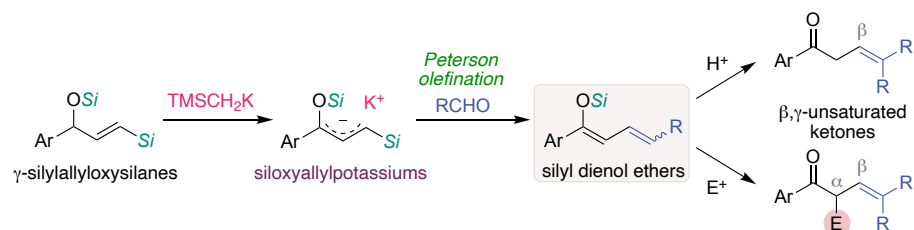


Synthesis of Silyl Dienol Ethers via Peterson Olefination of Siloxyallylpotassium Species

Masahiro Sai*

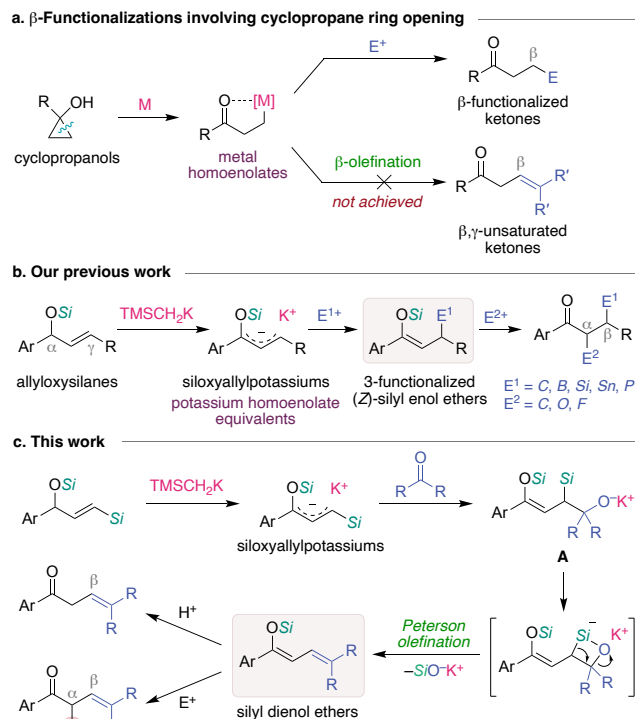
Faculty of Materials for Energy, Shimane University, 1060 Nishikawatsu-cho, Matsue, Shimane 690-8504, Japan



ABSTRACT: We report herein a general method for synthesizing a diverse array of silyl dienol ethers via the Peterson olefination of aldehydes using 3-silyl-substituted siloxyallylpotassium species. The reaction proceeds cleanly at -78°C and tolerates a wide range of functional groups on aldehyde substrates (OMe, NMe_2 , F, Cl, Br, CN, CO_2Bu , CF_3 , and epoxide). Under our conditions, organolithium bases are ineffective, underscoring the critical role of potassium carbanions. The resulting silyl dienol ethers are readily converted to β,γ -unsaturated ketones. This two-step sequence thus constitutes a formal β -olefination of ketones.

Metal homoenolates are valuable nucleophiles for introducing functional groups at the β -position of carbonyl compounds.¹ In recent years, metal-mediated ring opening of cyclopropanols has emerged as an efficient approach for generating metal homoenolates and has been applied to the synthesis of β -functionalized ketones. This strategy has enabled a broad range of β -functionalization reactions, including arylation, alkylation, allylation, alkynylation, fluorination, trifluoromethylation, trifluoromethylthiolation, acylation, cyanation, amination, amidation, and sulfonylation.² However, while acid-mediated transformations of 2-(1-hydroxyalkyl)-substituted cyclopropanols to β,γ -unsaturated ketones have been reported,³ the β -olefination of ketones via metal homoenolates has not yet been achieved (Scheme 1a). To address this challenge, we recently developed an efficient protocol for generating siloxyallylpotassium species from α -substituted allyloxysilanes using (trimethylsilyl)methylpotassium (TMSCH_2K) as the base.⁴ These species serve as potassium homoenolate equivalents and react readily with a variety of electrophiles to afford 3-functionalized (Z)-silyl enol ethers, which can be further converted to α,β -difunctionalized ketones (Scheme 1b).⁵ Guided by these results, we envisioned that siloxyallylpotassium species derived from γ -silylallyloxysilanes would undergo nucleophilic addition to carbonyl compounds to give adduct **A**, in which the proximity of the silyl substituent to the potassium alkoxide moiety would promote a Peterson olefination,⁶ thereby furnishing silyl dienol ethers (Scheme 1c). The resulting silyl dienol ethers can then be transformed into β,γ -unsaturated ketones by desilylation or into α -substituted β,γ -unsaturated ketones by α -functionalization. Thus, this sequence can be regarded as a formal β -olefination of ketones.

