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Development of Odorless Organosulfur Reagents and Asymmetric Reaction Using Odorless Thiols

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ABSTRACT: *Odorless organosulfur reagents were developed by increasing their molecular weights to suppress volatility. 1-Dodecanethiol (***4***), dodecyl methyl sulfide (***5***), p-heptylphenylmethanethiol (***6***), p-dodecylbenzenethiol (***7***), p-heptylbenzenethiol (***8***), 2-dodecyl-1,3-propanedithiol (***11***), p-octyloxyphenylmethanethiol (***18b***), and p-octyloxybenzenethiol (***19***) are typical examples of the odorless thiols and sulfides. 6-Morpholinohexyl thiol (***15***), methyl 6-morpholinohexyl sulfide (***16***), and methyl 6-morpholinohexyl sulfoxide (***17***) were also developed as separable reagents from reaction products by facile acid-base extraction. In addition, p-tetramethylsilylphenylmethanethiol (***18***) and p-tetramethylsilylbenzenethiol (***14***) were synthesized as the odorless synthetic substitutes of benzyl mercaptan and benzenethiol, respectively. In a similar way, silylated diphenyl disulfide (***26***) and diselenide (***27***) were prepared as odorless disulfide and diselenide. Moreover, 10-sulfanylisoborneol (***1***) was found to be an excellent chiral odorless substitute of hydrogen sulfide in Michael addition.* © 2007 Wiley Periodicals, Inc. Heteroatom Chem 18:572–583, 2007; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20348

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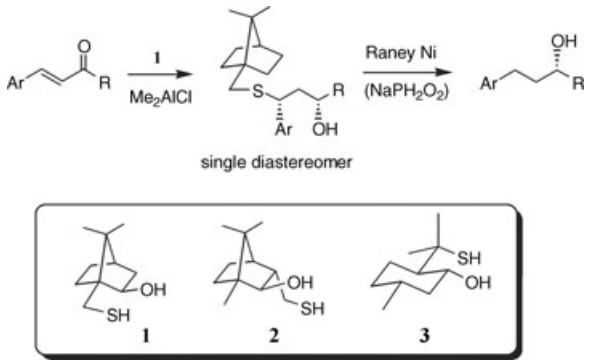
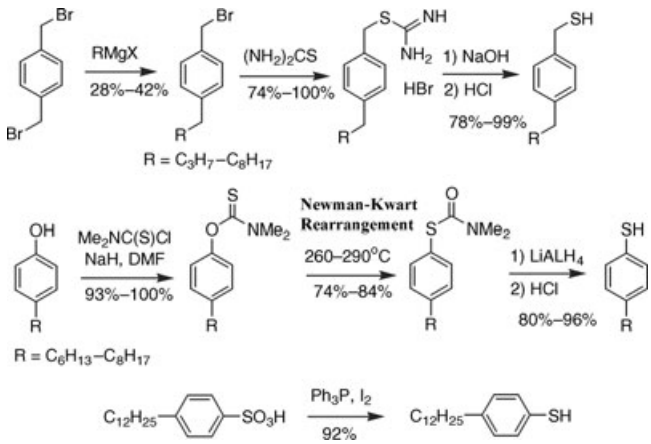
INTRODUCTION

Organosulfur reagents are indispensable in organic synthesis; however, the malodor of commonly used organosulfur reagents such as ethanethiol, benzyl mercaptans, benzenethiols, and dimethyl sulfide makes their use difficult and unpleasant. This shortcoming causes more serious problems in industry where these reagents are used on a large scale. The offensive odor control law for prevention of environmental pollution regulates the use of foul-smelling organosulfur reagents. Thus, development of odorless substitutes for the malodorous organosulfur reagents is desired, and several practical reagents have been reported in the last decade. For example, bulky benzenethiols [1] and sodium dithiocarboxylates [2] were developed as odorless substitutes that were applicable to demethylation reactions of aryl methyl ethers and methyl phosphates.

Recently, we found that 1,3-mercapto alcohols **1–3** do not have any malodor at all during our study on their asymmetric Michael addition to α,β-unsaturated ketones [3,4]. Therefore, the reactions in Scheme 1 could be performed without generating foul smell. Encouraged by this finding, we embarked on the development of odorless thiols. We herein report our recent studies on the development of new odorless organosulfur reagents that are used



SCHEME 1 Asymmetric Michael Addition using Chiral 1,3-Mercapto Alcohols.



SCHEME 2 Synthesis of odorless benzyl mercaptans and benzenethiols.

as substitutes for the foul-smelling ones, as well as their applications to organic synthesis and asymmetric reactions.

DEVELOPMENT OF ODORLESS THIOLS AND SULFIDES

We started our study with a test of the odor grade of various alkanethiols based on the fact that the odorless thiols **1–3** contain a monoterpenoid skeleton of 10 to 11 carbon atoms. 1-Alkanethiols, except 1-tetradecanethiol, listed in Table 1 are commercially available in spite of containing foul-smelling impurities. Thus, these thiols were purified by HPLC for the odor test. The relative odor index of thiols as perceived by two human testers is listed in the table, where the most malodorous thiol was evaluated as 5 and the odorless one was indexed as 0. Among these 1-alkanethiols, 1-dodecanethiol (**4**) was found to be completely odorless, whereas thiols carrying a shorter carbon chain were malodorous [5]. Therefore, the former was chosen as the odorless substitute of the foul-smelling alkanethiols for further studies.

TABLE 1 The Odor Scale for Alkanethiols

Entry	*Thiols*	*Carbon length*	*Odor scale*		*Bp (°C)*
			A	*B*	
1	CH_3CH_2SH	2	5	5	35
2	$CH_3(CH_2)_2SH$	3	5	5	67
3	$CH_3(CH_2)_3SH$	4	5	4	98
4	$CH_3(CH_2)_4SH$	5	4	3	126
5	$CH_3(CH_2)_5SH$	6	3	3	150
6	$CH_3(CH_2)_6SH$	7	4	3	173
7	$CH_3(CH_2)_7SH$	8	2	1	197
8	$CH_3(CH_2)_8SH$	9	2	1	220
9	$CH_3(CH_2)_9SH$	10	1	1	114/13 mmHg
10	$CH_3(CH_2)_{10}SH$	11	1	0	103/3 mmHg
11	$CH_3(CH_2)_{11}SH$ (4)	12	0	0	266
12	$CH_3(CH_2)_{13}SH$	14	0	1	298
13	$CH_3(CH_2)_{14}SH$	15	0	1	187/7 mmHg

In addition, we examined the odor of alkyl methyl sulfides, which were prepared by methylation of 1-alkanethiols listed in Table 1. Since the alkyl methyl sulfides having an alkyl chain of more than 12 carbon atoms were found to be odorless among the tested samples, dodecyl methyl sulfide (DMS, Dod-S-Me) (**5**) was chosen as the odorless substitute for dimethyl sulfides from the viewpoint of atom economy [6,7].

