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Solvolysis of 4-Methylcyclohexylidenemethyliodonium Salt: Chirality Probe Approach to a Primary Vinyl Cation Intermediate

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Optically active 4-methylcyclohexylidenemethyl(aryl)iodonium tetrafluoroborate ($1 \cdot BF_4^-$) was prepared and its solvolysis was carried out at 60 °C in various solvents. The main product is optically active 4-methylcycloheptanone (or its enol derivative) in unbuffered solvents, accompanied by the iodoarene. The rearranged product always maintains the optical purity of the starting **1**. Its stereochemistry conforms to a mechanism involving the rearrangement via the σ-bond participation in departure of the nucleofuge, followed by trapping of the resulting chiral 5-methylcyclohept-1-enyl cation with a nucleophilic solvent. That is, the achiral, primary vinyl cation is not involved during the reaction. The unrearranged substitution product is also obtained in a minor fraction in unbuffered methanol, ethanol, and acetic acid, but not in trifluoroethanol or hexafluoro-2-propanol: the methoxy product from methanolysis is largely racemized, but the acetolysis product is obtained mainly via retention of configuration. Reactions of **1** with bromide, acetate, and trifluoroacetate in chloroform give unrearranged substitution products in different degrees of inversion. These unrearranged products are concluded to be formed via the direct nucleophilic substitutions. Added bases such as sodium acetate in methanol lead to the unrearranged methoxy products of complete racemization, which is ascribed to the α elimination (to give an alkylidenecarbene) followed by the solvent insertion.

Introduction

The chemistry of vinyl cations has been developed through electrophilic additions to alkynes and allenes as well as solvolyses of vinylic substrates.[1,2] For the latter reactions, triflates (trifluoromethanesulfonates) were developed as an important class of substrates and have been extensively investigated in the 1970s.[3] Gas-phase stabilities of vinyl cations were evaluated both experimentally and theoretically,[4,5] and primary vinyl cations having no α substituent are considered to be thermochemically very unstable. The more stable structure was found to be a nonclassical bridged form rather than a classical linear form.[4,5] Primary vinyl cations are also kinetically labile in solution, and they were only observed under very special conditions such as in strong acid,[6,7] under photoirradiation,[8] and by nuclear decay,[9] although

no information about the structure of the cation is available in solution.

Vinyl iodonium salts are good progenitors of vinyl cations owing to the excellent nucleofugality of the iodonio group, which is evaluated to be about 10^6 times better as leaving group than triflate.[10] Since the recent developments of general preparation methods of this class of compounds,[11] we have searched for the evidence for formation of a classical primary vinyl cation as an intermediate of solvolysis reactions.[12] Although extensive rearrangements have been observed during the reactions of 2-phenylvinyl[13,14,15a] and 2,2-dialkylvinyl iodonium

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salts,[15,16] no definitive evidence for the simple heterolysis to give a primary vinyl cation was found even in non-nucleophilic polar solvents such as 2,2,2-trifluoroethanol (TFE). Unrearranged substitution products were also obtained from vinyl iodonium salts. The *E/Z* isomeric ratios of the solvolysis products were initially argued for suggesting the formation of primary vinyl cation,[15,16] but this suggestion was later disregarded.[15c,17] The confusion comes from the diversity of possible interpretations of these experimental results.

Alkenediazonium salts should also be good precursors for vinylic cations. However, no definitive examples showing formation of primary vinyl cation have been found, although their reactions usually result in formation of rearranged products.[18–20] On the other hand, Hanack and co-workers[21] suggested that solvolysis of cyclohexylidenemethyl triflate took place via the primary vinyl cation in aqueous methanol (eq 1). The solvolysis

(1)
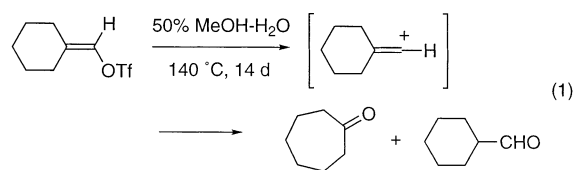
in 50% aqueous methanol afforded rearranged cycloheptanone and unrearranged cyclohexanecarbaldehyde at 140 °C in 2 weeks, but no reaction occurred in less polar, pure methanol. However, the suggestion was questioned from the stereochemical examinations of a similar reaction system.[22]

These observations have much ambiguity because the rearrangement can occur not only via primary vinyl cation but also through σ-bond participation, and the unrearranged products may be derived from the bimolecular nucleophilic substitution[23–25] as well as trapping of a possible primary vinyl cation. We wanted to make more definite observations to show whether the

