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Rearrangement of the *trans*-Tricyclo[4.2.0.0^{1,3}]oct-4-enyl Skeleton

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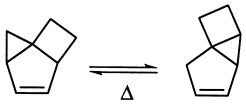
Abstract—The acetolysis of a tosylate with a novel tricyclic skeleton was examined. Two major products (a tosylate and an acetate) are formed and both are the result of a skeletal rearrangement. A mechanism to account for the observed products is proposed and preliminary kinetic data are reported.

Introduction

We recently reported a synthesis of *trans*-tricyclo-[4.2.0.0^{1,3}]oct-4-ene (**1**) and described some of its reactivity.[1,2] This hydrocarbon has a unique structure consisting of fused three-, four- and five-membered rings along with a double bond. Its strained ring skeleton is poised to undergo a variety of rearrangements and two were originally described (Eqs. (1) and (2)). In this paper we report on a cationic rearrangement brought about by the solvolysis of *p*-toluenesulfonate **2**.[3] This substrate can be viewed as a cyclopropylcarbinyl and 4-spiro[2.3]hexyl cation precursor, in which these subunits are embedded in a larger molecular framework. Strained constituents in complex structures have been studied less thoroughly than simpler model systems and are of some interest.[4]



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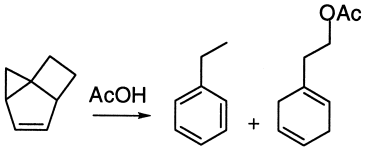

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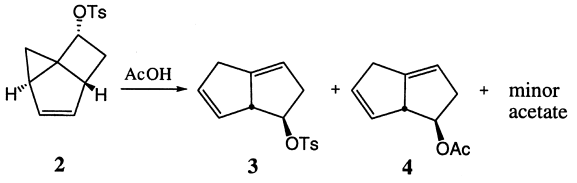
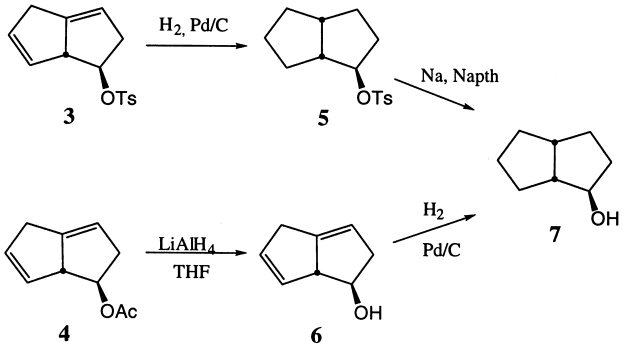
Results and Discussion

Tricyclic tosylate **2** was prepared as reported previously and solvolyzed in acetic acid at 25, 35 and 50°C. Two major products, tosylate **3** and acetate **4**, along with a minor and unidentified acetate were formed in a 11:3:1 ratio, respectively (Eq. (3)).[5] The product distribution is insensitive over the temperature range and reaction times that were examined. In addition, no deuterium incorporation was detected in **3** or **4** when acetic acid-d_4 was used as the solvent, suggesting that their ratio reflects the primary product distribution. As for the structural assignments, they are based upon the NMR spectral data (^{1}H, ^{13}C and COSY) for both species.



2 **3** **4** (3)

To secure the product and stereochemical assignments, we converted individually **3** and **4** to a known compound (Scheme 1). In particular, hydrogenation of the tosylate (**3**) on Pd/C gave the saturated *syn*,*syn*-2-bicyclo[3.3.0]octyl tosylate (**5**), which was subsequently reduced with sodium naphthalenide to afford *syn*,*syn*-bicyclo[3.3.0]octan-2-ol (**7**). Likewise, the acetate (**4**) was reduced with $LiAH_4$ to yield alcohol **6**, which was hydrogenated on Pd/C to give the



3 **5** **7** **4** **6**

Scheme 1.

Keywords: solvolysis; kinetics; tricyclo[4.2.0.0^{1,3}]oct-4-enyl skeleton; rearrangements.