Scheme 1. Strategies for β -Functionalization and β -Olefination of Ketones



To demonstrate the feasibility of our strategy, γ -silylallyloxysilane **1a** was treated with various bases in THF, and the resulting siloxyallyl anion was trapped with benzophenone (Table 1). Substrate **1a** was prepared in three steps: (i) addition of trimethylsilylacetylene to benzaldehyde, (ii) E -selective reduction of the resulting propargylic alcohol with

Red-Al, and (iii) silylation of the corresponding allylic alcohol. When TMSCH₂K, which we previously demonstrated to be effective for the deprotonation of α -arylallyloxysilanes,⁵ was employed, the desired silyl dienol ether **2aa** was formed in 72% NMR yield (entry 1). Increasing the amount of base to 2.0 equiv led to complete consumption of **1a** and improved the yield of **2aa** to 87% (entry 2). Reducing the amount of benzophenone from 1.5 to 1.3 equiv had no detrimental effect, and **2aa** was isolated in 92% yield (entry 3). In this reaction, a small amount of silyl enol ether **3a** was also detected, presumably formed by protonation of the siloxyallylpotassium intermediate rather than by trapping with benzophenone. Increasing the amount of benzophenone to 2.0 equiv did not suppress the formation of **3a** (entry 4). In contrast, with ^tBuLi as the base, **2aa** was not observed, and **1a** was fully recovered (entry 5).⁷ Addition of hexamethylphosphoramide (HMPA) to enhance the reactivity of ^tBuLi decreased the recovery of **1a** to 28%; however, **2aa** was not detected, and **3a** became the major product (entry 6). Raising the reaction temperature from –78 °C to 0 °C, in an attempt to promote the reaction of the putative siloxyallyllithium species with benzophenone, resulted in a complex mixture with no formation of **2aa** (entry 7). These results indicate that potassium carbanions are essential for the success of this transformation.

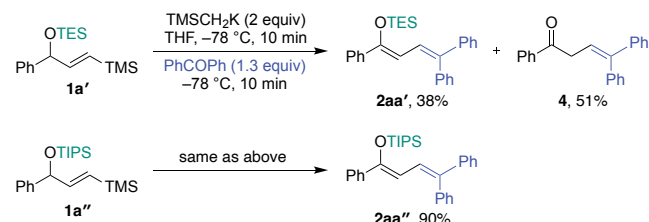
Table 1. Optimization of the Reaction Conditions^a

entry	1	base	X	Y	yield (%) ^b		
					1a	2aa	3a
1	1a	TMSCH ₂ K	1.5	1.5	14	72	7
2	1a	TMSCH ₂ K	2.0	1.5	<1	87	5
3	1a	TMSCH ₂ K	2.0	1.3	<1	89 (92) ^c	6
4	1a	TMSCH ₂ K	2.0	2.0	<1	90	6
5	1a	^t BuLi	2.0	1.3	95	0	0
6	1a	^t BuLi/HMPA	2.0	1.3	28	0	48
7 ^d	1a	^t BuLi/HMPA	2.0	1.3	19	0	5

^aReaction conditions: **1a** (80.2 mg, 0.25 mmol), base, and additive in THF (3 mL) at –78 °C for 10 min, followed by addition of benzophenone at –78 °C for 10 min. ^bDetermined by ¹H NMR analysis of the crude reaction mixture. ^cIsolated yield. ^dThe reaction with benzophenone was conducted at 0 °C.

