Kinetic Resolution of Racemic α-Methylbenzyl Methacrylate: Asymmetric Selective Polymerization Catalyzed by Grignard Reagent–(−)-Sparteine Derivative Complexes

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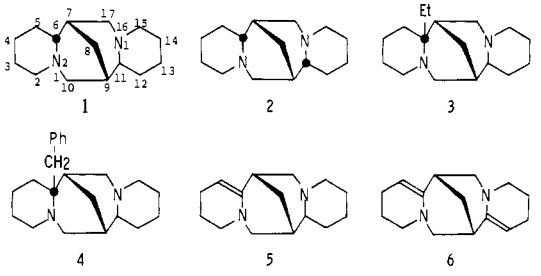
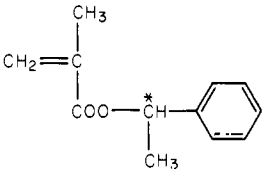
Abstract: Enantiomer-selective polymerization of racemic (*RS*)-α-methylbenzyl methacrylate (MBMA) was investigated with homogeneous Grignard reagent–(−)-spareteine and its derivative catalysts in toluene at −78 °C. A variety of Grignard reagents (RMgX) were combined with (−)-sparteine (**1**), (−)-α-isosparteine (**2**), (−)-6-ethylsparteine (**3**), (+)-6-benzylsparteine (**4**), (−)-Δ^5-dehydrosparteine (**5**), and (−)-$\Delta^{5,11}$-didehydrosparteine (**6**). The activity and selectivity of the catalysts depended greatly on the kinds of ligands and RMgX. Some RMgX–**1** complexes showed very high *S* selectivity, the optical purity of initially formed polymer being greater than 90%. The catalysts involving **2**, **3**, and **4** showed very low catalytic activity. Most RMgX–**5** complexes polymerized preferentially (*S*)-MBMA over (*R*)-MBMA with low selectivity, but *t*-BuMgCl and PhMgBr complexes showed reverse selectivity. RMgX–**6** complexes polymerized (*R*)-MBMA in slight excess. The crystals of EtMgBr–**1**, *t*-BuMgCl–**1**, EtMgBr–**2**, and EtMgBr–**4** were isolated, and their structures in solution were estimated by ^{1}H and ^{13}C NMR spectroscopy with the aid of the structural data obtained by X-ray analyses. The activity and selectivity of the catalysts were discussed on the basis of these structural data. Other anionic initiators such as butyllithium, sodium bis(2-methoxyethoxy)aluminum hydride, octylpotassium, and diethylaluminum diphenylamide showed no selectivity in the presence of **1** and **2**.

(−)-Sparteine (**1**) has often been used as a chiral bidentate ligand[2] since Eberhardt used it for the activation of anions[3] and Nozaki and co-workers found the asymmetric addition of alkyllithium and Grignard reagent to prochiral carbonyl compounds.[4] However, the optical yields of most reactions with **1**



were rather low, and Grignard reagent–**1** complexes were not effective chiral reagents in the asymmetric addition reactions. Fortunately, we found recently that some of the complexes are very useful in the enantiomer-selective (asymmetric selective)[5] polymerization of racemic α-methylbenzyl methacrylate (MBMA) in toluene at low temperatures.[6] The polymer obtained in the



early stage of the polymerization with cyclohexylmagnesium bromide (cHexMgBr) complex with **1** was rich in *S* antipode, whose optical purity was 93%, and the monomer recovered at about 65% conversion was almost optically pure. Thus, the monomer was kinetically resolved in the polymerization. Although various kinetic resolutions have been reported, the selectivity of the reactions seems to be rather low, except for the systems involving enzymes[7a] and the titanium alkoxide–tartrate catalyst found recently by Sharpless.[7b]

The present work was undertaken to obtain more detailed information on this novel enantiomer-selective polymerization. We synthesized five (−)-sparteine derivatives (**2**–**6**) and used them as the chiral ligands in the polymerization of MBMA with Grignard reagents. Some of the complexes were isolated and their structures in solution were estimated by ^{1}H and ^{13}C NMR spectroscopy with the aid of X-ray analysis data.

Experimental Section

Materials. MBMA and toluene were purified by a previously described method.[6b] Grignard reagents were prepared from alkyl halides and magnesium turnings in diethyl ether. Diethylmagnesium (Et_2Mg) was prepared according to the method of Schlenk with diethyl ether.[8]

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Butyllithium (BuLi), octylpotassium, and diethylaluminum diphenylamide (Ph_2NAlEt_2) were prepared in heptane, hexane, and toluene, respectively. Sodium bis(2-methoxyethoxy)aluminum hydride [$Na(O\text{-}C_2H_4OCH_3)_2AlH_2$] (Nakarai Chemical Co.) was used as a toluene solution. (−)-Sparteine (**1**) (Sigma Chemical Co.) was stirred over CaH_2 overnight and distilled under reduced pressure; $[\alpha]^{20}_D$ −17.8° (*c* 3.9, ethanol).

Preparation of (−)-Sparteine Derivatives (2–6). Derivatives **2–6** were prepared by the method shown in Scheme I, according to the literature[9,10] but with several modifications. However, **2** and **4** obtained had melting points different from those reported in the literature, and **3** and **5** showed different specific rotations. The purity of **2–6** was confirmed by ^1H NMR spectroscopy.

Scheme I

$$\mathbf{1} \xrightarrow{(CH_3COO)_2Hg} \mathbf{5} \xrightarrow[2.\ RMgX]{1.\ HClO_4} \mathbf{3} \text{ and } \mathbf{4}$$

$$\mathbf{1} \xrightarrow{(CH_3COO)_2Hg} \mathbf{6} \xrightarrow{NaBH_4} \mathbf{2}$$

(−)-Δ⁵-Dehydrosparteine (5). A solution of **1** (11.8 g, 0.050 mol) in 10% aqueous acetic acid (110 mL) was added to a solution of mercuric acetate (64.7 g, 0.20 mol) in water (150 mL) with stirring under nitrogen in the dark, and the reaction was continued for 24 h at 35 °C. The mercurous acetate formed was separated by filtration, and hydrogen sulfide was passed through the filtrate. After separating the precipitates, the solution was basified (pH >11) with sodium hydroxide and extracted with ether. The ether solution was dried over magnesium sulfate and concentrated. The residual oil was distilled under reduced pressure. The main fraction was dried over calcium hydride and distilled again to give 5.7 g (49%) of **5**: bp 92–96 °C (0.10 mm) [lit.[9] 98 °C (0.2 mm)]; $[\alpha]^{20}_D$ −184° (*c* 5.9, ethanol) [lit.[11] $[\alpha]_D$ −124° (*c* 2.9, ethanol)]; ^1H NMR ($CDCl_3$) δ 4.2 (m, 1 H, —CH═), 1.0–3.1 (m, 23 H, other H).