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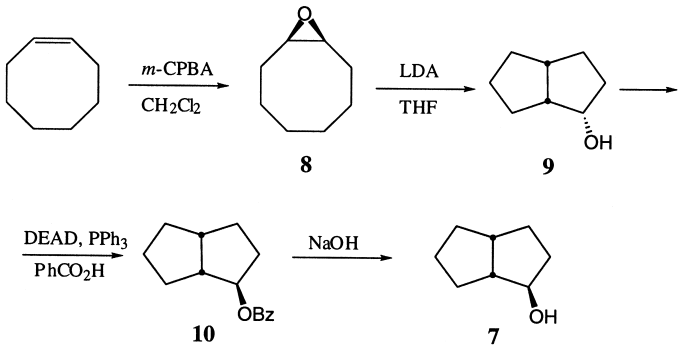
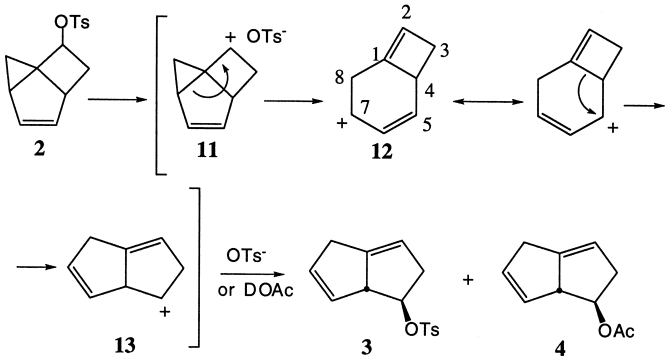


Scheme 2.



Scheme 3.

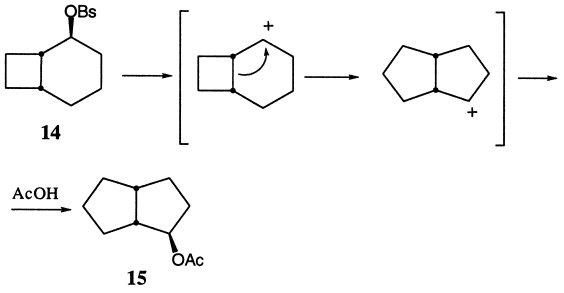
same bicyclic alcohol as in the tosylate case (**7**). In both instances the ^{1}H NMR spectra were found to be the same as that reported for **7**.[6]

There is confusion in the literature regarding the ^{1}H NMR spectrum of **7** relative to **9**, its *syn*,*anti*-epimer. Consequently, we independently prepared both *syn*-bicyclo[3.3.0]octan-2-ols (**7** and **9**, Scheme 2). Their synthesis was accomplished in four steps starting from *cis*-cyclooctene by following the literature procedure for the *anti* isomer (**9**)[7] and inverting it to the *syn* derivative (**7**) via the Mitsunobu method.[8] As a result, we have spectral data for both diastereomeric alcohols and can confidently assign their relative stereochemistry.

The proposed mechanism for the cationic rearrangement of the tricyclic skeleton is shown in Scheme 3. Solvolysis of **2** would be expected to afford the cyclopropylcarbinyl cation **11** as the first formed intermediate, but semiempirical (AM1), ab initio (HF) and density functional theory (B3LYP) calculations with the 6-31G(d) basis set lead either directly to the ring-opened allylic cation **12** or to a delocalized species with an extremely long C1–C7 bond (1.84 Å) that is well on its way to **12**. Subsequent migration of the C1–C4 bond leads to bicyclo[3.3.0]octadienyl cation **13**; strain relief provides the driving force for the isomerization. Trapping of this ion with the leaving group (OTs^-) or solvent gives the observed products.

Consistent with our proposed mechanism, B3LYP calculations indicate that ion **11** is 5.2 kcal mol^{-1} less stable than **12** and that the isomerization barrier is only 0.2 kcal mol^{-1}. We were unable to locate a stationary point corresponding to **13** at the same level of theory (all attempts led to a 1,2-hydride shift and the formation of the corresponding pentadienyl cation), but found that it is 3.2 kcal mol^{-1} more stable than **12** using AM1. In addition, an analogous transformation was reported by Cope et al.[9] to account for the formation of *syn*,*syn*-2-bicyclo[3.3.0]octyl acetate (**15**) from the acetolysis of 2-bicyclo[4.2.0]octyl brosylate (**14**, Scheme 4).

Preliminary kinetic results for the solvolysis of **2** were carried out at various temperatures in acetic acid-d_4 and monitored by ^{1}H NMR spectroscopy. The rate constants were measured over a 25°C range from 25 to 50°C (Table 1). An example of the kinetic data is shown in Fig. 1. A linear Eyring plot leads to $\Delta H^{\ddagger}$=24.6 kcal mol^{-1} and $\Delta S^{\ddagger}$=7.3 cal mol^{-1} K^{-1}. This contrasts with 4-spiro[2.3]-hexyl tosylate (**16**), which solvolyzes five times faster at 25°C and has activation parameters of $\Delta H^{\ddagger}$=18.4 kcal



Scheme 4.