Next, we tried to develop odorless substitutes for malodorous benzyl mercaptans and benzenethiols. We prepared several samples bearing an alkyl chain at the *para*-position on the benzene rings. Their synthetic pathways are shown in Scheme 2, of which the key reactions include the formation of thiolonium salts and Newmann–Kwart rearrangement, respectively [5,8]. It is noteworthy that no foul-smelling reagents were involved in the whole synthetic pathway.

The odor scale for benzyl mercaptans is shown in Table 2, where phenyl and *tert*-butyl groups were respectively counted as four and two carbons in length. As a result, *p*-heptylphenylmethanethiol (**6**) was found to be odorless among the *para*-alkylated benzyl mercaptans and was chosen as an odorless substitute for benzyl mercaptans. In addition, it was observed that the *tert*-butyl group had a dramatic effect on odor reduction [5].

Moreover, the odor scale for *p*-alkylated benzenethiols is shown in Table 3. *p*-Dodecylbenzenethiol (**7**) was found to be odorless among the benzenethiol derivatives; however, thiol **7** derived

TABLE 2 The Odor Scale for Benzyl Mercaptans

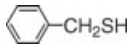
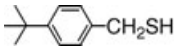
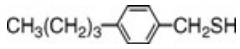
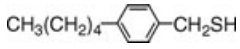
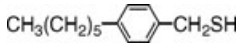
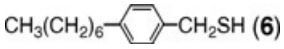
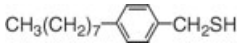
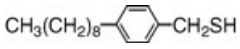
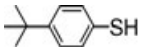
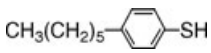
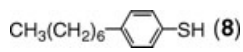
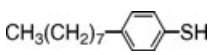
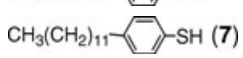
Entry	Thiols	Carbon length	Odor scale A	Odor scale B
1		5	5	5
2		7	1	1
3		9	2	1
4		10	2	1
5		11	0	1
6		12	0	0
7		13	1	0
8		14	1	1

TABLE 3 The Odor Scale for Thiophenols

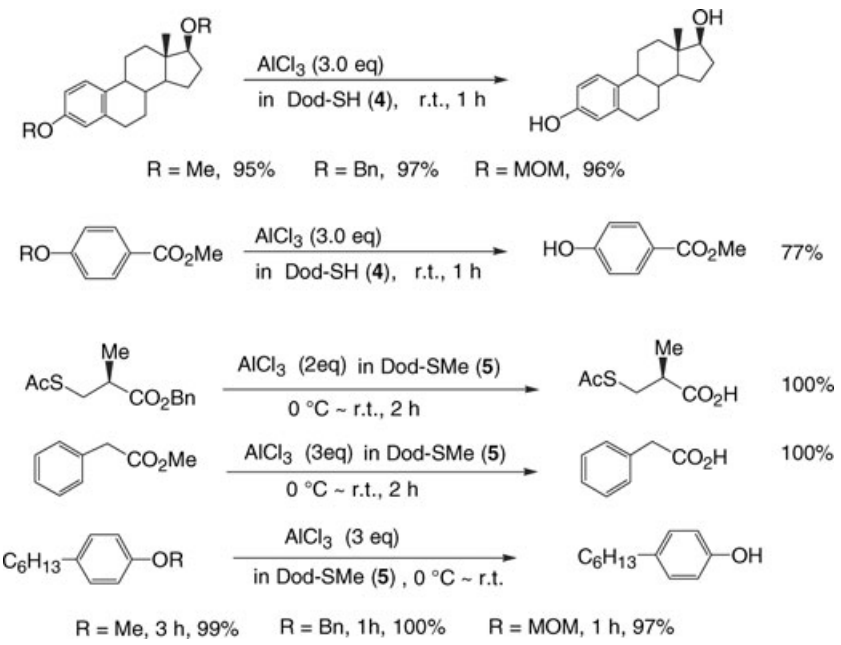
Entry	Thiols	Carbon length	Odor scale A	Odor scale B
1		4	5	5
2		6	2	1
3		10	0	2
4		11	1	0
5		12	1	1
6		16	0	0

from an industrial-grade material often contained a small amount of unseparable analogs having more or less a methylene group. Thus, *p*-heptylbenzenethiol (**8**) was chosen as the faint-smelling thiol for further studies.

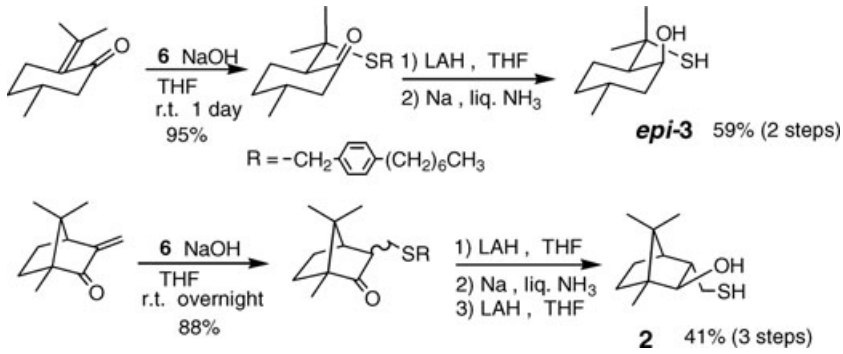
Some applications of the above odorless organosulfur reagents are shown in Scheme 3. Previously, we developed novel systems composed of a hard Lewis acid and a thiol as reagents for demethylation of aliphatic and aromatic methyl ethers [9]. Dealkylations of methyl, benzyl, and methoxymethyl (MOM) ethers using the odorless thiol **1** as substitute for the malodorous reagent in the system gave the corresponding alcohols and phenols in high yields as the reactions with the original reagent system [6]. Similarly, dodecyl methyl sulfide (DMS) **5** was applicable for dealkylation of alkyl (Me, Bn) esters and alkyl (Me, Bn, MOM) ethers (K. Nishide, S. Ohsugi, M. Node, unpublished results, 2003).

