

Synthetic Application of Benzothiazole Ring System as an On-Off Type of Leaving Group. Synthesis of Ketones and Carboxylic Acid Derivatives from 2-(1-Substituted 1-Hydroxyalkyl)- and 2-(1-Hydroxyalkyl)benzothiazoles

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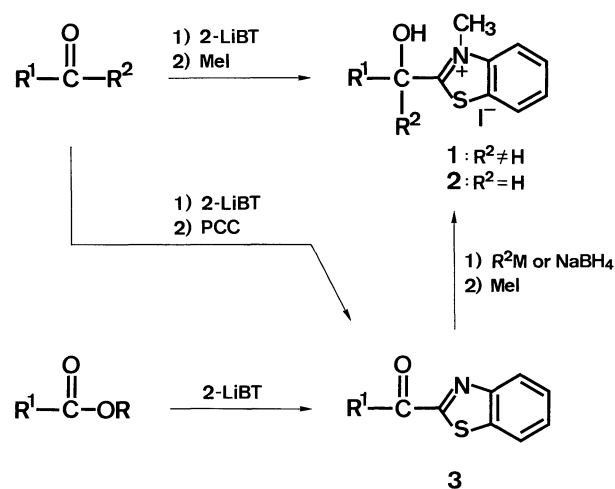
A synthetic and systematic use of benzothiazole ring system as an "on-off" type of leaving group was developed for the preparation of ketones and carboxylic acid derivatives from a variety of 2-(1-substituted 1-hydroxyalkyl)- and 2-(1-hydroxyalkyl)benzothiazoles (off state) via the corresponding benzothiazolium salts (on state) obtained by the quaternization (on switch). A variety of 3-methyl-2-(1-substituted 1-hydroxyalkyl)benzothiazolium iodides (**1**) underwent a carbon-carbon bond cleavage at the 2-position to give the corresponding ketones on the simple treatment with a base under mild reaction conditions. The similar reaction of 3-methyl-2-(1-hydroxyalkyl)benzothiazolium iodides (**2**) to aldehydes proceeded less efficiently. The oxidative reaction of a variety of **2** with base and nonactivated MnO_2 in ethanol afforded the corresponding ethyl esters. This type of oxidative reaction could be also achieved in THF with different nucleophiles such as alcohol, water, thiol, and amine to give the corresponding ester, carboxylic acid, thioester, and amide, respectively.

Thiamine pyrophosphate (TPP) is a coenzyme which participates in a number of important biochemical reactions involving formation and cleavage of carbon-carbon bonds as well as oxidation reactions.¹⁾ The catalytic unit of TPP on these reactions is the thiazolium ring. It is known that various simple thiazolium salts effect TPP type of transformations even in the absence of enzyme,²⁾ and up to now much interest has been focused on model reaction systems of TPP coenzyme.³⁾ From the standpoint of synthetic chemistry, these reactions can be regarded to offer a unique example of a heterocyclic molecule acting as an efficient leaving group because the release of the thiazolium salt unit as a thiazolium ylide by carbon-carbon bond fission is a key step and plays an essential role in the model systems. Although reaction intermediates derived from thiazolium salt catalysts have recently been of interest from a synthetic viewpoint,⁴⁾ there is little study dealing with synthetic and systematic applications of thiazole ring system by utilizing potential reactivities of the intermediate-like stable compounds themselves such as 2-(1-hydroxyalkyl)thiazolium salts. In our recent studies on benzazole field, we found several functionalities of the benzothiazole ring system available for organic synthesis and reported their applications to the novel synthetic methodologies.⁵⁾ In connection with these studies, we now investigated the preparation and reactivities of a variety of 2-(1-substituted 1-hydroxyalkyl)- and 2-(1-hydroxyalkyl)benzothiazolium salts structurally related to the intermediates on the TPP-model reactions and found that ketones and carboxylic acid derivatives were systematically obtained via these salts from the corresponding benzothiazole derivatives, revealing a novel functionality of benzothiazole ring system as an "on-off" type of leaving group. As a different type of systematic use of benzothiazole ring system in organic synthesis, we wish to report here a novel preparation method for ketones and carboxylic

acid derivatives based on this concept of leaving group.

