Pergamon

*Tetrahedron Letters*, Vol. 37, No. 7, pp. 1035-1038, 1996

0040-4039/96 $15.00 + 0.00

0040-4039(95)02341-0

# Solvolysis of [3-$^{13}$C]-3,4-Dimethyl-4-homoadamantyl *p*-Nitrobenzoate. Comparison of the Barriers to the Wagner–Meerwein Rearrangement of the Secondary and Tertiary 4-Homoadamantyl Cations

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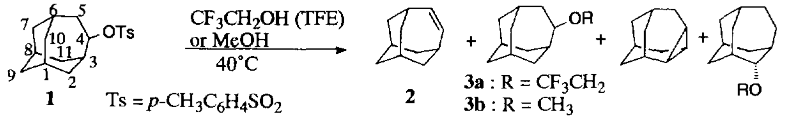
***Abstract***: The trifluoroethanolysis of [3-$^{13}$C]-3,4-dimethyl-4-homoadamantyl *p*-nitrobenzoate gave 3,4-dimethyl-4-homoadamantene (**10**), 3-methyl-4-methylenehomoadamantane (**11**), and trifluoroethyl ether (**12a**) in the ratio 62:36:2 at 40 °C. The $^{13}$C labels were exclusively distributed at the positions C(3) and C(4), and redistribution ratios were 92.8:7.2 in **10**, 93.3:6.7 in **11**, and 61.1:38.9 in **12a**. Comparison of these results with those for the solvolysis of secondary [3-$^{13}$C]-4-homoadamantyl *p*-toluenesulfonate suggests that the barrier to the Wagner-Meerwein rearrangement of the tertiary 4-homoadamantyl cation is higher than that of the secondary cation by at most 3.3 kcal mol$^{-1}$.

It is generally accepted that the degenerate Wagner–Meerwein rearrangement in secondary carbocations is faster than that in the corresponding tertiary cations.[1,2] However, there have been no examples that quantitatively show the difference in the activation barrier between classical secondary and tertiary carbocations, probably because of the occurrence of side reactions and possible formation of bridged ions in the secondary carbocations. Typically, the secondary 3-methyl-2-butyl cation could undergo the degenerate 3,2-alkyl shift, but actually the faster 3,2-hydride shift prevails to give the tertiary 2-methyl-2-butyl cation under stable ion conditions.[2] The tertiary 1,2-dimethyl-2-norbornyl cation was shown to be a rapidly equilibrating cation,[3] but it has been controversial whether the secondary 2-norbornyl cation is a bridged single species or a pair of rapidly equilibrating cations.[1,4]

In this respect, the secondary 4-homoadamantyl cation is unique in that it is a classical ion and that the hydride shift is much slower than the Wagner–Meerwein rearrangement. Nordlander et al.[5] and present authors[6] examined the solvolysis of 4-homoadamantyl *p*-toluenesulfonate (tosylate, **1**), which yielded 4-homoadamantene (**2**), 4-substitution product **3**, 2,4-dehydrohomoadamantane, and an *exo*-2-substitution product. It was concluded that **1** solvolyzes through not nonclassical ion **5** but classical ion **4**, and that the degenerate Wagner–Meerwein rearrangement is much faster than the 5,4-hydride shift. Therefore, we presumed that the 4-homoadamantyl system would be an appropriate model to estimate the difference between the barriers to the Wagner–Meerwein rearrangement of the secondary and the tertiary *classical* cations.

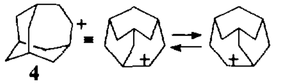
We now report the solvolysis of [3-$^{13}$C]-3,4-dimethyl-4-homoadamantyl *p*-nitrobenzoate ([3-$^{13}$C]-**6**) in 2,2,2-trifluoroethanol (TFE) and methanol buffered with 2,6-lutidine, and $^{13}$C redistributions in the solvolysis



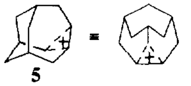
**1** Ts = $p$-$CH_3C_6H_4SO_2$

**2**

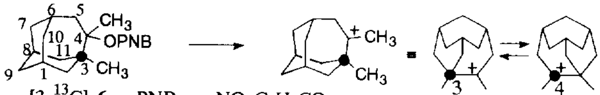
**3a** : R = $CF_3CH_2$
**3b** : R = $CH_3$



**4**



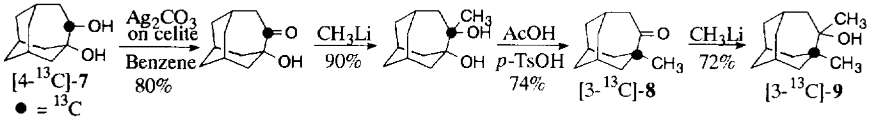
**5**



[3-$^{13}$C]-**6** PNB = $p$-$NO_2C_6H_4CO$

products as determined by quantitative $^{13}$C NMR measurements. By comparing the $^{13}$C redistributions with those for the solvolysis of the secondary tosylate ([3-$^{13}$C]-**1**),[6a] we were able to quantitatively estimate the difference between the activation barriers to the Wagner–Meerwein rearrangement of the *classical* secondary[5,6] and the tertiary 4-homoadamantyl carbocations.

