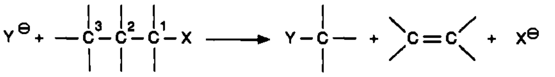
Fragmentation of Destabilized 2-Bicyclo[2.1.1]hexyl Cations. Primary Carbon as the Electrofuge

Bernhard Goer, Wolfgang Kirmse,* and Aribert Wonner

Fakultät für Chemie, Ruhr-Universität Bochum
D-44780 Bochum, Federal Republic of Germany

Received April 7, 1993

The Grob fragmentation, eq 1, is promoted by electron donation to the electrofugal carbon atom (C-3) and by the relief of ring strain.[1] Numerous derivatives of bicyclo[2.2.1]heptane,[2–4] bicyclo[3.1.1]heptane,[5–7] and bicyclo[2.1.1]hexane[8] were found to undergo ring cleavage with departure of a tertiary carbon atom.

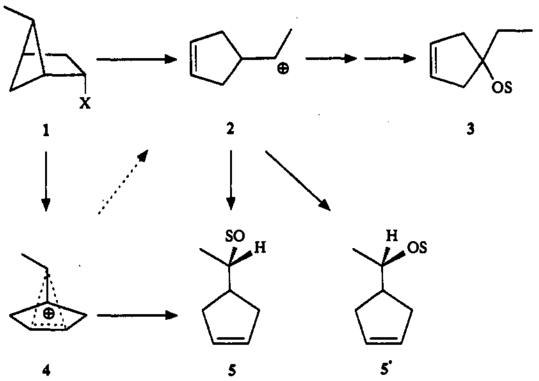


$$Y^{\ominus} + -\overset{|}{\underset{|}{C^3}}-\overset{|}{\underset{|}{C^2}}-\overset{|}{\underset{|}{C^1}}-X \longrightarrow Y-\overset{|}{\underset{|}{C}}- + >C=C< + X^{\ominus} \qquad (1)$$

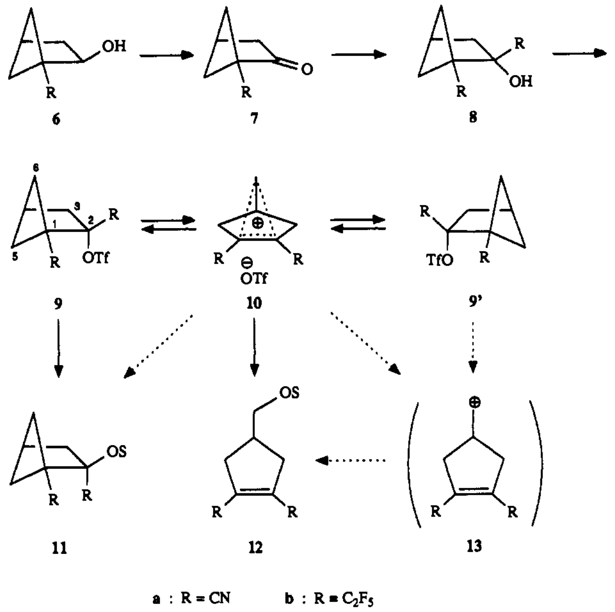
More recently, we observed fragmentation reactions of bicyclo[2.1.1]hexanes (e.g., **1** → **5**) in which the electrofugal carbon is secondary.[9] Both bridged and open carbocations are apparently involved (Scheme I). Predominant inversion of configuration (93% for **1**-OBs) suggests that **5** originates mainly from the bridged ion **4**. Partial racemization (→ **5′**) and 1,2-hydride shift (→ **3**) point to a minor contribution of the open ion **2**.[10]

The previous work relied on ring strain to compensate for poor leaving groups. It occurred to us that inductive destabilization[11] of the precursor ions could provide additional driving force. We now report on fragmentation reactions of electronegatively disubstituted 2-bicyclo[2.1.1]hexyl triflates that involve primary carbon as the electrofuge.

