, 0.44 mmol) followed by a solution of TsN_3 (130 mg, 0.66 mmol) in THF (1 mL). After the addition of reagents had been completed, the external cold bath was removed, and reaction mixture was allowed to warm gradually to ambient temperature and then was stirred at that temperature for 7 days. The reaction mixture was extracted with CH_2Cl_2 (2 x 15 mL). The organic layer was washed with water (10 mL), dried (MgSO_4), and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by using a 10-30% EtOAc-hexane gradient elution scheme.

The first chromatography fraction contained recovered TsN_3 (25 mg, 19%). Continued elution of the chromatography column afforded a second fraction that contained **9**. When this fraction was concentrated *in vacuo*, pure **9** (63 mg, 51%) was obtained as a colorless microcrystalline solid: mp 81-82 °C (lit.,^{6c} mp 81-82 °C). The IR, ^1H NMR and ^{13}C NMR spectra of this material are identical in all respects with the corresponding spectra reported previously for authentic **9**.^{6c}

Continued elution of the chromatography column afforded a third fraction that contained **12** (2.0 mg, 2.5%), which was isolated from this chromatography fraction as a colorless oil. The IR, ^1H NMR and ^{13}C NMR spectra of this material are identical in all respects with the corresponding spectra obtained previously for authentic **12** (*vide supra*).

The fourth chromatography fraction, when concentrated *in vacuo*, afforded pure **8** (26 mg, 23%) as a colorless oil that slowly solidified upon standing at ambient temperature. The resulting solid material displayed mp 72-73 °C. The IR, ¹H NMR and ¹³C NMR spectra of this material are identical in all respects with the corresponding spectra obtained previously for authentic **8** (*vide supra*).

Reaction of 3-Phenyl-1-azabicyclobutane (1) with TsCl. Method A. A solution of Na₂CO₃ (106 mg, 1.0 mmol) in H₂O (30 mL) and acetone (50 mL) was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution were added sequentially with stirring a solution of **1** (660 mg, 5.0 mmol) in acetone (5 mL) followed by solution of TsCl (1.43 g, 7.5 mmol) in acetone (5 mL). After the addition of reagents had been completed, the external cold bath was removed, and the resulting clear homogeneous mixture was stirred at ambient temperature overnight. The reaction mixture was concentrated *in vacuo* at 20 °C to minimum volume (to remove most of the acetone solvent), and the resulting aqueous suspension was extracted with CH₂Cl₂ (2 x 30 mL). The combined organic extracts were dried (MgSO₄) and filtered, and the filtrate was concentrated *in vacuo*. Careful integration of the ¹H NMR spectrum of the semi-solid residue (1.44 g) thereby obtained revealed the presence of **14** (965 mg, 60%) and **15** (455 mg, 30%) along with a trace amount of unreacted TsCl. The residue was purified *via* column chromatography on silica gel by eluting with CH₂Cl₂. Workup of the main chromatography fraction afforded *N-p*-toluenesulfonyl-3-chloro-3-phenylazetidine (**14**) as a colorless microcrystalline solid. Recrystallization of this material from CH₂Cl₂-hexane afforded analytically pure **14** as a colorless microcrystalline solid: mp 101-103 °C; IR (KBr) 1600 (m), 1500 (m), 1450 (m), 1350 (vs), 1300 (m), 1190 (s), 1180 (vs), 1100 (s), 1080 (m), 760 (s), 680 (s), 610 (m), 540 cm⁻¹ (s); ¹H NMR (CDCl₃) δ 2.42 (s, 3 H), 4.32 (AB, *J*_{AB} = 8.0 Hz, 2 H), 4.45 (AB, *J*_{AB} = 8.0 Hz, 2 H), 7.35 (AB, *J*_{AB} = 8.0 Hz, 2 H), 7.73 4.45 (AB, *J*_{AB} = 8.0 Hz, 2 H); ¹³C NMR (CDCl₃) δ 21.6 (q), 61.0 (s), 66.3 (t), 125.6 (d), 128.7 (d), 128.9 (d), 129.1 (d), 130.2 (d), 132.2 (s), 141.2 (s), 144.9 (s); Low-resolution MS (EI, 70 eV), *m/z* (relative intensity) 323 [(M + 2)⁺, 0.4], 322 [(M + 1)⁺, 0.7], 321(M⁺, 1), 285 (0.3), 168 (13), 166 (55), 155 (17), 141 (12), 140 (100), 139 (53), 138 (98), 130 (54), 104 (22), 103 (99), 102 (13), 91 (99). Anal. Calcd for C₁₆H₁₆NO₂ClS: C, 59.71; H, 5.01; N, 4.35; Cl, 11.02; S, 9.96. Found: C, 59.93; H, 5.08; N, 4.41; Cl, 11.09; S, 9.47.

