α,β-エポキシシランと求核剤との反応を利用する新しい反応の開発

課題番号（10671986）

平成１０年度~平成１２年度科学研究費補助金（基盤研究Ｃ(2)）研究成果報告書

平成１３年３月

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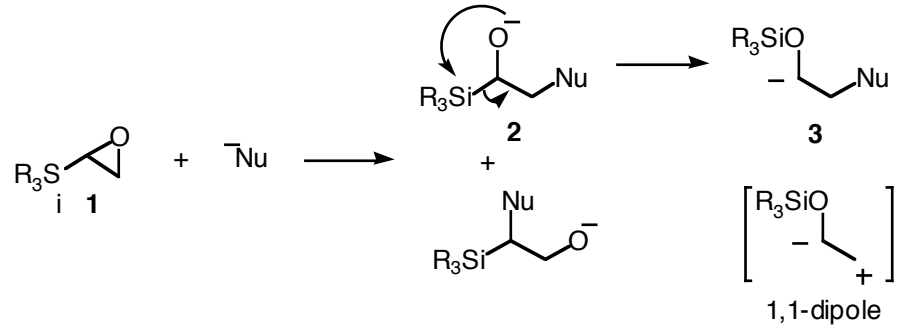
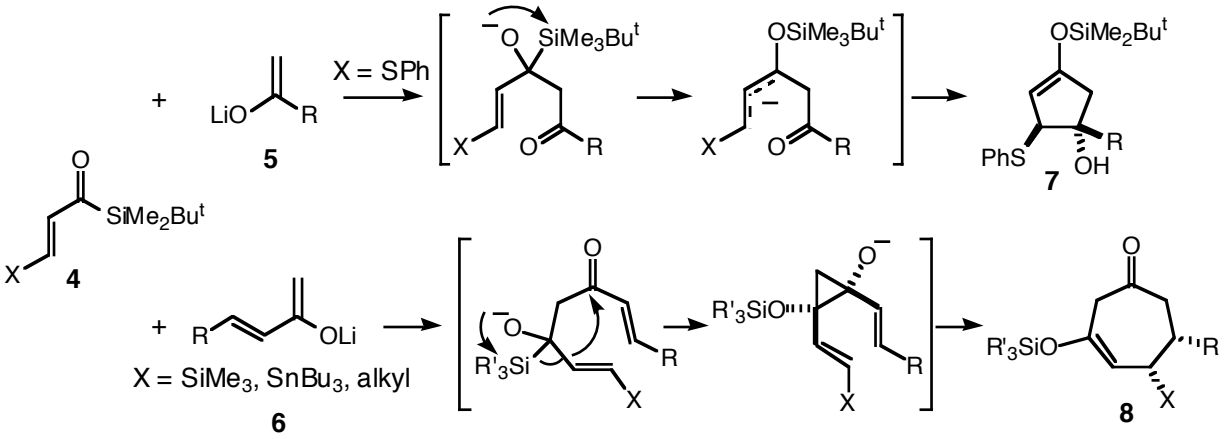
はじめに

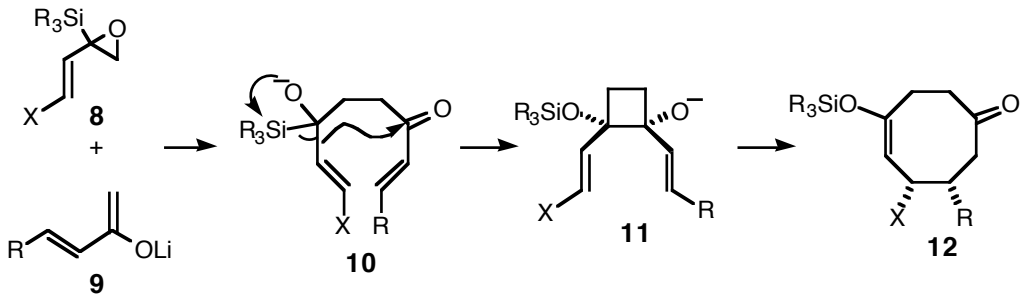
α,β-エポキシシラン **1** と求核剤との反応における反応点は二つあるが，シリル基の逆側の結合が開裂した場合，生成するα-シリルアルコキサイド **2** においてケイ素の 1,2-アニオニック転位が起これば **3** のようなα-シロキシカルバニオンが発生し，1,2-dipole 等価体として機能することが期待される．著者は，α,β-エポキシシランと求核剤との反応が，求核剤を工夫することによって種々の有用な新規合成反応の開発につながるのではないかとの着想を持った．



著者は，本研究を開始する以前に，ケイ素の 1,2-アニオニック転位いわゆる Brook 転位を利用した新規合成反応の開発研究を行っており，この転位の有用性を明らかにしつつあった．すなわち，以下に示すように，β-(フェニルチオ) アクリロイルシラン **4** (X = SPh) とアルキルメチルケトンのエノレート **5** を反応させると，シクロペンテノール誘導体 **7** が高収率で得られ，β-シリル，β-スタンニル，あるいはβアルキル-アクリロイルシラン **4** とアルケニルメチルケトン **6** との反応ではシクロヘプテノン **8** が立体特異的に生成するというものである．

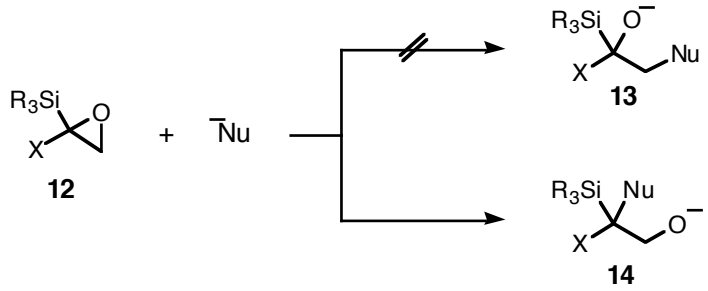


上記の [3 + 4] アニュレーションにおいて，アクリロイルシランの代わりにβ-アルケニル-α,β-エポキシシラン **8** を用いれば，アルケニルメチルケトンのエノレート **9** との反応で，エポキシの開環 (**8** + **9**→**10**)/Brook 転位-分子内アルドール反応 (**10**→**11**)/anionic oxy-Cope 転位 (**11**→**12**) が連続的に起こり，八員環が生成するのではないかと考えた．

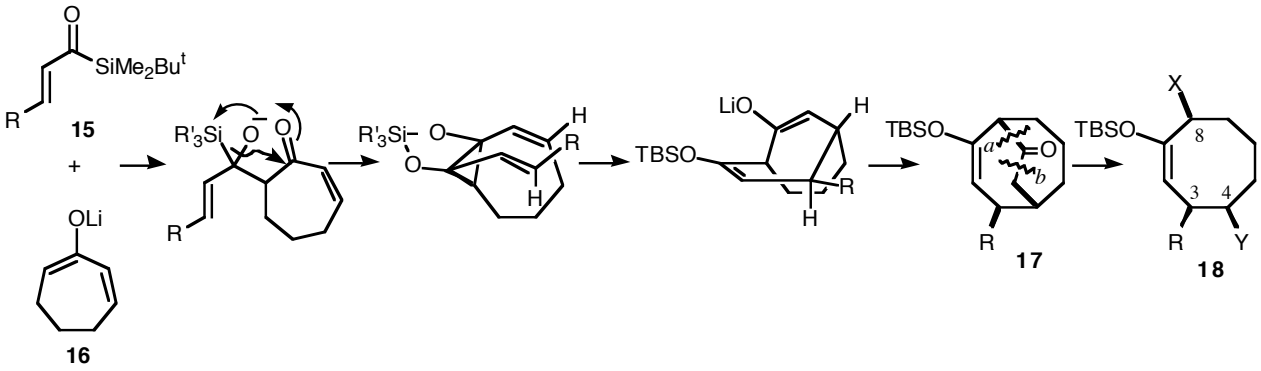


八員炭素環には，渡環相互作用などの八員環固有の高度の環歪みが存在するため，その環形成反応は六員環などと比較してかなり限定されており，特に立体選択的な置換基の導入が可能な方法は少ない．一方，タキサン類などの有用な天然物が八員炭素環を含むことから，立体選択的で効率的な八員炭素環形成反応の開発が求められている．

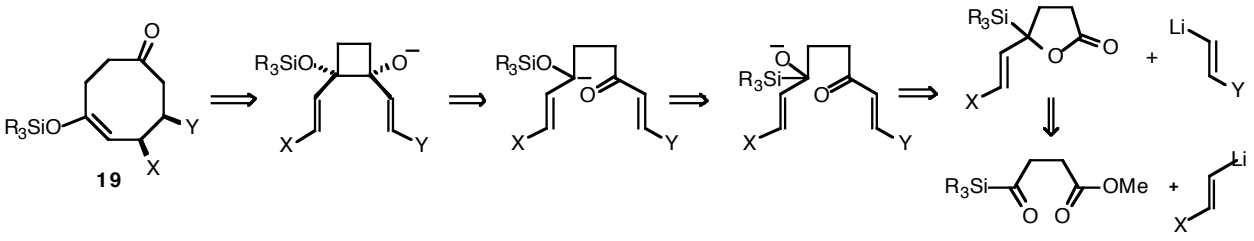
α,β-エポキシシランと求核剤との反応の報告例はそれほど多くはないが，多くの場合α位で反応が起っている．そこで，予備実験として，ビニル基を持たないα,β-エポキシシラン**12**と種々の求核剤との反応を検討した． しかし，ほとんどの場合求核剤の攻撃はα位で起こり，またXとして嵩高い置換基を導入すると原料回収に終わった．