On the other hand, the odorless sulfide **5** could be employed instead of foul-smelling dimethyl sulfide in the Corey–Kim oxidation, an oxidation of alcohols using dimethyl sulfide and *N*-chlorosuccinimide, which gives products in high yields without generating any foul smell [6,7]. Similarly, the Swern oxidation was capable of being improved by using dodecyl methyl sulfoxide **9** prepared by the oxidation of DMS **5** as a substitute for dimethyl sulfoxide, and the modified reaction proceeded effectively as the conventional method without generating any malodor [6,7].

Moreover, we demonstrated that the odorless thiol **6** could be utilized as a substitute for benzyl



SCHEME 3 Application of odorless thiols and sulfides to dealkylation.



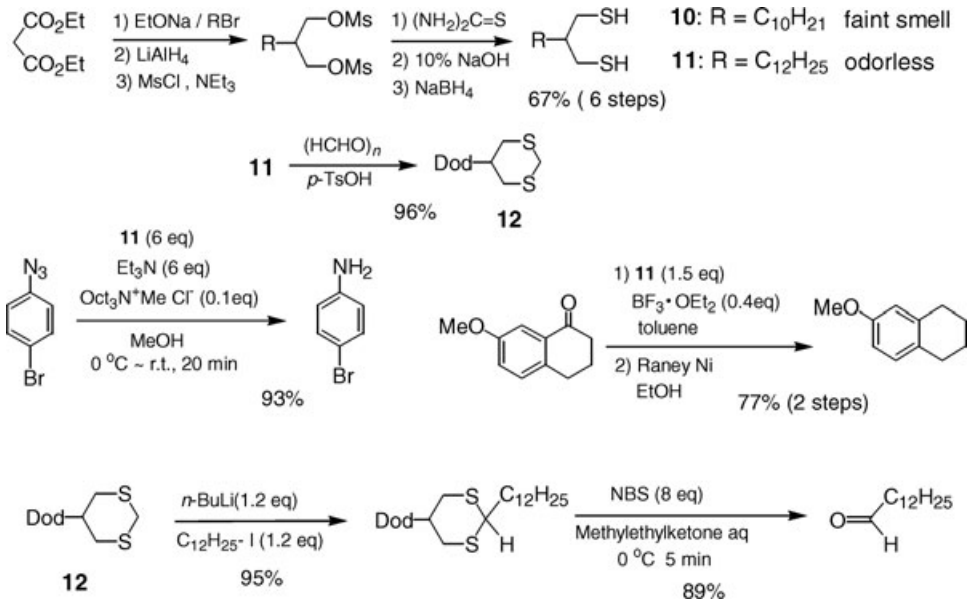
SCHEME 4 Application of odorless benzyl mercaptans to synthesis of mercapto alcohols.

mercaptans in a reductive Michael addition, where a formal conjugated addition of hydrogen sulfide to α, β-unsaturated ketones giving 1,3-mercapto alcohols (**2**, ***epi*-3**) was performed by a nuclephilic attack of the odorless thiol followed by a reductive cleavage of the benzylic carbon—sulfur bond and reduction of the ketone with sodium metal in liquid ammonia, as shown in Scheme 4 [5].

Since 1,3-propanedithiols and 1,3-dithianes have stronger malodor than the corresponding thiol, that is, propanethiol, we tested the odor grade of 2-alkylated propanedithiols that were prepared by the method of Shon et al. [10] as shown in Scheme 5 [11]. While 2-decyl-1,3-propanedithiol (**10**) has a faint smell, 2-dodecyl-1,3-propanedithiol (**11**) is an odorless reagent that could be used in place of 1,3-propanedithiols in organic reactions, for example, reduction of azides and protection of carbonyl groups. The 1,3-dithioacetals obtained in the latter reaction were effectively reduced to methylene groups with Raney nickel and reconverted to the original carbonyl compounds by hydrolysis with *N*-bromosuccinimide in aqueous 2-butanone. In addition, 1,3-dithiane **12** prepared from **11** and formaldehyde was found to be odorless, and the anion of **12** could be utilized as a synthetic equivalent of an anionic carbonyl carbon.

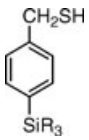
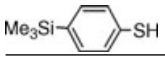
IMPROVED ODORLESS ORGANOSULFUR REAGENTS

Odorless thiols **6** and **7** could not be employed when introduction of benzylthio and phenylthio groups as functional groups was desired because no practical methods to remove the heptyl and dodecyl groups from benzene rings could be availed.



SCHEME 5 Preparation of odorless 1,3-propandithiols and their applications.

TABLE 4 The Odor Scale of Silylated Benzyl Mercaptans and Benzenthiol

Substrate	R	Odor scale A	Odor scale B
	Me (**13**)	0	1
	Et	1	1
	Pr	0	2
	(**14**)	1	1

Therefore, novel odorless thiols carrying a removable substituent on the phenyl and benzyl groups were next developed because the *tert*-butyl group on the benzene ring has an odor-reducing effect (see Table 2). Trialkylsilyl groups might contain removable protection groups to make benzenethiols and benzyl mercaptans nonodorous because of the probability of the odor-reducing effect such as that of the *tert*-butyl group and facility of desilylation reaction with acids, that is, protodesilylation. In fact, the silylated benzyl mercaptans have considerably lesser odor than benzyl mercaptans as shown in Table 4. Because the trimethylsilyl group on the benzene ring had a remarkable effect in reducing the foul smell and almost no differences depending upon the alkyl species were observed, trimethylsilylated thiols **13** and **14** were chosen as the faint-smelling thiols [12].

The Michael addition of **13** and **14** to α,β-unsaturated carbonyl compounds and the protodesilylation of the Michael adducts were performed to exemplify the utility of the silylated thiols. In fact, the Michael addition proceeds smoothly in the presence of a base, for example, tetrabutylammonium fluoride or triethylamine, and successive protodesilylation with trifluoroacetic acid realized the introduction of the benzylthio and phenylthio groups under odorless conditions as shown in Scheme 6.

