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Rearrangement Pathways of the Tricyclo[4.1.0.0^{1,3}]heptyl Skeleton

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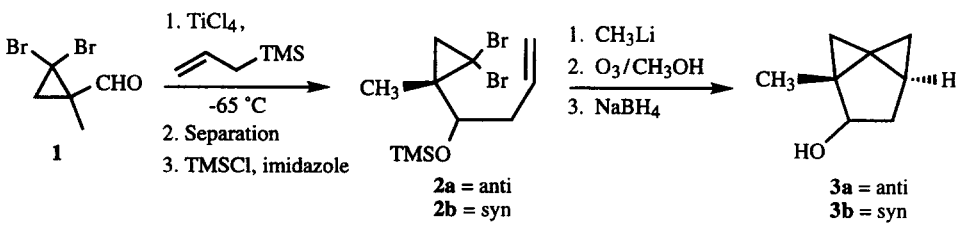
Abstract: *Syn*- and *anti*-1-methyltricyclo[4.1.0.0^{4,6}]heptan-2-ol derivatives (**4a** and **4b**) have been prepared. Their buffered solvolyses in anhydrous 2,2,2-trifluoroethanol were studied. Anti dinitrobenzoate **4a** solvolyzes to give mainly *m*-xylene and two trifluoroethyl ethers (**5** and **6**). Solvolysis of the syn mesylate **4b** gives 6-methyl-1-(2,2,2-trifluoroethoxy)tricyclo[4.1.0.0^{3,5}]heptane (**7**), the product of a solvent trapped cyclopropyl cation. © 1997 Elsevier Science Ltd.

The solvolysis of cyclopropyl derivatives typically affords ring opened products derived from allylic cation intermediates.[2] It is generally accepted that the mechanism involves ionization and isomerization occurring in concert, which is consistent with *ab initio* calculations that indicate cyclopropyl cation is a transition structure.[3] Cyclopropylium ions have been trapped and direct spectroscopic evidence has been obtained nonetheless in select cases where the ring opening is geometrically constrained or the ion is stabilized by π-electron donation.[4,5] While exploring the rearrangement pathways available to the tricycloheptyl ring system we discovered a novel example of cyclopropyl cation stabilization and trapping. These results are presented herein.[6]

Aldehyde **1**[7] was treated with $TiCl_4$ at -65 °C and then allyltrimethylsilane was added to afford a 3.9 : 1 syn to anti mixture of alcohols in an 82% yield (Scheme 1).[8] These compounds were readily separated by preparative HPLC (12% EtOAc/88% hexanes) and each isomer was treated separately.[9] Protection of the alcohols with chlorotrimethylsilane and imidazole proceeded in 86% (anti) and 89% (syn) isolated yields. The

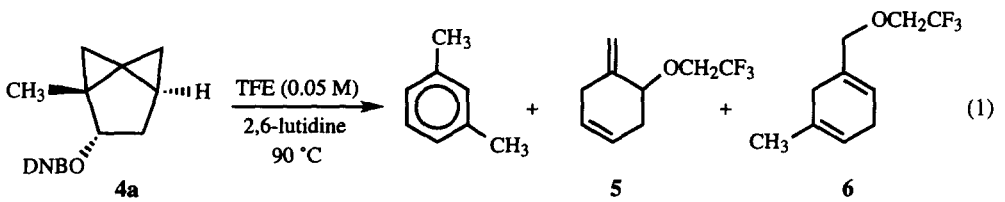


Scheme 1. The preparation of *syn*- and *anti*-tricyclo[4.1.0.0^{4,6}]heptan-2-ol (**3a** and **3b**)

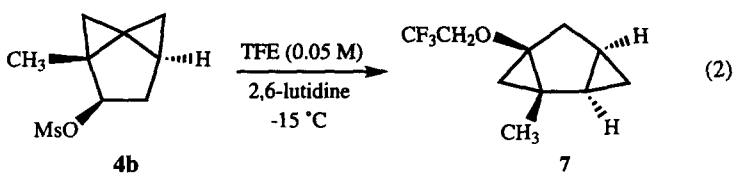
resulting silyl ethers were treated with methyllithium at -78 °C to give the desired spiropentane derivatives along with an allene byproduct. Removal of the allene contaminant and desilylation of the silyl ethers was accomplished most easily by ozonizing the product mixtures (O_3/CH_3OH, -78 °C) and carrying out a reductive workup with sodium borohydride. Clean samples of the desired tricyclic alcohols (**3a** and **3b**) were obtained in this way in moderate yield (30-60%).[10]