Results and Discussion

Preparation and Properties of 3-Methyl-2-(1-substituted 1-Hydroxyalkyl)- and 3-Methyl-2-(1-hydroxyalkyl)benzothiazolium Iodides (1** and **2**).** Benzothiazolium salts **1** and **2** were prepared as outlined in Scheme 1. The two typical procedures for large scale preparation of **1** and **2** are the following: (i) The reaction of lithiated benzothiazole (2-LiBT) with ketones and aldehydes followed by quaternization of the resulting 2-(1-substituted 1-hydroxyalkyl)- and 2-(1-hydroxyalkyl)benzothiazoles with methyl iodide in DMF; and (ii) the acylation of 2-LiBT with esters and the subsequent alkylation with organometallic reagents or hydride reduction of the resulting 2-acylbenzothiazole **3** under standard conditions, followed by the quaternization with methyl iodide in DMF. As shown in our previous paper,^{5f)} each step in both methods proceeds in high

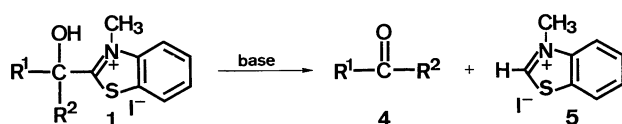


Scheme 1.

Table 1. Conversion of Benzothiazolium Salt **1a** into Acetophenone (**4a**)

Entry	Base (equiv)	Solvent	Temp/°C	Time/h	Isolated yield/%
1	K ₂ CO ₃ (1.5)	H ₂ O/ethanol	Reflux	7	92
2	K ₂ CO ₃ (1.5)	H ₂ O/hexane	60	2	95
3	AcONa (3.0)	H ₂ O/hexane	60	2	91
4	DBU (1.0)	Ethanol	r.t.	2	86
5	DBU (0.2)	Ethanol	Reflux	2	90
6	TEA (1.0)	Ethanol	r.t.	2	89
7	None	90% aq Ethanol	Reflux	72	77 ^{a)}

a) 3-Methylbenzothiazolium iodide (**5**) was isolated in 83% yield.



- a** : R¹=Ph, R²=Me
b : R¹=Ph, R²=Ph
c : R¹=n-C₆H₁₃, R²=Me
d : R¹=n-Pr, R²=Ph
e : R¹=, R²=Me
f : R¹-R²=(CH₂)₁₁-
g : R¹-R²=(CH₂)₅-
h : R¹=PhCH=CH-, R²=Ph

Scheme 2.

yields and benzothiazolium salts **1** and **2** are obtained in good total yields. In addition, benzothiazolium salt **1** could be easily prepared from aldehydes via 2-acylbenzothiazole **3** obtained by the reaction with 2-LiBT followed by pyridinium chlorochromate (PCC) oxidation. Benzothiazolium iodides **1** and **2** are generally obtained as very stable crystalline compounds and can be easily purified by recrystallization from methanol.

Ketone- and Aldehyde-Generating Reactions of 1 and 2. We started our studies by examining the ketone-generating reaction of the salt **1a** under a variety of reaction conditions (Scheme 2). The results are summarized in Table 1. When **1a** was homogeneously treated with 1.5 equiv of 10% aqueous K₂CO₃ in ethanol under refluxing, acetophenone (**4a**) was obtained in excellent yield after a 7-h reaction time (Entry 1). However, heterogeneous reaction by stirring the two-layer mixture consisting of **1a**, hexane, and 1.5 equiv of 10% aqueous K₂CO₃ at lower temperature was found to be more effective and ketone **4a** was obtained in nearly quantitative yield after shortened reaction time (Entry 2). In this reaction, 10% aqueous K₂CO₃ could be replaced by a weaker base such as 10% aqueous AcONa, and excellent yield of ketone **4a** was obtained under similar reaction conditions (Entry 3). On the other hand, we have found that organic bases such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or triethylamine (TEA) were also effective for this type of cleavage reaction. Thus, the treatment of **1a** with 1 equiv of DBU or TEA in ethanol at room temperature afforded ketone **4a** in high yield (Entries 4,6). The use of a catalytic amount of DBU (0.2 equiv) in ethanol at refluxing temperature was also useful for producing ketone **4a** from **1a** in excellent yield (Entry 5). Furthermore, it