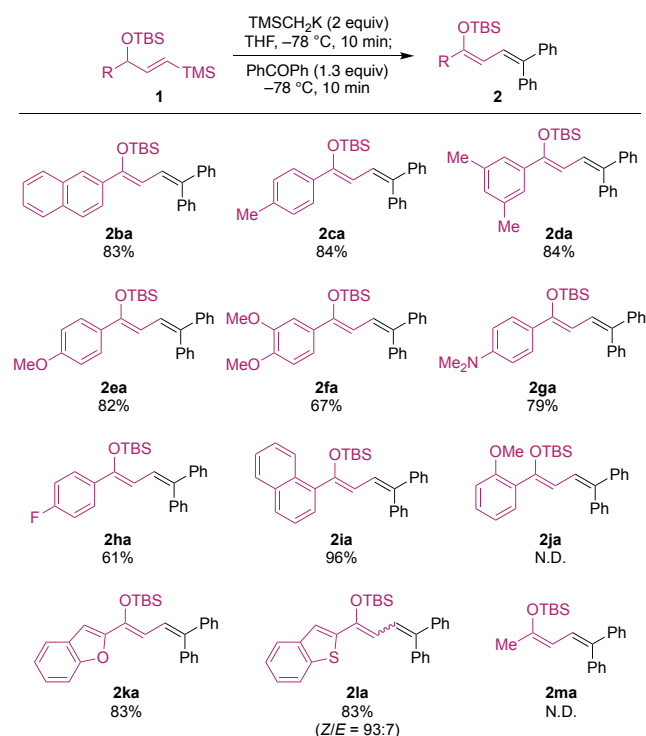
We next examined the influence of the siloxy substituent on the reaction outcome (Scheme 2). When triethylsilyl (TES) derivative **1a'** was used, the reaction proceeded efficiently; however, partial desilylation occurred, affording **2aa'** in 38% yield together with β,γ -unsaturated ketone **4** in 51% yield. In contrast, triisopropylsilyl (TIPS) derivative **1a''** underwent complete conversion to provide **2aa''** in 90% isolated yield, despite the steric bulk of the TIPS group.

Scheme 2. Influence of the Siloxy Substituent on the Reaction Outcome



The substrate scope of allyloxysilanes was examined using benzophenone as the electrophile (Scheme 3). Allyloxysilanes **1b–1h** were readily converted into the corresponding silyl dienol ethers **2ba–2ha** in 61–84% yields with excellent *Z*-selectivity, regardless of the electronic properties of the aryl substituents. *Ortho*-substituted aryl substrates were also investigated. As a result, 1-naphthyl derivative **1i** furnished **2ia** in 96% yield, whereas *ortho*-anisyl derivative **1j** gave no desired product and was recovered unchanged, likely due to steric congestion at the α position. The reaction was also applicable to substrates bearing heteroaryl groups, affording **2ka** and **2la** in high yields, although the *Z/E* ratio of **2la** decreased slightly to 93:7. Unfortunately, no reaction was observed with alkyl-substituted allyloxysilane **1m**, as the alkyl substituent renders the C1–H bond less acidic, preventing the initial deprotonation.

Scheme 3. Scope of γ -Silylallyloxysilanes^a

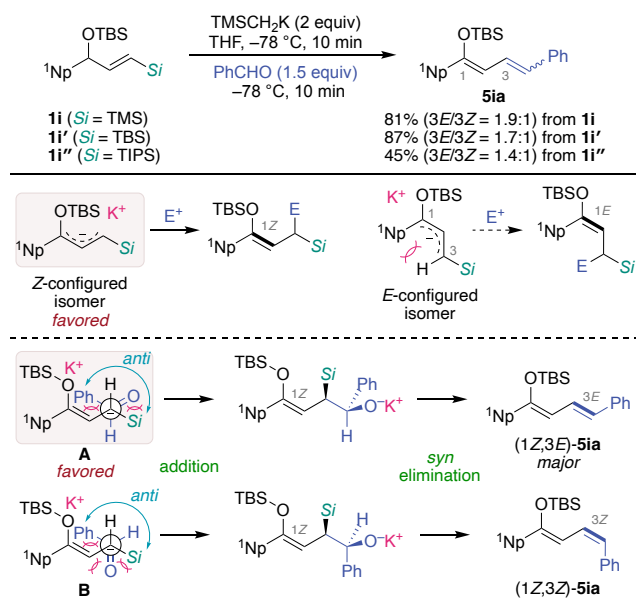


^aConditions: **1** (0.25 mmol) and TMSCH₂K (63.2 mg, 0.50 mmol) in THF (3 mL) at –78 °C for 10 min, followed by addition of benzophenone (59.2 mg, 0.325 mmol) at –78 °C for 10 min. Yields of isolated products are shown.