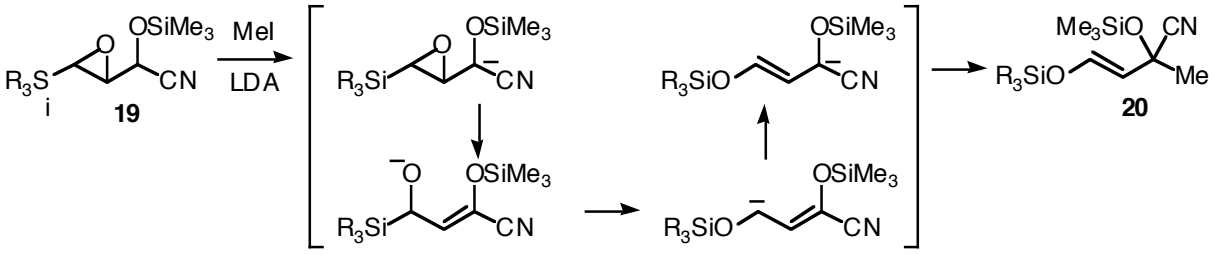
ここで，当初の計画は若干の変更を余儀なくされた．すなわち，α,β-エポキシシランの反応から，新しい八員環形成反応へ研究の比重を移すこととし，以下に示す二つのルートを案出した．１番目の経路は，[3 + 4] アニュレーションにおける四炭素単位として，シクロヘプテノンのエノレート**16**を用いるもので，生成するビシクロ体**17**の架橋部分*a,b*のいずれかを切断すれば，３，４，８位の置換基がすべてシスである八員環**18**が選択的に生成するのではないかと考えた．



２番目のルートは，1,2-ジビニルシクロブタノレートのアニオニックオキシ Cope 転位を利用するもので，以下に示すように，Brook 転位/分子内アルドール反応/Cope 転位のタンデム過程に特徴がある．



これら二つの経路は以下の章で述べるように，ほぼ所期の目的を達成しつつあるが，本研究の期間の終了間近になって，当初の課題であったα,β-エポキシシランを用いる新しい反応の開発研究において，新しい発見があった．すなわち，α,β-エポキシシラン **19** のγ位に求電子剤の存在下カルボアニオンを発生させると，エポキシ環の開環/Brook 転位/アリル転位/求電子剤との反応，が低温下瞬時に起こり，合成化学的に有用な官能基を備えたエノールシリルエーテル **20** が生成するというものである．



求電子剤が存在しているにもかかわらず，*O*-メチル化体や中間体のメチル化成績体が全く生成しないという結果は，一連の過程が協奏的に進行していることを示唆している．したがって，不斉エポキシドを用いた反応では，キラリティーが保持される可能性が極めて高いと予想される．今後新たに研究費を得て，さらに不斉反応へと展開する予定である．

連続的炭素-炭素結合形成反応を利用する八員炭素環形成反応の開発

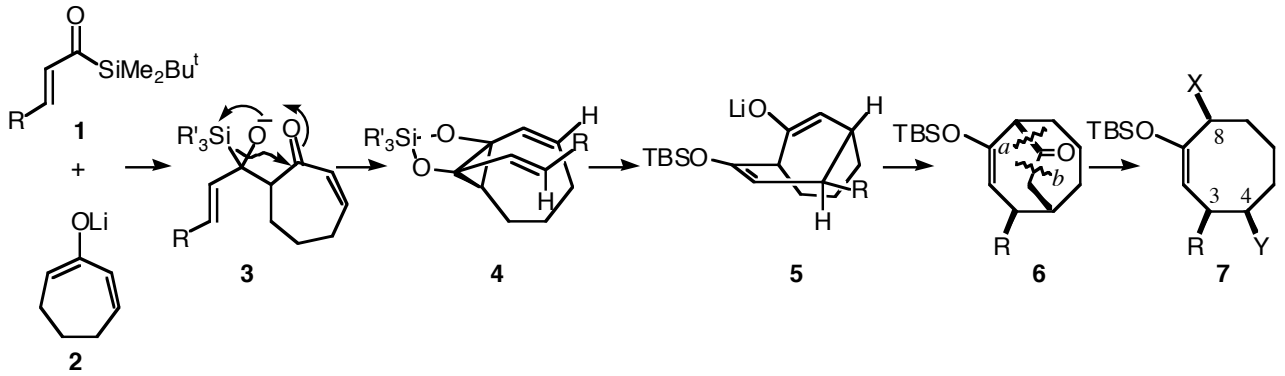
富山医薬大・薬　○武田　敬,[1)] 鷲見浩一，岡本康志，泉　恵美

八員炭素環には，渡環相互作用などの八員環固有の高度の環歪みが存在するため，その環形成反応は六員環などと比較してかなり限定されており，特に立体選択的な置換基の導入が可能な方法は少ない．一方，タキサン類などの有用な天然物が八員炭素環を含むことから，立体選択的で効率的な八員炭素環形成反応の開発が求められている．

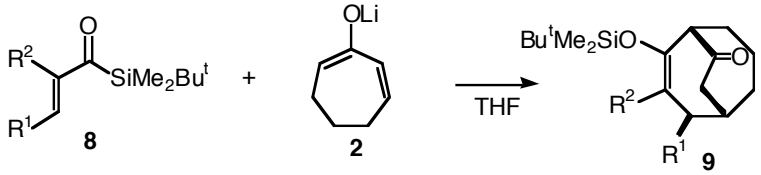
われわれは，以前に Brook 転位を利用した [3 + 4] アニュレーションによる七員炭素環形成反応の開発に成功しているが，[2)] 今回本法を八員炭素環形成反応に拡張すべく検討を行い，連続的炭素-炭素結合形成反応を利用する２種の新しい反応を開発することに成功した．

[3 + 4] アニュレーションによる八員炭素環の形成

以前に報告した [3 + 4] アニュレーションにおいて，四炭素単位として 2-cycloheptenone の enolate **2** を用いれば，付加体 **3** において Brook 転位/分子内 aldol 反応/anionic oxy-Cope 転位 (**3** → **4** → **5**) を経て bicylo[3.3.2]decane 誘導体 **6** が生成し，架橋結合 *a* あるいは *b* を開裂すれば，3, 4, 8 位の置換基がすべてシスである cyclooctene 誘導体 **7** が立体選択的に生成するのではないかと考えた．

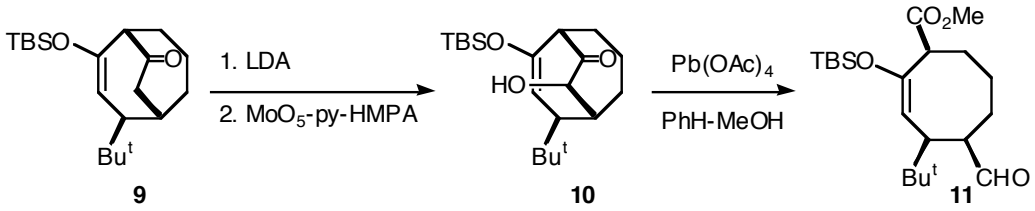


種々の acryloylsilane **8** と **2** との反応を行ったところ，満足すべき収率で環化体 **9** が得られた．



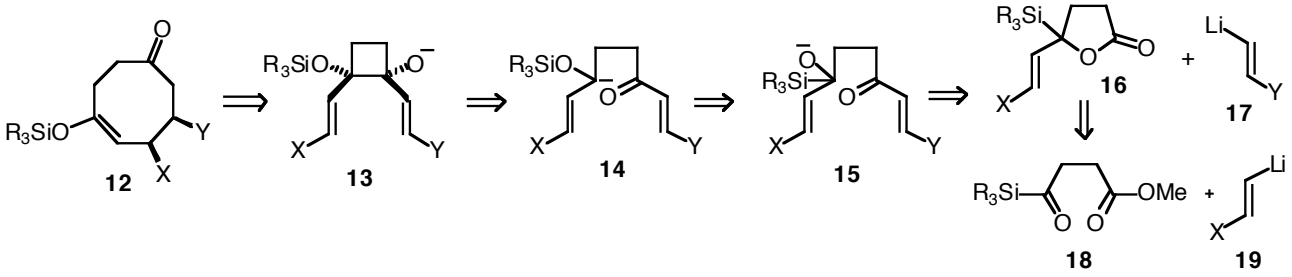
R^1	R^2	conditions	yield (%)
$SiMe_3$	H	-80 °C, 30 min	30
i-Pr	H	-80 °C, 30 min	45
t-Bu	H	-80 ° to 0 ℃	84
c-C_6H_{11}	H	-80 ° to 0 ℃	45
-$(CH_2)_4$-		0 ℃	31

次に，最も収率の良かった **9** (R = *t*-Bu) を用いて架橋結合の開裂を検討した．その結果，Baeyer-Villiger 酸化によるラクトン体の生成，*n*-butyl nitrite との反応によるエステル-オキシムの生成などは不成功に終わったが，MoO_5-pyridine-HMPA により α-ヒドロキシル体 **10** とした後，$Pb(OAc)_4$ で酸化することによりエステルアルデヒド体 **11** に変換できることがわかった．