Scheme 3.

was discovered that this acetophenone-generating reaction could proceed in the absence of bases by prolonged refluxing in 90% aqueous ethanol giving ketone **4a** in 77% yield together with 3-methylbenzothiazolium iodide (**5**) which was isolated in 83% yield (Entry 7). Although satisfactory results were obtained in all cases examined, the two-layer method using K₂CO₃ in hexane-water is the best reaction in terms of the yield of product and rapidity and cleanliness of the reaction. In fact, almost pure ketone **4a** could be obtained simply by evaporating the organic layer. In contrast to these, the cleavage of benzothiazolium salt **2a** by the methods employed for the cleavage of **1a** or by the heterogeneous reaction with aq NaOH and benzene in the presence of 6-aminohexanoic acid as a trapping agent produced benzaldehyde in generally very low yield (Scheme 3), although the homogeneous reaction in ethanol employing 10% aqueous K₂CO₃ afforded benzaldehyde in 30% isolated yield. In addition, it should be noted that the reactions employing DBU and TEA led to the formation of benzoin derived from 2 equiv of benzaldehyde. The reason for these unsuccessful results will be discussed later.

We next examined a general applicability of the ketone-generating reaction of a variety of 2-(1-substituted 1-hydroxyalkyl)benzothiazolium salts **1b–h** with the two-layer method using K₂CO₃ (Scheme 2). The results are summarized in Table 2. Benzothiazolium salts **1b–e** were all cleanly cleaved to the corresponding aliphatic and aromatic ketones **4b–e** and the reactions were completed within 2 h with nearly quantitative yields of the products (Entries 1–4). Cycloundecyl compound **1f** was similarly reacted to afford cycloundecanone (**4f**) in nearly quantitative yield, hence the reaction of cyclohexyl compound **1g** gave cyclohexanone (**4g**) in modest yield (Entries 5,6). On the other hand, the reaction of the benzothiazolium salt possessing a vinylic substituent, **1h**, under the present conditions did not produce the expected ketone,

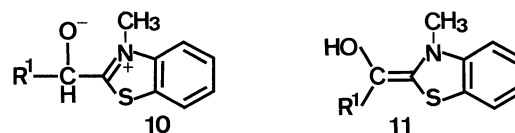
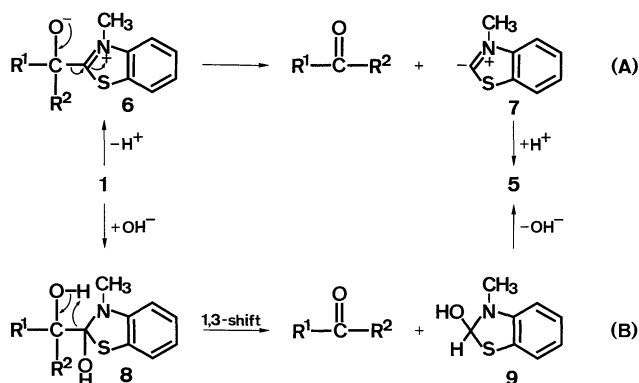
Table 2. Preparation of Ketones **4** from a Variety of 2-(1-Substituted 1-Hydroxyalkyl)benzothiazolium Salts **1**^{a)}

Entry	Salt 1	Product 4	Isolated yield/%
1	1b	4b	94
2	1c	4c	97
3	1d	4d	94
4	1e	4e	95
5	1f	4f	95
6	1g	4g	40
7	1h	4h	0

a) All reactions were carried out with the salts **1** (4 mmol) in two-layer mixture of hexane (4 ml) and 10% aqueous K₂CO₃ (8 ml) at 60°C for 2 h under stirring.