Substrate **1i**, which gave the highest yield in Scheme 3, was reacted with benzaldehyde, and the yield and 3*E*/3*Z* ratio of **5ia** were determined (Scheme 4). The reaction provided **5ia** in 81% yield with a 3*E*/3*Z* ratio of 1.9:1. Replacing the TMS group on the vinylsilane unit with TBS (**1i'**) decreased the 3*E*/3*Z* ratio slightly to 1.7:1. Substitution with TIPS (**1i''**) caused a significant drop in both the yield (45%) and the 3*E*/3*Z* ratio (1.4:1). To rationalize the diastereoselectivity and

the effect of the silyl substituent in this transformation, we propose the stereochemical models shown in Scheme 4. According to our previous computational study,^{5b} the *E*-configured siloxyallylpotassium isomer is considered less stable than the *Z*-configured isomer owing to steric repulsion between the C1 aryl substituent and the C3 hydrogen atom. The addition to benzaldehyde is therefore proposed to proceed via the *Z*-isomer, yielding a *Z*-configured double bond at C1. As benzaldehyde approaches this *Z*-configured organopotassium species, the phenyl group is oriented *anti* to the bulky silyl group. In conformer **A**, the principal steric repulsions are between the phenyl group and the silyl enol ether moiety, and between the carbonyl oxygen and the silyl group. In contrast, conformer **B** involves these interactions as well as an additional repulsion between the carbonyl oxygen and the silyl enol ether moiety. Consequently, addition via conformer **A** is favored, affording (1*Z*,3*E*)-**5ia** as the major product. However, increasing the steric bulk of the silyl substituent enhances the repulsion between the silyl group and the carbonyl oxygen and diminishes the relative contribution of other steric interactions. As a result, the energy gap between **A** and **B** narrows, explaining the observed decrease in the 3*E*/3*Z* ratio.

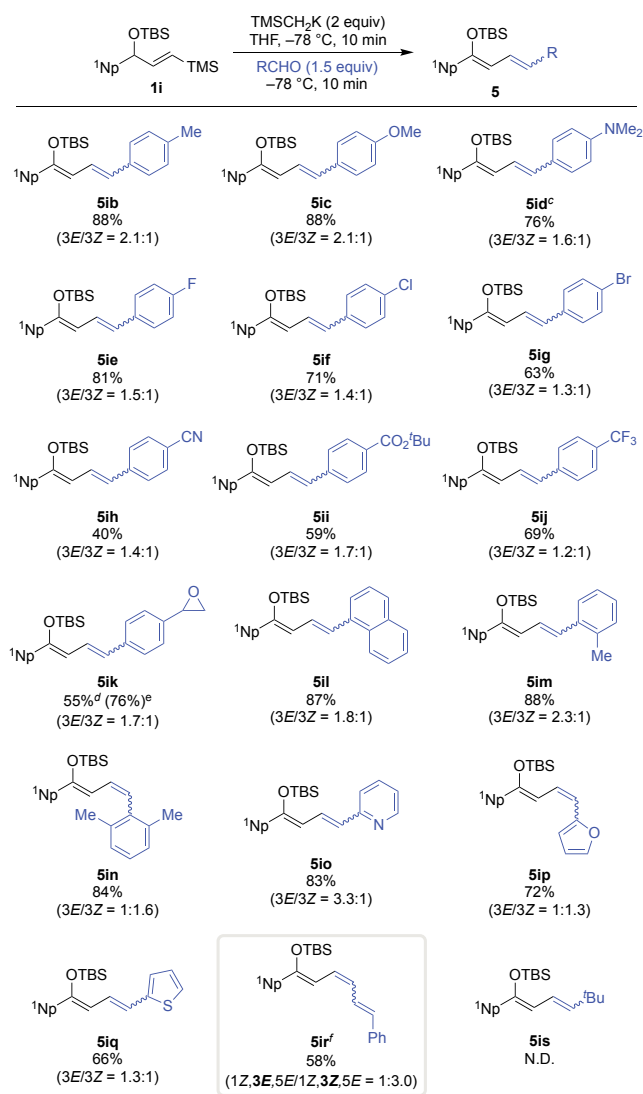
Scheme 4. Effect of the Vinylsilane Substituent on Diastereoselectivity and Proposed Stereochemical Models