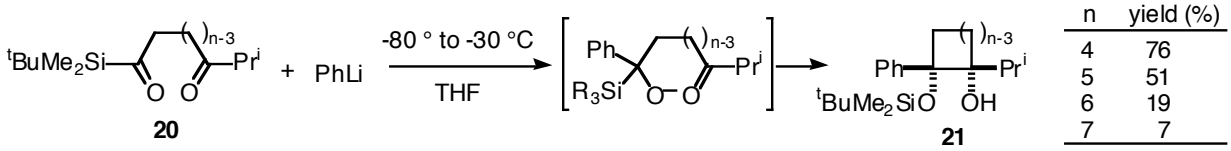


[6 + 2] 及び [4 + 2 + 2] アニュレーションによる八員炭素環の形成

divinylcyclopropanolate の anionic oxy-Cope 転位を経る [3 + 4] アニュレーション法を，八員環形成反応に拡張するために，以下のような経路を考えた．すなわち，anionic oxy-Cope 転位の基質である divinylcyclobutanolate **13** は **15** の Brook 転位/分子内アルドール反応により，また **15** はラクトン体 **16** と vinyllithium **17** との反応で，そして **16** はエステルアシルシラン **18** と vinyllithium **19** との反応で合成できるのではないかと考えた．

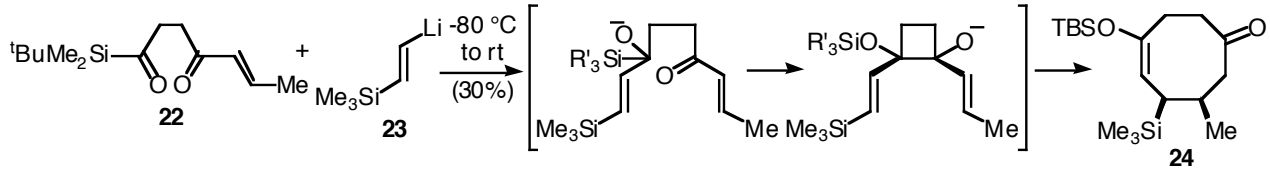


まず，**15**→**14**→**13** の Brook 転位/分子内アルドール反応で四員環が生成するかどうかを調べるために，ケトアシルシラン **20** と PhLi との反応を行った．その結果，収率良く四員環が生成することが明らかになった．興味深いことに，比較のために行った五，六，七員環形成反応と比較しても四員環の収率が最も良かった．

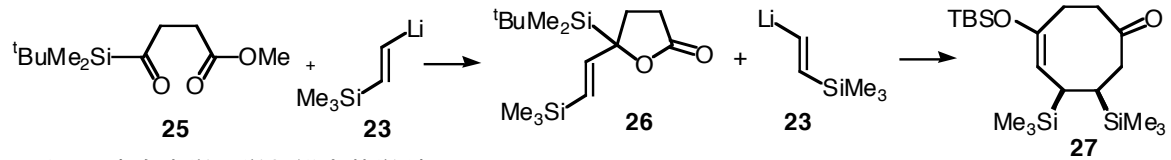


n	yield (%)
4	76
5	51
6	19
7	7

そこで，β -alkenoylacylsilane **22** と vinyllithium **23** を反応させたところ，[6 + 2] アニュレーション成績体 **24** が生成した．



Brook-aldol-Cope が期待通り進行することがわかったので，次に，ラクトン体 **26** と vinyllithium **23** との反応で一挙に八員環が生成するかどうか調べることにした．エステルアシルシラン **25** から導いた **26** に **23** を反応させたところ，低収率ながら形式的な [4 + 2 + 2] アニュレーション成績体 **27** が得られた．



1) 現所属：広島大学医学部総合薬学科

2) (a) Takeda, K.; Takeda, M.; Nakajima, A.; Yoshii, E. *J. Am. Chem. Soc*. **1995**, *117*, 6400-6401. (b) Takeda, K.; Nakajima, A.; Yoshii, E. *Synlett* **1996**, 753-754. (c) Takeda, K.; Nakajima, A.; Takeda, M.; Okamoto, Y.; Sato, T.; Yoshii, E.; Koizumi, T.; Shiro, M. *J. Am. Chem. Soc*. **1998**, *120*, 4947-4959. (d) Takeda, K.; Nakajima, A.; Takeda, M.; Yoshii, E.; Zhang, J.; Boeckman, Jr., R. K. *Org. Synth*. **1999**, *76*, 199-213.

Synthesis of 4-Hydroxy-2-cyclopentenone Derivatives by [3 + 2] Annulation of β-Heteroatom-Substituted Acryloylsilanes and Lithium Enolate of Methyl Ketones

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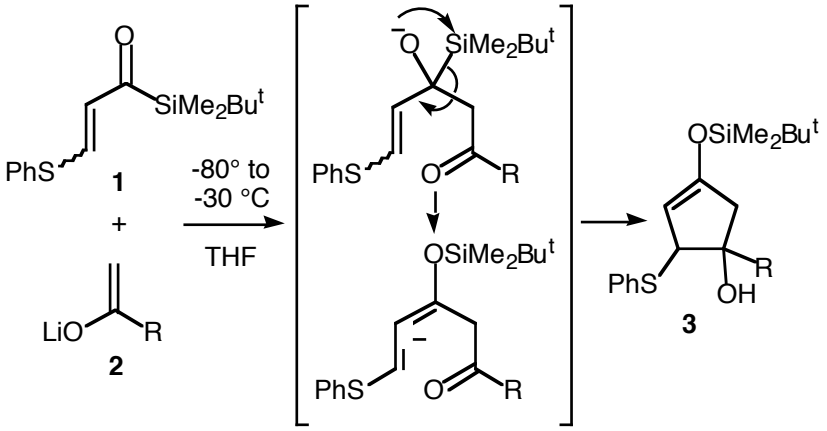
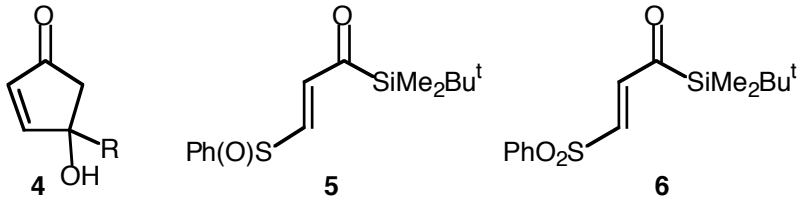
The [3 + 2] annulation using β-[2-(pyridyl)thio] and β,β-dichloro derivatives of acryloylsilane and the lithium enolate of methyl ketones successfully proceeded to afford 4-alkyl-4-hydroxy-3-(2-pyridylthio)cyclopentanone and 4-alkyl-3-chloro-4-hydroxy-2-cyclopentenone, respectively.

The construction of highly functionalized cyclopentenone derivatives has attracted a great deal of attention in recent years because the skeleton has been found in a variety of biologically important molecules. Earlier investigations[1-3] in our laboratory have shown that the [3 + 2] annulation employing a combination of (β-(phenylthio)acryloyl)silanes **1** and the lithium enolate of methyl ketones **2** provided an efficient route for the rapid construction of polyfunctionalized cyclopentenol derivatives **3**.

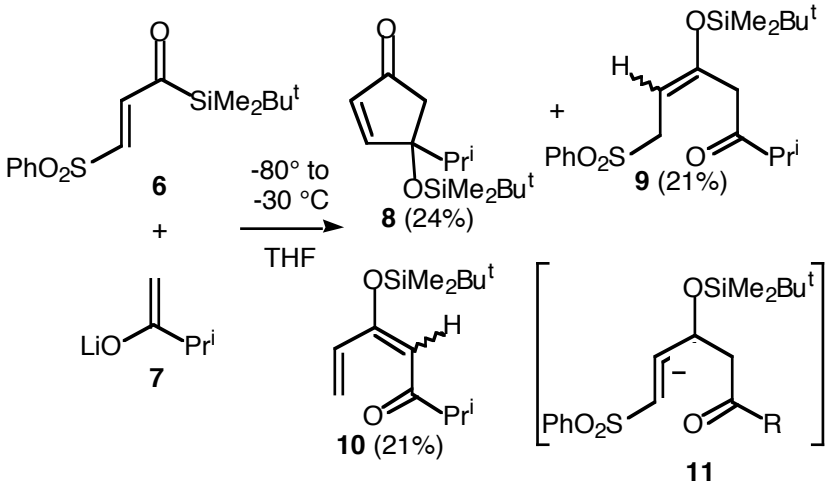


Scheme 1.

Although the cyclopentenols **3** resulting from the annulation are themselves useful structural entities because they contain potentially useful functionalities for further derivatization, the versatility of the annulation would be greatly enhanced if direct formation of 4-hydroxy-2-cyclopentenone derivative **4** from the annulation becomes possible. This prompted us to investigate the annulation using the acryloylsilane bearing a better leaving group than the phenylthio group as the β-substituent. First, we examined the reaction using the β-sulfinyl and β-sulfonyl derivatives, **5**[4] and **6**[4], which were prepared by the mCPBA oxidation of the phenylthio derivative **1**.

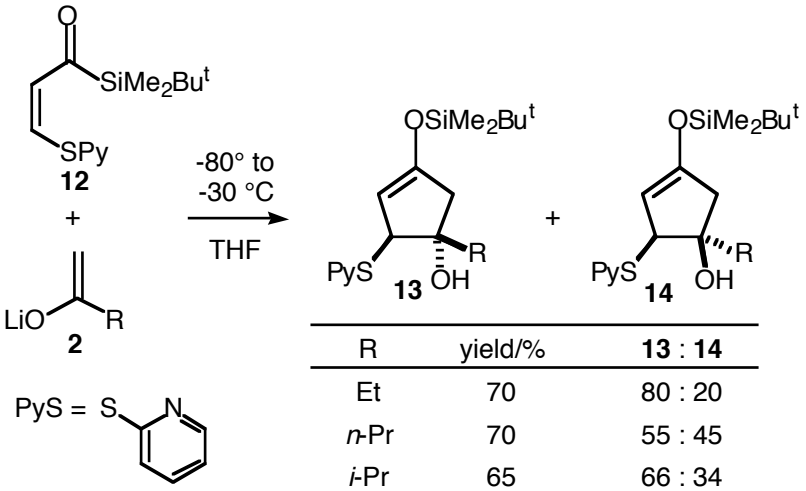


Although the sulfinyl derivative **5** afforded a complex mixture, the reaction of the sulfonyl derivative **6** produced the cyclopentenone **8** together with uncyclized products **9** and **10**. Compound **10** can be formed by the elimination of phenylsulfinate from the enolate of **9** which is generated by intramolecular and/or intermolecular proton abstraction involving the delocalized allylic anion intermediate **11**. The formation of **9** and **10** suggests that **11** is not reactive enough to cyclize in order to form **8** due to the carbanion stabilizing ability of the sulfonyl group and consequently undergoes the competing proton abstraction leading to **9** and **10**.