Table 1. Acetolysis rates and activation parameters (data for **16** come from Ref. 10; the rate constant was obtained from the activation parameters)

Compound	T (°C)	k (s^{-1})	k_{rel}	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$
2	25	$(2.78\pm.08)\times10^{-4}$	1	24.6	7.3
	35	$(7.51\pm.16)\times10^{-4}$			
	50	$(7.12\pm.22)\times10^{-3}$			
 **16**	25	1.32×10^{-3}	5	18.4	−10

Figure 1. Kinetic data at 25°C for the solvolysis of **2**.

mol^{-1} and $\Delta S^{\ddagger}=-10$ cal mol^{-1} K^{-1}.[10] It might seem surprising that the tricyclic tosylate reacts more slowly than its bicyclic analog but there is poorer overlap between the C–OTs bond and the Walsh orbitals of the cyclopropane in the former (more rigid) case.[11] As a result, **2** either directly isomerizes to **12** or it affords **11** in which there is considerable weakening of the C1–C7 bond. This explanation accounts for the difference in activation parameters and is consistent with the fact that all of the products derived from **2** are rearranged whereas a small amount of unrearranged material is obtained from **16**.

Experimental

Solvolysis of tricyclo[4.2.0.0^{1,3}]oct-4-en-8-tosylate (2). A solution of tosylate **2** (0.20 g, 0.73 mmol) in 10 ml of AcOH was heated to reflux for 2 min. Upon cooling to room temperature, 20 ml of Et_2O was added. This solution was washed with H_2O, sat. $NaHCO_3$ and sat. NaCl, and then the organic layer was dried over $MgSO_4$. Concentration under reduced pressure afforded a 11:3:1 mixture of **3**, **4** and an unknown acetate, respectively. Separation of the products via column chromatography (5% EtOAc/hexanes) afforded 40 mg (20%) of tosylate **3** and 30 mg (25%) of a mixture of acetates (**4** and an unknown compound). Tosylate **3**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, 2H), 7.35 (d, 2H), 5.83 (m, 1H), 5.69 (m, 1H), 5.30 (s, 1H), 4.60 (dd, J=6.0 and 9.6 Hz, 1H), 3.75 (m, 1H), 2.66–2.78 (m, 3H), 2.59 (m, 1H), 2.45 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.2, 131.5, 130.0, 128.1, 117.2, 103.0, 86.6, 59.8, 40.3, 32.5, 21.9 (two quaternary carbons were not assigned). HRMS-CI (NH_3) M+NH_4^+ calcd for $C_{15}H_{20}NO_3S$ 294.1164, found 294.1168. Acetate **4**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.03 (m, 1H), 5.87 (m, 1H), 5.37 (m, 1H), 4.91 (dd, J=7.5 and 16 Hz, 1H), 3.61 (m, 1H), 2.79 (m, 3H), 2.60 (m, 1H), 2.15 (s, 3H).

Preparation of *syn*,*syn*-bicyclo[3.3.0]octyl-2-tosylate (5). A solution of tosylate **3** (0.010 g, 0.036 mmol) and 10 mg of 10% Pd/C in 1 ml of EtOAc was stirred overnight under 1 atm of H_2. The reaction mixture was filtered through a plug of silica gel and concentrated under reduced pressure to afford 8.6 mg (86%) of tosylate **5**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J=8.1 Hz, 2H), 7.35 (d, J=8.1 Hz, 2H), 4.58 (m, 1H), 2.5 (m, 1H), 2.44 (s, 3H), 1.92 (m, 2H), 1.71 (m, 3H), 1.43 (m, 2H), 1.26 (m, 2H), 1.10 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.4, 134.6, 129.7, 127.7, 90.6, 49.9, 41.5, 34.0, 31.9, 31.2, 29.9, 26.5, 21.6. HRMS-EI M^+ calcd for $C_{15}H_{20}O_3S$ 280.1133, found 280.1128.