The odorless alkanethiols and sulfides developed so far required chromatographic separation of products from the reagents in the reaction mixture. To

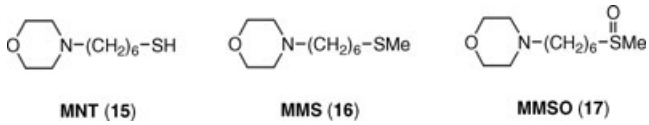


FIGURE 1 Improved odorless organosulfur reagents carrying a morpholino unit.

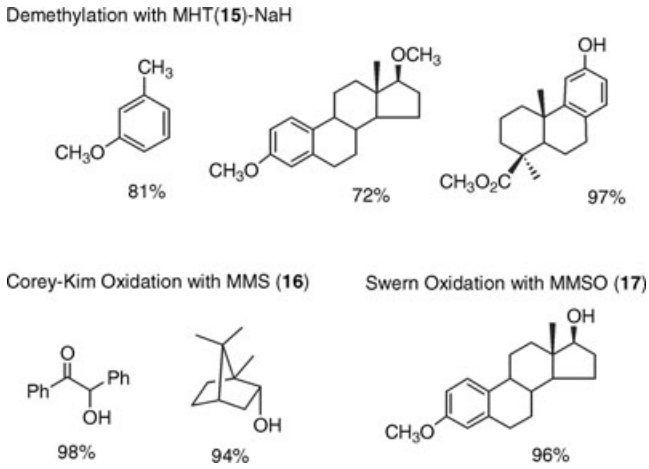
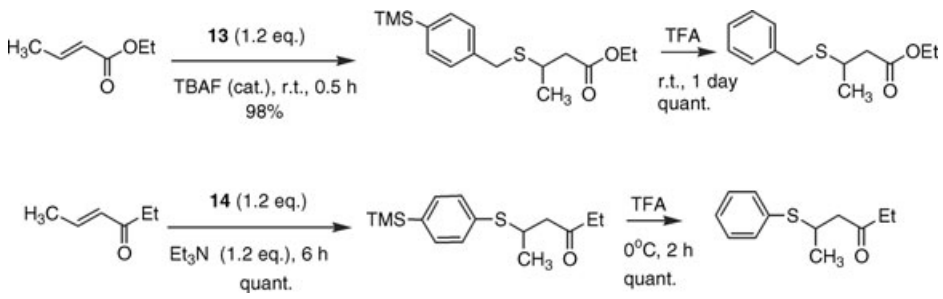


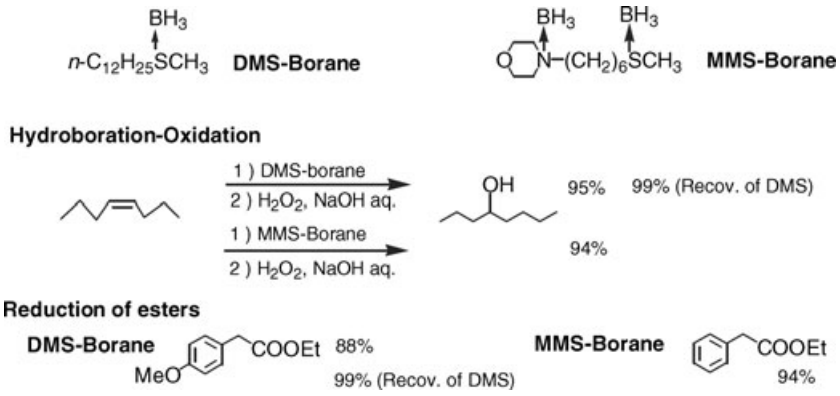
FIGURE 2 Applications of the improved odorless organosulfur reagents.

avoid the tedious procedure, a novel odorless alkanethiol bearing a morpholino group (MHT, **15**) was developed for their facile separation by conventional acid–base extraction. While designing a thiol, carbon length between the morpholino and mercapto groups is an important factor in reducing the odor. Furthermore, taking advantage of the basic property of morpholine, the other odorless organosulfur reagents, that is, sulfide **5** and sulfoxide **9**, were modified similarly as shown in Fig. 1. Both methyl sulfide (methyl 6-morpholinohexyl sulfide (MMS), **16**) and methyl sulfoxide (MMSO, **17**) derivatives were found to be odorless and reusable by the acid–base extraction [13].

Applications of the improved organosulfur reagents (MHT **15**, MMS **16**, and MMSO **17**) are shown in Fig. 2. Dealkylation of MHT (**15**) with sodium thiolate, Corey–Kim oxidation with MMS



SCHEME 6 Applications of silylated benzyl mercaptan and benzenethiol.



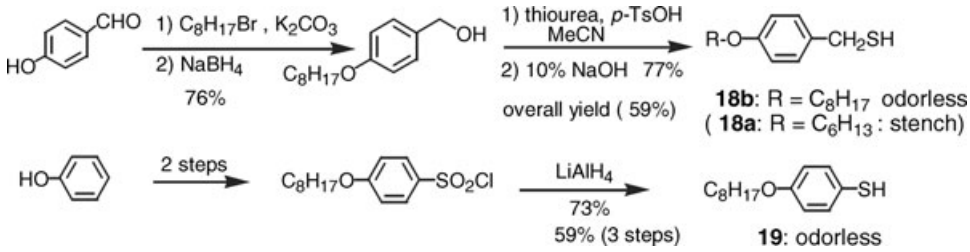
SCHEME 7 Boran complexes with odorless sulfides.

(**16**), and the Swern oxidation with MMSO (**17**) proceeded smoothly as the original reactions [13].

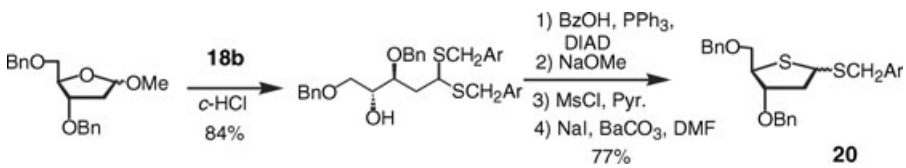
Moreover, DMS (**5**) and MMS (**16**) could be employed as efficient borane carriers. Scheme 7 shows their preparation and applications to hydroboration-oxidation and reduction of esters. These reactions were carried out in high yields and without generating any foul smell [14].