Scheme 2.

Next, we examined the reaction of acryloylsilane **12**[5] bearing the β-(2-pyridyl)thio group which has lithium chelating ability[6] and is more electron-withdrawing than the phenylthio group but less than the phenylsulfonyl group. When the reaction of **12** with the enolates **2** was conducted under the same conditions as those for **1**, diastereomeric cyclopentenols **13** and **14** rather than the cyclopentenol **4** were obtained as summarized in Scheme 3.

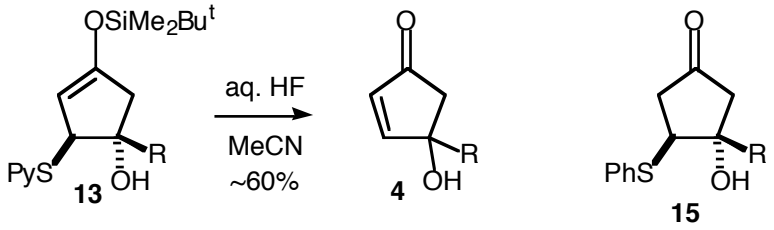


R	yield/%	**13** : **14**
Et	70	80 : 20
n-Pr	70	55 : 45
i-Pr	65	66 : 34
n-octyl	54	67 : 33

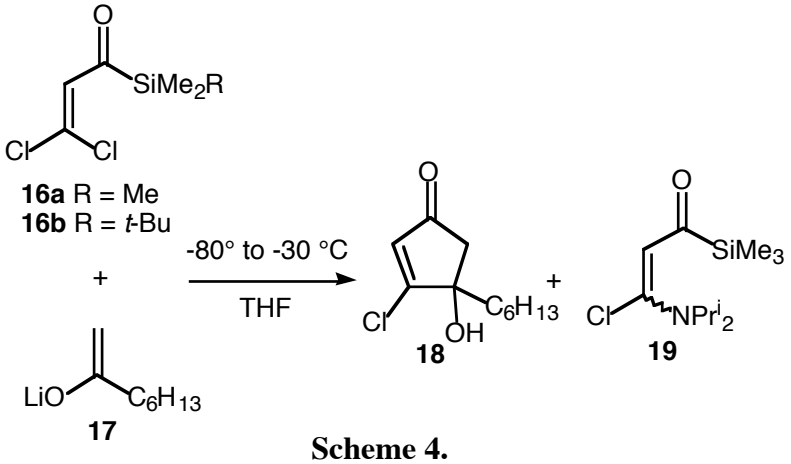
Scheme 3.

Treatment of **13** with aqueous HF in MeCN, however, afforded 2-cyclopentenone **4**, in contrast to the reaction of **3** under same conditions which provided the 3-(phenylthio)cyclopenta-none derivatives **15**.[1]

We next turned to the use of (*β*,*β*-(dichloro)acryloyl)trime-thylsilane (**16**), readily prepared according to the protocol of

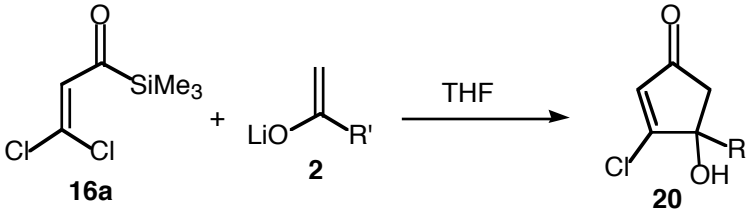


Cunico and Cui-ping[7,8] and expected it to give the 3-chloro-4-hy droxy-2-cyclopentenone derivative **18**, a potentially useful compound for further synthetic manipulation, during the annulation. We first attempted the reaction of **16a** with the lithium enolate of 2-octanone, generated from LDA, but 3-chloro-4-hexyl-4-hydroxy-2-cyclopentenone (**18**) was obtained in only 13% yield. The major side products were the enamine **19** which can be formed by an addition-elimination reaction of the diisopropylamine to **16a**, and the aldol condensation products of the ketone. The aldol condensation can be attributed to the generation of the ketone by the enolate-mediated dehydrochlorination of **16a**.



Scheme 4.

Next, we examined the reaction under the amine-free conditions using mesityllithium as a base to prevent the formation of the side products. When **16a** was treated with lithium enolate **2** at -80° to -30° or 0 °C, 3-chloro-4-hydroxy-2-cyclopentenones **20** were obtained in moderate to good yields as shown in Scheme 5.[9]



R	conditions	yield/%
Et	-80° to 0 °C	43
i-Pr	-80° to -30 °C	65
i-Bu	-80° to 0 °C	62
t-Bu	-80° to -30 °C	70
hexyl	-80° to 0 °C	42
c-C_3H_5	-80° to -30 °C	48

Scheme 5.

Somewhat lower yields relative to the original annulation using **1**, especially in the normal chain ketones, might be attributed to the decomposition via the enolate-mediated dehydrochlorination. No enol silyl ether corresponding to **3**, even when *t*-butyldime-thylsilyl derivatives **16b** was used, was detected. Slightly lower yields (39-53%) of **20** were obtained from the reaction of **16b**. The use of β,β-dibromo derivative resulted in a poor yield (~10%) of **20**.

In summary, we have demonstrated that the Brook rearrangement-mediated [3 + 2] annulation was successfully applied to the direct synthesis of the 3-chloro-4-hydroxy-2-cyclopentenone derivatives.

We thank the Grant-in-Aid for Scientific Research (No. 10671986 (K.T.)) from the Ministry of Education, Science, Sports and Culture, Japan, and the Hoan Sha Foundation for partial support of this research.

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9 General procedure for the [3 + 2] annulation using **16a**: Reaction of **16a** with Li enolate of 3,3-dimethyl-2-butanone. To a cooled (-80 °C) solution of 2-bromomesitylene (149 mg, 749 μmol) in THF (0.8 mL) was added *t*-BuLi (1.15M in pentane, 1.43 mL, 1.64 mmol). The solution was stirred at the same temperature for 20 min. To this mixture was added dropwise a solution of 3,3-dimethyl-2-butanone (94 μL, 749 μmol) in THF (1.5 mL). After being stirred at -80 °C for 30 min, the solution was added dropwise to a solution of (3,3-(dichloro)propanoyl)trimethylsilane (134.3 mg, 681 μmol) in THF (29 mL). The reaction mixture was allowed to warm to -30 °C over 30 min, and quenched using saturated aqueous NH_4Cl solution (10 mL). The mixture was extracted with Et_2O (30 mL x 2), and the combined organic phases were washed with saturated brine, dried ($MgSO_4$), and concentrated. The residual oil was subjected to column chromatography (silica gel, 10 g; elution with 1:1 hexane-Et_2O) to give **20** (R = Et) (90 mg, 70%).

Formation of Four- to Six-Membered Carbocycles by Tandem Brook Rearrangement-Intramolecular Michael Reaction

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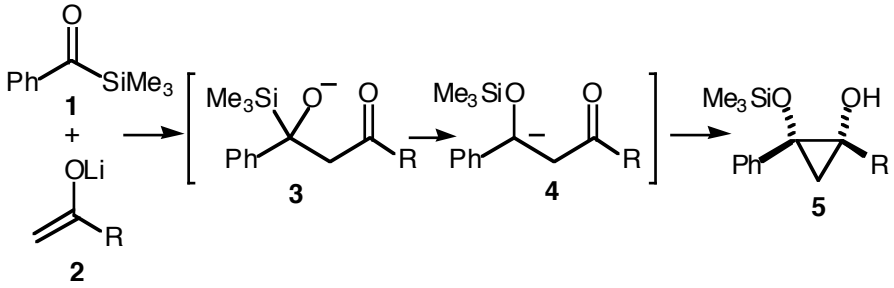
Abstract: A tandem Brook rearrangement-intramolecular Michael reaction has been developed as a synthetic route to functionalized carbocycles. Acylsilanes, tethered by a two-, three-, or four-carbon chain to an acrylate Michael acceptor, have been prepared and used as the cyclization substrates. Treatment of these compounds with PhLi or $LiP(O)(OMe)_2$ at temperatures below 0 °C results in the formation of four- to six-membered carbocycles in good yields.