Scheme I



Scheme II



Syntheses of the alcohols **6a**[12] and **6b**[13] have been described. Sulfonates and diazonium ions related to **6a,b** solvolyze without fragmentation.[12,13] PCC oxidation of **6a,b** provided the ketones **7a,b**, which were treated with Me_3SiCN and C_2F_5Li, respectively, to give the alcohols **8a,b** and the triflates **9a,b** derived therefrom (Scheme II). Solvolyses of **9a** afforded products of fragmentation (**12a**) and substitution (**11a**) in the solvent-dependent ratios of 2.3:1 in acetone–water (1:1), 4.3:1 in formic acid, and 13:1 in trifluoroacetic acid. The half-life of **9a** in HCO_2H–1.5 M NaOCHO at 80 °C was found to be 44 ± 3 min, whereas only 23% of **9a** had reacted after 4 days in CF_3CO_2H–2 M $NaOCOCF_3$ at 80 °C. Thus, the half-life of **9a** *increased* with decreasing nucleophilicity of the solvent, suggesting a significant k_s component. Starting with [2-^{13}CN]**9a** in HCO_2H–1.5 M NaOCHO, scrambling of the label in the recovered triflate (32% after 50% conversion, 46% after 75% conversion) uncovered the degenerate Wagner–Meerwein rearrangement, **9a** ⇄ **9a′**. The distribution of ^{13}CN in **11a** lagged behind the scrambling in **9a** (36% and 46%, respectively, after 75% conversion of **9a** in HCO_2H–1.5 M NaOCHO at 80 °C). Nucleophilic displacement at **9a**, rather than capture of **10a**, appears to be the major route to **11a**.

Analogous substitution of **9b** should be seriously impeded, owing to the voluminous C_2F_5 group. As expected, solvolyses of **9b** in dioxane–water (8:2), trifluoroacetic acid (TFA), and 2,2,2-trifluoroethanol (TFE) did not produce significant amounts of **11b**, the virtually exclusive product being **12b**. Degenerate rearrangements were detected by means of [3-$^2H_2$]**9b**. Equilibration of **9b** and **9b′**, mediated by **10b**, was found to proceed readily (53% in TFA and 68% in TFE after 2 half-lives). Interconversion of **10b** with open ions should lead to exchange of C-3,5 with C-6, i.e., to equivalence of all CH_2 groups.[14–16] Only a minor fraction (1–3%) of the label was recovered in the

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exocyclic CH_2 group of the solvolysis product **12b**. Therefore, we invoke the bridged ion **10** as the predominant intermediate and precursor to **12**. The intervention of **13** on the reaction path to **12** is very unlikely. Aside from the instability of primary carbocations, no 1,2-hydride shift was observed (cf. **2** → **3** in Scheme I).

In summary, we have adduced evidence for *degenerate* 1,2-carbon shifts in electronegatively substituted carbocations (ion pairs). Associated with the degeneracy is a unique fragmentation in which primary carbon assumes the role of the electrofuge. We postulate that bridged ions or ion pairs (**10**) are germane to both reactions.[17] The electron-withdrawing groups are thought to divert solvent attack at **10** from C-1,2 to C-6.

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(14) For the parent 2-bicyclo[2.1.1]hexyl cation, equivalence of all CH_2 groups is attained in superacids (NMR)[15] and in TFA (solvolysis of labeled substrates)[16] but not in more nucleophilic media.[16]

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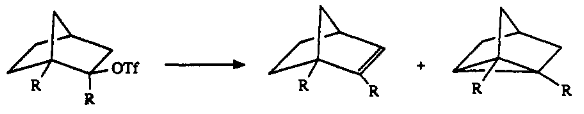
(17) Ring strain remains an important factor. 2-Norbornyl analogues of **9** do not undergo fragmentation. The homologues of the bridged ion **10** appear to be deprotonated rather than substituted (Siegfried, R.; Wonner, A., unpublished results). Deprotonation of **10** would lead to a prohibitively strained tricyclo[2.2.0.0^{2,6}]hexane.



R= CN	dioxane-H_2O (2:1), 80° C, 24 h	70 %	26 %
R= C_2F_5	acetone-H_2O (4:1) 80° C, 24 h	80 %	18 %