(−)-Δ⁵,¹¹-Didehydrosparteine (6). A solution of **1** (13.8 g 0.059 mol) in 10% aqueous acetic acid (110 mL) was added with stirring to a solution of mercuric acetate (129 g, 0.41 mol) in water (400 mL) under nitrogen at room temperature, and the reaction was continued for 1 h at room temperature and 5 h at 80 °C. The reaction mixture was treated in the same manner as described above. Concentration of the ethereal extract gave crude **6**, which was then purified by sublimation at 70 °C (0.02 mm) to yield 1.8 g (13.4%) of a colorless crystal: mp 108–109 °C (lit.[9] 105–107 °C); $[\alpha]^{20}_D$ −645° (*c* 0.25, benzene) [lit.[9] $[\alpha]^{25}_D$ −698° (*c* 1.98, benzene)]; ^1H NMR ($CDCl_3$) δ 3.5–4.2 (br, 2 H, —CH═), 1.3–3.2 (m, 20 H, other H).

(−)-α-Isosparteine (2).[12] A mixture of **6** (1.8 g, 0.0079 mol) and $NaBH_4$ (12 g) in methanol (80 mL) was stirred for 5 h at room temperature under nitrogen and refluxed for 3 h. The mixture was then poured into ice water, made strongly basic with sodium hydroxide, and extracted with ether. After the ether was evaporated, the residue was sublimed. The crude product was dissolved in hexane and dried with CaH_2. Hexane was evaporated, and the residue was sublimed again to yield 1.6 g (84%) of **2**: mp 68–70 °C (lit. mp 102–108 °C,[9] 118 °C[11]); $[\alpha]^{20}_D$ −57.2° (*c* 1.1, methanol) [lit.[11] $[\alpha]_D$ −56.2 (*c* 6.8, methanol)]; ^1H NMR ($CDCl_3$) δ 2.4–2.9 (m, 4 H), 1.1–2.0 (m, 22 H). Anal. Calcd for $C_{15}H_{26}N_2 \cdot 0.41H_2O$: C, 74.52; H, 11.18; N, 11.59. Found: C, 74.52; H, 11.06; N, 11.50. **2** was very hygroscopic compared to **1**.

(−)-6-Ethylsparteine (3). Aqueous $HClO_4$ (60%) was added to a solution of **5** in ethanol to adjust to pH 8 at 0 °C. The precipitated salt was separated and recrystallized from ethanol [mp 163–165 °C (lit.[9] mp 160–161 °C)]. To the perchlorate (8.0 g, 0.024 mol) was added with stirring ethylmagnesium bromide (0.060 mol) in ether. Then the mixture was refluxed for 2 h and added to cooled aqueous NH_4Cl. The precipitates formed were separated, added to aqueous NaOH, and extracted with ether. After the ether was evaporated, the residue was distilled under reduced pressure. The oily product was dried over CaH_2. Distillation gave 2.5 g (27%) of **3**: mp 58–59 °C (lit.[9] mp 61–63 °C); $[\alpha]^{20}_D$ −6.9° (*c* 1.7, ethanol) [lit.[9] $[\alpha]^{20}_D$ −16.2° (*c* 7.2, ethanol)]; ^1H NMR ($CDCl_3$) δ 0.72 (t, 3 H, CH_3), 1.1–2.9 (m, 27 H, other H). Anal. Calcd for $C_{17}H_{30}N_2$: C, 77.80; H, 11.52; N, 10.68. Found: C, 77.54; H, 11.38; N, 10.76.

(+)-6-Benzylsparteine (4). This was prepared by using benzylmagnesium chloride in the same manner as described for **3**. Crystallization of crude product from methanol afforded **4** in 27% yield: mp 91–92 °C (lit.[9] mp 115 °C); $[\alpha^{20}_D$ +30.4° (*c* 1.0, ethanol) [lit.[9] $[\alpha]^{20}_D$ +30.6° (*c* 3.51, ethanol)]; ^1H NMR ($CDCl_3$) δ 7.20 (s, 5 H, Ph), 1.1–3.1 (m, 27 H, other H). Anal. Calcd for $C_{22}H_{32}N_2$: C, 81.43; H, 9.94; N, 8.63. Found: C, 81.38; H, 9.87; N, 8.63. The compounds **1–6** were stored in toluene solutions immediately after purification.

Polymerization. The polymerization was carried out in a glass ampule under dry nitrogen. Grignard reagent (0.20 mmol) in ether and a ligand (0.24 mmol) in toluene were mixed in toluene (15 mL) at room temperature. The homogeneous catalyst solution was then cooled at −78 °C, and the monomer (1.52 g, 8.0 mmol) was added. The polymerization was terminated by adding a small amount of methanol, and the polymer was precipitated by adding a large amount of methanol. After the polymer was separated by filtration, unreacted monomer was recovered by distillation.

Preparation of Ethylmagnesium Bromide–1 Complex. A solution of EtMgBr (1.71 M, 3.23 mL) in ether was added to **1** (1.30 g) in toluene (5 mL) at room temperature under dry nitrogen. After 3 h at room temperature, the crystals formed were separated, washed with toluene at −40 °C, and dried to give ca. 0.8 g (40%) of the crude complex, which was then recrystallized from toluene under dry nitrogen. The ^1H NMR spectrum of the purified complex in toluene-d_8 indicated that the molar ratio of EtMgBr to **1** was 1:1.

Preparation of *t*-BuMgCl–1, Et_2Mg–1, EtMgBr–2, and EtMgBr–4 Complexes. These complexes were prepared in the same manner as described for EtMgBr–**1** complex and recrystallized from toluene.

Cryoscopic Determination of Molecular Weight of EtMgBr–1 Complex. Determination of the molecular weight of EtMgBr–**1** complex was done cryoscopically in dry benzene. The freezing points of four sample solutions (*c* = 26–103 g/kg) were measured.

X-ray Analyses. All the crystals of EtMgBr–**1**, *t*-BuMgBr–**1**, EtMgBr–**2**, and EtMgBr–**4** belong to the orthorhombic system, space group $P2_12_12_1$. The intensity data were collected on a Rigaku automated diffractometer using Mo Kα radiation. Structures were solved by the heavy-atom method and refined by the block-diagonal least-squares procedure. The final *R* indices for EtMgBr–**1**, *t*-BuMgCl–**1**, EtMgBr–**2**, and EtMgBr–**4** were 0.100, 0.098, 0.074, and 0.169 for 1272, 1199, 1235, and 1445 observed reflections, respectively. Details of the X-ray analyses of the complexes EtMgBr–**1**,[13a] *t*-BuMgCl–**1**,[13b] EtMgBr–**2**,[13c] and EtMgBr–**4**[13b] will be published elsewhere.