Benzenethiols and benzyl mercaptans have also been widely used in carbohydrate chemistry, a most active field of medicinal chemistry, for the synthesis of 1-thioglycosides and thiosugars. Especially, 1-thiosugars prepared with benzenethiols have been used as glycosyl donors in glycosylation reactions even in solid-phase synthesis or polymer-supported synthesis of bioactive oligosaccharides [15,16]. However, unpleasant odor accompanied with the preparation of 1-thioglycosides and during glycosylation reactions due to the liberated thiols. Making matters worse, neither the odorless thiols **8** nor **14** were convenient reagents for the preparation of 1-thioglycosides, as the low-yield synthesis of **8** and production of malodorous benzenethiol from **14** by the protodesilylation reaction in the presence of acids were essential for activating these 1-thioglycosides. Therefore, not only a benzenethiol derivative but also benzyl mercaptan derivatives having an alkyloxy group at the *p*-position were prepared in a facile manner as the new organosulfur reagents as shown in Scheme 8.

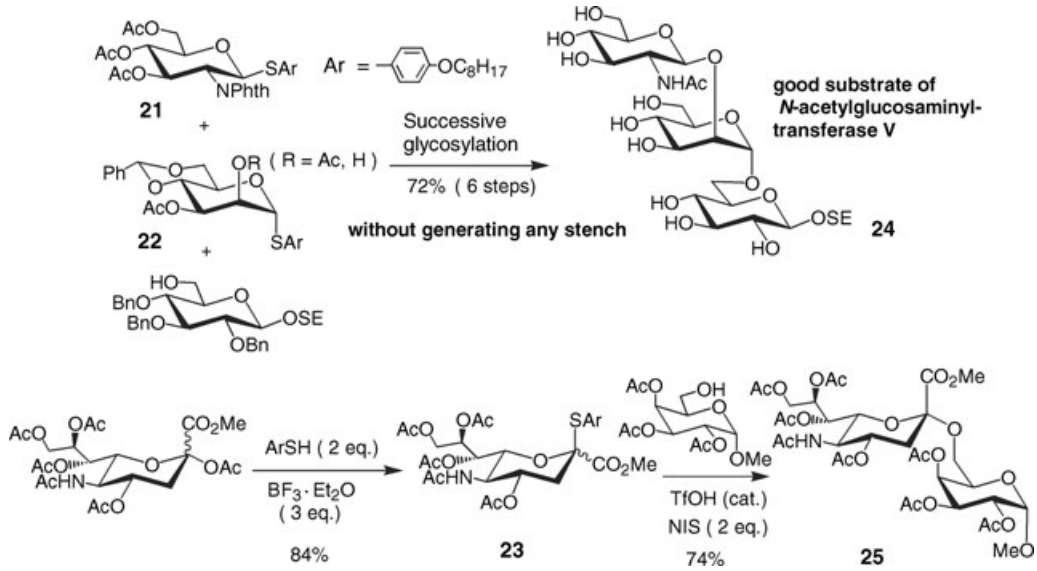
While *p*-hexyloxybenzyl mercaptan (**18a**) was malodorous, both *p*-octyloxybenzyl mercaptan (**18b**) and *p*-octyloxybenzenethiol **(19)** were odorless. As an example, mercaptan **18b** was effectively used in the synthesis of 4-thiopentofuranoses **20** as shown in Scheme 9 [8], and 1-thioglycosides **21–23**



SCHEME 8 Preparation of odorless benzylmercaptan and benzenethiol.



SCHEME 9 Application of benzyl mercaptan to synthesis of thiosugar.



SCHEME 10 Application to the synthesis of oligosaccharides.

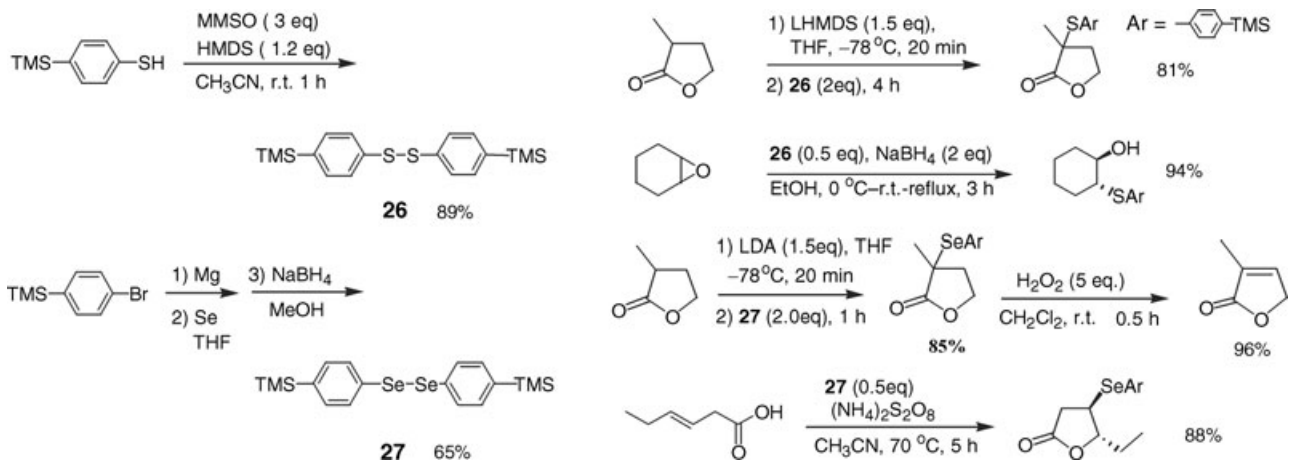
prepared from peracetates of monosaccharides and **19** were employed as excellent glycosyl donors in the synthesis of an oligosaccharide (**24**), including a silaloside **25**, as shown in Scheme 10 [17].

Finally, besides being odorless, diphenyl disulfides and diphenyl diselenides liberate malodorous benzenethiols and benzeneselenols during reactions such as sulfanylation and selenation. On the basis of our previous observation that the trimethylsilyl groups in **13** and **14** had an odor-reducing effect, we designed silylated diphenyl disulfide **26** and silylated diphenyl diselenide **27** that do not liberate unpleasant smell. As expected, reactions using disulfide **26** and diselenide **27** were attainable without generating foul smell, and the new reagents have the same reactivity in comparison with the original reagents as shown in Scheme 11 [18].