SCHEME 1
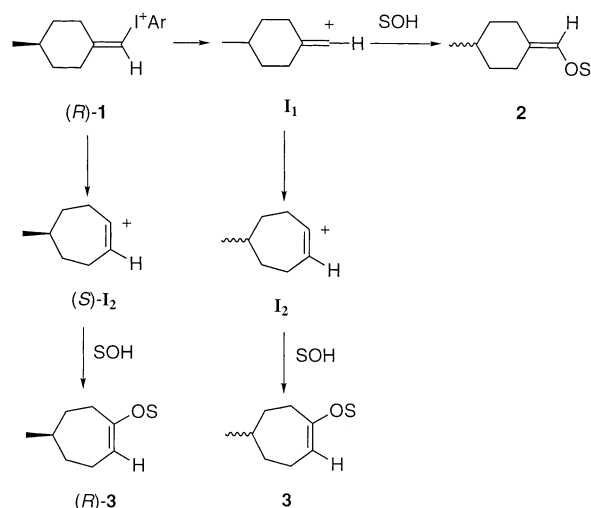
primary vinyl cation is involved in the reaction. We consider that the most suitable substrate for this purpose is a chiral 4-substituted cyclohexylidenemethyl derivative. If the achiral, primary vinyl cation is formed from the optically active starting material, the chirality should be lost, leading to completely racemized products. In contrast, if the rearrangement occurs via the σ-bond participation, the optical purity of the substrate would be maintained throughout the reaction via the chiral secondary vinyl cation, as illustrated in Scheme 1. This kind of chirality probe approach has been applied to carbanion (the Grignard reaction)[26] and carbenoid[27] chemistry. Similar axial chiralities were also used for examinations of the ion-pair processes of vinylic solvolysis.[28,29] We have now prepared optically active 4-methylcyclohexylidenemethyl(aryl)iodonium tetrafluoroborates (**1·BF₄⁻**), and the solvolysis of (*R*)- and (*S*)-**1** has been examined as well as some other nucleophilic substitution reactions. This paper describes the full account of these results to show that the primary vinyl cation is *not* involved in the reactions[17] and that unrearranged substitution products are formed via in-plane and out-of-plane vinylic S$_N$2 reactions.

Results

Preparation of Optically Active Vinyliodonium Salts. Tetrafluoroborate salts of (*R*)- and (*S*)-4-methylcyclohexylidenemethyl(phenyl)iodonium (**1a**) and 3-trifluoromethylphenyl (**1b**) and 4-methoxyphenyl derivatives (**1c**) were prepared from the corresponding enantiomers of 4-methylcyclohexylidenemethyl bromide, which were obtained according to the literature procedure[30] (the

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R counterpart is shown in eq 2). The last step of the
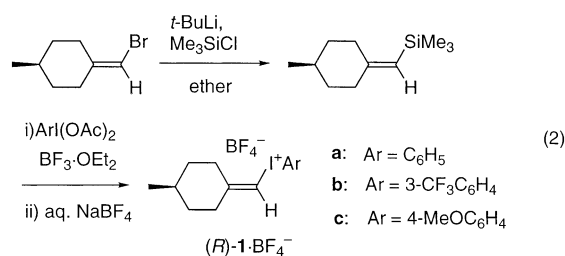
preparation, the conversion of the vinylsilane to the vinyliodonium salt, is established to proceed with complete retention of configuration,[11b,31] and the enantiomeric excesses (ee) of **1a−c·BF4^{−}** should be identical to that of the precursor vinylsilane, unless racemization or stereochemical resolution of **1a−c·BF4^{−}** occurs during the workup. This was confirmed, but crystallizations of the crude (*R*)-**1a−c·BF4^{−}** from dichloromethane−hexane were found to diminish their ee. An oily crude sample of 78% ee of (*R*)-**1a·BF4^{−}** was used for the product isolation. However, crystallized (*R*)-**1a·BF4^{−}** (69% ee), (*R*)-**1b·BF4^{−}** (63% ee), and (*R*)-**1c·BF4^{−}** (70% ee) were used for most of the reactions described below. The *S* isomer of **1a·BF4^{−}** was obtained at 79% ee and used for some of the reactions.

Solvolysis of Iodonium Salts. Solvolysis of optically active iodonium salts **1a−c·BF4^{−}** was carried out at 60 °C in various protic solvents. Solvents employed include methanol, 50 (v/v) % aqueous methanol, ethanol, acetic acid, 2,2,2-trifluoroethanol (TFE), and 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP). The reaction was slower in less nucleophilic solvents. Products include the unrearranged enol derivative **2OS** (and/or 4-methylcyclohexanecarbaldehyde **2C**)[32] and rearranged 4-methylcycloheptanone (**3C**) (and/or its enol derivative **3OS**)[32] as well as iodoarene (eq 3). For product isolation, a crude sample of
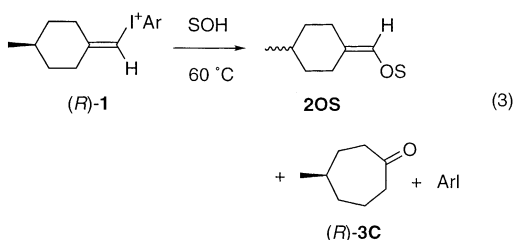
(*R*)-**1a·BF4^{−}** of 78% ee was employed for solvolysis in 50 (v/v) % aqueous methanol at 60 °C for 8 h to quantitatively give ketone **3C**. Isolated **3C**, which was found to be 77% ee by chiral GC, showed a negative optical rotation, indicating that the **3C** is in excess of the *R* form.[33]

The product yields were determined by normal gas chromatography (GC) with tetradecane as an internal

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(32) The acetals were also formed in some runs.

TABLE 1. Products of Solvolysis of 1 at 60 °C

(*R*)-1 (%ee)[a]	solvent	time (h)	yield (%)			ee (%)	
			2OS	3C	ArI	2OS	(*R*)-3C[a]
1a (69)	MeOH	6	15	57	86	8[b]	68
1a (−79)	MeOH (Bu4NBF4)[c]	5	29	65	98	−15[b]	−77
1a (−79)	MeOH (Bu4NClO4)[d]	5	20	71	86	−14[b]	−79
1a (69)	MeOH/H2O[e]	7	11[f]	80	79		68
1a (−79)	MeOH/H2O[e]	2	10[f]	89	93		−78
1a (69)	AcOH	4	15	68[g]	100[h]	50(R)	69[g]
1a (69)	EtOH	6	31	60	78	5[b]	67
1a (69)	TFE	9	0	75	84		69
1a (69)	HFIP	20	0	41	60		69
1b (63)	MeOH/H2O[e]	2	13[f]	85	63		62
1b (63)	TFE	7	0	95	51		63
1c (70)	MeOH/H2O[e]	6	25[f]	72	52		70
1c (70)	TFE	16	0	90	75		69