The synthesis of [3-$^{13}$C]-3,4-dimethyl-4-homoadamantanol ([3-$^{13}$C]-**9**) is shown in Scheme 1. [3-$^{13}$C]-3-Methyl-4-homoadamantanone ([3-$^{13}$C]-**8**) was prepared from [4-$^{13}$C]-3,4-homoadamantanediol ([4-$^{13}$C]-**7**) following the previously reported method[6a,7,8] and then converted to [3-$^{13}$C]-**9** with $CH_3Li$. The $p$-nitrobenzoate ([3-$^{13}$C]-**6**) was prepared by the usual method. The $^{13}$C NMR showed that [3-$^{13}$C]-**6** was quantitatively labeled at the position C(3).

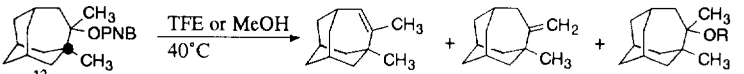


[4-$^{13}$C]-**7**
● = $^{13}$C
[3-$^{13}$C]-**8**
[3-$^{13}$C]-**9**

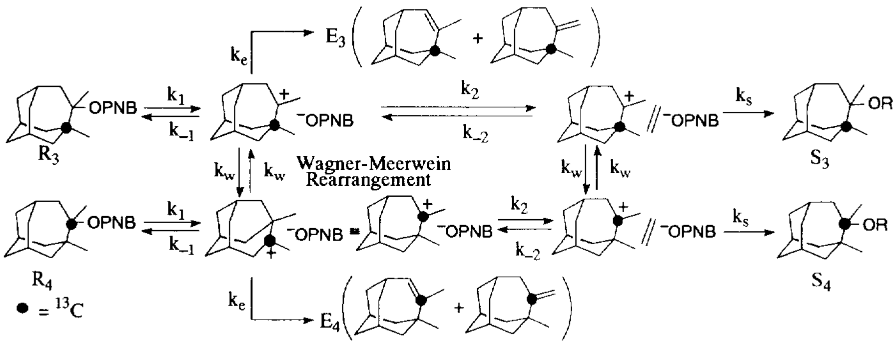
Scheme 1

The solvolysis rate constants of unlabeled **6**[9,10] in TFE and MeOH buffered with 2,6-lutidine were determined at 40 °C to be 2.49 × $10^{-3}$ $s^{-1}$ and 2.61 × $10^{-5}$ $s^{-1}$, respectively.[11] The solvolysis products from [3-$^{13}$C]-**6** consisted of 3,4-dimethyl-4-homoadamantene (**10**), 3-methyl-4-methylenehomoadamantane (**11**), and substitution product (**12a** or **12b**) in the ratio 62:36:2 in TFE or 66:27:7 in MeOH, respectively, at the time of 20 half-lives at 40°C as determined by glc. After aqueous work-up, $^{13}$C distributions in the products were measured by quantitative $^{13}$C NMR in the presence of a relaxation reagent, $Fe(acac)_3$.[6a] The $^{13}$C labels were exclusively distributed at the C(3) and C(4) positions. The redistribution ratios are shown in Table 1.

The redistributions of the $^{13}$C labels for olefins **10** and **11** in Table 1 are essentially identical with each other within experimental errors, but they are much less advanced than that for substitution products **12** both in methanolysis and trifluoroethanolysis. If the products are formed from the carbocation intermediate of the same stage, the values of $^{13}$C redistribution should be identical.[3b,c,5,6a] The present results indicate that olefins **10** and **11** and substitution products **12** are formed at different stages of ion–pair; the elimination occurs at the stage of the tight ion pair, and the substitution at a second stage (e.g. solvent separated ion–pair).