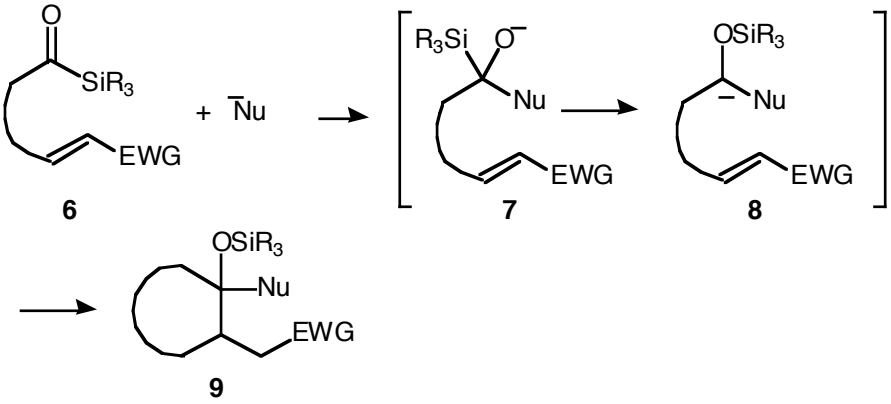
Key words: tandem reaction, acylsilane, Brook rearrangement, intramolecular Michael reaction, carbocycles

Intramolecular Michael reaction constitutes one of the most efficient methodologies for constructing carbocycles and has been widely applied for syntheses of naturally occurring products.[1,2] In many cases, carbanions stabilized by an electron-withdrawing group stronger than the Michael acceptor or by two electron-withdrawing groups have been employed as a Michael donor, allowing selective proton abstraction with bases in the presence of the Michael acceptor. In contrast, intramolecular Michael reactions of unstabilized carbanion centers have received much less attention, with the lithium-halogen exchange-initiated conjugate addition reactions of Cooke being the only examples reported to the best of our knowledge.[3-5]

Six years ago we reported that the reaction of benzoylsilane **1** with ketone enolates **2** affords *cis*-1,2-cyclopropanediol derivatives **5** via the Brook rearrangement[6,7] in the adduct **3** followed by the internal attack of the generated α-siloxy carbanion **4** on the β-carbonyl group.[8]

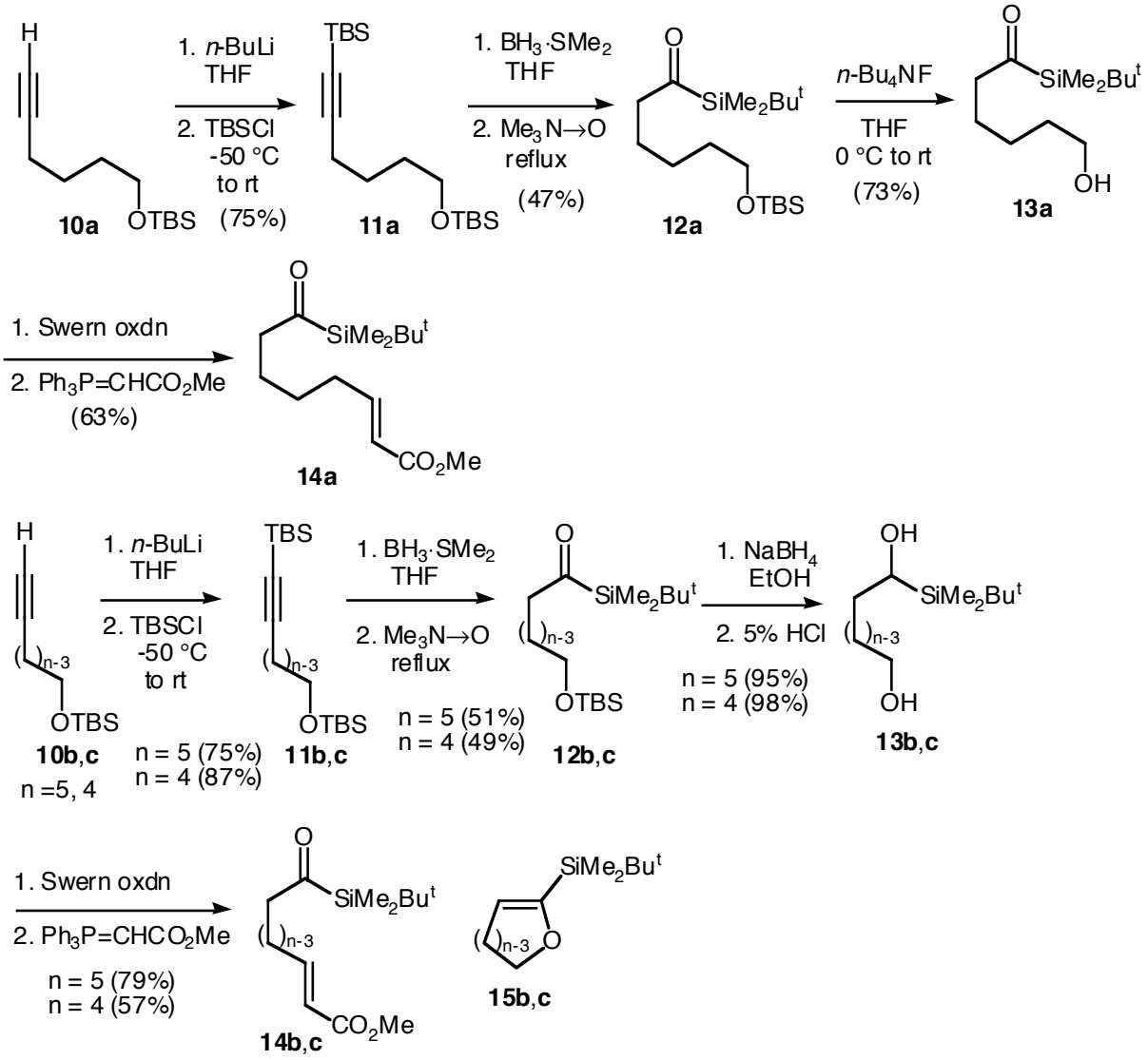


These results led us to expect that the reaction of acylsilanes **6** bearing a Michael acceptor at the appropriate position in the same molecule with a suitable nucleophile would provide a new entry to the construction of carbocycles via a tandem sequence of the Brook rearrangement (**7** to **8**) and the intramolecular Michael reaction (**8** to **9**).



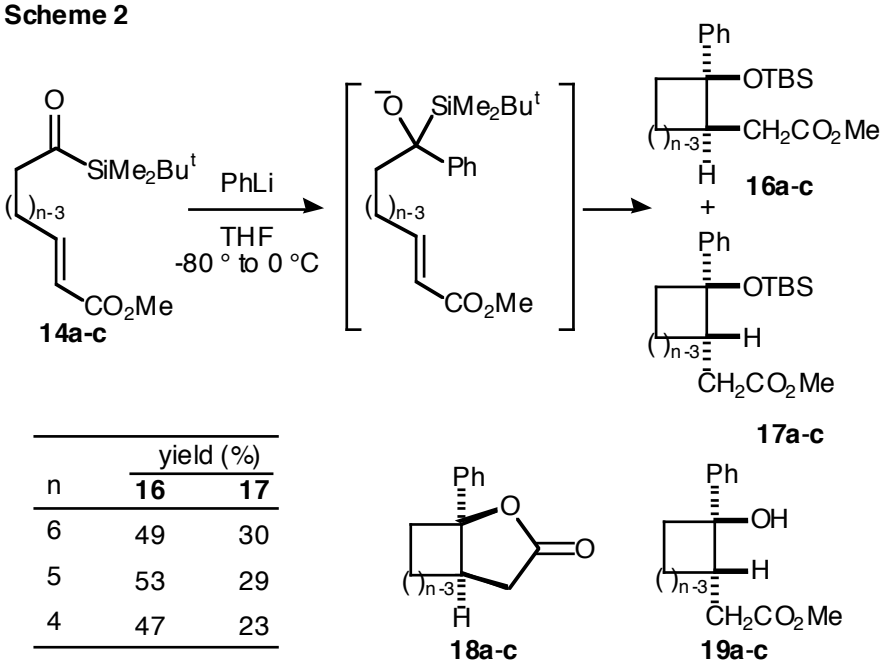
For the investigations of the tandem reaction, we chose phenyllithium and lithium dimethyl phosphite as the nucleop\hile, because the Brook rearrangement is usually accelerated by a carbanion stabilizing group. The cyclization precursor **14a**[9] for a six-membered ring system was prepared by a five-step sequence involving hydroboration,[10] starting with *O*-protected 5-heptyn-1-ol **10a**[11] (Scheme1). In the case of the acylsilanes **14b**,**c**[9] for four- and five-membered rings, reduction of the carbonyl group of the acylsilane before Swern oxidation was required because the oxidation of ω-hydroxyacylsilanes corresponding to **13a** afforded dihydrofuran or dihydropyran derivatives **15b**,**c**, cyclization and a dehydration product.

Scheme 1



When phenyllithium (1 equiv) was added to a THF solution (0.01 M) of acylsilanes **14a**-**c** at –80 °C and the solution was allowed to warm to 0 °C, the tandem Brook rearrangement-intramolecular Michael reaction proceeded smoothly to afford two diastereomeric cycloalkanols **16** and **17** in good yields (Scheme 2).[12] Their stereochemistries were assigned by conversion to bicyclic cis-lactones **18a**-**c** and hydroxy esters **19a**-**c**, respectively, by brief treatment with *n*-Bu_4NF in THF.