Continued elution of the chromatography column by eluting with 2% MeOH-hexane afforded crude **15**. Additional purification of this material *via* preparative TLC (SiO₂ stationary phase) followed by recrystallization of the eluate thereby obtained from CH₂Cl₂-hexane afforded analytically pure **15** as a colorless microcrystalline solid: mp 142-144 °C; IR (CHCl₃) 3380 (br, m), 1600 (m), 1450 (m), 1350 (s), 1180 (vs), 1100 cm⁻¹ (m); ¹H NMR (CDCl₃) δ 2.43 (s, 3 H), 2.83 (br s, 1 H), 3.92 (AB, *J*_{AB} = 8.5 Hz, 2 H), 4.08 (AB, *J*_{AB} = 8.5 Hz, 2 H), 7.30 (s, 5 H), 7.37 (AB, *J*_{AB} = 8.0 Hz, 2 H), 7.72 (AB, *J*_{AB} = 8.0 Hz, 2 H); ¹³C NMR (CDCl₃) δ 21.6 (q), 65.4 (t), 124.9 (d), 128.4 (d), 128.8 (d), 128.9 (d), 130.2 (d), 132.2 (s), 142.6 (s), 144.7 (s); Low-resolution MS (EI, 70 eV), *m/z* (relative intensity) 304 [(M+1)⁺, 0.8], 198 (16), 184 (61), 155 (84), 148 (26), 121 (18), 120 (99), 105 (93), 91 (100), 78 (51). Anal. Calcd for C₁₆H₁₇NO₃S: C, 63.34; H, 5.65; N, 4.62; S, 10.57. Found: C, 63.38; H, 5.69; N, 4.76; S, 9.94.

Reaction of 3-Phenyl-1-azabicyclobutane (1) with TsCl. Method B. To a solution of **1** (130 mg, 1.0 mmol) in CDCl₃ (1 mL) in a 5 mL round bottom flask under nitrogen at ambient temperature was added dropwise with stirring a solution of TsCl (230 mg, 1.2 mmol) in CDCl₃ (1 mL). After the reaction

had proceeded for *ca.* 1 h, the ^1H NMR spectrum of the crude reaction mixture was obtained. Careful examination of the spectral region between δ 4.2-4.6 revealed only the presence of the characteristic AB absorption pattern that corresponds to **14**. The reaction mixture then was concentrated *in vacuo*, and the solid residue thereby obtained was triturated with a small amount of hexane. The resulting solution was cooled in a refrigerator, whereupon crystals precipitated from the hexane solution. The precipitate was collected by filtration, and the residue was air-dried, thereby affording crude **14** (310 mg, 97%) as a colorless microcrystalline solid: mp 97-101 °C. The IR, ^1H NMR, and ^{13}C NMR spectra of this material are essentially identical to the corresponding spectra obtained previously for authentic **14** (*vide supra*).

Reaction of 3-Phenyl-1-azabicyclobutane (1) with TsCl in the Presence of Excess NaCl (10 equivalents). A solution of Na_2CO_3 (106 mg, 1.0 mmol) and NaCl (2.95 g, 50 mmol) in H_2O (30 mL) and acetone (50 mL) was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution were added sequentially with stirring a solution of **1** (660 mg, 5.0 mmol) in acetone (5 mL) followed by solution of TsCl (1.43 g, 7.5 mmol) in acetone (5 mL). After the addition of reagents had been completed, the external cold bath was removed, and the clear homogenous mixture was stirred at ambient temperature overnight. The reaction mixture was concentrated *in vacuo* at 20 °C to minimum volume (to remove most of the acetone solvent), and the resulting aqueous suspension was extracted with CH_2Cl_2 (2 x 30 mL). The combined organic extracts were dried (MgSO_4) and filtered, and the filtrate was concentrated *in vacuo*. Careful integration of the ^1H NMR spectrum of the solid residue (1.60 g) revealed the presence of **14** (1.375 g, 85%) and **15** (190 mg, 12%) along with a trace amount of unreacted TsCl.

Reaction of 3-Phenyl-1-azabicyclobutane (1) with TsCl in the Presence of Excess NaI (10 equivalents). A solution of Na_2CO_3 (106 mg, 1.0 mmol) and NaI (7.5 g, 50 mmol) in H_2O (30 mL) and acetone (50 mL) was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution were added sequentially with stirring a solution of **1** (660 mg, 5.0 mmol) in acetone (5 mL) followed by solution of TsCl (1.43 g, 7.5 mmol) in acetone (5 mL). After the addition of reagents had been completed, the external cold bath was removed, and the clear homogenous mixture was stirred at ambient temperature overnight. The reaction mixture was concentrated *in vacuo* at 20 °C to minimum volume (to remove most of the acetone solvent). A crystalline solid which had precipitated during this operation was isolated by suction filtration, washed with a minimal amount of cold MeOH, and air-dried. Crude *N-p*-toluenesulfonyl-3-iodo-3-phenylazetidene (**16**, 1.86 g, 90%) was thereby obtained. This material was further purified *via* recrystallization from MeOH, thereby affording analytically pure **16** as a pale yellow microcrystalline solid: mp 105-106 °C. Compound (**16**) decomposes slowly during storage at ambient temperature with evolution of I_2 ; IR (KBr) 1600 (m), 1450 (m), 1350 (vs), 1280 (s), 1160 (vs), 1105 (s), 1090 (s), 1020 (m), 700 (m), 660 (vs), 620 (m), 580 (m), 540 (s), 505 cm^{-1} (s); ^1H NMR (CDCl_3) δ 2.38 (s, 3 H), 4.50 (s, 4 H), 7.22 (br s, 5 H), 7.32 (AB, $J_{\text{AB}} = 8.0$ Hz, 2 H), 7.72 (AB, $J_{\text{AB}} = 8.0$ Hz, 2 H); ^{13}C NMR (CDCl_3) δ 21.6 (q), 25.3 (s), 69.2 (t), 125.2 (d), 128.3 (d), 128.6 (d), 129.2 (d), 130.1 (d), 132.3 (s), 144.8 (s), 146.4 (s); Low-resolution MS (EI, 70 eV), m/z (relative intensity) (no molecular ion), 286 (41), 155 (14), 131 (31), 130 (100), 104 (26), 103 (65), 91 (68), 77(17). Anal. Calcd for $\text{C}_{16}\text{H}_{16}\text{NO}_2\text{IS}$: C, 46.50; H, 3.90; N, 3.39; I, 30.71; S, 7.76. Found: C, 46.71; H, 3.87; N, 3.37; I, 30.46; S, 7.62.