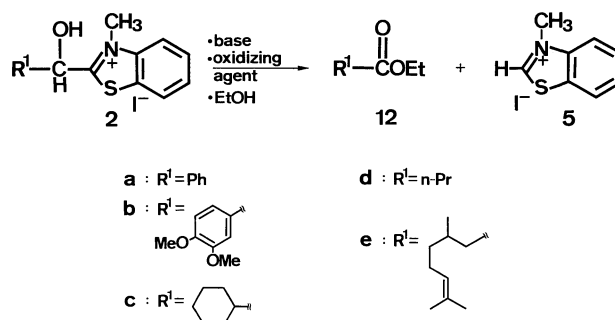
chalcone (**4h**), at all. Thus, the present method was found to be generally applicable to the synthesis of a variety of ketones except for α,β -unsaturated ketones.

Two possible reaction mechanisms for the present cleavage reaction of **1** can be proposed as illustrated in Scheme 4. They involve deprotonation at the HO-site by the base followed by leaving the ylide **7** from the resulting zwitterion intermediate **6** (mechanism A); and hydroxylation at the benzothiazolium ring followed by leaving 2-hydroxy-3-methyl-2,3-dihydrobenzothiazole **9** from the dihydroxy intermediate **8** via 1,3-shift (mechanism B). In the chemistry of thiazolium salt catalyzed reactions, however, the mechanism involving the regeneration of a thiazolium ylide by carbon-carbon bond fission at the 2-position of the thiazolium ring in 2-(1-hydroxyalkyl)thiazolium intermediates has been accepted. In the present case, this type of mechanism is also supported by the fact that the reactions using tertiary amines in a nonaqueous system could proceed in excellent yields. Accordingly, mechanism A via active-aldehyde like intermediate **6** is most likely mechanism for the present ketone-generating reaction and well conforms to the driving force for the formation of the stable benzothiazolium ylide **7**. In addition, this type of mechanism releasing the ylide **7** has been reasonably proposed for the aldehyde formation in the reaction of **2** with organometallic reagents.^{5f)} On the other hand, the reaction of **2** in the presence of a base would cause rather



complicated equilibria derived from the reactivity of so called "active-aldehyde" molecules **10** and **11** on the analogy of model reactions of TPP coenzyme.²⁻⁴⁾ The unsuccessful results in the case of an aldehyde-generating reaction of **2** are well understood based on the formation of these complicated and indiscriminate equilibria.

Oxidative Ester-Generating Reaction of 2. Treatment of benzothiazolium salt **2** with a base would easily produce the foregoing active-aldehyde molecules **10** and **11** which are intermediates similar to those in TPP-dependent enzymatic pathway and in its catalytic model reactions. It is well known that active-aldehyde molecules in later cases are oxidized in the presence of a variety of oxidizing agents (e.g., flavin or K₃Fe(CN)₆) to afford carboxylic acids, esters, or benzoin type of products depending on the reaction conditions.^{3,4)} If the intermediate **10** or **11** possessing a variety of substituents can be oxidized controllably in an alcoholic solvent, this would provide a different type of useful application of benzothiazolium unit as a leaving group for the preparation of esters **12** in organic synthesis (Scheme 5). We have first examined this type of oxidative ester-generating reaction of **2a** in ethanol in the presence of a base by employing 10 equiv of nonactivated MnO₂ and K₃Fe(CN)₆ as convenient oxidizing agents. As shown in Table 3, all the reactions examined afforded the expected ester, ethyl benzoate (**12a**), even in the absence of a base. Among the series of reactions employing MnO₂ as an oxidizing agent (Entries 1-8), the reaction with 1 equiv of AcONa was found to give the best results affording ester **12a** in 76% isolated yield (Entry 4), while the reaction with relatively strong bases such as K₂CO₃ and Na₂CO₃ or tertiary amines such as DBU and TEA generally gave the product **12a** in modest yield. The result of the reaction in the absence of a base may indicate that compound **2a** itself can be directly oxidized under the present conditions (Entry 8). On the other hand, the reaction employing K₃Fe(CN)₆ in the presence of 1 equiv of AcONa proceeded less effectively



to give ester **12a** in low yield (Entries 9,10). Thus, this type of oxidative ester synthesis was then applied to several different benzothiazolium salts **2b–e** under the optimum conditions, with the results summarized in Table 4. Benzothiazolium salts possessing a 2-(substituted hydroxymethyl) group, **2b,c,e**, reacted well under the conditions to give the corresponding ethyl