Scheme 2

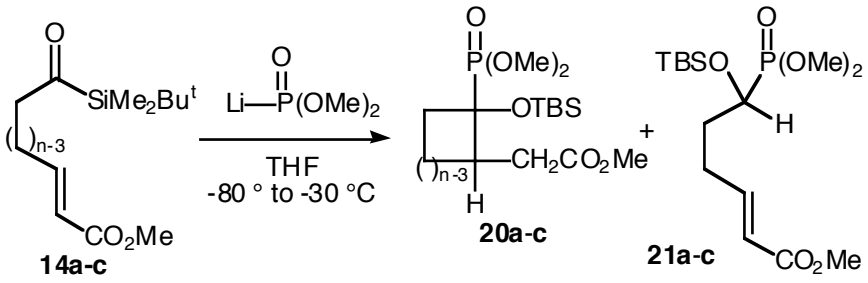


	yield (%)	
n	**16**	**17**
6	49	30
5	53	29
4	47	23

Although the origin of stereoselectivity in the cyclization are unclear at present, these results indicate that the tandem sequence of the Brook rearrangement and intramolecular Michael reaction is a facile process and that an unstabilized carbanion such as α-siloxycarbanion can function as a Michael donor.

Reaction of **14a**-**c** with lithium dimethyl phosphite, conducted in a similar manner to the reaction with phenyllithium, resulted in the formation of a single cyclized product **20a**-**c** with undetermined stereochemistry and a Brook rearranged but uncyclized product **21a**-**c** (Scheme 3).[13]

Scheme 3



	yield (%)	
n	**20**	**21**
6	46	23
5	40	31
4	55	9

The somewhat lower yields of the cyclization products and the formation of the uncyclized products may be due to the bulkiness of the phosphoryl group and/or the increased stabilization of the α-phosphoryl carbanion relative to the phenyl group.

In conclusion, we have developed an unprecedented, tandem Brook rearrangement-intramolecular Michael reaction sequence that is potentially useful for the construction of functionalized carbocycles.

Acknowledgments

This research was partially supported by a grant-in-aid for Scientific Research (No. 10671986 from the Japanese Ministry of Education, Sciences, Sports and Culture, and the Ciba-Geigy Foundation (Japan) for the Promotion of Science.

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(9) Characteristic data for **14a**-**c**. **14a**: a colorless oil, R_f (hexane : AcOEt = 5 : 1) = 0.46. IR (film) 1725, 1655, 1640 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 0.12 (6H, s, $SiMe_2$), 0.87 (9H, s, *t*-Bu), 1.33-1.39 (2 H, m, H-5), 1.45-1.51 (2 H, m, H-6), 2.12-2.16 (2 H, m, H-4), 2.55 (2 H, t, *J* = 7.1 Hz, H-7), 3.66 (3 H, s, OMe), 5.76 (1 H, dt, *J* = 15.8, 1.5 Hz, H-2), 6.89 (1 H, dt, *J* = 15.8, 7.1 Hz, H-3). ^{13}C NMR (125 MHz, $CDCl_3$) δ –6.90 ($SiMe_2$), 16.6 (CMe_3), 21.5 (C-6), 26.5 (CMe_3), 27.8 (C-5), 32.2 (C-4), 49.9 (C-7), 51.5 (OMe), 121.1 (C-2), 149.2 (C-3), 167.1 (CO_2Me), 247.2 (SiC=O). HRMS calcd for $C_{11}H_{19}O_3Si$ (M^+ - *t*-Bu) 227.1103, found 227.1110. **14b**: a colorless oil, R_f (hexane : AcOEt = 5 : 1) = 0.46. IR (film) 1725, 1655, 1640 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 0.14 (6H, s, $SiMe_2$), 0.89 (9H, s, *t*-Bu), 1.63-1.69 (2 H, m, H-5), 2.12-2.16 (2 H, m, H-4), 2.59 (2 H, t, *J* = 7.1 Hz, H-6), 3.69 (3 H, s, OMe), 5.76-5.80 (1 H, dm, *J* = 15.8 Hz, H-2), 6.88 (1 H, dt, *J* = 15.8, 7.1 Hz, H-6). ^{13}C NMR (125 MHz, $CDCl_3$) δ -6.87 ($SiMe_2$), 16.6

(*C*Me$_3$), 20.3 (C-5), 26.5 (C*Me*$_3$), 31.7 (C-4), 49.2 (C-6), 51.6 (OMe), 121.4 (C-2), 148.9 (C-3), 167.1 (*C*O$_2$Me), 246.8 (SiC=O). **14c**: a colorless oil, R_f (hexane : AcOEt = 5 : 1) = 0.46. IR (film) 1725, 1655, 1640 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.14 (6H, s, SiMe$_2$), 0.88 (9H, s, *t*-Bu), 2.34-2.39 (2 H, m, H-4), 2.70 (2 H, t, *J* = 7.3 Hz, H-5), 3.66 (3 H, s, OMe), 5.77 (1 H, dt, *J* = 15.6, 1.7 Hz, H-2), 6.88 (1 H, dt, *J* = 15.6, 7.1 Hz, H-3). ^{13}C NMR (125 MHz, CDCl$_3$) δ -6.93 (SiMe$_2$), 16.6 (*C*Me$_3$), 24.6 (C-4), 26.5 (C*Me*$_3$), 48.2 (C-5), 51.6 (OMe), 121.4 (C-2), 148.4 (C-3), 167.0 (*C*O$_2$Me), 244.9 (SiC=O). HRMS calcd for C$_{13}$H$_{24}$O$_3$Si 256.1495, found 256.1479.

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(12) General procedure for the tandem Brook rearrangement-Michael reaction using phenyllithium. Reaction of **14a** with phenyllithium. To a cooled (-80 °C) solution of **14a** (142 mg, 0.50 mmol) in THF (50 mL) was added phenyllithium (1.07 M in cyclohexane-Et$_2$O, 514 μL, 0.550 mmol). The solution was stirred at the same temperature for 30 min, and then allowed to warm to –30 °C before the addition of AcOH (32 μL, 0.550 mmol) in THF (2 mL). The reaction mixture was diluted with saturated NH$_4$Cl solution (20 mL), and then extracted with Et$_2$O (50 mL x 1, 10 mL x 2). Combined organic phases were washed with saturated brine (20 mL), dried (MgSO$_4$), and concentrated. The residual oil was subjected to column chromatography (silica gel, 15 g; elution with 10:1 hexane:AcOEt) to give a 1.6:1 mixture of **16a** and **17a** (142 mg, 79%), which could be separated by medium pressure liquid chromatography (10 μ silica gel). **16a** a colorless oil, R_f (hexane : AcOEt = 15 : 1) = 0.32. IR (film) 1740 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$) δ -0.16 and 0.08 (each 3 H, s, SiMe$_2$), 0.99 (9H, s, *t*-Bu), 1.35-1.44 (1 H, m, H-5), 1.45-1.55 (2 H, m, H-6), 1.58-1.64 (1 H, m, H-4), 1.69-1.74 (1 H, m, H-5), 1.76-1.81 (1 H, m, H-4), 1.88 (1 H, dm, *J* = 12.2 Hz, H-3), 2.15-2.23 (3 H, m, H-1, H-3, and C*H*$_2$CO$_2$Me), 2.42 (1 H, d, *J* = 12.2 Hz, C*H*$_2$CO$_2$Me), 3.53 (3 H, s, OMe), 7.20-7.31 (3 H, m, Ar-H), 7.46-7.48 (2 H, m, Ar-H). ^{13}C NMR (125 MHz, CDCl$_3$) δ -1.65 and –0.89 (SiMe$_2$), 19.5 (*C*Me$_3$), 22.7 (C-4), 24.7 (C-5), 26.7 (C*Me*$_3$), 28.0 (C-6), 35.3 (*C*H$_2$CO$_2$Me), 37.5 (C-3), 45.0 (C-1), 51.5 (OMe), 79.1 (C-2), 126.7, 126.9, 127.8 and 146.3 (Ar), 174.5 (C=O). HRMS calcd for C$_{17}$H$_{25}$O$_3$Si (M$^+$ - *t*-Bu) 305.1573, found 305.1575. **17a**: a colorless oil, R_f (hexane : AcOEt = 10 : 1) = 0.46. IR (film) 1740 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$) δ -0.10 (6H, s, SiMe$_2$), 0.90 (9H, s, *t*-Bu), 1.36-1.59 (3 H, m, H-3 and H-4), 1.62-1.68 (1 H, m, H-5), 1.73 (1 H, ddd, *J* = 15.4, 3.5, 0.9 Hz, C*H*$_2$CO$_2$Me), 1.77-1.86 (1 H, m, H-5), 1.94 (1 H, ddd, *J* = 13.4, 13.4, 3.8 Hz, H-6), 2.00 (1 H, dm, *J* = 13.4 Hz, H-6), 2.17 (1 H, dd, *J* = 15.4, 11.2 Hz, C*H*$_2$CO$_2$Me), 2.14-2.22 (1 H, m, H-3), 2.63-2.68 (1 H, m, H-1), 3.52 (3 H, s, OMe), 7.22-7.32 (3 H, m, Ar-H), 7.42 (2 H, d, *J* = 7.32 Hz, Ar-H). ^{13}C NMR (125