Measurements. Optical rotation was measured with a JASCO DIP-181 polarimeter at 20 °C; the precision of rotation was ±0.002°. The rotation of the polymer was measured in toluene, and its optical purity was calculated on the basis of $[\alpha]^{20}_D$ +125° (toluene) for optically pure isotactic poly(MBMA).[6b] The rotation of MBMA (neat) was measured with 0.1–1.0-cm cells, and its optical purity was estimated from $[\alpha]^{20}_D$ −53° (neat) of (*S*)-MBMA.[6b] The ^1H NMR spectra were measured on JNM-MH-100 (100 MHz) and JNM-FX-100 (100 MHz) spectrometers; the ^{13}C NMR spectra were taken on the latter at 25 MHz. The tacticity of the polymer was estimated from the ^1H NMR spectrum of poly(methyl methacrylate) derived from poly(MBMA).[6b] Spin–lattice relaxation time (T_1) was measured by the inversion–recovery method.

Results

The results of the polymerization of (*RS*)-MBMA with various Grignard reagent complexes are summarized in Table I. The polymerization was carried out in toluene at −78 °C by using cyclohexylmagnesium chloride (cHexMgCl), *tert*-butylmagnesium chloride (*t*-BuMgCl), ethylmagnesium bromide (EtMgBr), isopropylmagnesium bromide (*i*-PrMgBr), isobutylmagnesium bromide (*i*-BuMgBr), cHexMgBr, phenylmagnesium bromide (PhMgBr), and cHexMgI as Grignard reagents. Most complexes of **1** polymerized preferentially (*S*)-MBMA, giving the polymers of negative rotations in over 30% yields within 10 h, but *t*-BuMgCl and PhMgBr complexes showed very low reactivity. The cHexMgI complex formed the polymer in a rather low yield even after 115 h, and the optical purity of the polymer[14] was low. The cHexMgBr–**1** complex, which was prepared by mixing at 60 °C, showed enantiomer selectivity analogous to that of the catalyst prepared at room temperature. However, when cHexMgBr and **1** were mixed at −78 °C, the catalyst showed only low selectivity, and the polymer was atactic. This is similar to the polymer

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(12) Absolute configuration of **1** is 6*R*,7*S*,9*S*,11*S* and that of **2** is 6*R*,7*S*,9*S*,11*R*.

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(14) Optical purity of polymer means optical purity of polymerized monomer that is in good agreement with its enantiomeric excess.[6b]

Table I. Polymerization of MBMA with Grignard Reagent Complexes in Toluene at −78 °C

ligand	Grignard reagent	time, h	yield, %	$[\alpha]^{20}_D$ (OP) polymer, deg	$[\alpha]^{20}_D$ (OP) recovered monomer, deg	tacticity, % I	H	S
1	cHexMgCl	4	48.1	−101.3 (81)	+40.5 (75)	92	5	3
1	*t*-BuMgCl	96	0.4	0 (0)	0 (0)			
1	EtMgBr	1	41.4	−102.2 (82)	+30.4 (57)	94	5	1
1	*i*-PrMgBr	1	31.7	−106.1 (85)	+20.7 (39)			
1	*i*-BuMgBr	6	32.0	−106.6 (85)	+20.4 (39)			
1	cHexMgBr	2	51.8	−95.5 (76)	+43.8 (83)	92	5	3
1	cHexMgBr[a]	3	38.9	−108.7 (87)	+29.4 (55)			
1	cHexMgBr[b]	8	34.4	−13.7 (11)	+3.0 (6)	35	35	30
1	cHexMgBr[c]	29	44.9			34	37	20
1	PhMgBr	129	0					
1	cHexMgI	115	32.6	−34.7 (28)	+6.9 (13)	70	18	12
1	Et_2Mg	96	0					
2	EtMgBr	22	0					
2	cHexMgBr	214	2.3	0 (0)	0 (0)			
2	cHexMgBr[d]	4	33.8	−112 (90)	+24 (45)			
2	cHexMgBr[e]	8	0.2	−82 (66)	+1 (2)			
3	EtMgBr	264	0					
3	EtMgBr[f]	5	61.9	−1.4 (1)		14	29	57
3	BuLi	0.1	79.6	+3.5 (3)		7	32	61
4	EtMgBr	99	14.1	−82.9 (66)	+6.2 (12)	77	14	9
4	EtMgBr[g]	29	17.3	−5.3 (4)	+0.5 (1)	10	28	62
4	cHexMgBr	96	1.1	−58.4 (47)	+0.5 (1)			
4	cHexMgBr[g]	98	2.9	−6.5 (5)	+0.1 (0)			
4	BuLi	0.1	45.2	+8.1 (7)	−3.1 (6)	6	29	65
5	cHexMgCl	4	40.6	−12.0 (10)	+4.0 (8)	32	34	34
5	*t*-BuMgCl	69	7.1	+18.8 (15)	−0.6 (1)	24	29	47
5	EtMgBr	4	26.1	−26.6 (21)		38	33	29
5	PhMgBr	118	20.1	+18.4 (15)	−1.6 (3)	26	31	43
5	cHexMgI	2	54.4	−22.7 (18)	+9.8 (19)	38	33	29
6	cHexMgCl	4	26.7	+13.8 (11)	−2.6 (5)	6	19	75
6	*t*-BuMgCl	3	5.0	+30.4 (24)	−0.5 (1)			
6	EtMgBr	23	45.0	+0.3 (0)	−0.6 (1)	18	32	50
6	PhMgBr	6	2.4	0 (0)	0 (0)			
6	cHexMgI	7	46.2	+1.5 (1)	−0.6 (1)	30	42	28

[a] 1 was added at 60 °C. [b] 1 was added at −78 °C. [c] Polymerization without 1. [d] cHexMgBr:1:2 = 1.0:0.6:0.6. [e] cHexMgBr:1:2 = 1.0:1.1:1.1. [f] Polymerization temperature = 0 °C. [g] Polymerization temperature = −40 °C.

obtained with cHexMgBr alone but contrary to the polymers obtained in the polymerization with high selectivity.

The catalysts involving **2** showed very low activity and no selectivity regardless of the kind of Grignard reagents used. Asymmetric selective polymerization proceeded by mixing cHexMgBr with 1.2 equiv of an equimolar mixture of **1** and **2**. However, almost no polymerization occurred at the molar ratio cHexMgBr:**1**:**2** = 1.0:1.1:1.1. The result indicates that **2** has a stronger complexing power with cHexMgBr than does **1**.