[a] The negative value means *S* excess. [b] Absolute stereochemistry was not determined. [c] In the presence of tetrabutylammonium tetrafluoroborate (0.1 M). [d] In the presence of tetrabutylammonium perchlorate (0.1 M). [e] 50(v/v)% aqueous methanol. [f] 4-Methylcyclohexanecarbaldehyde, achiral but of a 1:2 diastereomeric mixture. [g] **3OAc**. [h] Relative amounts of products, normalized to ArI = 100%.

standard after ether extraction, while the ee of the products were determined by chiral GC. The results are summarized in Table 1.

In unbuffered alcoholic solvents, the rearranged ketone **3C** was usually obtained as a major product. Addition of tetrafluoroborate or perchlorate salts did not significantly affect the product distribution of methanolysis. The seven-membered cyclic acetal was detected from methanolysis upon careful alkaline workup, but enol ether **3OMe** was not detected, even with this aqueous treatment. Enol ether **3OMe** is very reactive in acidic solution[34] and may be readily converted to the acetal in methanol catalyzed by HBF4 byproduct. The acetolysis product, 5-methylcyclohept-1-enyl acetate (**3OAc**), was obtained as a stable compound, accompanied by 4-methylcyclohexylidenemethyl acetate (**2OAc**). Un-rearranged products **2** were not obtained in TFE or HFIP.

The *R* iodonium salt (*R*)-**1a** always gives the *R* enantiomer of the rearranged substitution product, **3C** or **3OAc**, while (*S*)-**1a** affords (*S*)-**3**. It should also be noted that the ee of the rearranged product **3C** or **3OAc** is equal to that of the starting iodonium salts within experimental errors. These results were not affected by the leaving ability of the aryliodonium group, as observed with (*R*)-**1b** and (*R*)-**1c**. In contrast, the unrearranged products, **2OMe** and **2OEt**, are largely racemized. Although the absolute stereochemistry was not determined for these products, the form of the excess enantiomer obtained from (*S*)-**1a** is opposite to that from (*R*)-**1a**. In contrast to the alcoholysis, acetolysis gave **2OAc** without much loss of ee (50%). The stereochemistry of **2OAc** obtained from (*R*)-**1a** was confirmed to be of the *R* configuration, indicating that the substitution by acetic acid proceeds mainly with *retention* of configuration.

Reactions with Some Nucleophiles. Reactions were also examined in the presence of acetate and trifluoro-

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TABLE 2. Reaction of 1a·BF₄⁻ in the Presence of Carboxylate[a]

% ee[c] (R)-1a	solvent (SOH)	carboxylate (Nu)	product yield (%)[b,c]				
			2OS	(R)-**2Nu**	**3C**	(R)-**3Nu**	**PhI**
−79	MeOH	NaOAc[d]	91 (0)	0	0	0	97
69	AcOH	NaOAc	48 (0)	0	0	26 (65)	83
0	EtOH	NaOAc	99	0	0	0	100[e,f]
0	TFE	NaOAc	96	0	0	0	100[e,f]
69	CHCl₃	Bu₄NOAc		86 (−6)	0		100[e]
−79	CHCl₃[g]	Bu₄NOAc		90 (6)	0		91
−79	CHCl₃	Et₄NOCOCF₃		89 (44)	0		100[e]

[a] Reaction at [**1a**·BF₄⁻] = 2.5 mM, [carboxylate] = 0.10 M, and 60 °C for 2 h. [b] Determined by GC unless noted otherwise. The values in parentheses show ee. [c] The negative value means *S* excess. [d] Similar results were also obtained at 0.01 M. [e] Relative amounts of products, normalized to PhI = 100%. [f] Determined by ¹H NMR. [g] In the presence of acetic acid (0.3 M).

TABLE 3. Reaction of 1·BF₄⁻ in the Presence of Tetrabutylammonium Bromide[a]

(R)-**1** (% ee)[b]	solvent	[Bu₄NBr] (M)	product yield (%)[b]			
			2OMe	(R)-**2Br**	(R)-**3C**	**ArI**
1a (−79)	MeOH	0.01	20 (−1)[c]	28 (65)	51 (−77)	91
1a (−79)	MeOH	0.1	3 (−1)[c]	55 (69)	41 (−77)	99
1a (69)	MeOH/H₂O	0.1	13[d]	3 (−57)	84 (69)	97
1a (69)	CHCl₃	0.1		82 (−58)		81
1a (−79)	CHCl₃	0.1		87 (67)		100[e]
1b (63)	CHCl₃	0.1		94 (−48)		78
1c (70)	CHCl₃	0.1		53 (−53)		84

[a] [**1**·BF₄⁻] = ca. 2 mM, at 60 °C. Reaction time was ca. 5 h for the reactions in methanolic solvents and ca. 2 h for the reactions in chloroform. [b] The values in parentheses show ee. The negative value means *S* excess. [c] Although the absolute configuration of **2OMe** was not determined, the major enantiomer of **2OMe** was comparable to the results of Table 1. [d] 4-Methylcyclohexanecarbaldehyde. [e] Relative amounts of products, normalized to ArI = 100%.

acetate salts in some solvents including chloroform (Table 2). In alcoholic solvents, added sodium acetate greatly accelerated the reaction and changed the product distribution dramatically to give exclusively the unrearranged substitution product **2OS** with the alcohol as a nucleophile, and it was completely racemized. The selective formation of **2OS** was generally observed during basic alcoholysis, e.g., in the presence of triethylamine. Enol ether **2OS** was isolated from the reaction of **1a**·BF₄⁻ under similar basic conditions as a mixture with iodobenzene, fully characterized by ¹H and ¹³C NMR, and used as an authentic sample for the unbuffered solvolysis. The reaction of **1a**·BF₄⁻ with carboxylate salts in chloroform quantitatively gave the carboxylate substitution product of unrearranged structure. The trifluoroacetate gave **2OCOCF₃** mainly with inversion (44% ee), while the acetate gave **2OAc** in largely racemized but still inverted form (6% ee).