MHz, $CDCl_3$) δ -3.35 and –2.17 ($SiMe_2$), 18.8 (CMe_3), 19.9 (C-4), 21.8 (C-5), 25.3 (C-3), 26.3 (CMe_3), 31.3 (C-6), 34.2 (CH_2CO_2Me), 42.9 (C-1), 51.6 (OMe), 76.8 (C-2), 126.6, 127.5, 128.2, and 146.0 (Ar), 173.8 (C=O). HRMS calcd for $C_{21}H_{34}O_3Si$ 362.2277, found 362.2271. **16b**: a colorless oil, R_f (hexane : AcOEt = 15 : 1) = 0.32. IR (film) 1740 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ -0.14 and 0.08 (each 3 H, s, $SiMe_2$), 0.98 (9H, s, *t*-Bu), 1.54-1.62 (1 H, m, H-5), 1.81-1.94 (2 H, m, H-4), 1.95-2.02 (1 H, m, H-5), 2.10 (1 H, ddddd, *J* = 9.4, 4.7, 4.7, 4.7, 4.7 Hz, H-3), 2.15-2.12 (1 H, m, H-1), 2.31 (1 H, dd, *J* = 15.6, 10.0 Hz, CH_2CO_2Me), 2.42 (1 H, dd, *J* = 15.6, 4.1 Hz, CH_2CO_2Me), 2.41-2.48 (1 H, m, H-3), 3.53 (3 H, s, OMe), 7.19-7.32 (3 H, m, Ar-H), 7.42-7.45 (2 H, m, Ar-H). ^{13}C NMR (125 MHz, $CDCl_3$) δ -2.58 and –2.27 ($SiMe_2$), 19.1 (CMe_3), 21.9 (C-4), 26.5 (CMe_3), 30.3 (C-5), 33.5 (CH_2CO_2Me), 39.4 (C-3), 51.3 (C-1), 51.5 (OMe), 86.2 (C-2), 125.9, 126.7, 127.9, and 145.8 (Ar), 174.4 (C=O). HRMS calcd for $C_{20}H_{32}O_3Si$ 348.2121, found 348.2152. **17b**: a colorless oil, R_f (hexane : AcOEt = 10 : 1) = 0.46. IR (film) 1740 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ -0.41 and –0.08 (each 3 H, s, $SiMe_2$), 0.86 (9H, s, *t*-Bu), 1.35-1.43 (1 H, m, H-5), 1.61 (1 H, dd, *J* = 15.2, 11.5 Hz, CH_2CO_2Me), 1.82-1.88 (1 H, m, H-4), 1.91-1.99 (1 H, m, H-4), 2.02 (1 H, dd, *J* = 15.2, 3.6 Hz, CH_2CO_2Me), 2.04-2.10 (1 H, m, H-3), 2.14-2.21 (1 H, m, H-5), 2.22-2.28 (1 H, m, H-3), 2.65-2.70 (1 H, m, H-1), 3.57 (3 H, s, OMe), 7.22-7.32 (3 H, m, Ar-H), 7.36-7.38 (2 H, m, Ar-H). ^{13}C NMR (125 MHz, $CDCl_3$) δ -3.21 and –2.61 ($SiMe_2$), 18.4 (CMe_3), 21.0 (C-4), 26.1 (CMe_3), 28.5 (C-5), 35.2 (C-3), 36.8 (CH_2CO_2Me), 48.9 (C-1), 51.6 (OMe), 87.1 (C-2), 127.5, 128.1, and 143.6 (Ar), 173.8 (C=O). HRMS calcd for $C_{20}H_{32}O_3Si$ 348.2121, found 348.2091. **16c**: a colorless oil, R_f (hexane : AcOEt = 10 : 1) = 0.46. IR (film) 1740 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ -0.46, -0.06 (each 3 H, s, $SiMe_2$), 0.84 (9H, s, *t*-Bu), 1.61-1.68 (1 H, m, H-4), 1.85-1.93 (1 H, m, H-4), 2.27-2.33 (1 H, m, H-3), 2.59 (1 H, dd, *J* = 15.6, 7.5 Hz, CH_2CO_2Me), 2.74-2.85 (2 H, m, H-1 and H-3), 2.88 (1 H, dd, *J* = 15.6, 7.5 Hz, CH_2CO_2Me), 3.67 (3 H, s, OMe), 7.23-7.27 (1 H, m, Ar-H), 7.31-7.35 (2 H, m, Ar-H), 7.45-7.47 (2 H, m, Ar-H). ^{13}C NMR (125 MHz, $CDCl_3$) δ -3.42 and –2.83 ($SiMe_2$), 18.3 (CMe_3), 20.1 (C-4), 26.0 (CMe_3), 31.9 (C-3), 35.3 (CH_2CO_2Me), 45.5 (C-1), 51.5 (OMe), 78.6 (C-2), 126.3, 127.3, 128.2, and 146.5 (Ar), 174.0 (C=O). HRMS calcd for $C_{15}H_{21}O_3Si$ (M^+ - *t*-Bu) 277.1260, found 277.1254. **17c**: a colorless oil, R_f (hexane : AcOEt = 15 : 1) = 0.32. IR (film) 1740 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ -0.24 and –0.02 (each 3 H, s, $SiMe_2$), 0.90 (9H, s, *t*-Bu), 1.28-1.36 (1 H, m, H-4), 1.50 (1 H, dd, *J* = 15.6, 10.7 Hz, CH_2CO_2Me), 2.05-2.12 (1 H, m, H-4), 2.16 (1 H, dd, *J* = 15.6, 4.9 Hz, CH_2CO_2Me), 2.31-2.38 (1 H, m, H-3), 2.68-2.72 (1 H, m, H-3), 2.94-3.01 (1 H, m, H-1), 3.57 (3 H, s, OMe), 7.24-7.27 (1 H, m, Ph), 7.32-7.35 (2 H, m, Ar-H), 7.38-7.41 (2 H, m, Ar-H). ^{13}C NMR (125 MHz, $CDCl_3$) δ -2.81 and –2.67 ($SiMe_2$), 18.2 (CMe_3), 20.1 (C-4), 26.1 (CMe_3), 34.1 (C-3), 36.7 (CH_2CO_2Me),

46.5 (C-1), 51.5 (OMe), 79.7 (C-2), 126.6, 127.3, 128.1, and 142.7 (Ar), 173.3 (C=O). HRMS calcd for $C_{15}H_{21}O_3Si$ (M^+ - ^{t}Bu) 277.1260, found 277.1259.

(13) General procedure for the tandem Brook rearrangement-Michael reaction using lithium dimethyl phosphite. Reaction of **14a** with lithium dimethyl phosphite. To a cooled (-80 °C) solution of dimethyl phosphite (50 mL, 0.550 mmol) in THF (2.6 mL) was added *n*-butyllithium (1.33 M in hexane, 0.41 mL, 0.550 mmol). After being stirred at the same temperature for 15 min, the mixture was added to a cooled (-80 °C) solution of **14a** (142 mg, 0.500 mmol) in THF (50 mL). The solution was stirred at the same temperature for 30 min, and then allowed to warm to –30 °C before the addition of AcOH (32 μL, 0.550 mmol) in THF (2 mL). The reaction mixture was diluted with saturated NH_4Cl solution (20 mL), and then extracted with Et_2O (50 mL x 1, 10 mL x 2). Combined organic phases were washed with saturated brine (20 mL), dried ($MgSO_4$), and concentrated. The residual oil was subjected to column chromatography (silica gel, 15 g; elution with 1:2 hexane:AcOEt) to give a 2.0:1 mixture of **20a** and **21a** (137 mg, 69%), which could be separated by medium pressure liquid chromatography (10 μ silica gel). **20a**: a colorless oil, R_f (hexane : AcOEt = 1 : 2) = 0.32. IR (film) 1735 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.15 (6H, s, $SiMe_2$), 0.91 (9H, s, *t*-Bu), 1.24-1.32 (1 H, m, H-5), 1.35-1.44 (1 H, m, H-6), 1.46-1.60 (3 H, m, H-4 and H-6), 1.62-1.69 (2 H, m, H-3 and H-5), 2.04-2.08 (1 H, m, H-3), 2.15 (1 H, dd, J = 16.2, 10.1 Hz, C$H_2$$CO_2$Me), 2.20-2.25 (1 H, m, H-1), 3.16 (1 H, dd, J = 16.2, 2.6 Hz, C$H_2$$CO_2$Me), 3.64 (3 H, s, CO_2*Me*), 3.72 (3 H, d, $J_{H\text{-}P}$ = 10.5 Hz, $P(OMe)_2$), 3.78 (3 H, d, $J_{H\text{-}P}$ = 10.3 Hz, $P(OMe)_2$). ^{13}C NMR (125 MHz, $CDCl_3$) δ -3.11 and –2.50 ($SiMe_2$), 19.5 (*C*Me_3), 20.1 (C-4), 25.3 (C-5), 26.4 (C*Me*$_3$), 27.8 (C-6), 33.3 (C-3), 37.2 (CH_2CO_2Me), 39.3 (C-1), 51.6 (CO_2Me), 52.0 ($J_{C\text{-}P}$ = 8.3 Hz, $P(OMe)_2$), 53.6 ($J_{C\text{-}P}$ = 7.4 Hz, $P(OMe)_2$), 77.9 (C-2), 174.2 (C=O). HRMS calcd for $C_{17}H_{35}O_6PSi$ 394.1941, found 394.1961. **20b**: a colorless oil, R_f (hexane : AcOEt = 2 : 1) = 0.27. IR (film) 1740 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.13 and 0.15 (each 3 H, s, $SiMe_2$), 0.87 (9H, s, *t*-Bu), 1.37-1.46 (1 H, m, H-5), 1.58-1.67 (1 H, m, H-4), 1.74-1.82 (1 H, m, H-4), 1.87-1.93 (1 H, m, H-3), 1.99-2.05 (1 H, m, H-5), 2.16-2.23 (1 H, m, H-3), 2.27 (1 H, dd, J = 16.2, 10.7 Hz, C$H_2$$CO_2$Me), 2.46-2.54 (1 H, m, H-1), 2.86 (1 H, dd, J = 16.2, 3.2 Hz, C$H_2$$CO_2$Me), 3.65 (3 H, s, CO_2Me), 3.74 (3 H, d, $J_{H\text{-}P}$ = 10.5 Hz, $P(OMe)_2$), 3.78 (3 H, d, $J_{H\text{-}P}$ = 10.5 Hz, $P(OMe)_2$). ^{13}C NMR (125 MHz, $CDCl_3$) δ -3.10 and –2.77 ($SiMe_2$), 19.0 (*C*Me_3), 22.4 (C-4), 26.0 (C*Me*$_3$), 30.9 (C-5), 34.7 (*C*$H_2$$CO_2$Me), 36.8 (C-3), 44.3 (C-1), 51.7 (CO_2Me), 52.7 ($P(OMe)_2$), 53.4 ($P(OMe)_2$), 82.9 (C-2), 174.1 (C=O). HRMS calcd for $C_{16}H_{33}PSi$ 380.1784, found 380.1764. **20c**: a colorless oil, R_f (hexane : AcOEt = 1 : 2) = 0.25. IR (film) 1740 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ -0.08 and –0.03 (each 3 H, s, $SiMe_2$), 0.67 (9H, s, *t*-Bu), 1.39-1.46 (1 H, m, H-4), 1.92-2.06 (2 H, m, H-3 and H-4), 2.23 (1 H, dd, J = 16.0, 9.0 Hz, C$H_2$$CO_2$Me), 2.32-2.40 (1 H, m, H-3), 2.45 (1 H, dd, J = 16.0, 6.8 Hz, C$H_2$$CO_2$Me),