The anti dinitrobenzoate **4a** was prepared in a 75% yield by reacting **3a** with dinitrobenzoyl chloride, two equivalents of triethylamine, and 25 mol % of 4-dimethylaminopyridine (DMAP) in dichloromethane. Treatment of a 0 °C dichloromethane solution of **3b**, one equivalent of triethylamine, and 25 mol % of DMAP with methanesulfonic anhydride for 1 hour gave the syn mesylate (**4b**) quantitatively. In order to successfully isolate **4b** several volumes of anhydrous ether had to be added to the cold reaction mixture before carrying out the aqueous work-up; precedent for the stabilizing influence of ether on sulfonates can be found in the work of Wiberg et al.[11] All attempts to isolate the mesylate of **3a** were unsuccessful.

Solvolysis of **4a** in anhydrous 2,2,2-trifluoroethanol buffered with 2 equivalents of 2,6-lutidine gave three isolable products, *m*-xylene and two allylic trifluoroethyl (TFE) ethers (**5** and **6**), in a 84 : 11 : 5 ratio (eq 1). Solvolysis of **4b**, on the other hand, afforded a single product (**7**) in a 60% yield after purification by gas phase chromatography (eq 2).[12] Compound **7**'s structure was established by spectroscopic means (NMR, IR and MS) making particular use of 2D NMR techniques such as COSY, DEPT, HSC and, especially, the INADEQUATE pulse sequence. The data from this last spectroscopic method enabled us to unambiguously assign the carbon skeleton connectivity, but the relative orientation of the methyl and TFE groups could not be made unequivocally and was assumed to be syn due to the instability of trans fused small ring systems.

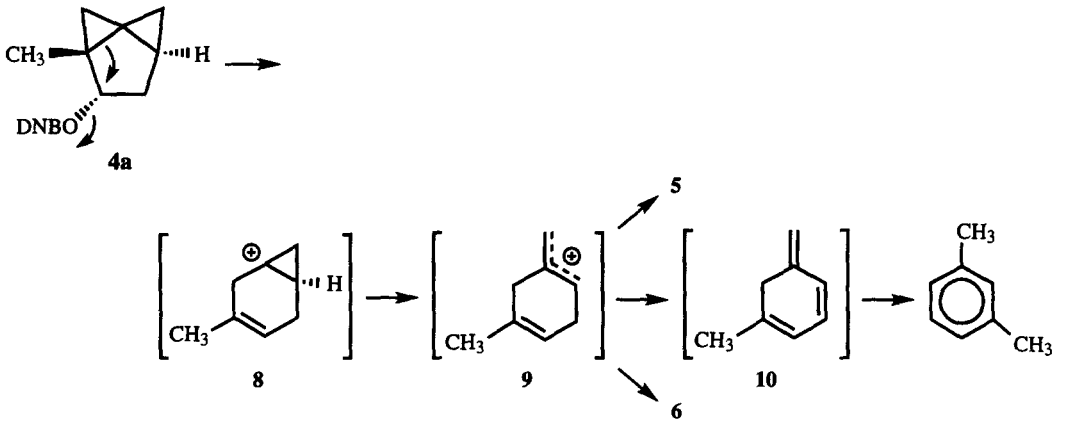


4a **5** **6**



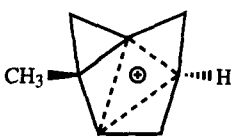
4b **7**

The product distribution observed from **4a** is consistent with that predicted from cyclopropylcarbinyl model systems.[13] Cleavage of the adjacent internal cyclopropyl C–C bond presumably leads to **8** or goes directly to the allylic cation **9** (Scheme 2). Addition of the solvent to **9** would afford **5** and **6**, whereas the loss of a proton would give *m*-xylene via the intermediacy of triene **10**.



Scheme 2. Proposed mechanism for the solvolysis of **4a**.

