

### Chirality Transfer from 4-Methylcyclohexylidenemethyl(phenyl)iodonium Tetrafluoroborate to 4-Methylcycloheptanone during Solvolysis: Evidence against a Primary Vinylic Cation as Intermediate

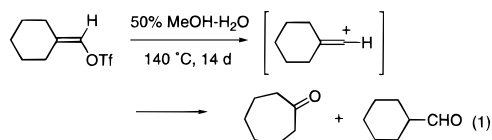
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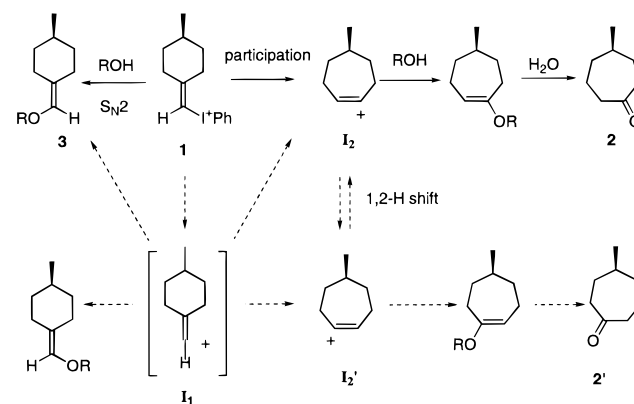
Primary vinylic cations, bearing a hydrogen atom at the  $\alpha$  carbon, are admittedly unstable,<sup>1–3</sup> and can only be generated under special conditions; for example, by nuclear decay of tritiated ethene,<sup>4</sup> by photolysis,<sup>5</sup> in a superacid,<sup>6</sup> or in strong sulfuric acid.<sup>7</sup> Vinyl cations are stabilized by  $\beta$ -alkyl substituents,<sup>3,8</sup> and there are indications for formation of primary  $\beta$ , $\beta$ -dialkylvinyl cations under normal conditions.<sup>9–11</sup> Cyclohexylidenemethyl triflate was suggested to undergo solvolysis via a transient primary vinylic cation in aqueous alcohols at high temperature (eq 1).<sup>9</sup> In this



contribution we report that solvolysis of the chiral 4-methylcyclohexylidenemethyl iodonium salt **1** results in complete chirality transfer to the rearranged product, 4-methylcycloheptanone (**2**), which serves as evidence against the involvement of a primary vinylic cation intermediate (Scheme 1).

We have recently shown that the solvolysis of unsymmetrically substituted  $\beta$ , $\beta$ -dialkylvinylidonium salts takes place with extensive rearrangements through  $\beta$ -alkyl participation, and concluded that primary vinylic cations are not formed in aqueous solution.<sup>10</sup> Nonetheless, it was suggested that primary cations may be partially involved in less nucleophilic solvents such as 2,2,2-trifluoroethanol (TFE) and acetic acid. The thermolysis of  $\beta$ , $\beta$ -dialkylvinylidonium triflates in chloroform is also proposed to occur via primary vinylic cations.<sup>11</sup> The conclusions are based on the E/Z stereochemistry of the unrearranged substitution products obtained from geometrically isomeric substrates. However, product profiles are quite complicated due to the presence of two different  $\beta$ -alkyl substituents, which leads to three pairs of substitution products and three elimination products via

Scheme 1



rearrangements.<sup>10</sup> The difference in migratory aptitudes of the  $\beta$ -alkyl groups further complicates the analysis of the reaction. Most of the complications are avoided by using the chiral 4-substituted cyclohexylidenemethyl derivative **1** as substrate. The two  $\beta$ -alkyl moieties are electronically as well as sterically the same. The only difference is the chirality and the primary vinylic cation **I**<sub>1</sub> formed from **1** is achiral due to the linear structure<sup>1,2</sup> of the cationic carbon atom. If the primary cation **I**<sub>1</sub> were generated, the chirality should be lost leading to reduced enantiomeric purity of the products. The only products expected are enantiomeric substitution products of unrearranged and rearranged form (Scheme 1). Elimination products are hard to produce since seven-membered cyclic acetylene and allene are subject to serious strain.

Optically active (*R*)-4-methylcyclohexylidenemethyl(phenyl)iodonium tetrafluoroborate (**1**)<sup>12,13</sup> was prepared from (*R*)-4-methylcyclohexylidenemethyl bromide which was obtained according to a literature procedure<sup>15</sup> (Scheme 2). The last step, conversion of the vinylsilane to the corresponding vinylidonium salt is established to proceed with complete retention of configuration,<sup>16</sup> and the enantiomeric excess (ee) of **1** is the same as that of the precursor vinylsilane unless racemization or optical resolution of **1** occurs during the workup. Crystallization of the crude **1** was found to diminish its ee. Crystallized **1** of 69% ee<sup>17</sup> was used for the solvolysis experiments.