The filtrate that remained after separation of **16** was extracted with CH_2Cl_2 . The organic layer was dried (MgSO_4) and filtered, and the filtrate was concentrated *in vacuo*. A very dark-colored residue (0.3 g) was thereby obtained which contained free I_2 and other decomposition products.

Reaction of 3-Phenyl-1-azabicyclobutane (1) with TsCl in the Presence of Excess NaN_3 (10 equivalents). A solution of Na_2CO_3 (106 mg, 1.0 mmol) and NaN_3 (3.26 g, 50 mmol) in H_2O (30 mL) was cooled to 0°C via application of an external ice-water bath. To this solution were added sequentially with stirring a solution of **1** (660.5 mg, 5.0 mmol) in THF (5 mL) followed by solution of TsCl (1.43 g, 7.5 mmol) in THF (5 mL). After the addition of reagents had been completed, the external cold bath was removed, and the heterogenous suspension was stirred overnight. The reaction mixture was concentrated *in vacuo* at 20°C to minimum volume (to remove most of the acetone solvent), and the resulting aqueous suspension was extracted with CH_2Cl_2 (2 x 30 mL). The combined organic extracts were dried (MgSO_4) and filtered, and the filtrate was concentrated *in vacuo*. Careful integration of the ^1H NMR spectrum of the semi-solid residue (1.93 g) thereby obtained revealed the presence of TsN_3 (550 mg, 38% based on TsCl), **14** (500 mg, 31%) and **2** (880 mg, 54%) along with a trace amount of **15**. A similar experiment performed by using aqueous acetone as solvent afforded a complex mixture of polymeric products, diacetone alcohol, and TsN_3 along with trace quantities of **2** and **14**. It thus appears that the conditions used in this experiment may have promoted rapid polymerization of **1** to the virtual exclusion of other possible reactions of **1** with TsCl- NaN_3 .

Competition Experiment: Reaction of 3-Phenyl-1-azabicyclobutane (1) with TsN_3 and TsCl (ratio 1 : TsN_3 : TsCl = 1 : 1 : 1) in Nonaqueous Solution. To a solution of **1** (130 mg, 1.0 mmol) in CDCl_3 (1 mL) under nitrogen at ambient temperature was added dropwise with stirring a solution that contained a mixture of TsCl (190 mg, 1.0 mmol) and TsN_3 (197 mg, 1.0 mmol) in CDCl_3 (1 mL). After the reaction mixture had been stirred at ambient temperature for 1 h, the ^1H NMR spectrum of the crude reaction mixture was obtained. Careful examination of the spectral region between δ 4.2-4.6 revealed only the presence of the characteristic AB absorption pattern that corresponds to **14**. In particular, there were no absorption signals present at δ 1.50 and 2.75 (due to unreacted **1**). In addition, there was no indication in the ^1H NMR spectrum of the crude reaction mixture that any detectable quantity of **2** had been formed.

Competition Experiment: Reaction of 3-Phenyl-1-azabicyclobutane (1) with TsN_3 and TsCl (ratio 1 : TsN_3 : TsCl = 1 : 0.7 : 0.3) in Nonaqueous Solution. To a solution of **1** (65 mg, 0.5 mmol) in CDCl_3 (1 mL) under nitrogen was added dropwise with stirring a solution that contained a mixture of TsCl (30 mg, 0.15 mmol) and TsN_3 (70 mg, 0.35 mmol) in CDCl_3 (1 mL). The ^1H NMR spectrum of the crude reaction mixture was obtained after the reaction had proceeded for a few minutes. Once again, careful examination of the spectral region between δ 4.2-4.6 revealed only the presence of the characteristic AB absorption pattern that corresponds to **14**. However, absorption signals at δ 1.50 and 2.75 persisted, thereby indicating the presence of remaining, unreacted **1**. In addition, there was no indication in the ^1H NMR spectrum of the crude reaction mixture that any detectable quantity of **2** had been formed, even after the reaction had been allowed to proceed at ambient temperature for an additional 4 h.

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