The scope of aldehydes was examined using allyloxysilane **1i** as the model substrate (Scheme 5).⁸ Because generation of the siloxyallylpotassium species from an allyloxysilane requires a highly reactive potassium carbanion, the allyloxysilane component exhibited limited functional-group tolerance. In contrast, addition of the siloxyallylpotassium species to aldehydes, followed by Peterson olefination, proceeded rapidly even at cryogenic temperatures, thereby allowing broad functional-group tolerance on the aldehyde component. Indeed, aldehydes bearing methoxy, amino, fluoro, chloro, bromo, cyano, ester, and trifluoromethyl groups were well tolerated (**5ib–5ij**). Notably, even an epoxide group, typically susceptible to nucleophilic ring opening, was tolerated (**5ik**) under the reaction conditions.⁹ *Ortho*-substituted aldehydes were compatible, providing **5il–5in** in 84–88% yields; however, with 2,6-dimethylbenzaldehyde, the 3*Z* isomer was obtained as the major product (**5in**). Heteroaromatic aldehydes

were also suitable electrophiles, affording **5io–5iq** in 66–83% yields. In addition to the synthesis of silyl dienol ethers, this reaction was applicable to the preparation of 1-siloxy-1,3,5-hexatriene **5ir** by employing *trans*-cinnamaldehyde as the electrophile. No reaction was observed with aliphatic aldehydes.

Scheme 5. Scope of Aldehydes^{a,b}

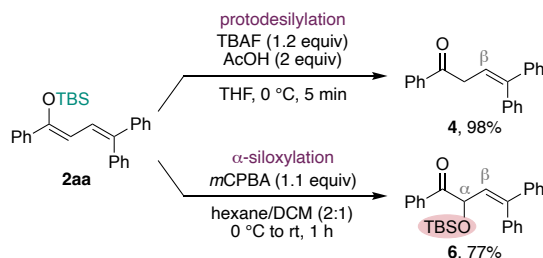


^aConditions: **1i** (92.7 mg, 0.25 mmol) and TMSCH₂K (63.2 mg, 0.50 mmol) in THF (3 mL) at -78 °C for 10 min, followed by addition of aldehyde (0.375 mmol) at -78 °C for 10 min. ^bThe 3*E*/3*Z* ratios were determined by ¹H NMR analysis of the crude reaction mixtures. ^cPurified by gel permeation chromatography. ^dPurified by column chromatography on amino-modified silica gel. ^eDetermined by ¹H NMR analysis of the crude reaction mixture. ^fThe reaction mixture was diluted with hexane (3 mL) prior to aldehyde addition.

Finally, we demonstrated the conversion of the silyl dienol ethers to β,γ-unsaturated ketones (Scheme 6). Silyl dienol ether **2aa** was converted to β,γ-unsaturated ketone **4** in 98% yield by protodesilylation with tetrabutylammonium fluoride (TBAF) and acetic acid (AcOH). In addition, Rubottom oxidation of **2aa** afforded the corresponding α-siloxy-β,γ-unsaturated ketone **6** in 77% yield.¹⁰ Thus, this transformation not only constitutes a formal β-olefination of ketones but also

enables sequential α -functionalization, leading to α -substituted β,γ -unsaturated ketones.

Scheme 6. Transformations of Product 2aa



In conclusion, we have developed an efficient method for synthesizing a variety of silyl dienol ethers via the Peterson olefination of aldehydes and benzophenone with siloxyallylpotassium species, generated by TMSCH_2K -mediated deprotonation of γ -silylallyloxysilanes. The reaction proceeds smoothly at -78 °C and exhibits broad functional-group tolerance toward aldehyde substrates, accommodating methoxy, amino, halogen, ester, trifluoromethyl, and epoxide functionalities. Moreover, the resulting silyl dienol ethers serve as valuable synthetic intermediates, as they can be readily transformed into β,γ -unsaturated ketones and α -substituted β,γ -unsaturated ketones.

AUTHOR INFORMATION

Corresponding Author

*saimasa@mat.shimane-u.ac.jp; orcid.org/0000-0001-5018-917X

Notes

The author declares no competing financial interest.

ACKNOWLEDGMENT

M.S. acknowledges the financial support from the Tokuyama Science Foundation.