The complexes of **3** afforded a small amount of the polymer even after prolonged polymerization at −78 and −40 °C. At 0 °C, EtMgBr–**3** complex yielded the polymer of low optical purity and isotacticity. When butyllithium (BuLi) was used in place of Grignard reagent, the reaction was very fast, and the (+) polymer of low optical purity was obtained.

The catalyst systems involving **4** were slightly more reactive than the corresponding systems of **3**. EtMgBr–**4** gave the isotactic polymer of rather high negative rotation at −78 °C. At −40 °C, however, the complex showed little selectivity, the resulting polymer being rich in syndiotacticity.

All Grignard reagent–**5** catalysts initiated the polymerization. However, the selection of enantiomers depended on Grignard reagent, and the complexes of *t*-BuMgCl and PhMgBr that showed no activity in the combination with **1** formed the polymer rich in (*R*)-MBMA. All the polymers were atactic. Most RMgX–**6** catalysts polymerized preferentially (*R*)-MBMA over (*S*)-MBMA, with low selectivity. The polymers were rich in syndiotactic triad.

The polymerization of (*RS*)-MBMA was also performed with other anionic initiators in the presence of excess **1** or **2** in toluene at −78 °C (Table II). The polymers were produced in a short time, particularly with BuLi, but showed no optical activity. The polymers prepared with BuLi and $Na(OC_2H_4OCH_3)_2AlH_2$ in the absence of the ligands were isotactic. However, the tacticity of the polymers was greatly changed in the presence of **1** and **2**, indicating that the complexation between these initiators and the ligands had occurred.

Table II. Polymerization of (*RS*)-MBMA with Various Initiators in the Presence of 1 and 2 in Toluene at −78 °C[a]

initiator	time, h	yield, %	$[\alpha]^{20}_D$ polymer, deg	tacticity, % I	H	S
BuLi	24	85.4		56	35	9
BuLi–**1**	0.2	71.0	−0.7	10	38	52
BuLi–**2**	0.1	94.7	0	6	18	76
$Na(OC_2H_4OCH_3)_2AlH_2$	0.6	68.2		70	29	1
$Na(OC_2H_4OCH_3)_2AlH_2$–**1**	2.4	31.5	−0.5	58	38	4
$Na(OC_2H_4OCH_3)_2AlH_2$–**2**	1.6	14.0	0	4	24	72
octylpotassium	1.0	72.4		47	46	7
octylpotassium–**1**	0.3	81.8	−0.7	49	44	7
Ph_2NAlEt_2	24	90.0		4	20	76
Ph_2NAlEt_2–**1**	1.5	70.1	−0.6	2	23	74
Ph_2NAlEt_2–**2**	2.1	92.1	0	7	22	71

[a] [Ligand]/[initiator] = 1.2.

The molecular weight of EtMgBr–**1** in a benzene solution was estimated to be about 360 ± 30, which agrees with the calculated value (367) of the complex. This implies that the complex scarcely associates in a diluted solution.

The structures of EtMgBr–**1**, *t*-BuMgCl–**1**, EtMgBr–**2**, and EtMgBr–**4** complexes have been determined by X-ray analyses, and those of EtMgBr–**1**, –**2**, and –**4** are shown in Figures 1, 2, and 3, respectively.[13] All complexes are four-coordinate with tetrahedral structures. No difference was observed in the structure of the (−)-sparteine skeleton in EtMgBr–**1** and *t*-BuMgCl–**1**, and the four six-membered rings of **1** were all in the chair form to

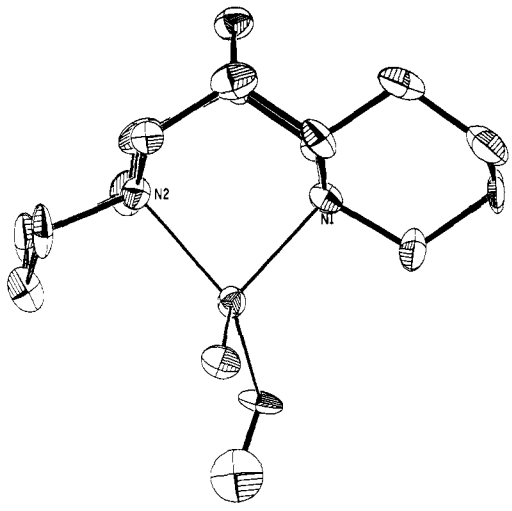


Figure 1. Structure of EtMgBr–**1** complex.

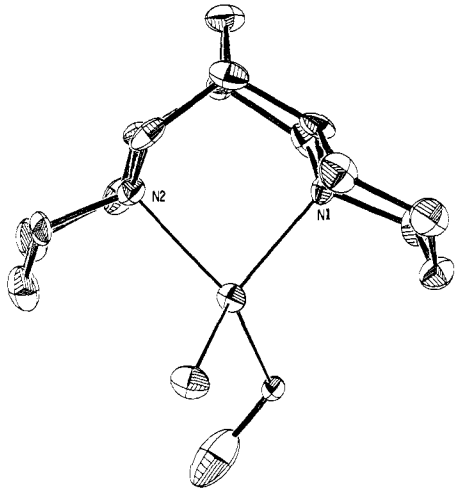


Figure 2. Structure of EtMgBr–**2** complex.

produce the cavity into which magnesium could enter. However, the positions of the alkyl group and halogen in the two complexes were reversed. The *tert*-butyl group in *t*-BuMgCl–**1** occupied the position at which the bromine of EtMgBr–**1** existed. Two different forms are feasible for the complex involving **1** because **1** has no symmetrical elements. However, only one tetrahedral structure exists for EtMgBr–**2** due to the C_2 symmetry of **2**.

Figure 4 shows the ^{1}H NMR spectra of EtMgBr–**1** complex in toluene-d_8. Although the methylene resonance of EtMgBr appears as a clear quartet at 0 ppm at 35 °C, its methyl group gives two triplets of different intensities at 1.8 ppm. These triplets were also observed in the spectra recorded at 0 °C and −78 °C.

The ^{1}H NMR spectra of *t*-BuMgCl–**1** (A), Et_2Mg–**1** (B), EtMgBr–**2** (C), EtMgBr–**3** (D), and EtMgBr–**4** (E) are presented in Figure 5. *t*-BuMgCl–**1** also shows two singlets of different intensities at 1.4 ppm. Spin–lattice relaxation time, T_1, of the main peak at low field was 1.70 s, while T_1 of the peak at high field was 1.33 s. This probably indicates that the *tert*-butyl group of a main complex is less sterically hindered. The methyl groups of Et_2Mg–**1** give two triplets of the same intensity, but its methylenes give a single quartet, as observed in EtMgBr–**1**. These results indicate that EtMgBr–**1** as well as *t*-BuMgCl–**1** in toluene exists as a mixture of two different forms. On the contrary, EtMgBr–**2** shows a single triplet due to the methyl group and two quartets due to the methylene group. In the complexes of **2**, only one form is possible because of its C_2 symmetry. The methyl resonances of EtMgBr–**3** and EtMgBr–**4** also appear as a single triplet. This result suggests that one form predominates over the other form in these complexes though the structure of the cavitities of **3** and **4** is rather similar to that of **1**.