Preparation of *syn*,*syn*-bicyclo[3.3.0]octan-2-ol (7) from *syn*,*syn*-bicyclo[3.3.0]octyl-2-tosylate (5). To a solution of naphthalene (0.012 g, 0.090 mmol) in 0.5 ml of THF under N_2 was added sodium metal (~2.1 mg, 0.090 mmol). The reaction mixture was stirred for 1 h until a dark blue color formed at which point tosylate **5** (8.6 mg, 0.030 mmol) in 0.5 ml of THF was added. The blue color disappeared within 5 min and 5 ml of H_2O was added. Ether (5 ml) also was added and the organic layer was dried over $MgSO_4$. Concentration under reduced pressure followed by column chromatography (5% EtOAc/hexanes) afforded 3.6 mg (95%) of alcohol **7**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.87 (q, J=6.0 Hz, 1H), 2.57 (m, 1H), 2.22 (m, 1H), 1.94 (m, 1H), 1.73 (m, 2H), 1.6 (br. s, 1H), 1.48 (m, 4H), 1.21 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 80.3, 52.9, 42.9, 34.5, 34.4, 31.8, 30.5, 26.7.

Preparation of *syn*-bicyclo[3.3.0]octa-1,6-dien-4-ol (6). To a 0°C solution of 0.030 g (0.18 mmol) of acetate **4** (with the unknown acetate) in 2 ml of Et_2O was added 0.3 ml of a 1 M solution of $LiAlH_4$ in THF. The reaction mixture was stirred for 1.5 h under reflux, cooled down to 0°C, and 10 ml of both Et_2O and sat. NH_4Cl were added. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to afford 0.018 g (80%) of alcohol **6**, which was of sufficient purity for the subsequent reactions. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.02 (m, 1H), 5.89 (m, 1H), 5.35 (m, 1H), 4.13 (dd, J=4.5 and 12.0 Hz, 1H), 3.50 (dt, J=3.0 and 6.3 Hz, 1H), 2.78 (m, 2H), 2.65 (m, 1H), 2.49 (m, 1H), 1.94 (br. s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.1, 133.5, 132.4, 117.9, 81.3, 62.8, 43.4, 32.7. HRMS-EI M^+ calcd for $C_8H_{10}O$ 122.0732, found 122.0732.

Preparation of *syn*,*syn*-bicyclo[3.3.0]octan-2-ol (7) from *syn*-bicyclo[3.3.0]octa-1,6-dien-4-ol (6). A solution of alcohol **6** (0.018 g, 0.15 mmol) and 20 mg of 10% Pd/C in 1 ml of EtOAc was stirred overnight under 1 atm of H_2. The reaction mixture was filtered through a plug of silica gel and concentrated under reduced pressure to afford 0.0179 g (95%) of alcohol **7**.

Preparation of *syn*-epoxycyclooctane (8).[6] To a 0°C solution of 3.0 g (0.027 mol) of cyclooctene in 50 ml of CH_2Cl_2 was added 7.0 g of 80% *m*-chloroperbenzoic acid. The

reaction mixture was stirred at room temperature for 2 h, cooled down to 0°C, and 50 ml of aqueous $NaHCO_3$ (saturated) was added. The organic layer was washed with 50 ml of H_2O and saturated NaCl solution, and dried over $MgSO_4$. Concentration under reduced pressure followed by vacuum distillation at 15 mm (bp 86–88°C at 30 mm (lit.))[12] afforded 2.8 g (82%) of epoxide **8**. ^1H NMR (300 MHz, $CDCl_3$) δ 2.89 (m, 2H), 2.16 (m, 2H), 1.26–1.66 (m, 8H), 1.15–1.26 (m, 2H).

Preparation of *syn*,*anti*-bicyclo[3.3.0]octan-2-ol (9). To a solution of *i*-Pr_2NH (3.09 ml, 0.022 mol) in 7 ml of Et_2O was added 11.2 ml (0.019 mol) of a 1.7 M *n*-BuLi solution in hexanes. The reaction mixture was stirred for 1 h and then a solution of *syn*-epoxycyclooctane (1.2 g, 9.5 mmol) in 1 ml of Et_2O was added. After refluxing the reaction mixture for 1 h, it was cooled down to room temperature and 5 ml of sat. NH_4Cl was added. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. Distillation at 15 mm (bp 103–105°C at 25 mm (lit.))[7] afforded 0.40 g (34%) of *syn*,*anti*-bicyclo[3.3.0]octan-2-ol (**9**). ^1H NMR (300 MHz, $CDCl_3$) δ 4.19 (m, 1H), 2.51 (m, 2H), 1.22–1.92 (m, 11H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 75.3, 47.4, 42.5, 34.9, 34.1, 29.3, 27.8, 26.5.