Reactions of **1**·BF₄⁻ with bromide were carried out in methanol and chloroform (Table 3). In methanol, some bromide substitution product **2Br** was obtained via about 90% inversion of configuration in addition to the normal solvolysis products. Bromide **2Br** is the sole substitution product in chloroform and has a similar ee to that obtained in methanol.

Discussion

Stereochemistry of Rearranged Products. The main product obtained in solvolysis of **1** is the rearranged

ketone **3C** (or **3OS**). Seven-membered ring enol ether **3OS** must first be formed, but it is very reactive to give the acetal in acidic alcohol.[34] The dimethyl acetal was obtained upon careful alkaline workup of the methanolysis products of (R)-**1a**. After usual treatment of the reaction mixture, the acetal (or enol ether) was not detected as a result of acid-catalyzed hydrolysis due to HBF₄ byproduct. The estimated half-lives of both the seven-membered ring acetal and enol ether are a few minutes at the acidity of the workup.[34,35] The acetolysis product **3OAc** was more easily obtained by usual workup due to its resistance to acid hydrolysis. These rearranged products obtained from (R)-**1**·BF₄⁻ are in excess of the *R* configuration and maintain the ee of the starting iodonium salt for any of the substrates and in all the solvents employed. That is, the chirality of the substrate was completely transferred to the rearranged product during the solvolysis.

The observed stereospecific reaction can be rationalized within the framework of the reaction pathways illustrated in Scheme 1. If the simple heterolysis provided the primary vinyl cation, 4-methylcyclohexylidenemethyl cation **I₁**, the ensuing 1,2-rearrangement to 5-methylcyclohept-1-enyl cation **I₂** should have occurred with considerable racemization due to the achiral structure of **I₁**. The *R* configuration of the rearranged product **3** from (R)-**1** is reasonably explained by a trans-σ-bond participation mechanism, leading directly and stereospecifically to the rearranged secondary cation (S)-**I₂**, which is trapped by a nucleophilic solvent to give (R)-**3OS**. Furthermore, the 1,2-hydride shift of the cyclic cation **I₂** across the double bond, leading to racemization, should be slower than trapping of the cation.

Although a similar hydride shift of acyclic vinyl cations occurs very readily, as demonstrated both theoretically and experimentally,[16] the degenerate hydride shift within cyclohept-1-enyl cation (eq 4) has a quite high activation


$$(4)$$
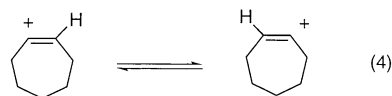
free energy of 20.8 kcal mol⁻¹, as obtained by ab initio calculations at the MP2/6-31G* level.[36] The optimized structures of the cation and the transition state for the 1,2-hydride shift are shown in Figure 1.

The structure of the hydrogen-bridged transition state looks like protonated acetylene, and that for the acyclic analogue has a linear carbon skeleton.[16b] In contrast, the seven-membered cyclic transition state is forced to be bent to the degree of 148.5°. This small angle induces a strain and must raise the barrier for the hydride shift of the intermediate **I₂** (Scheme 1).

Racemization of the rearranged product could also be induced by elimination addition of cation **I₂**, which involves cycloheptyne as an intermediate. This possibility did not occur during the solvolysis, but it did occur in the reaction of **1** with sulfonates, as presented in the accompanying paper.[37]
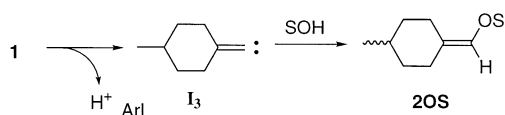
(35) Kreevoy, M. M.; Taft, Jr., R. W. *J. Am. Chem. Soc.* **1955**, *77*, 5590−5595.
(36) The B3LYP/6-31G* calculations gave 26.0 kcal mol⁻¹ for the same free energy barrier.
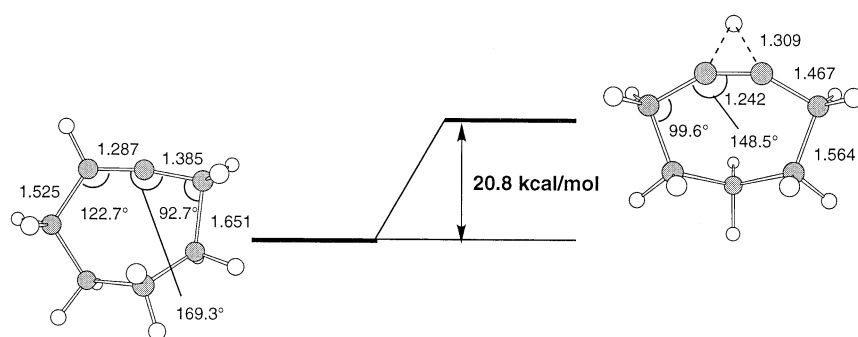
FIGURE 1. Optimized structures of cyclohept-1-enyl cation and the transition state for the 1,2-hydride shift and the free energy difference (MP2/6-31G*), where bond lengths are in angstroms.