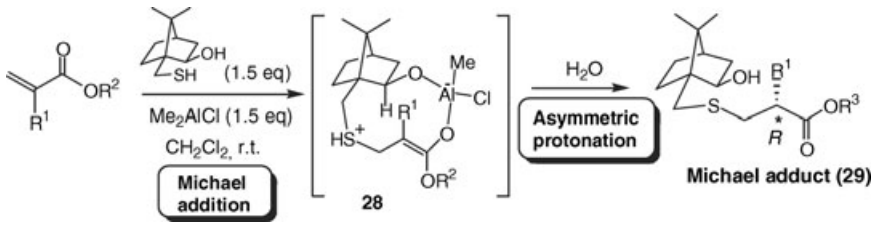
In a short conclusion so far, we have succeeded in developing new odorless organosulfur reagents that are excellent substitutes for malodorous reagents.

ASYMMETRIC REACTIONS USING ODORLESS THIOLS

1,3-Mercapto alcohols **1**, **2**, and **3** derived from optically active camphorsulfonic acid, camphor, and pulegone, respectively, were not only odorless but



SCHEME 11 Synthesis of bis[4-(trimethylsilyl)phenyl]disulfide (**26**) and -diselenide (**27**) and their application.

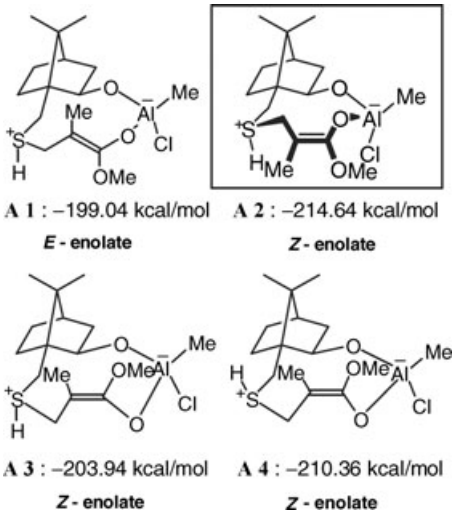


SCHEME 12 Strategy and results of asymmetric protonation in Michael addition.

also effective as chiral reagents for the asymmetric Michael addition to the α,β-unsaturated carbonyl compounds. Namely, in the asymmetric Michael addition of the chiral thiols to α-alkylated acrylates in the presence of dimethylaluminum chloride as Lewis acid, 1,4-adducts formed a 10-membered ring of aluminum enolate **28**, which could be converted to sulfides **29** by intramolecular protonation as shown in Scheme 12 [19].

Herein, it was presumed that the protonation at the α-carbon atom of the enolate **28** occurred with high diastereoselectivity, and the results are summarized in Table 5. Because the absolute configuration *R* of the resulting esters **29** was determined by the chemical conversion to known compounds, it was suggested in the beginning that the protonation to *E*-enolate took place from the outer face of the 10-membered ring. However, MOPAC PM3 calculations revealed that *Z*-enolate (A-2) was the most stable among the proposed four enolates (A-1 to A-4) having minimum values of free energy. Therefore, the protonation should occur from the inside of the 10-membered intermediate (A-2).

TABLE 5 Heat of Formation for Proposed Enolates A1-A4 Calculated by MOPAC PM3

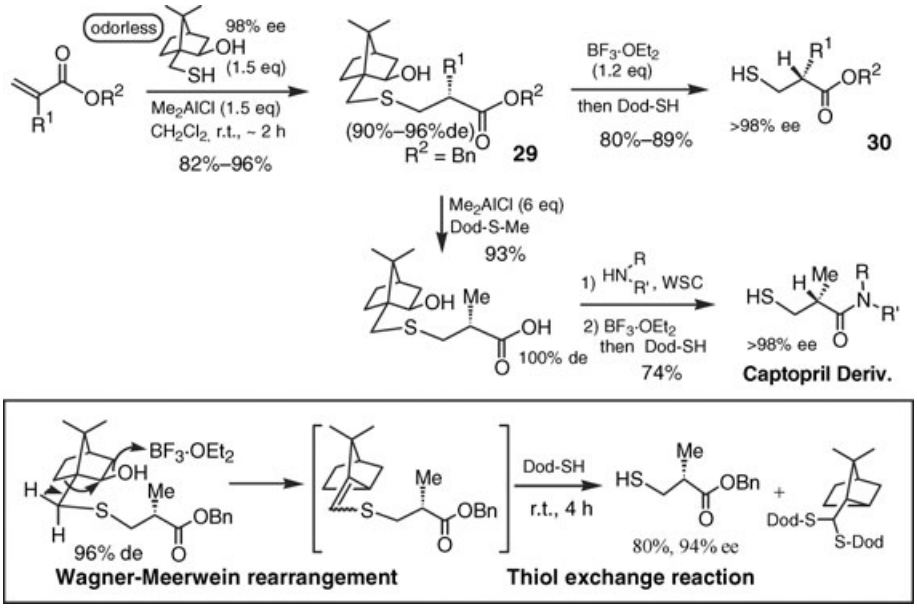


	Substrate				
Entry	R^1	R^2	*Time (h)*	*Yield (%)*	*de (%)*
1	Me	Bn	1.5	96	96
2	Et	Bn	2	82	90
3	Bn	Bn	2	90	93
4	Me	Me	2	86	85
5	Bn	Me	2	92	84
6	Bn	Et	2	90	96

To adapt the diastereoselective Michael addition for an asymmetric synthesis of β-mercapto amides or esters **30**, Michael adducts **29** were treated with boron trifluoride etherate complex, followed by the addition of odorless dodecanethiol **4**. Because the removal of the chiral moiety of the reagent proceeded smoothly and in good yield at room temperature, a novel method for the formal asymmetric Michael addition of hydrogen sulfide to α,β-unsaturated esters was established, that is, the chiral thiol **1** was served as an odorless chiral hydrogen sulfide equivalent as shown in Scheme 13 [19–21]. This synthetic route could be applied for the synthesis of captopril, an antihypertensive agent, and its derivatives.

Next, Meerwein-Pondorf-Verley (MPV) reduction was focused as a target reaction for the Michael addition of the chiral thiols. Although asymmetric MPV reductions have been reported by many research groups to date [22,23], no general methods have been developed except some intramolecular reactions where substrates are limited to those having special structures [24,25]. Therefore, we designed a new type of intramolecular MPV reduction using the optically active 1,3-mercapto alcohols that could be added to α,β-unsaturated ketones in the presence of a Lewis acid as shown in Scheme 14.