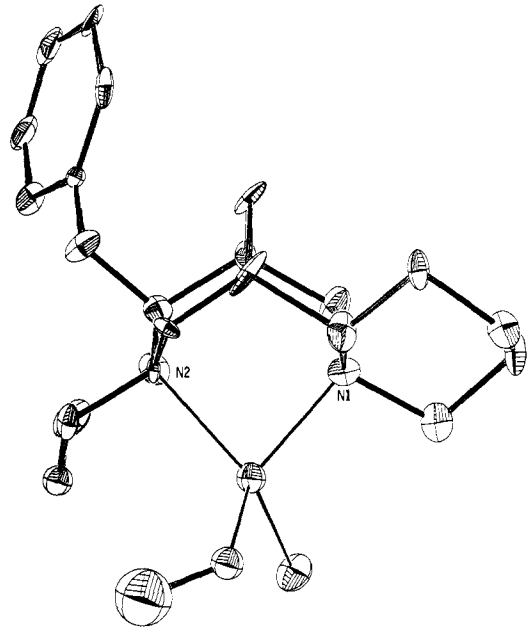


Figure 3. Structure of EtMgBr–**4** complex.

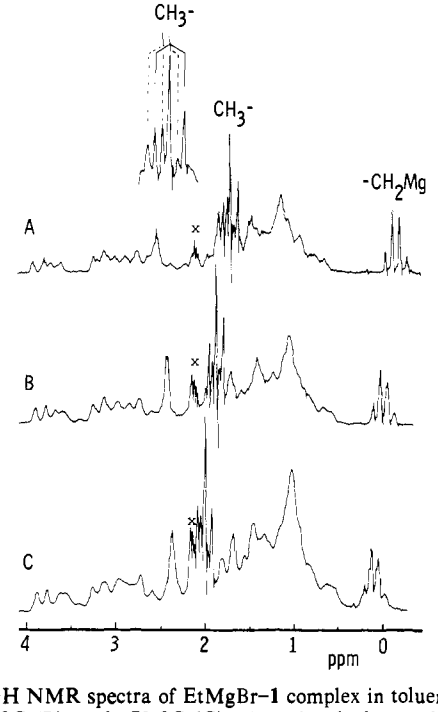


Figure 4. ^{1}H NMR spectra of EtMgBr–**1** complex in toluene-d_8 at 35 °C (A), 0 °C (B), and −78 °C (C). (×: signals due to the solvent.)

The ^{13}C NMR spectra of the complexes were well correlated with the ^{1}H NMR data (Figure 6). Most carbons of EtMgBr–**1** and *t*-BuMgCl–**1** show two peaks, the intensity ratios of which are similar to those of the methyl resonances shown in Figures 4 and 5. The intensity ratio of two peaks due to each carbon of **1** is reversed between EtMgBr and *t*-BuMgCl complexes. Therefore, the predominant form in EtMgBr–**1** may correspond to the minor form in *t*-BuMgCl–**1**.

The ^{13}C NMR spectra of the EtMgBr–**2** and −**3** complexes showed a single peak for each carbon in the complexes, as expected from the results of the ^{1}H NMR spectra. The spectrum of EtMgBr–**2** was rather simple because of the symmetry, and the peaks due to CH_2Mg and CH_3 appeared at 2.5 and 13.4 ppm, respectively. The spectrum of EtMgBr–**3** showed a peak due to CH_2Mg at 7.3 ppm.

Discussion

Previously we demonstrated that the asymmetric selective polymerization of (*RS*)-MBMA with *c*HexMgCl– or

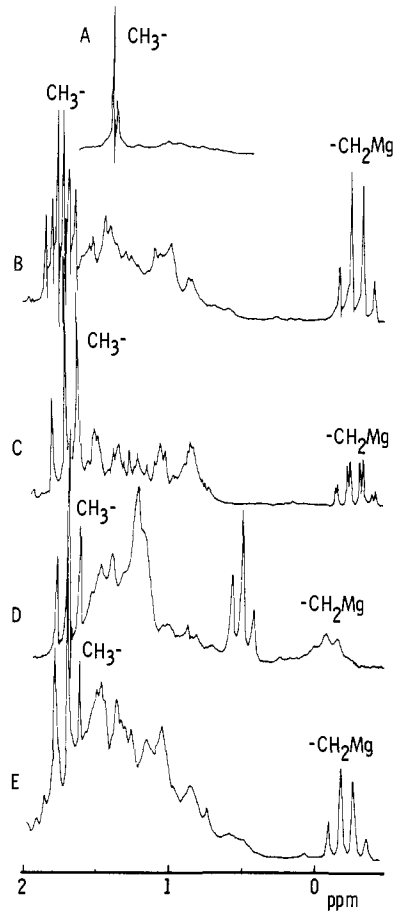


Figure 5. ^{1}H NMR spectra of *t*-BuMgCl–**1** (A), Et_2Mg–**1** (B), EtMgBr–**2** (C), EtMgBr–**3** (D), and EtMgBr–**4** (E) complexes in toluene-d_8 at 35 °C.

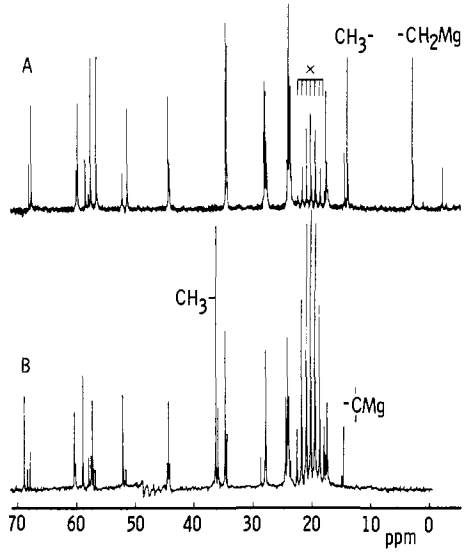


Figure 6. ^{13}C NMR spectra of EtMgBr–**1** (A) and *t*-BuMgCl–**1** (B) complexes in toluene-d_8 at 27 °C. (×: signals due to the solvent.)