SCHEME 2

SCHEME 3

Formation of Unrearranged Products. Solvolysis of **1** in methanol, ethanol, aqueous methanol, and acetic acid gives the unrearranged **2OS** (or **2C**) as a minor product, but none at all is seen in TFE or HFIP (Table 1). Methanolysis and ethanolysis products are largely racemized. In the presence of sodium acetate, **2OMe** and **2OEt** (with accompanying iodobenzene) are the sole products in the alcohols, and they are completely racemized (Table 2). In chloroform, acetate gives acetate substitution product **2OAc** with slightly preferred inversion, and the trifluoroacetate substitution occurs with considerable inversion of configuration (Table 2). Bromide, on the other hand, gives **2Br** with more than 90% inversion in both methanol and chloroform (Table 3). In contrast, acetolysis (in acetic acid) gives **2OAc** mainly with stereochemical retention. Since the stereochemistry of nucleophilic substitution of the same substrate ranges from inversion to retention, how can the variety of results be rationalized?

The racemic unrearranged products can be formed through nucleophilic alcoholic trapping of the achiral primary vinyl cation **I₁** (Scheme 1) or through the insertion of the alkylidenecarbene intermediate **I₃** formed by α elimination (Scheme 2). An alternative mechanism for the formation of the (partially) racemic unrearranged products is competition of the two direct reactions, in-plane (inversion) and out-of-plane (retention) S_N2 pathways[23] (Scheme 3).

The α elimination reaction of 1-alkenyliodonium salts can occur in neutral methanol.[23] In this case, a rapid 1,2-hydride shift of the alkylidenecarbene leads to the alkyne product. However, a 2,2-dialkylvinyl derivative was found to give an O–H insertion product via the carbene intermediate, due to the poor migratory aptitude of the alkyl group.[16] In the present case (neutral methanolysis of **1**), α elimination can well be a possible route to give racemic substitution product **2OS** by insertion. The vinylic H atom of this product (**2OS**) from the carbene insertion should originate exclusively from the solvent,
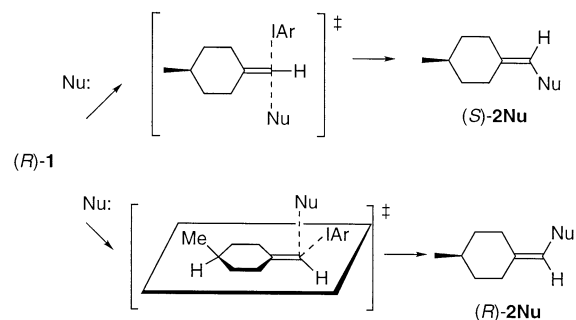
and this can be easily examined by using a deuterium solvent. To confirm this expectation, the reaction of **1a·BF₄⁻** was carried out in MeOD, but the product **2OMe** contained essentially no deuterium, as analyzed by mass spectrometry. Sodium acetate promotes the α elimination as a base, and the **2OMe** obtained in MeOD containing 0.1 M NaOAc was in fact a deuterated one, as expected. The completely racemized product under these conditions can therefore be ascribed to the α elimination. However, that obtained in unbuffered methanol cannot be ascribed to this route. This makes a sharp contrast to a similar reaction of an acyclic 2,2-dialkylvinyliodonium salt via the α elimination.[16] Suggestion of this route for the formation of **2OMe** from **1a** presented in a preliminary report[17] should be corrected. So, another route should be involved for racemization of **2OMe** obtained in neutral methanol.

An alternative mechanism involving primary vinyl cation **I₁** is also unlikely, because **I₁** should rearrange extremely readily without barrier to cyclic cation **I₂** and the rearranged product should largely racemized. Theoretical calculations at both the MP2 and B3LYP levels show that cyclohexylidenemethyl cation is of high energy and not in a local minimum on the potential energy surface, but instead, an unsymmetric β-carbon-bridged form can be optimized, which is 1.9 kcal mol⁻¹ (MP2)[38] higher in free energy than the rearranged cycloheptenyl cation (Figure 2). The unrearranged product could have been obtained via this mechanism, only if **I₁** were trapped by a nucleophilic solvent faster than its barrierless rearrangement to **I₂**. In less nucleophilic solvents such as TFE or HFIP, which have a stronger ionizing power than methanol, ethanol, and acetic acid, no unrearranged

(37) (a) Fujita, M.; Sakanishi, Y.; Nishii, M.; Okuyama, T. *J. Org. Chem.* **2002**, *67*, 8138–8146. (b) Fujita, M.; Sakanishi, Y.; Okuyama, T. *J. Am. Chem. Soc.* **2001**, *123*, 9190–9191.