Preparation of *syn*,*syn*-bicyclo[3.3.0]octyl-2-benzoate (10). Diethyl azodicarboxylate (0.33 g, 1.9 mmol) was added over a 5 min period to a room temperature mixture of alcohol **9** (0.20 g, 1.5 mmol), PPh_3 (0.49 g, 1.9 mmol) and benzoic acid (1.2 g, 1.9 mmol) in 6 ml of THF. The resulting solution was stirred overnight and then concentrated under reduced pressure. Column chromatography (5% EtOAc/hexanes, R_f=0.67) afforded 0.29 g (81%) of compound **10**. ^1H NMR (300 MHz, $CDCl_3$) δ 8.02 (m, 2H), 7.54 (m, 1H), 7.43 (m, 2H), 5.06 (td, J=2.1 and 3.9 Hz, 1H), 2.60 (m, 2H), 1.9 (m, 6H), 1.6 (septet, J=6.3 Hz, 1H), 1.4 (m, 2H), 1.26 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 132.9, 131.1, 129.7, 128.4, 83.3, 50.1, 42.1, 34.4, 31.9, 31.6, 30.8, 27.0. HRMS-EI M^+ calcd for $C_{15}H_{18}O_2$ 230.1307, found 230.1305.

Preparation of *syn*,*syn*-bicyclo[3.3.0]octan-2-ol (7) from *syn*,*syn*-bicyclo[3.3.0]octyl-2-benzoate (10). To a solution of benzoate **10** (0.15 g, 0.65 mmol) in 5 ml of EtOH was added a solution of NaOH (0.056 g, 1.4 mol) in 2.5 ml of H_2O. The reaction mixture was stirred overnight and 15 ml of CH_2Cl_2 and 10 ml of H_2O were added. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography (5% EtOAc/hexanes, R_f=0.2) afforded 0.048 g (59%) of compound **7**.

Kinetics. A 20 mg portion of tosylate **2** was added to approximately 0.5 ml of acetic acid-d_4 in an NMR tube flushed with dry N_2. The probe of a 500 MHz Varian™ NMR was preheated to the desired temperature and did not vary by more than half a degree over the course of a kinetic run. Data were collected as a series of 5–23 four scan spectra at 2–5 min intervals over a period of at least 2 half-lives at 25, 35 and 50°C. First-order rate constants were obtained by monitoring the disappearance of **2** via the integration of its cyclopropyl resonance at 0.34 δ relative to the residual acid proton in acetic acid. The results given in Table 1 represent the average of 2 determinations at 35 and 50°C and 1 run at 25°C, where the uncertainties are the standard deviations in the measurements except for the 25°C rate, which is estimated to have an error of ±3%. Eyring parameters were obtained from a plot of $\ln(k/T)$ vs. $1/T$.

Acknowledgements

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References

1. Koltun, E. S.; Kass, S. R. *J. Org. Chem.* **2000**, in press.
2. Koltun, E. S. PhD Thesis, University of Minnesota, 1999.
3. Only the *syn* isomer of tosylate **2** was obtained in the synthesis of **1**.
4. For example, see: Dombrowski, G. W. PhD Thesis, University of Minnesota, 1995, and references therein.
5. ^1H NMR data of the unknown acetate indicates that it is not the unrearranged acetate of **2**.
6. Fujita, K.; Hata, K.; Oda, R.; Tabushi, I. *J. Org. Chem.* **1973**, *38*, 2640–2644.
7. Whitesell, J. K.; White, P. D. *Synthesis* **1975**, *102*, 602–603.
8. Overman, L. E.; Bell, K. L.; Ito, F. *J. Am. Chem. Soc.* **1984**, *106*, 4192–4201.
9. Cope, A. C.; Gleason, R. W.; Moon, S.; Park, C. H. *J. Org. Chem.* **1967**, *32*, 942–946.
10. Wiberg, K. B.; Hiatt, J. E. *J. Am. Chem. Soc.* **1968**, *90*, 6495–6500.
11. Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*; 3rd ed.; Harper & Row: New York, 1987, pp 454–463.
12. Kato, H.; Miyamoto, N.; Kawanisi, M.; Nozaki, H. *Tetrahedron* **1970**, *26*, 2975–2979.