[3-$^{13}$C]-**6**
**10**
**11**
**12a** : R = $CF_3CH_2$
**12b** : R = $CH_3$



Scheme 2

Table 1. The $^{13}C$ Redistributions in the Products and the Differences in Free Energy of Activation between the Elimination and the Wagner–Meerwein Rearrangement ($\Delta G^{\ddagger}_e - \Delta G^{\ddagger}_w$) in the Solvolyses of [3-$^{13}C$]-4-Homoadamantyl Tosylate ([3-$^{13}C$]-**1**, 0.040 M) and [3-$^{13}C$]-3,4-Dimethyl-4-homoadamantyl *p*-Nitrobenzoate ([3-$^{13}C$]-**6**, 0.020 M or 0.005 M) in TFE or MeOH at 40.0 °C.[a]

| Substrate | Solvent | Product | Yield, | $^{13}C$ Redistribution in the product, % [b] | | | $k_w / k_e$ | $\Delta G^{\ddagger}_e - \Delta G^{\ddagger}_w$, |
|---|---|---|---|---|---|---|---|---|
| | | | % | C(3) | C(4) | others | | kcal mol$^{-1}$ |
| [3-$^{13}C$]-**1** | TFE | **2** | 18 [c] | 55.4 [c] | 42.4 [c] | 2.2 [c] | 16.9 | 1.76 |
| [3-$^{13}C$]-**1** | TFE | **3a** | 73 [c] | 46.6 [c] | 45.6 [c] | 7.8 [c] | | |
| [3-$^{13}C$]-**1** | MeOH | **2** | 26 [c] | 62.3 [c] | 37.6 [c] | 0.1 [c] | 5.57 | 1.07 |
| [3-$^{13}C$]-**1** | MeOH | **3b** | 69 [c] | 54.7 [c] | 43.9 [c] | 1.4 [c] | | |
| [3-$^{13}C$]-**6** | TFE | **10** | 62 | 92.8 | 7.2 | 0.0 | 0.0817 [d] | -1.56 [d] |
| [3-$^{13}C$]-**6** | TFE | **11** | 36 | 93.3 | 6.7 | 0.0 | | |
| [3-$^{13}C$]-**6** | TFE | **12a** | 2 | 61.1 | 38.9 | 0.0 | | |
| [3-$^{13}C$]-**6** | MeOH | **10** | 66 | 99.1 | 0.9 | 0.0 | 0.0101 [d] | -2.86 [d] |
| [3-$^{13}C$]-**6** | MeOH | **11** | 27 | 99.0 | 1.0 | 0.0 | | |
| [3-$^{13}C$]-**6** | MeOH | **12b** | 7 | 94.0 | 6.0 | 0.0 | | |

[a] The solvolyses were conducted for 20 half-lives in the presence of 0.050M 2,6-lutidine. [b] Determined by quantitative $^{13}C$ NMR within the experimental error of ± 0.3%. [c] Ref. 6a. [d] Averaged value for **10** and **11**.

The product formation at different stages and the exclusive distributions of the label on C(3) and C(4) suggest the mechanistic model illustrated in Scheme 2. The symbols of $k_1$, $k_{-1}$, $k_2$, $k_{-2}$, $k_w$, $k_e$, and $k_s$ are the rate constants of ionization, internal return, further ionization at the first stage, ion-pair return at the second stage, the Wagner–Meerwein rearrangement, the elimination, and the solvent capture of the cation intermediate, respectively. The symbols of R, E, and S stand for the reactant (**6**), the elimination products (**10** and **11**), and substitution products (**12**), respectively, and [R] is the concentration of the compound R. The number n in $R_n$ means the position of $^{13}C$ label in the compound.

Very recently, Richard estimated the life-time of the *t*-butyl cation in 50% aq. TFE to be $10^{-12}$ s.[12] It can be safely assumed that this life-time is also applicable to the 3,4-dimethyl-4-homoadamantyl cation.[13] Since the life-time of $10^{-12}$ s is close to the period of bond vibration (~$10^{-13}$ s), both the tertiary 3,4-dimethyl-4-homoadamantyl and the secondary 4-homoadamantyl cations would show $k_s$ values of $10^{12}$–$10^{13}$ s$^{-1}$. Since the rate constants $k_2$ and $k_{-2}$ are expected to be close to the theoretical value for a diffusion-limited reaction (~$5 \times 10^9$ s$^{-1}$), the $k_{-2}/k_s$ value is estimated to be much less than 1.[14] By applying the steady state with respect to the carbocation intermediates in Scheme 2 and $k_{-2}/k_s << 1$, the following equations (1)–(3) were respectively derived for the rate ratios $k_e/k_2$ and $k_w/k_e$, and the difference in the activation free energy between the elimination ($\Delta G^{\ddagger}_e$) and the Wagner–Meerwein rearrangement ($\Delta G^{\ddagger}_w$):

$$\frac{k_e}{k_2} = \frac{[E_3]_{t=\infty} + [E_4]_{t=\infty}}{[S_3]_{t=\infty} + [S_4]_{t=\infty}} \tag{1}$$