(38) The B3LYP/6-31G* calculations show that the bridged form is 10.2 kcal mol⁻¹ higher than the cycloheptenyl cation.
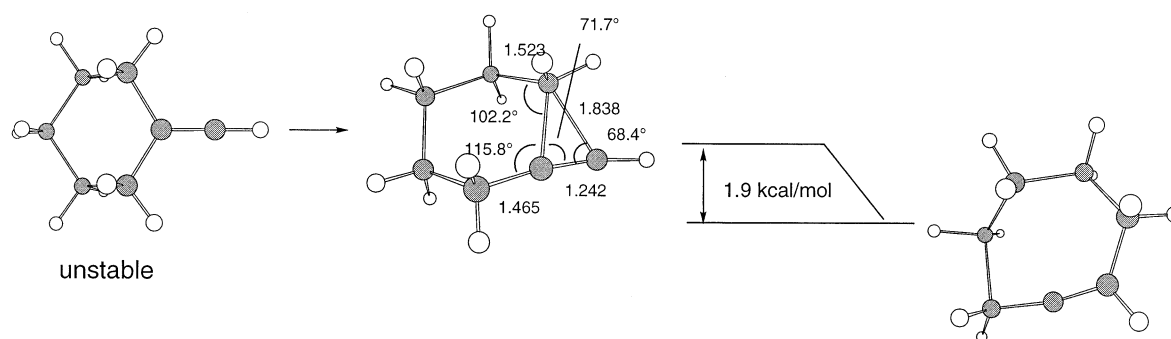
FIGURE 2. An optimized structure of the intermediate bridged cation in the rearrangement of cyclohexylidenemethyl to cyclohept-1-enyl cation and the free energy difference determined by the MP2/6-31G* method.

product was obtained, but the rearranged product **3C** still retained the stereochemical purity of the substrate. These results are incompatible with the primary cation route, because the less nucleophilic solvent would not decrease the efficiency of the unimolecular heterolysis of **1** to give **I₁** and would prolong the lifetime of **I₁** to promote the rearrangement to **I₂**, resulting in the racemic product. Bromide-trapping experiments are also incompatible with this mechanism. In methanol, bromide only gave unrearranged **2Br** at a high inversion rate but no rearranged bromide **3Br**. The formation of **2Br** cannot be ascribed to trapping of **I₁**, but it would be a product of direct nucleophilic substitution, as will be discussed below.

In contrast to these unlikely possibilities, the direct substitution mechanisms (Scheme 3) are more probable and must be responsible for the decrease in ee of the unrearranged products. The two pathways illustrated in Scheme 3 are theoretically feasible for the vinylic S$_N$2 reaction.[25] The substitution can proceed either by the in-plane vinylic S$_N$2 mechanism (nucleophilic attack at the σ^* orbital) leading to inversion or by the out-of-plane S$_N$2 mechanism (attack at the π^* orbital) leading to retention of configuration. The latter process can occur more easily with iodonium salts via the ligand-coupling (LC) mechanism within the λ^3-iodane adduct, in which the nucleophile coordinates to the iodonium iodine atom.[25c] Two typical cases were found in the present reaction systems. The stereochemically inverted product **2Nu** is mainly obtained in the reaction of **1** with nucleophilic reagents, bromide and trifluoroacetate salts, in chloroform, while the stereochemically retained product **2OAc** was obtained during solvolysis of **1a** in acetic acid. The bromide product in methanol has a similar inversion rate to that obtained in chloroform and must be derived via the same mechanism. The acetolysis occurring mainly via retention is remarkable compared to other observations of different degrees of inversion. This result substantiates a contribution from a mechanism leading to retention, although most of the results can be rationalized by competition between inversion and racemization. The LC mechanism for formation of **2OAc** in acetolysis must occur within the iodane intermediate, and acetic acid has interaction with the iodine atom at the transition state like **T$_A$**.

Although the acetate ion leads to α elimination of **1a** as a base in methanol, it reacts with **1a** as a nucleophile in chloroform to give largely racemized **2OAc**. To examine the contribution of the alkylidenecarbene intermediate, deuterium labeling and trapping experiments were
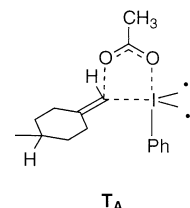
carried out for the acetate reaction in chloroform. In the presence of acetic acid-*d* (0.18 M), deuterium incorporation was essentially not observed in the acetate-substitution product **2OAc**. For reference, it was confirmed that an addition of acetic acid did not affect the product distribution, including the ee of **2OAc** (Table 2). The alkylidenecarbene **I₃** can easily be generated by a treatment of **1a** with triethylamine in chloroform and effectively trapped by cyclohexene[39] to give an cyclopropylidene adduct **4** (eq 5).
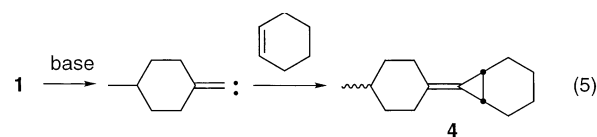
However, in the acetate reaction, only a small amount of carbene-trapping product **4** was detected (8% yield) together with the major acetate-substituted product **2OAc** (92% yield) when 0.1 M cyclohexene was added. The results indicate that the carbene route is not a major one of the acetate reaction in chloroform. The acetate product **2OAc** must be formed via the direct nucleophilic reaction of acetate ion with **1a**, which includes two stereochemically different pathways. A similar mechanism of competitive in-plane and out-of-plane S$_N$2 pathways may be operative in solvolysis reactions to give unrearranged products **2OS**. These considerations indicate that *the stereochemistry of the unrearranged products cannot provide evidence for the primary vinyl cation intermediate.*

In conclusion, achiral primary vinyl cation **I₁** is not involved in the solvolysis and related nucleophilic substitution reactions of the chiral cyclohexylidenemethyliodonium salt. Nucleophiles can react with this vinyl derivative via direct σ^* and π^* routes of substitution reaction, leading to the unrearranged products of both inversion and retention. The intramolecular σ-bond

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participation to give the rearranged, ring-expanded, chiral cation $\mathbf{I_2}$ can compete with the external nucleophilic attack under poorly nucleophilic conditions. The rearranged products completely maintain the chirality of the substrate due to the high barrier for the hydride-shift racemization of the chiral cation $\mathbf{I_2}$.