REFERENCES

- (1) For reviews, see: (a) Kuwajima, I.; Nakamura, E. Metal Homoenoates. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I. Eds.; Pergamon: Oxford, 1991; Vol. 2, pp 441–454. (b) Nithiy, N.; Rosa, D.; Orellana, A. Carbon–Carbon Bond Formation through Palladium Homoenoates. *Synthesis* **2013**, *45*, 3199–3210. (c) Mills, L. R.; Rousseaux, S. A. L. Modern Developments in the Chemistry of Homoenoates. *Eur. J. Org. Chem.* **2019**, 8–26.
- (2) For reviews, see: (a) Nikolaev, A.; Orellana, A. Transition-Metal-Catalyzed C–C and C–X Bond-Forming Reactions Using Cyclopropanols. *Synthesis* **2016**, *48*, 1741–1768. (b) Cai, X.; Liang, W.; Dai, M. Total Syntheses via Cyclopropanols. *Tetrahedron* **2019**, *75*, 193–208. (c) Le Bras, J.; Muzart, J. Pd-Catalyzed Reactions of Cyclopropanols, Cyclobutanols and Cyclobutenols. *Tetrahedron* **2020**, *76*, 130879. (d) Pirenne, V.; Muriel, B.; Waser, J. Catalytic Enantioselective Ring-Opening Reactions of Cyclopropanes. *Chem. Rev.* **2021**, *121*, 227–263. (e) Sekiguchi, Y.; Yoshikai, N. Metal-Catalyzed Transformations of Cyclopropanols via Homoenoates. *Bull. Chem. Soc. Jpn.* **2021**, *94*, 265–280. (f) McDonald, T. R.; Mills, L. R.; West, M. S.; Rousseaux, S. A. L. Selective Carbon–Carbon Bond Cleavage of Cyclopropanols. *Chem. Rev.* **2021**, *121*, 3–79. (g) Jha, N.; Mishra, P.; Kapur, M. Strained Cycloalkanol in C–C Bond Formation Reactions: A Boon in Disguise! *Org. Chem. Front.* **2023**, *10*, 4941–4971. (h) Doraghi, F.; Pegah Aledavoud, S.; Fakhriolaei, A.; Larijani, B.; Mahdavi, M. Ring-Opening Cross-Coupling/Cyclization Reaction of Cyclopropanols with Organic Compounds. *ChemistrySelect* **2023**, *8*, e202301438. (i) Laktsevich-Iskryk, M.; Hurski, A.; Ošeka, M.; Ka-

nanovich, D. Recent Advances in Asymmetric Synthesis via Cyclopropanol Intermediates. *Org. Biomol. Chem.* **2025**, *23*, 992–1015. (j) Basak, S.; Paul, T.; Mandal, S.; Barman, M.; Nanjgowda, M. V.; Punniyamurthy, T. Transition-Metal-Catalyzed Auxiliary-Assisted C–H Functionalization Using Vinylcyclopropanes and Cyclopropanols. *Chem. Commun.* **2025**, *61*, 6055–6068.

(3) (a) Toratsu, C.; Fujii, T.; Suzuki, T.; Takai, K. Cross-Coupling Reactions between α,β -Unsaturated Ketones and Aldehydes with CrCl_2 : Aldol Condensation and Cyclopropanol Formation. *Angew. Chem., Int. Ed.* **2000**, *39*, 2725–2727. (b) Ohe, T.; Ohse, T.; Mori, K.; Ohtaka, S.; Uemura, S. Iridium-Catalyzed Cross-Coupling Reactions between α,β -Unsaturated Carbonyl Compounds and Aromatic Aldehydes. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 1823–1827. (c) Nomura, K.; Matsubara, S. Stereoselective Synthesis of β,γ -Unsaturated Ketones by Acid-Mediated Julia-Type Transformation from 2-(1-Hydroxyalkyl)-1-alkylcyclopropanols. *Synlett* **2008**, *2008*, 1412–1414. (d) Nowaki, A.; Kawano, M.; Hori, F.; Fuse, Y.; Yoshimura, T.; Matsuo, J. Aldol/Brook/Carbon Skeletal Rearrangement Cascade Reactions of β -Silyl Ketones with Aldehydes. *Eur. J. Org. Chem.* **2023**, *26*, e202300351.