Table 3. Conversion of Benzothiazolium Salt **2a** into Ethyl Benzoate (**12a**)^{a)}

Entry	Oxidizing agent ^{b)}	Base (equiv)	Isolated yield/%
1	MnO ₂	K ₂ CO ₃ (1.0)	49
2	MnO ₂	K ₂ CO ₃ (3.0)	53
3	MnO ₂	Na ₂ CO ₃ (1.0)	41
4	MnO ₂	AcONa (1.0)	76
5	MnO ₂	AcONa (3.0)	64
6	MnO ₂	TEA (1.0)	45
7	MnO ₂	DBU (1.0)	56
8	MnO ₂	None	45
9	K ₃ Fe(CN) ₆ ^{c)}	AcONa (1.0)	22
10	K ₃ Fe(CN) ₆	AcONa (1.0)	28

a) All reactions were carried out in ethanol at reflux temperature for 5 h. b) Ten equiv of oxidizing agent was used unless otherwise noted. c) Two equiv of K₃Fe(CN)₆ was used.

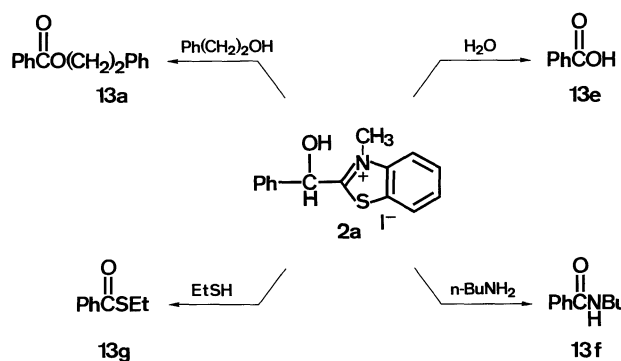
Table 4. Preparation of Esters **12** from a Variety of 2-(1-Hydroxyalkyl)benzothiazolium Salts **2a**)

Entry	Salt 2	Product 12	Isolated yield/%
1	2b	12b	78
2	2c	12c	52
3	2d	12d	17
4	2e	12e	70

a) All reactions were carried out with the salts **2** (2 mmol), MnO₂ (10 mmol), and AcONa (2 mmol) in ethanol (30 ml) at reflux temperature for 5 h.

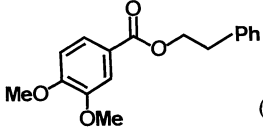
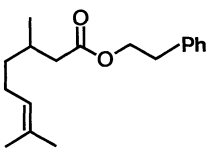
esters **12b,c,e** in good isolated yields (Entries 1,2,4), although the reaction with **2d** exceptionally showed low yield of product **12d** (Entry 3).

Oxidative Preparation of Carboxylic Acid Derivatives from **2 in Nonnucleophilic Solvent.** If it is possible that the active-aldehyde molecule **10** or **11** is also generated and oxidized efficiently in a nonnucleophilic solvent system, the reaction can be carried out in the presence of a variety of nucleophiles. To examine this possibility, we have carried out the reaction of **2** in THF in the presence of AcONa (1 equiv), MnO₂ (10 equiv), and an excess amount of alcohol at refluxing temperature. The results are summarized in Table 5. The reaction of **2a** with a large excess amount of ethanol in THF efficiently proceeded under the conditions to afford ethyl ester **12a** in good yield. Similarly, **2a,b,d,e** reacted with 3 equiv of 2-phenylethanol in THF to give the corresponding phenethyl esters **13a–d**. These results clearly show that the formation of active-aldehyde molecule **10** or **11** and its subsequent oxidation by MnO₂ followed by the reaction with an alcohol can proceed in THF as well as in ethanol solvent. We next tried the preparation of the carboxylic acid derivatives by the reaction of **2a** in the presence of several different nucleophiles as a



Scheme 6.