Experimental Section

1-Methyl-4-(trimethylsilylmethylene)cyclohexane. To a solution of bromide **2Br**[30] (1.34 g, 7.1 mmol) in ether (14 mL) cooled at −65 °C was added *tert*-butyllithium (7.8 mL of a 1.57 M solution in pentane, 12.2 mmol) dropwise for 90 min. Then, trimethylsilyl chloride (1.0 mL, 7.9 mmol) was added to the mixture at −65 °C. The mixture was allowed to warm to room temperature, quenched by water, and extracted with ether two times. The combined organic extracts were dried (MgSO$_4$) and concentrated in vacuo. The residue was purified by chromatography (SiO$_2$; eluent, hexane) to give the title compound (0.86 g, 4.7 mmol, 66% yield) as a colorless oil. When (*R*)-**2Br** (85% ee) and (*S*)-**2Br** (82% ee) were employed, the *R* and *S* isomers were obtained at 78% and 71% ee, respectively. The ee was determined by a chiral GC (DEX-CB, 80 °C, 32 cm s^{-1}). The retention times of the *S* and *R* isomers are 15.5 and 16.3 min, respectively. *S* isomer (71% ee): [α]$_D^{20}$ = +10.6 (CHCl$_3$, *c* = 0.36); ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.09 (s, 1H), 2.46−2.42 (m, 1H), 2.21−2.09 (m, 2H), 1.99−1.91 (m, 1H), 1.76−1.72 (m, 2H), 1.57−1.47 (m, 1H), 1.19−0.92 (m, 2H), 0.89 (d, *J* = 6.8 Hz, 3H), 0.06 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 159.5, 120.7, 39.9, 37.2, 36.8, 33.8, 32.4, 21.8, 0.4; MS (EI) *m/z* (relative intensity, %) 182 (M$^+$, 19), 167 (70), 73 (100); HRMS (EI) calcd for C$_{11}$H$_{22}$Si (M) 182.1491, found 182.1482.

4-Methylcyclohexylidenemethyl(phenyl)iodonium Tetrafluoroborate (1a·BF$_4^-$). To a solution of 1-methyl-4-(trimethylsilylmethylene)cyclohexane (1.0 g, 5.5 mmol) and PhIO[40] (1.25 g, 5.7 mmol) in dichloromethane (20 mL) was added BF$_3$·Et$_2$O (0.7 mL, 5.7 mmol) dropwise at 0 °C under nitrogen, and the reaction mixture was stirred for 100 min at 0 °C. A saturated aqueous sodium tetrafluoroborate solution was added to the reaction mixture. The mixture was stirred vigorously for 20 min and extracted with dichloromethane twice. The organic layer was concentrated in vacuo to give an oil. Crystallization of the crude mixture from dichloromethane−ether−hexane gave **1a·BF$_4^-$** (1.1 g, 2.75 mmol, 50% yield) as a white solid: mp = 93.7−94.2 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 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), 1.92−1.83 (m, 2H), 1.65−1.58 (m, 1H), 1.15−1.00 (m, 2H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 164.6, 134.5, 132.3, 132.2, 110.4, 91.8, 36.5, 36.1, 35.7, 35.1, 31.4, 21.0; MS (FAB+) *m/z* (relative intensity, %) 313 (100); HRMS (FAB+) calcd for C$_{14}$H$_{18}$I (**1a**) 313.0453, found 313.0445.

The *R*-enriched **1a·BF$_4^-$** was prepared by the same procedure using the *R* isomer of the vinylsilane (78% ee, 0.40 g, 2.2 mmol) to give a crude mixture (0.66 g). Crystallization of a part of the crude mixture (0.4 g) from dichloromethane−ether−hexane gave (*R*)-**1a·BF$_4^-$** of 69% ee (0.15 g) as a white solid: mp = 91.8−93.0 °C; [α]$^{20}_D$ = −20.4 (CHCl$_3$, *c* = 0.91) (69% ee).

(*S*)-**1a·BF$_4^-$** (79% ee) was also prepared from the (*S*)-vinylsilane.

4-Methylcyclohexylidenemethyl(3-trifluoromethylphenyl)iodonium Tetrafluoroborate (1b·BF$_4^-$). The titled compound was prepared in the same way as **1a·BF$_4^-$** using 3-trifluoromethyl(diacetoxyiodo)benzene.[41] Crystallization from dichloromethane−hexanes−ether gave **1b·BF$_4^-$** as a white solid in 45% yield: mp = 77.8−78.0 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.22 (d, *J* = 7.8 Hz, 1H), 8.08 (s, 1H), 7.81 (d, *J* = 7.8

Hz, 1H), 7.60 (t, *J* = 7.8 Hz, 1H), 6.75 (s, 1H), 2.72−2.68 (m, 2H), 2.47−2.35 (m, 2H), 1.88−1.82 (m, 2H), 1.64−1.60 (m, 1H), 1.18−0.97 (m, 2H), 0.89 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 165.9, 138.1, 133.9 (q, *J* = 33 Hz), 132.6, 130.7, 128.8, 122.4 (q, *J* = 273 Hz), 110.1, 92.1, 36.6, 36.2, 35.8, 35.2, 31.4, 20.9; MS (FAB+) *m/z* (relative intensity, %) 381 (100); HRMS (FAB+) calcd for C$_{15}$H$_{17}$F$_3$I (**1b**) 381.0327, found 381.0343. The *R*-enriched **1b·BF$_4^-$** was prepared by the same procedure using the *R* isomer of the vinylsilane (65% ee). Crystallization of the crude mixture from dichloromethane−ether−hexane gave (*R*)-**1b·BF$_4^-$** of 37% ee in 17% yield as a white solid and a filtrate of 83% ee. The following crystallization of the filtrate gave (*R*)-**1b·BF$_4^-$** of 63% ee in 4% yield as an oily solid: [α]$^{21}_D$ = −4.4 (CHCl$_3$, *c* = 0.91) (63% ee).