cHexMgBr–**1** catalyst in toluene at −78 °C could be treated as a copolymerization of R and S monomers:[6d,e]

$$\sim S^-C^* + S \underset{}{\overset{K_{SS}}{\rightleftharpoons}} \sim S^-C^*S \xrightarrow{k_{SS}} \sim S^-C^*$$

$$\sim S^-C^* + R \overset{K_{SR}}{\rightleftharpoons} \sim S^-C^*R \xrightarrow{k_{SR}} \sim R^-C^*$$

$$\sim R^-C^* + S \overset{K_{RS}}{\rightleftharpoons} \sim R^-C^*S \xrightarrow{k_{RS}} \sim S^-C^*$$

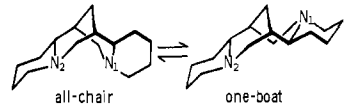
$$\sim R^-C^* + R \overset{K_{RR}}{\rightleftharpoons} \sim R^-C^*R \xrightarrow{k_{RR}} \sim R^-C^*$$

where $\sim S^-$ and $\sim R^-$ are polymer chains that have (*S*)- and (*R*)-MBMA units as growing ends, respectively, and C* is the counterion to which **1** coordinates. The enantiomer selectivity ratios, r_S ($= k_{SS}K_{SS}/k_{SR}K_{SR}$) and r_R ($= k_{RR}K_{RR}/k_{RS}K_{RS}$), have been estimated to be 33.7 and 0.27, respectively. These values indicate that enantiomer selection depends on the configuration of the ester group of the growing end; the *S* end polymerizes preferentially S monomer over R monomer by a factor of 33.7 and the *R* end also prefers S monomer, but only about fourfold. Using these values, we can determine how the optical yields of the polymer and unreacted monomer change with an increase of polymer yield starting from the racemic monomer.[6e] The data obtained with EtMgBr–, *i*-PrMgBr–, and *i*-BuMgBr–**1** catalysts (Table I) are well-fit to the theoretical curve for $r_S = 33.7$ and $r_R = 0.27$, indicating that these catalysts possess selectivities similar to those of cHexMgCl– and cHexMgBr–**1**. This also suggests that the difference in size between chlorine and bromine is not important, although iodine resulted in low selectivity.

Grignard reagents have been considered to exist as a mixture represented by the Schlenk equation:[15]

$$RMgX \rightleftarrows R_2Mg + MgX_2$$

In our polymerization with **1**–**6** as ligands, R_2Mg is unimportant because Et_2Mg–**1** catalyst showed no activity (Table I). Furthermore, the NMR data on EtMgBr complexes showed the absence of Et_2Mg complex. Conformation of free **1** is known to be the "one-boat" form[16] but changes to the "all-chair" form to



work as a bidentate ligand in the presence of metals.[2] This is also the case for the Grignard reagent complexes both in the solid state and in a toluene solution. However, this conformation change must be depressed at low temperature, because the complexation did not take place by mixing **1** with cHexMgBr at −78 °C (Table I).

The X-ray analyses of EtMgBr–**1** and *t*-BuMgCl–**1** indicate that the complexes in the solid state take a single form. In toluene, however, each complex exists as a mixture of two forms. The most probable structures are those in which the positions of alkyl group and halogen are reversed with each other. The space-filling molecular model (CPK) of **1** in the all-chair form is shown in Figure 7. The molecule has a cavity in which a magnesium ion can coordinate, and the upper part of the cavity is spatially more open than the lower part. The bromine in EtMgBr–**1** in the solid state occupies the upper part and the ethyl group the lower part. This form (A) may be predominant in toluene. On the other hand, in *t*-BuMgCl–**1** in the solid state, the *tert*-butyl group is in the upper part, probably because of its bulkiness, and the form B appears to be the major one in toluene. This assignment is also supported by the measurement of T_1 of *t*-BuMgCl–**1**. Since in toluene forms A and B are possible for both EtMgBr and *t*-BuMgCl, the extremely low activity of *t*-BuMgCl in the polymerization is ascribed to the steric factor. The bulk *tert*-butyl group, which covers the magnesium ion, likely prevents the monomer from getting in between the magnesium ion and the *tert*-butyl group. The CPK model of **2** shows that its cavity is smaller than that of **1** (Figure 7). The upper part of **2** is the same as its lower part due to C_2 symmetry, and these parts are almost identical with the lower part of **1**. Therefore, the open upper part of **1** must be responsible for the catalytic activity of the Grignard reagent complexes.

The inactive catalyst EtMgBr–**4** takes form B in the solid state and exists in a single form in toluene, which is most likely form B. The cavity of **4** is slightly narrower than that of **1** because

(15) Coates, G. E.; Wade, K. "Organometallic Compounds"; Methuem: London, 1969; Vol. I, p 85.
(16) (a) Bohlmann, F.; Schumann, D.; Arndt, C. *Tetrahedron Lett.* **1965**, 2705. (b) Wiewiorowski, M.; Edwards, O. E.; Bratek-Wiewiorowska, M. D. *Can. J. Chem.* **1967**, *45*, 1447.