Table 5. Preparation of Esters from a Variety of 2-(1-Hydroxyalkyl)benzothiazolium Salts **2** in THF^{a)}

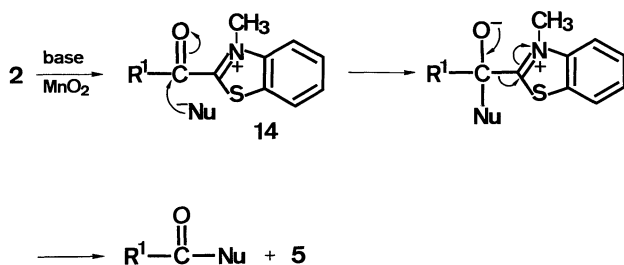
Entry	Salt 2	Nucleophile	Product	Isolated yield/%
1	2a	EtOH ^{b)}	12a	73
2	2a	Ph(CH ₂) ₂ OH ^{c)}	PhCO ₂ (CH ₂) ₂ Ph (13a)	54
3	2b	Ph(CH ₂) ₂ OH	 (13b)	35
4	2d	Ph(CH ₂) ₂ OH	<i>n</i> -C ₅ H ₁₁ CO ₂ (CH ₂) ₂ Ph (13c)	21
5	2e	Ph(CH ₂) ₂ OH	 (13d)	52

a) All reactions were carried out with the salts **2** (2 mmol), MnO₂ (10 mmol), and AcONa (2 mmol) in THF (30 ml) at reflux temperature for 5 h. b) Large excess amount of ethanol (10 ml) was used. c) In all cases, 3 equiv of 2-phenylethanol was used.

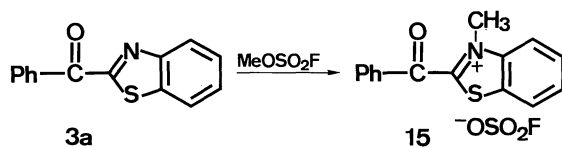
representative example, as illustrated in Scheme 6. The reaction of **2a** in the presence of an excess amount of water at refluxing temperature gave benzoic acid (**13e**) in 76% isolated yield, while the reaction with 3 equiv of butylamine at 60 °C and the reaction with 3 equiv of ethanethiol at 38 °C also produced the corresponding amide **13f** and thioester **13g** in 42% and 57% isolated yields, respectively. However, it should be noted that the similar reaction employing a secondary amine affording a secondary amide was unsuccessful in contrast to the reaction with a primary amine.

The mechanism of the present oxidative reactions can be explained according to that proposed in a TPP-dependent enzymatic pathway and in its catalytic model reactions (Scheme 7).^{3,4} However, so-called "active acyl" molecule such as **14** which is the key species to react with nucleophiles in the mechanism has not been isolated yet. We tried the direct synthesis of the active-acyl compound **15** by the *N*-methylation of 2-benzoylbenzothiazole **3a** (Scheme 8). Although the *N*-methylation of **3a** by the standard method using methyl iodide or dimethyl sulfate was very difficult due to the low nucleophilicity at the nitrogen atom, we have found that the *N*-methylation of **3a** with the powerful methylating reagent, methyl fluorosulfate, in dichloromethane at 100 °C proceeds efficiently to give the salt **15** in excellent isolated yield. The compound **15** is slightly unstable in air but can be stored in vacuo for several days. When compound **15** was treated in ethanol under refluxing, ethyl benzoate (**12a**) could be obtained in 85% isolated yield. Similarly, compound **15** reacted with an excess amount of water and butylamine in THF to give benzoic acid (**13e**) and *N*-butylbenzamide (**13f**) in 63% and 56% isolated yields, respectively. This result directly indicates that the active-acyl intermediate **14** can efficiently react with nucleophiles giving the corresponding carboxylic acid derivatives.