Namely, the Michael addition of the 1,3-mercapto alcohol was supposed to result in sulfides having a 10-membered chelated ring as an intermediate, in which the following 1,7-hydride shift afforded a desired keto-alcohols (**31**) with high diastereoselectivities. We succeeded in tandem Michael addition–MPV reduction, and the removal of the chiral moiety of the reagent gave an optically active alcohol. Results of this asymmetric



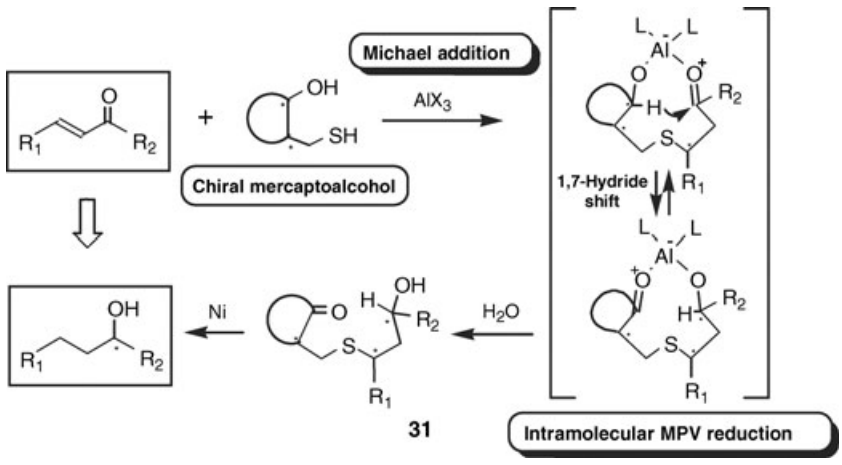
SCHEME 13 Formal asymmetric Michael addition of H_2S using odorless thiols.

reduction of α,β-unsaturated ketones are summarized in Table 6, and the sulfides were removed in a reductive manner from **31** using a combination of Raney nickel and sodium hypophosphite to give the corresponding secondary alcohols **32** [3,4]. In addition, the sulfides were converted to optically active allyl alcohols by oxidative desulfurization.

Moreover, the mechanistic study confirmed that the reaction was controlled by a dynamic kinetic resolution through reversible Michael addition as shown in Scheme 15. Namely, the Michael addition is an equilibrium reaction that gives two diastereomers, and the following intramolecular MPV reduction is controlled kinetically to give a single product.

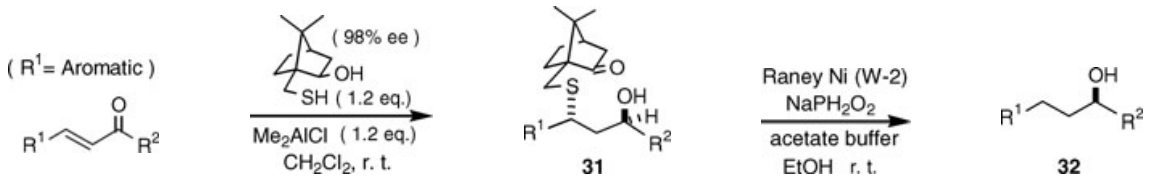
The above hydroxyl sulfides were also converted to *anti*-1,3-mercapto alcohols **33** by the reduction of ketones **31** and successive treatment with a combination of boron trifluoride etherate complex and dodecanethiol **4** [21]. On the other hand, tandem Michael addition–MPV reduction of α,β-unsaturated ketones using chiral odorless mercapto alcohol **2** afforded the same type of hydroxyl sulfides that were easily transformed to *syn*-1,3-mercapto alcohols **34** by treatment with a base [26]. Asymmetric syntheses of 1,3-mercapto alcohols are summarized in Scheme 16.

Because we have succeeded in controlling the two chiral centers on 1,3-mercapto alcohols, a one-step synthesis of three contiguous chiral

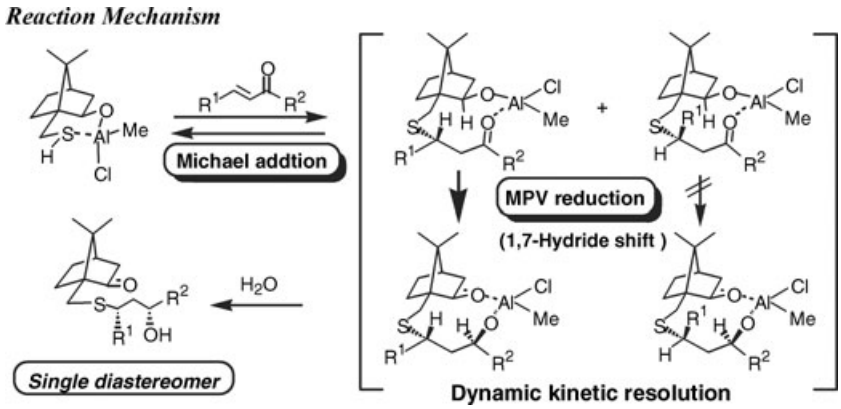


SCHEME 14 Asymmetric reduction *via* a tandem Michael-MPV reaction.

TABLE 6 Asymmetric Reduction of α,β-Unsaturated Ketones



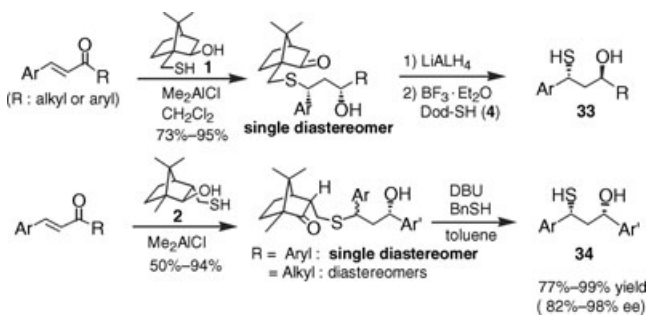
	Tandem Michael-MPV reaction				*Reductive desulfurization*			
	Substrate							
Entry	R^1	R^2	*Time (h)*	*Yield (%)*	*Time (h)*	*Yield (%)*	*% ee*	*Config*
1	Ph	Me	12	83	0.6	89	97	S
2	Ph	Et	13	90	0.3	91	98	S
3	Ph	*n*-Pr	16	81	0.3	95	98	S
4	Ph	*n*-Bu	12	83	0.3	89	97	S
5	Ph	*n*-Oc	12	90	0.6	99	98	S
6	Ph	Ph	24	85	0.3	96	96	R
7	4-MePh	Ph	16	73	0.3	90	98	R
8	4-MeOPh	Ph	33	75	0.3	97	96	R



SCHEME 15 Tandem Michael-MPV reaction using chiral mercapto alcohol.

centers by using the tandem reaction of acyclic α,β-unsaturated ketones was designed next as shown in Scheme 17.