The formation of **7** is consistent with either a delocalized cyclopropyl cation (**11**) or solvent addition to the quaternary spiro carbon with concomitant mesylate displacement. Since exposure of **4b** to five equivalents of thiophenol and two equivalents of 2,6-lutidine in dichloromethane at room temperature gave no reaction after 48 hours, and its solvolysis in the presence of two equivalents of thiophenol only led to solvent trapped product (**7**), it is unlikely that trifluoroethanol displaces the mesylate to form the product by a remote S_N2' type displacement. These admittedly crude tests suggest either a k_c (unassisted) or k_Δ (anchimeric) rather than a k_s (solvent assisted) ionization process. Therefore, we believe that the formation of **7** is consistent with a delocalized cation such as **11**. This species is unique in that it is a trishomocyclopropenyl cation[14] as well a cyclopropyl and cyclopropylcarbinyl carbocation.



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3. The fully optimized C_{2v} cyclopropyl cation is an energy minimum at the HF/6-31G(d) level but the MP2/6-31G(d) and MP2/6-311G(2df,2pd) structures correspond to transition states (the imaginary frequencies are 547i and 531i, respectively).
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9. Syn and anti are used in this paper to refer to the relative orientation between the OR substituent and the distal cyclopropyl ring in the tricyclic product. Both epimers of **2** were treated independently because the syn/anti mixture of **3** could only be separated on an analytical scale.
10. All new compounds were characterized by ^1H and ^{13}C NMR, infrared, and high-resolution mass spectrometry. Spectroscopic data for **3a**: ^1H NMR (300 MHz, $CDCl_3$) 4.07 (m, 1 H), 2.39 (m, 1 H), 1.56 (m, 5 H), 1.22 (m, 1 H), 1.00 (s, 3 H), 0.79 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) 87.5 (d), 47.1 (t), 35.3 (s), 30.6 (s), 23.8 (t), 20.4 (t), 19.4 (d), 17.1 (q); IR (thin film) 1002, 1027, 1048, 1069, 1083, 1092, 1195, 1303, 1341, 1432, 1437, 1456, 3039, 3325 cm^{-1}; HRMS (CI, isobutane) calcd for $C_8H_{12}O$ ($M+H^+$) 125.0966, found 125.0977. Spectroscopic data for **3b**: ^1H NMR (300 MHz, $CDCl_3$) 4.06 (dd, J = 10.9, 5.8 Hz, 1 H), 2.38 (m, 1 H), 1.58 (m, 4 H), 1.52 (m, 1 H), 1.21 (m, 1 H), 0.99 (s, 3 H), 0.78 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) 83.6 (d), 45.4 (t), 30.9 (s), 28.9 (t), 24.6 (s), 19.6 (t), 12.6 (q), 11.8 (d); IR (thin film) 1027, 1050, 1096, 1107, 1328, 1335, 1377, 1444, 1459, 1709, 3037, 3368 cm^{-1}; HRMS (CI, isobutane) calcd for $C_8H_{12}O$ ($M+H^+$) 125.0966, found 125.0969.
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12. Spectroscopic data for **7**: ^1H NMR (300 MHz, C_6D_6) 3.27 (m, 2 H), 2.00 (dd, J = 12.6, 5.9 Hz, 1 H), 1.81 (d, J = 12.6 Hz, 1 H), 1.16 (s, 3 H), 0.98 (m, 1 H), 0.55 (m, 1 H), 0.40 (m, 2 H), 0.34 (d, J = 5.0 Hz, 1H), 0.04 (m, 1H); ^{13}C NMR (125 MHz, C_6D_6) 124.4 (q, J_{C-F} = 277 Hz), 71.9 (s), 66.4 (q, J_{C-F} = 34 Hz), 36.6 (t), 36.2 (s), 27.7 (d), 25.3 (t), 14.6 (q), 14.3 (t), 12.8 (d); IR (thin film) 975, 1084, 1096, 1134, 1161, 1234, 1281, 1339, 1449, 1459, 2870, 2934, 2954, 2973, 2991, 3069 cm^{-1}; HRMS (EI) calcd for $C_{10}H_{13}OF_3$ 206.0918, found 206.0919.
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