Summary. Synthesis of carbonyl compounds from 2-(1-substituted 1-hydroxyalkyl)- and 2-(1-hydroxyalyl)-



Scheme 7.



Scheme 8.

benzothiazoles (**16** and **17**) via the corresponding benzothiazolium salts **1** and **2** developed in the present study is summarized as follows. The present study reveals that the benzothiazole ring unit can be used as an "on-off" type of leaving group in the synthesis of ketones and carboxylic acid derivatives under simple operations and mild reaction conditions. That is, benzothiazole unit (off state) was found to be able to act as a leaving group only after conversion (turning on) to benzothiazolium structure (on state) by the treatment with methylating agent (on switch). A simple advantage of this method is that the off-state compounds can be treated under a variety of severe conditions. For example, in the ketone synthesis, **16** (off state) can be regarded as a protected form for ketones because the parent ketones of **16** are regenerated via **1** (on state). In fact, benzothiazoles **16** survived the severe conditions commonly required for removal of other protecting groups.⁶ This type of protection requiring an activation step for deprotection is a new method in organic synthesis and is called "locked protection" (i.e., **16** as locked form, MeI as key, **1** as delocked form, and ketones as opened form).⁷ Similarly, in the ester synthesis, **17** (off state) can be considered to be a protected form for esters because the parent esters of **3** are regenerated via **2** and **14** (on states). We have already developed the synthetic application of functions of the benzothiazole ring system as a hydride- and enolates-transferring auxiliary, protecting group, and carbonyl equivalent.⁵ Thus, the present chemistry of the benzothiazole ring system as an "on-off" type of leaving group should prove a useful addition of function of the system in organic synthesis.

Experimental

Melting points were recorded on a Yanagimoto micro melting point apparatus and are uncorrected. ¹H NMR spectra were measured on a JEOL JNX PMX-60 spectrometer at 60 MHz with tetramethylsilane as an internal standard. IR spectra were recorded on a JASCO A-202 spectrophotometer. Gas chromatographic analyses were carried out on a Shimadzu Gas chromatograph GC-6AM equipped with a hydrogen flame ionization detector using glass columns (1.5 m) packed with 2% silicone OV-7 on Uniport HP (60–80 mesh). Silica gel (Wakogel C-300) was used for short-column chromatography (SCC).

Materials. 3-Methyl-2-(1-substituted 1-hydroxyalkyl)- and 3-methyl-2-(1-hydroxyalyl)benzothiazolium iodides (**1** and **2**) and 2-benzoylbenzothiazole (**3a**) were prepared according to the previously reported methods.^{5f} Methyl fluorosulfate was prepared by the literature procedure.⁸ Solvents were purified according to standard procedures. The other reagents were supplied as high-grade commercial products and used without further purification.

Product Analyses. Identification of ketones and carboxylic acid derivatives obtained in the present reactions was performed by spectroscopic (¹H NMR and IR) and GLC methods. These spectral and GLC data were in good agreement with those of the corresponding authentic samples.

General Procedure for the Preparation of Ketone 4 from 3-Methyl-2-(1-substituted 1-Hydroxyalkyl)benzothiazolium Iodide (1). To a two-layer mixture of hexane (4 ml) and 10% aqueous K_2CO_3 (8 ml) was added the benzothiazolium salt **1** (4 mmol) and the mixture was then stirred at 60 °C for 2 h. The aqueous layer was extracted with dichloromethane and the combined organic layer and the extract was dried over $MgSO_4$. Concentration of the solution under reduced pressure afforded almost pure ketone **4**.

Reaction of Benzothiazolium Iodide 1a in Aqueous Ethanol in the Absence of Base. A solution of the benzothiazolium salt **1a** (1.59 g, 4 mmol) in 90% aqueous ethanol (20 ml) was stirred under refluxing for 3 d and then concentrated under reduced pressure. The crystalline residue was triturated with ether, filtered, and washed thoroughly with ether. Recrystallization from methanol–acetone gave pure 3-methylbenzothiazolium iodide (**5**) (0.92 g, 83%): Mp 216–217 °C (decomp) (lit.^{5b}) 217 °C (decomp); 1H NMR ($DMSO-d_6$) δ =4.38 (s, 3H, NCH_3), 7.81 (m, 2H, Arom), 8.40 (m, 2H, Arom), and 10.42 (s, 1H, CH).