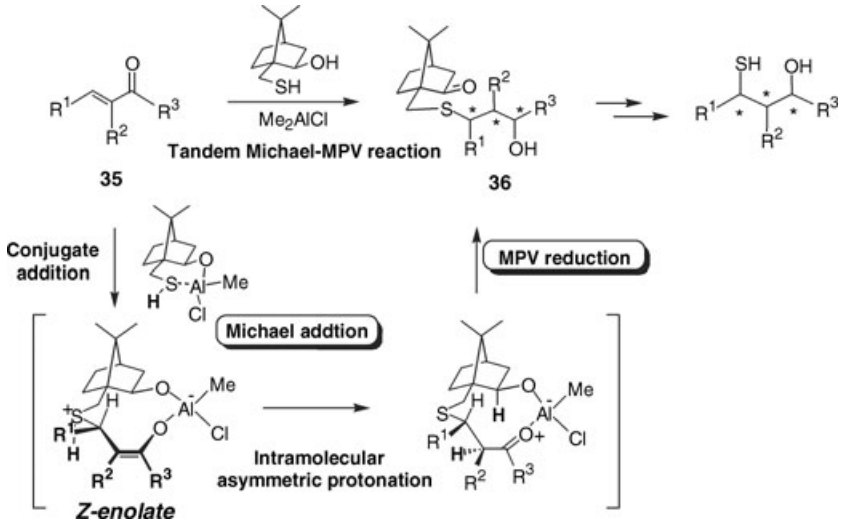
Among eight possible isomers, the reaction of a mixture of *E*- and *Z*-α-alkyl-α,β-unsaturated ketones



SCHEME 16 Asymmetric synthesis of 1.3-mercapto alcohols.

35 with chiral mercapto alcohol **1** and dimethyl aluminum chloride at room temperature gave only two diastereomers at the C-2 position. This result suggested that the tandem reaction was controlled by a dynamic kinetic resolution. In the case of R^2 = phenyl, the diastereomeric excess of the products **36** rose to more than 98% with increasing bulkiness of the R^1 group. Meanwhile, in the case of R^2 = alkyl, the products were obtained with low diastereomeric excess. However, addition of pentafluorobenzoic acid (PFBA) surprisingly resulted in improved diastereomeric excess as shown in Table 7 [20].

The resulting products **36** in the above tandem reaction were transformed to 1,3-mercapto alcohols, for example, **37**, as shown in Scheme 18. As a result, asymmetric synthesis of 1,3-mercapto alcohols having three contiguous chiral carbons from acyclic α,β-unsaturated ketones was achieved in high ee and de forms. Asymmetric synthesis of *cis*-cognac lactone

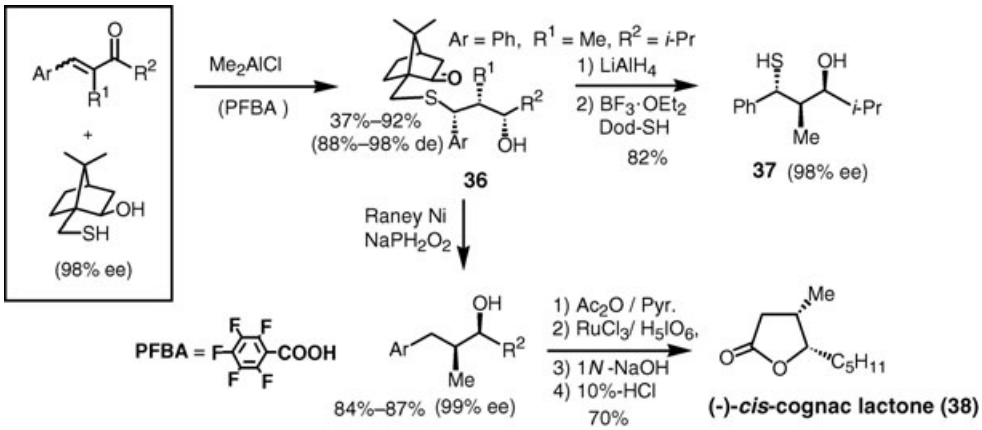


SCHEME 17 Asymmetric construction of contiguous three chiral carbons.

TABLE 7 Asymmetric Construction of Three Contiguous Chiral Carbons

Entry	Substrate R^1	Substrate R^2	Additive (1 eq)	Time (day)	Yield (%)	de (%)
1	Me	Ph	—	2	92	89
2	Et	Ph	—	2	60	93
3	Pr	Ph	—	3	44	>98
4	Bn	Ph	—	3	37	>98
5	Me	*i*-Pr	PFBA	3	55 (46)[a]	96 (48)[a]
6	Me	*c*-Hex	PFBA	3	50 (31)[a]	96 (60)[a]

[a]Numbers in parentheses are results in the reaction without PFBA.



SCHEME 18 Applications of tandem Michael-MPV reaction.

38 from the product of the tandem reaction was performed to exemplify a practical application of the method as shown in Scheme 18 [27].

Finally, a [$4^+ + 2$] cycloaddition-elimination reaction was performed by using **3** to afford dihydrothiopyran derivatives with moderate stereoselectivities under completely odorless condition [28].

Consequently, we succeeded in the preparation of a number of odorless thiols, sulfides, as well as selenides, and exhibiting a wide range of their applications in organic synthesis including asymmetric synthesis [29–31]. It is noteworthy to emphasize that all the reactions shown above were carried out under odorless environment in spite of utilizing thiol-containing reagents. We believe that these odorless organosulfur reagents could greatly serve the chemical community in preserving environmental benignity, especially where large-scale syntheses are concerned.

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