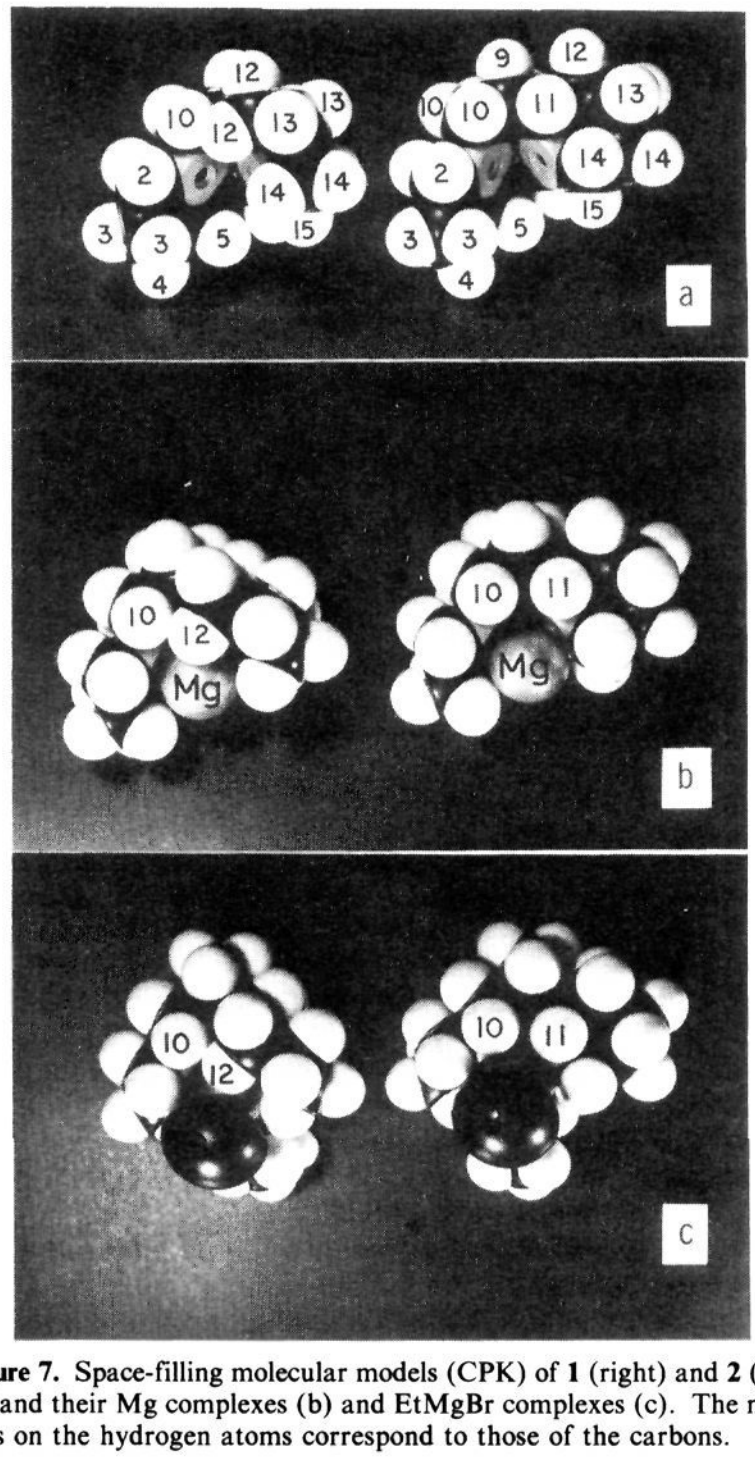


Figure 7. Space-filling molecular models (CPK) of **1** (right) and **2** (left) (a) and their Mg complexes (b) and EtMgBr complexes (c). The numbers on the hydrogen atoms correspond to those of the carbons.

of the existence of the 6-benzyl group, which forces the terminal six-membered rings to come closer together. This small difference in the cavities must be very important for the action of these ligands. It may be concluded that the active species of EtMgBr–**1** complex is in form A.

Then why must Grignard reagent–**1** be in form A to initiate the polymerization of MBMA? We have reported that the polymerization proceeds in a coordination mechanism; that is, the monomer always coordinates to an active center before being incorporated into a polymer chain end, and therefore the rate of the polymerization is independent of the monomer concentration.[6b,c] This means that at least five ligands coordinate to the magnesium in the process of the polymerization: one halogen, two nitrogens of **1**, one growing end, and one monomer. For this, four-coordinate form A must be altered to a five- or six-coordinate structure. One of the probable five-coordinate structures is schematically shown in Figure 8, in which the halogen is considered to occupy the open space of **1** and is pushed more to the inside of the cavity than in the EtMgBr–**1** complex. This structure may be possible only in form A. In the complexes involving **2** and those in form B, there seems to be no room for the halogen to move inside. Therefore, these complexes do not react with the monomer and remain unreacted in the polymerization system, even after a long time.[6c] Several five- and six-coordinate organomagnesium compounds have been reported.[17] The possibility of a four-coordinate growing end is also excluded by the following reason.

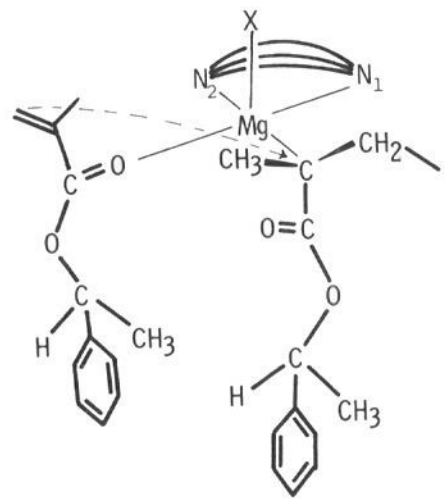


Figure 8. Schematical structure of an active center. N≡N and X represent **1** and halogen, respectively. The monomer is (*S*)-MBMA.

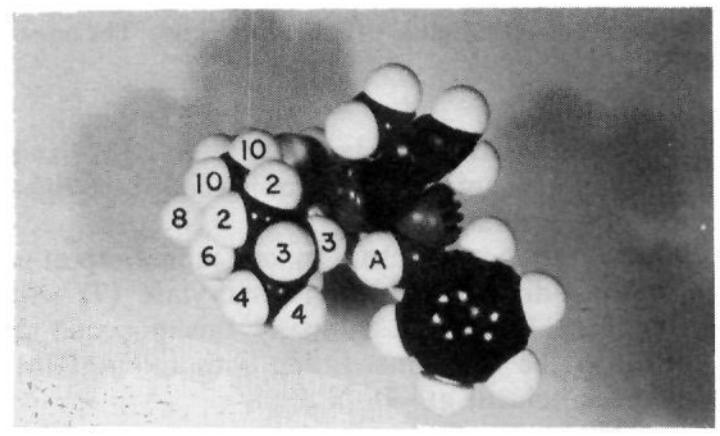


Figure 9. Molecular model of **1**, Mg, and (*S*)-MBMA.

The growing end is a more bulky tertiary center than *t*-BuMgCl, whose complex is four-coordinate and cannot initiate the polymerization because of steric hindrance. Consequently, if the growing end was four-coordinate, it could not add the monomer. In Figure 8, enantiomer selection should be controlled by two main interactions. One is the interaction between the ester group of the monomer and **1**, and the other is the interaction between the ester group of the monomer and the growing end.

Figure 9 shows the CPK model of **1** and (*S*)-MBMA that coordinate to Mg. Although exact conformation of the monomer has not yet been determined owing to the difficulty of obtaining a proper crystal for X-ray analysis, here we assume that the large phenyl group is placed at the remote position from the carbonyl group and two smaller groups, methyl and hydrogen A, are in a staggered position. This conformation is analogous to those proposed for α-keto esters by Prelog.[18] The C=C double bond and C=O groups are in a trans position.[19] In the case of (*S*)-MBMA, the close position of the hydrogen on asymmetric carbon makes it easy for this monomer to coordinate to Mg and add to the growing end. However, in (*R*)-MBMA, the position of the hydrogen and methyl group are reversed, and the methyl group hits **1** in coordinating to Mg in the same way as shown in Figures 8 and 9. Therefore, since the growing end is situated at the right-hand side of **1** in Figure 7 and the monomer coordinates to Mg in the direction shown in Figure 8, (*S*)-MBMA will be more reactive. The coordination of S monomer to Mg seems to proceed exclusively in the same direction. Actually, the homopolymerization of optically pure (*S*)-MBMA with cHexMgCl–**1** yielded the polymer of 100% isotacticity.[6b] Therefore, the slightly lower than 100% isotacticity of the polymer obtained from racemic monomer may be caused by the incorporation of R monomer, which coordinates to Mg upside down to avoid the steric repulsion between **1** and its methyl group (Figure 10). The structure in which the positions of the growing end and monomer are reversed from those in Figure 8 may be less favorable because the left-hand

(17) (a) Percaud, M. C.; Ducon, M. J.; Vallino, M. *C.R. Hebd. Seances Acad. Sci., Ser. C* **1967**, *264*, 571. (b) Toney, J.; Stucky, G. D. *J. Organomet. Chem.* **1971**, *28*, 5. (c) Sarma, R.; Ramirez, F.; Narayanan, P.; McKeever, B.; Marecek, J. F. *J. Am. Chem. Soc.* **1979**, *101*, 5015.