(12)  $[\alpha]_D^{20} = -20.4$  (CHCl<sub>3</sub>, *c* = 0.91); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.90 (d, *J* = 7.8 Hz, 2H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 2H), 6.65 (s, 1H), 2.75–2.66 (m, 2H), 2.47–2.34 (m, 2H), 1.91–1.58 (m, 3H), 1.15–1.00 (m, 2H), 0.91 (d, *J* = 6.8 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  164.6, 134.5, 132.3, 132.2, 110.4, 91.8, 36.5, 36.1, 35.7, 35.1, 31.4, 21.0.

(13) Although the synthesis of optically active diaryliodonium salts has recently been achieved,<sup>14</sup> this is the first example of iodonium salts carrying a chiral and reactive vinyl moiety.

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(17) Determination of the ee of the neutral organic samples was performed using a gas chromatograph equipped with a chiral column (CHROMPACK-Chirasil-DEX CB (i.d. 0.25 mm  $\times$  25 m)) usually within  $\pm 1\%$  in ee. The vinylsilane of 78% ee was converted to the iodonium salt **1** by an established procedure.<sup>16</sup> Part of the crude **1** was converted to the vinyl bromide by treating it with tetrabutylammonium bromide (0.1 M) in chloroform.<sup>18</sup> The vinyl bromide obtained was 66% excess of the *S* form, determined using the chiral GC-column. This indicates that the substitution proceeds with 92% [= 100  $\times$  (66/78 + 1)/2] inversion. A sample of **1** obtained by crystallization of the crude mixture was also converted under the same conditions to the vinyl bromide which was of 58% ee. This means that the ee of the sample of **1** was 69% [= 58/(2  $\times$  0.92–1)]. If the conversion of the vinylsilane to **1** would proceed with partial loss of ee, the ee of the crystallized **1** should be lower than 69%. On the contrary, the 69% ee of product **2** obtained in the solvolysis experiments implies that the ee of the substrate **1** is not lower than 69% unless enantiomeric enrichment occurs during the reaction. These results are also consistent with complete retention of configuration in the formation of vinylidonium salts from the corresponding vinylsilanes.

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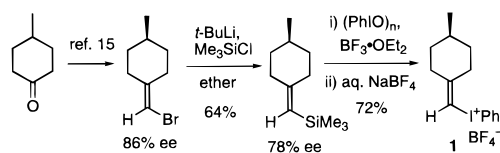
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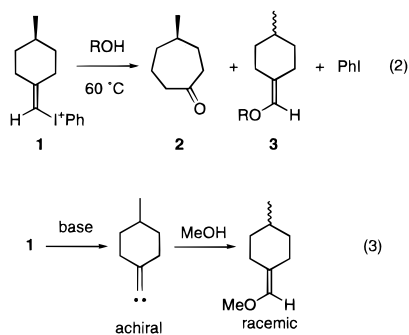
## Scheme 2

**Table 1.** Solvolysis Products Obtained at 60 °C

solvent	time (h)	2		PhI
		ee (%)	yield (%)	yield (%)
MeOH <sup>a</sup>	6	68	57	86
(1/1) MeOH/H <sub>2</sub> O	7	68	80	79
CF <sub>3</sub> CH <sub>2</sub> OH	9	69	75	84
(CF <sub>3</sub> ) <sub>2</sub> CHOH	20	69	41	60

<sup>a</sup> Ether **3** (15% yield) with 8% ee and the acetal products (~10% yield) were also obtained.

Solvolysis of **1** as well as of racemic **1** was carried out at 60 °C in methanol, 50 (v/v) % aqueous methanol, TFE, and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), respectively.<sup>19</sup> In all cases the major product was 4-methylcyclohexanone (**2**), the rearranged substitution product, accompanied by iodobenzene (eq 2). In unbuffered methanol, also 1-methoxymethylene-4-methylcyclohexane (**3**), the unrearranged substitution product, was obtained. The results are summarized in Table 1. Enol ether derivatives of **2** were obtained upon careful alkaline workup, but were not detected after the usual aqueous treatments of the reaction mixture, as the result of acid-catalyzed hydrolysis of the enol ether.<sup>20</sup> It is remarkable that product **2** in all solvents retains the ee of the starting iodonium salt **1** within experimental error. Product **2** has a negative optical rotation and its stereochemistry is determined to be *R* as depicted in eq 2 by comparison with an authentic sample.<sup>21</sup> Thus, the chirality of **1** is completely transferred to product **2**.