4-Methylcyclohexylidenemethyl(4-methoxylphenyl)iodonium Tetrafluoroborate (1c·BF$_4^-$). The titled compound was prepared in the same way as **1a·BF$_4^-$** using 4-methoxy(diacetoxyiodo)benzene.[41] Crystallization from dichloromethane−hexanes−ether gave **1c·BF$_4^-$** as a white solid in 41% yield: mp = 104.0−105.0 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.83 (d, *J* = 8.8 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 6.62 (s, 1H), 3.82 (s, 3H), 2.76−2.72 (m, 1H), 2.66−2.62 (m, 1H), 2.42−2.33 (m, 2H), 1.91−1.88 (m, 1H), 1.82−1.79 (m, 1H), 1.65−1.57 (m, 1H), 1.31−1.01 (m, 2H), 0.90 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 163.6, 162.8, 136.9, 118.2, 98.3, 92.7, 55.8, 36.4, 36.1, 35.7, 35.2, 31.5, 21.0; MS (FAB+) *m/z* (relative intensity, %) 343 (100); HRMS (FAB+) calcd for C$_{15}$H$_{20}$OI (**1c**) 343.0559, found 343.0574.

The *R*-enriched **1c·BF$_4^-$** was prepared by the same procedure from the (*R*)-vinylsilane of 72% ee. Crystallization of the crude mixture from dichloromethane−ether−hexane gave (*R*)-**1c·BF$_4^-$** of 70% ee in 54% yield as a white solid: mp = 84.0−85.0 °C; [α]$^{20}_D$ = −18.3 (CHCl$_3$, *c* = 0.91) (70% ee).

Determination of the ee of Vinyliodonium Salts. A typical procedure for (*R*)-**1a·BF$_4^-$** follows. (*R*)-1-Methyl-4-(trimethylsilylmethylene)cyclohexane of 78% ee was converted to the iodonium salt (*R*)-**1a·BF$_4^-$** by the established procedure described above. A part of the crude (*R*)-**1a·BF$_4^-$** was converted to **2Br** by treating it with tetrabutylammonium bromide (0.1 M) in chloroform. The **2Br** obtained was 66% ee in the *S* form, determined by the chiral GC. This indicates that the substitution proceeds with 92% [=100 × (66/78 + 1)/2] inversion. A sample of (*R*)-**1a·BF$_4^-$** obtained by crystallization of the crude mixture was also converted under the same conditions to **2Br**, which was found to be of 58% ee. From these results, the ee of the sample of (*R*)-**1a·BF$_4^-$** is calculated to be 69% [=58/(2 × 0.92 − 1)]. If the conversion of the vinylsilane to (*R*)-**1a·BF$_4^-$** proceeded with a partial loss of ee, the ee of the crystallized (*R*)-**1a·BF$_4^-$** should have been lower than 69%. Nonetheless, the solvolysis product **3C** has 69% ee, the ee of the substrate (*R*)-**1a·BF$_4^-$** should not be lower than 69%, unless enantiomeric enrichment could occur during the reaction. These results are also consistent with complete retention of the configuration during the preparation of vinyliodonium salts from the corresponding vinylsilanes. Determination of the ee of **2Br** was performed using a gas chromatograph equipped with a chiral column (DEX-CB, i.d. 0.25 mm × 25 m), at a column temperature of 100 °C and a linear velocity of 32 cm s^{-1}. The retention times of (*R*)- and (*S*)-**2Br** are 9.0 and 9.8 min, respectively. The ee values of the other salts were determined in the same way. For details, see the Supporting Information.

Standard Procedure for Solvolysis of 1. The tetrafluoroborate salt of **1** (1 mg) was dissolved in 1 mL of alcohol or acetic acid and kept at 60 °C. After the addition of 1 mL of an ether solution containing tetradecane (5 μmol), the products were extracted with ether and washed with water. The yields of the products were determined by GC with tetradecane as an internal standard and the ee values were found by chiral GC. Details are given in the Supporting Information.

(40) Saltzmann, H.; Sharefkin, J. G. *Org. Synth.* **1973**, *Coll. 5*, 658−659.

(41) (a) McKillop, A.; Kemp, D. *Tetrahedron* **1989**, *45*, 3299−3306. (b) Sharefkin, J. G.; Saltzmann, H. *Org. Synth.* **1973**, *Coll. 5*, 660−663.

Standard Procedure for Reaction of 1 with Nucleophile in Chloroform. The tetrafluoroborate salt of **1** (1 mg) was dissolved in 1 mL of chloroform containing an appropriate amount of a nucleophilic salt and kept at 60 °C. The products were analyzed in the same way as those of solvolysis.

Calculations. The compounds studied in the present paper were optimized by using Gaussian 98 program.[42] All calculations were carried out at the second-order Møller−Plesset perturbation (MP2)[43] using the hybrid density functional B3LYP[44] methods with the 6-31G* basis set.[45] Optimized structures were verified by means of their Hessian matrixes to be local minima or a saddle point on the potential energy surfaces. The symmetrical hydride-shift transition state of cyclohept-1-enyl cation showed one imaginary reaction-coordinate frequency of 645i (MP2) or 1047i (B3LYP).

Supporting Information Available: Experimental procedures and characterization of products **2** and **3** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JO020398C

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