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(19) Ukaji, T. *Bull. Chem. Soc. Jpn.* **1959**, *32*, 1275. (b) Kageyama, H.; Miki, K.; Tanaka, N.; Kasai, N.; Okamoto, Y.; Hatada, K.; Yuki, H. *Markomol. Chem.*, in press.

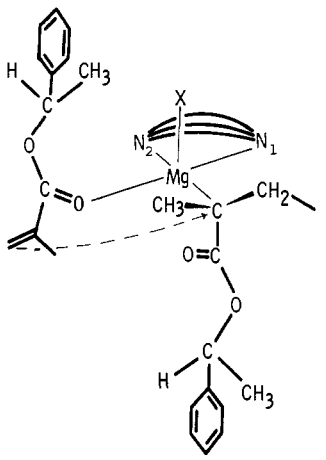
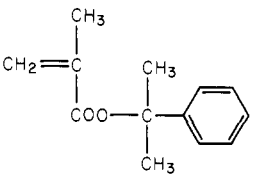


Figure 10. Schematical structure of an active center. The monomer is (*R*)-MBMA.

side of **1** is more sterically hindered than the right-hand side. Therefore, the existence of the bulky growing end at the right-hand side seems more favorable.

According to the above mechanism, one cannot expect polymerization of α,α-dimethylbenzyl methacrylate (**7**) with the Grignard reagent–**1** catalysts. Actually, this monomer showed no reactivity in the copolymerization with (*RS*)-MBMA by cHexMgCl–**1** in toluene at −78 °C.[6c]



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The cavities of **5** and **6** are less hindered than that of **1**. Therefore, most Grignard reagent complexes of these ligands initiated the polymerization of MBMA, but enantiomer selection became low compared with that of the complexes of **1**. The activity and selectivity of the catalysts are very sensitive to the ligands and the cations. Highly asymmetric selective polymerization of vinyl monomers seems to be attainable only under restricted conditions.

Acknowledgment. A part of this work was supported by a Grant-in-Aid for Scientific Research by the Ministry of Education.

Registry No. **1**, 90-39-1; EtMgBr-**1**, isomer 1, 82335-32-8; EtMgBr-**1**, isomer 2, 82335-33-9; *t*-BuMgCl-**1**, isomer 1, 82281-69-4; *t*-BuMgCl-**1**, isomer 2, 82335-34-0; Et_2Mg-**1**, 82281-70-7; **2**, 446-95-7; EtMgBr-**2**, 82281-68-3; **3**, 82209-19-6; EtMgBr-**3**, 82281-67-2; **4**, 82263-24-9; EtMgBr-**4**, 82281-66-1; **5**, 2130-67-8; **5** $2HClO_4$, 82209-20-9; **6**, 82209-21-0; *c*-HexMgCl, 931-51-1; *t*-BuMgCl, 677-22-5; EtMgBr, 925-90-6; *i*-PrMgBr, 920-39-8; *i*-BuMgBr, 926-62-5; *c*-HexMgBr, 931-50-0; PhMgBr, 100-58-3; *c*-HexMgI, 931-52-2; Et_2Mg, 557-18-6; (±)-MBMA, 19321-42-7; ethyl bromide, 74-96-4; benzyl bromide, 100-39-0.

Acyl Transfer Reactions in the Gas Phase. Ion–Molecule Chemistry of Vinyl Acetate

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Abstract: An ion cyclotron resonance study of the ion–molecule reactions of vinyl acetate with methanol in the gas phase has revealed the formation of structurally different ions having the composition of protonated vinyl acetate. Deuterium-labeled reactants ($CD_3CO_2CH{=}CH_2$ with CH_3OH or CD_3OD) gave product ions showing incorporation of up to two deuteriums in the vinyl group, indicating coexistence and interconversion of O-protonated and C-protonated vinyl acetate. Evidence was also obtained for a third MH^+ ion for which the proposed structure is protonated 3-oxobutanal. This ion is believed to be formed by attack of CH_3CO^+ at the terminal vinylic carbon with loss of the ester acyl group as ketene. The ion reacts with methanol to give m/z 101 by loss of water. In contrast, protonated vinyl acetate reacts with methanol by an acyl transfer process to give $(AcOCH_3)H^+$, m/z 75. The related ion chemistry of vinyl propanoate, vinyl 2,2-dimethylpropanoate, and isopropenyl acetate is also described. Each of the acyl transfer reactions observed is consistent with formation of intermediate acylium ion complexes rather than tetracovalent addition complexes. Attempts were made to generate tetracovalent intermediates by an independent route from ortho esters of vinyl acetate. Dissociation of the ortho ester $CH_3C(OCH{=}CH_2)_2(OCH_3)$ to dioxacarbocations was the dominant reaction, but the product ions were unreactive with H_2O, CH_3OH, or t-C_4H_9OH. The mechanistic implications of these results are discussed.

Acyl transfer reactions are among the most important reactions in organic and bioorganic chemistry and, for this reason, have been studied intensively with respect to their scope and mechanisms. A wealth of data exists on acid-catalyzed bimolecular acylation of nucleophiles ($A_{Ac}2$ in the Ingold notation) that supports an addition–elimination pathway involving tetrahedral addition intermediates.[1] Related ion–molecule reactions occur in the gas phase and have been the object of several investigations by ion-cyclotron resonance (ICR) techniques.[2] Recently, we reported evidence that $A_{Ac}2$ reactions in the gas phase under ICR conditions do not involve tetrahedral addition intermediates but rather proceed by way of acyl cation transfer, as in eq 1.[3] With one

$$HY + AcXH^+ \rightarrow [HY{\cdots}Ac^+{\cdots}XH] \rightarrow AcYH^+ + HX \quad (1)$$

(1) (a) Ingold, C. K. "Structure and Mechanism in Organic Chemistry"; Cornell University Press: Ithaca, NY, 1953; Chapter 14. (b) For a review, see: Euranto, E. K. In "The Chemistry of Carboxylic Acids and Esters"; S. Patai, Ed.; Interscience: New York, 1969; Chapter 11.

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