In contrast, the unrearranged methyl ether **3** obtained in methanol was largely racemized (8% ee). Product **3** presumably is formed through  $\alpha$ -elimination followed by insertion of the

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(19) A sample of **1** or the racemic salt (1–5 mg) was dissolved in 1–5 mL of the solvent and kept at 60 °C under stirring for a specified reaction time. The products were extracted with ether and washed with water. The yields of the products from the racemic substrate were determined by gas chromatography with tetradecane as an internal standard, while the ee of the products from **1** were determined using the chiral GC-column.

achiral alkylidenecarbene intermediate in the O–H bond of the solvent (eq 3). The elimination reaction already occurs with neutral methanol as base.<sup>10,22</sup> Ether **3** formed in the methanolysis may be derived mainly from this pathway. The amount of unrearranged vinyl ethers was essentially negligible in the less nucleophilic, less basic solvents.

Formation of the rearranged product **2** with complete chirality transfer can be rationalized within the framework of the reaction pathways illustrated in Scheme 1. If simple heterolysis formed the primary vinylic cation **I**<sub>1</sub> and the ensuing 1,2-rearrangement led to the cyclic cation **I**<sub>2</sub> and its enantiomer **I**<sub>2</sub><sup>′</sup>, considerable racemization should have occurred. The stereochemistry of product **2** is consistent with formation of cation **I**<sub>2</sub> by participation of the  $\beta$  C–C bond from the *trans* position. Furthermore, the 1,2-hydride shift across the double bond of **I**<sub>2</sub> leading to racemization has to be slower than trapping of the cation by the nucleophilic solvent. This type of 1,2-shift is very rapid in acyclic secondary vinylic cations, for example, CH<sub>3</sub>–CH=C<sup>+</sup>–CH<sub>3</sub>, and the barrier calculated for this process is very low (0.77 kcal mol<sup>–1</sup> by MP2/6-31G\*<sup>10</sup>). However, the barrier for a 1,2-hydride shift across the C=C bond of the cyclic vinylic cation **I**<sub>2</sub> was calculated to be quite high, due to the triple bond nature of the transition state (23.2 kcal mol<sup>–1</sup>).<sup>23</sup> The clear-cut observation that no racemization occurs during the rearrangement of the iodonium salt **1** indicates not only that the reaction does not involve a primary vinylic cation **I**<sub>1</sub><sup>24</sup> but also that the barrier for the 1,2-hydride shift of the cyclic vinylic cation **I**<sub>2</sub> is significantly greater than that for reaction of **I**<sub>2</sub> with the solvent. It is also worth noting that this is even the case in a very poorly nucleophilic and highly ionizing solvent such as HFIP. The earlier suggestion that a cyclohexylidenemethyl cation was generated from the triflate in aqueous methanol at 140 °C<sup>9</sup> is incompatible with the present observations.

In conclusion, the rearrangement of the cyclohexylidenemethyl system occurs via  $\beta$  C–C bond participation from the *trans* position. No primary vinylic cation is involved during the solvolysis of the iodonium salt in a highly ionizing and poorly nucleophilic solvent.

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(20) Kresge, A. J.; Sagatys, D. S.; Chen, H. L. *J. Am. Chem. Soc.* **1977**, *99*, 7228–7233. This seven-membered-ring enol ether is very readily hydrolyzed; its half-life during the aqueous workup may be a few min at the acidity due to the HBF<sub>4</sub> byproduct.

(21) An authentic sample of optically active **2** was prepared from commercially available (*R*)-3-methylcyclohexanone. It was reacted with ethyldiazoacetate to give a diastereomeric mixture of (4*R*)-4-methyl- and (3*R*)-3-methyl-2-ethoxycarbonylcycloheptanones, which was subjected to hydrolysis and decarboxylation to afford a mixture of (*R*)-4-methyl- and (*R*)-3-methylcycloheptanones. The former isomer coincided with the major enantiomer of product **2** upon co-injection in the chiral GC-column.

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(24) Our previous suggestion<sup>10</sup> that a primary vinylic cation is formed from  $\beta,\beta$ -dialkylvinylidonium salt in poorly nucleophilic solvents should be reconsidered. It was based solely on the stereochemistry of the minor, unrearranged substitution products. Our recent results imply that an S<sub>N</sub>2-type reaction with retention (via perpendicular attack) is a viable alternative.