$$\frac{k_w}{k_e} = 0.5 \times \left\{ \frac{[R_3]_{t=0} - [R_4]_{t=0}}{[R_3]_{t=0} + [R_4]_{t=0}} \, \frac{[E_3]_{t=\infty} + [E_4]_{t=\infty}}{[E_3]_{t=\infty} - [E_4]_{t=\infty}} - 1 \right\} \times \left\{ 1 + \frac{[S_3]_{t=\infty} + [S_4]_{t=\infty}}{[E_3]_{t=\infty} + [E_4]_{t=\infty}} \right\} \tag{2}$$

$$\Delta G^{\ddagger}_e - \Delta G^{\ddagger}_w = RT \left( \ln \frac{k_w}{k_e} \right) \tag{3}$$

The $k_w/k_e$ and the $\Delta G^{\ddagger}_e - \Delta G^{\ddagger}_w$ values were calculated and shown in Table 1 with the results for the solvolyses of [3-$^{13}C$]-4-homoadamantyl tosylate ([3-$^{13}C$]-**1**) in TFE and MeOH.[6a]

When the deprotonation steps are used as a clock, the difference ($\Delta\Delta G^{\ddagger}_w$) in $\Delta G^{\ddagger}_w$ between the 4-homoadamantyl and 3,4-dimethyl-4-homoadamantyl cations is calculated to be 3.3 [= 1.76 – (– 1.56)] kcal mol$^{-1}$ in TFE or 3.9 [= 1.07 – (– 2.86)] kcal mol$^{-1}$ in MeOH. In E1 reactions a counter anion is believed to abstract the proton of a cation intermediate.[15,16] The deprotonation by the 3,5-dinitrobenzoate anion, whose basicity is similar to that of $PNBO^-$, has been estimated to be only three times faster than that of $TsO^-$.[16] This might reduce the above $\Delta\Delta G^{\ddagger}_{w}$ values by up to 0.8 kcal $mol^{-1}$. Since TFE is much more acidic than MeOH, the former would more strongly solvate the counter anion than the latter, making the basicity of $PNBO^-$ close to that of $TsO^-$. Therefore, the rate constant $k_e$ for the tertiary cation would become close to $k_e$ for the secondary cation, which would permit the use of $k_e$ in TFE as a clock.[17]

Saunders reported that the barrier to the methyl migration in the 2,3,3-trimethyl-2-butyl cation is 3.5 kcal $mol^{-1}$ (–140 °C).[18] This means that the assumed $\Delta\Delta G^{\ddagger}_{w}$ value with respect to the methyl migration in the tertiary 2,3,3-trimethyl-2-butyl and secondary 3-methyl-2-butyl cations must be smaller than 3.5 kcal $mol^{-1}$, supporting the appropriateness of the $\Delta\Delta G^{\ddagger}_{w}$ value of at most 3.3 kcal $mol^{-1}$ obtained in the present work.

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10 **6**: colorless crystals; mp 226.5–227.5 °C; IR (KBr) 2910, 1707, 1521, 1292 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 270 MHz), δ 1.14 (s, 3H), 1.48–1.61 (m, 6H), 1.76 (s, 3H), 1.78–2.01 (m, 5H), 2.07 (m, 1H), 2.40 (m, 1H), 2.49 (m, 1H), 2.72 (m, 1H), 8.16 (d, 2H, *J* = 9.1 Hz), 8.28 (d, 2H, *J* = 9.1 Hz); $^{13}C$ NMR ($CDCl_3$, 67.8 MHz), δ 24.7 ($CH_3$), 28.1 (CH), 28.2 (CH), 30.4 ($CH_3$), 30.6 (CH), 36.8 ($CH_2$), 36.9 ($CH_2$), 37.4 ($CH_2$), 40.0 ($CH_2$), 40.5 ($CH_2$), 42.3 (C), 49.1 ($CH_2$), 93.9 (C), 123.5 (2CH), 130.3 (2CH), 138.2 (C), 150.2 (C), 163.7 (C). Satisfactory microanalytical data were obtained: Reference 9.

11 The methanolysis rate at 40 °C was interpolated from the data at other temperatures. The activation enthalpy and entropy ($\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$) are calculated to be 21.3 kcal $mol^{-1}$ and –2.9 cal $mol^{-1}$ $K^{-1}$ in TFE or 26.0 kcal $mol^{-1}$ and 3.4 cal $mol^{-1}$ $K^{-1}$ in MeOH, respectively.

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(*Received in Japan* 18 *September* 1995; *revised* 16 *November* 1995; *accepted* 7 *December* 1995)