The combined filtrate and washings were dried over $MgSO_4$ and concentrated under reduced pressure to give almost pure acetophenone (**4a**) as a pale yellow oil (0.37 g, 77%).

General Procedure for the Oxidative Preparation of Ethyl Ester 12 from 3-Methyl-2-(1-hydroxyalkyl)benzothiazolium Iodide (2) in Ethanol. To a solution of the benzothiazolium salt **2** (2 mmol) in dry ethanol (30 ml), MnO_2 (1.74 g, 20 mmol) and $AcONa$ (0.16 g, 2 mmol) were added with stirring and the suspended mixture was then stirred under refluxing for 5 h. After cooling to room temperature, the insoluble materials were removed by filtration and the filtrate was concentrated under reduced pressure. The residue was diluted with hexane–dichloromethane and filtered through silica-gel pad (Wakogel C-300). Concentration of the filtrate under reduced pressure and SCC purification of the residue gave pure ester **12**.

General Procedure for the Oxidative Preparation of Carboxylic Acid Derivative 13 from 3-Methyl-2-(1-hydroxyalkyl)benzothiazolium Iodide (2) in THF. To a suspension of the benzothiazolium salt **2** (2 mmol) in dry THF (30 ml) was added MnO_2 (1.74 g, 20 mmol), $AcONa$ (0.16 g, 2 mmol), and a nucleophile (6 mmol) and the mixture was stirred under refluxing for 5 h. After cooling to room temperature, the insoluble materials were removed by filtration and the filtrate was concentrated under reduced pressure. The residue was diluted with hexane–dichloromethane and filtered through silica-gel pad (Wakogel C-300). Concentration of the filtrate under reduced pressure and SCC purification of the residue gave pure carboxylic acid derivative **13**.

Preparation of 2-Benzoyl-3-methylbenzothiazolium Fluorosulfate (15). A solution of 2-benzoylbenzothiazole (**3a**) (1.20 g, 5 mmol) in dry dichloromethane (10 ml) was mixed with methyl fluorosulfate (1.71 g, 15 mmol) in a glass tube and the mixture was then degassed several times in vacuo. The tube was sealed in vacuo and kept at 100 °C in an oil bath for 5 h (after about 1 h, yellow needles started to separate). The yellow crystalline product was collected by suction filtration, washed thoroughly with dry dichloromethane and then dried in vacuo to give almost pure salt **15** as yellow needles (1.66 g, 94%): Mp 85–87 °C (decomp). Found: C, 50.27; H, 3.74; N, 3.76%. Calcd for $C_{15}H_{12}NO_4S_2F$: C, 50.98; H, 3.42; N, 3.96%.

The Reaction of Active-Acyl Compound 15 in Ethanol. A mixture of compound **15** (0.71 g, 2 mmol) and dry ethanol (10 ml) was refluxed with stirring for 5 h and then concentrated

under reduced pressure. The residue was diluted with hexane–dichloromethane and filtered through silica-gel pad (Wakogel C-300). Concentration of the filtrate under reduced pressure and SCC purification of the residue gave pure ester **12a** in 85% yield.

The Reaction of Active-Acyl Compound 15 with Water and Butylamine in THF. To a suspension of compound **15** (0.71 g, 2 mmol) in dry THF (30 ml) was added water (1 ml) or butylamine (0.44 g, 6 mmol) and the mixture was then stirred under refluxing for 5 h under a nitrogen atmosphere. After cooling to room temperature, the insoluble materials were removed by filtration and the filtrate was concentrated under reduced pressure. The residue was diluted with hexane–dichloromethane and filtered through silica-gel pad (Wakogel C-300). Concentration of the filtrate under reduced pressure and SCC purification of the residue gave pure carboxylic acid derivative **13e** in 63% yield or **13f** in 56% yield.

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