(4) For reports on TMSCH_2K , see: (a) Clegg, W.; Conway, B.; Graham, D. V.; Hevia, E.; Kennedy, A. R.; Mulvey, R. E.; Russo, L.; Wright, D. S. Structurally Defined Potassium-Mediated Zincation of Pyridine and 4-R-Substituted Pyridines (R = Et, *i*Pr, *t*Bu, Ph, and Me_2N) by Using Dialkyl-TMP-Zincate Bases. *Chem. Eur. J.* **2009**, *15*, 7074–7082. (b) Sato, I.; Yamashita, Y.; Kobayashi, S. Alkylpotassium-Catalyzed Benzylic C–H Alkylation of Alkylarenes with Alkenes. *Synthesis* **2019**, *51*, 240–250. (c) Hirata, T.; Sato, I.; Yamashita, Y.; Kobayashi, S. Asymmetric $\text{C}(\text{sp}^3)\text{--H}$ Functionalization of Unactivated Alkylarenes such as Toluene Enabled by Chiral Brønsted Base Catalysts. *Commun. Chem.* **2021**, *4*, 36. (d) Hayashi, R.; Udagawa, T.; Sai, M. β -Functionalized and α,β -Difunctionalized Ketones from 1-Arylallylic Alcohols via Dipotassium α,β -Dianion Intermediates. *Adv. Synth. Catal.* **2023**, *365*, 826–833. (e) Hayashi, R.; Narita, Y.; Sai, M. One-Pot Synthesis of 3-Functionalized (Z)-Silyl Enol Ethers from 1-Arylallylic Alcohols by C,O-Difunctionalization of Dipotassium α,β -Dianion Intermediates. *Org. Biomol. Chem.* **2023**, *21*, 4206–4209. For a review, see: (f) Yamashita, Y.; Kobayashi, S. New Dimensions of Brønsted Base Catalyzed Carbon–Carbon Bond-Forming Reactions. *Synlett* **2021**, *32*, 14–22.

(5) (a) Okuda, S.; Narita, Y.; Hayashi, R.; Sai, M. Regio- and Diastereoselective Synthesis of Unsymmetrical 1,4-Diketone-Derived (Z)-Monosilyl Enol Ethers via Siloxyallylpotassium Intermediates. *Chem. Commun.* **2023**, *59*, 2939–2942. (b) Okuda, S.; Narita, Y.; Hayashi, R.; Udagawa, T.; Sai, M. 1-Arylallyloxysilanes as Formal Precursors to Ketone-Derived Potassium Homoenoate Equivalents. *Org. Lett.* **2025**, *27*, 4762–4766.

(6) (a) Peterson, D. J. A Carbonyl Olefination Reaction Using Silyl-Substituted Organometallic Compounds. *J. Org. Chem.* **1968**, *33*, 780–784. (b) Ager, D. J. The Peterson Olefination Reaction. *Org. React.* **1990**, *38*, 1–223. (c) van Staden, L. F.; Gravestock, D.; Ager, D. J. New Developments in the Peterson Olefination Reaction. *Chem. Soc. Rev.* **2002**, *31*, 195–200.

(7) For the generation of siloxyallyllithium species and their reactions with electrophiles, see: (a) Still, W. C.; Macdonald, T. L. Allyloxy Carbanions. A New Synthesis of Aldehydes via a β -Acyl Carbanion Equivalent. *J. Am. Chem. Soc.* **1974**, *96*, 5561–5563. (b) Still, W. C.; Macdonald, T. L. Allyloxy Carbanions. A Synthesis of 3,4-Dihydroxy-1-Olefins from Carbonyl Compounds. *J. Org. Chem.* **1976**, *41*, 3620–3622. (c) Oppolzer, W.; Snowden, R. L. Electrophilic Substitutions of 3-Triethylsilyloxypentadienyl Lithium. *Tetrahedron Lett.* **1976**, *17*, 4187–4190. (d) Davies, D. H.; Hall, J.; Smith, E. H. C–C Bond Cleavage of 2-Acylimidazolium Salts in a Sequence Involving a New Ester Homoenoate Equivalent. A Synthesis of γ -Lactones. *J. Chem. Soc., Perkin Trans. 1* **1989**, 837–838.

(8) The 3E/3Z ratios were determined by ^1H NMR analysis; for **5ir**, the assignment was corroborated by $^1\text{H}\text{--}^1\text{H}$ COSY (see the Supporting Information for details).

(9) **5ik** decomposed during column chromatography on silica gel. Thus, it was purified by column chromatography on amino-modified silica gel.

(10) Brook, A. G.; Macrae, D. M. 1,4-Silyl Rearrangements of Siloxyalkenes to Siloxyketones during Peroxidation. *J. Organomet. Chem.* **1974**, *77*, C19–C21.