2.94-3.01 (1 H, m, H-1), 3.43 (3 H, s, CO_2Me), 3.56 (3 H, d, $J_{H\text{-}P}$ = 10.5 Hz, $P(OMe)_2$), 3.60 (3 H, d, $J_{H\text{-}P}$ = 10.5 Hz, $P(OMe)_2$). ^{13}C NMR (125 MHz, $CDCl_3$) δ -3.29 and –2.54 ($SiMe_2$), 18.6 (*C*Me_3), 21.3 (C-4), 25.9 (C*Me*$_3$), 31.2 (C-3), 34.8 (*C*H_2CO_2Me), 38.9 (C-1), 51.6 (CO_2*Me*), 53.1 ($P(OMe)_2$), 73.9 (C-2), 173.0 (C=O). HRMS calcd for $C_{15}H_{31}O_6PSi$ 366.1628, found 366.1652.

Enantioselective Reduction of α,β-Unsaturated Acylsilanes by Chiral Lithium Amides

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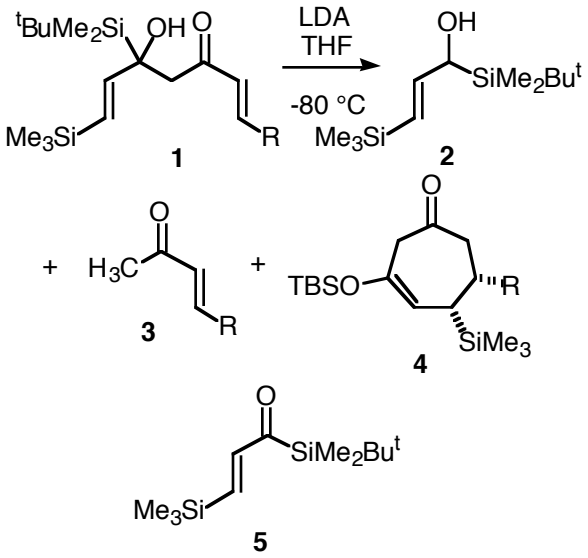
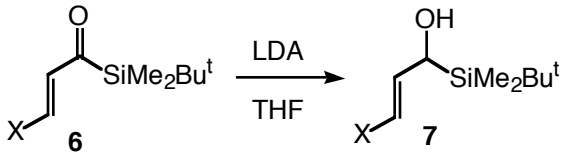
During our investigation of the mechanism of the Brook rearrangement-mediated [3 + 4] annulation,[1] we observed that treatment of α-silyl-β-ketoalcohol **1** with LDA (1 equiv) afforded α-silylalcohol **2** in 16% yield in addition to cycloheptenone **4** (37%), and 3-nonen-2-one (**3**) (36%).[2] The formation of **2** suggests that reduction of acryloylsilane **5**, a retro aldol product, by LDA via the hydride transfer of the Meerwein-Ponndorf-Verley type occurred at –80 °C.

Scheme 1



Although there have been reports on the reduction of a carbonyl group by LDA,[3] the ability of LDA as a reducing agent has attracted far less attention and there has been no report concerning the reduction of α,β-unsaturated acylsilanes by LDA. Therefore, we first examined the reduction of acylsilanes by LDA. When acryloylsilanes **6**[4] were treated with 1 equiv of LDA in THF at -80 °C for 30 to 60 min, the corresponding α-silylalcohols **7** were obtained in yields depending on the β-substituent. Thus, the substrates bearing no γ-hydrogen being abstracted afforded better yields of **7** (Table 1, entries 5-9), whereas in the case of the substrate with γ-hydrogen, significant amounts of the starting acryloylsilane were recovered, suggesting the competitive formation of dienolate in the latter cases.[51]

Table 1



entry	6	X	conditions	yield (%) 7	yield (%) recovery of 6
1	**a**	Me	-80 °C, 30 min	49	50
2	**b**	*i*-Pr	-80 °C, 30 min	64	30
3	**c**	*c*-C_6H_{11}	-80 °C, 30 min	58	37
4	**d**	*c*-C_3H_5	-80 °C, 30 min	36	56
5	**e**	*t*-Bu	-80 °C, 60 min	93	3
6	**f**	$SiMe_3$	-80 °C, 30 min	67	-
7	**g**	$SiMe_2Ph$	-80 °C, 60 min	81	-
8	**h**	$SiMePh_2$	-80 °C, 60 min	82	-
9	**i**	$SiPh_3$	-80 °C, 30 min	88	-
10	**j**	H	-80 °C, 30 min	26	-

On the basis of the above result, we envisioned that the use of lithium amide of chiral secondary amines instead of LDA would offer the possibility of enantioselective reduction. To the best of our knowledge, there are only two reports in the literature on the enantioselective reduction of a carbonyl group via formal hydride transfer from chiral lithium amides. In 1969 Wittig and Thiele reported the enantioselective reduction of phenyl α-naphthyl ketone by lithium (*R*)-(-)-α-phenylethylanilide to give the corresponding alcohol in 25% yield and ee less than 60%.[6] Cervinka and co-workers used (*S*)-(+)-2-methylpiperidine as a chiral source in the reaction with diaryl ketones with little success.[7] Since α-hydroxysilanes have shown promise as versatile synthons for synthetically useful transformations, the generation of such spieces in enatiomerically pure form would be desirable.[8,9,10] We first examined the enantioselective reduction by several known lithium amides **8**-**12**[11] using **6e** as a substrate. Among the five lithium amides examined, **12** gave the best result in terms of chemical and optical yields; that is, the reaction proceeded smoothly to give alcohol **13** with excellent optical purity. Assignment of absolute configuration of **13** was made by the method of Trost[12] using *O*-methylmandelate and the modified Mosher method.[13] Changes in the solvent from THF to THF-HMPA (3 equiv) or toluene caused a decrease in chemical yield and/or ee.

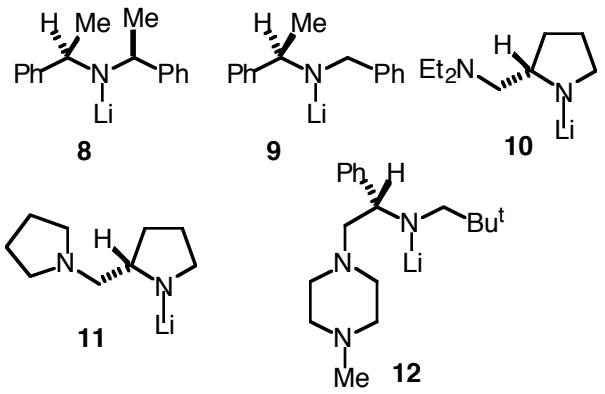
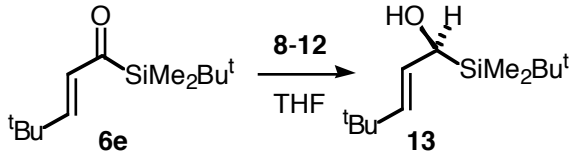


Table 2. Enantioselective Reduction of 6e

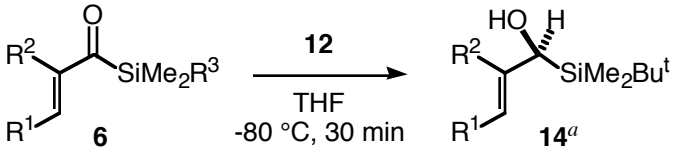


lithium amide	temperature	yield (%)	ee (%)[b]
8	-80 °C to -15 °C	16[a]	66
9	-80 °C to -15 °C	55	57
10	-80 °C	85	9
11	-80 °C	99	14
12	-80 °C	88	>99

[a] 63% of **6e** was recovered. [b] Enantiomeric purity was determined by chiral HPLC assay (Daicel Chiralcel-OD)

Encouraged by these results, we examined the enantioselective reduction of some α.β-unsaturated acylsilanes, including cycloalkenylcarbonylsilanes, by **14**. The results are summarized in Table 4. Although the chemical yields depended upon the presence of an abstractable γ-hydrogen, as was the case for LDA, α-silylalcohol **16** was obtained in excellent optical yield. Unfortunately, β-silyl derivatives **6e**-**g** produced a complex mixture in sharp contrast to the case of LDA. Elevated reaction temperatures and/or longer reaction times resulted in the Brook rearrangement and in some cases followed by allylic rearrangement of the generated carbanion.

Table 3. Asymmetric Reduction of α,β-Unsaturated Acylsilanes 6

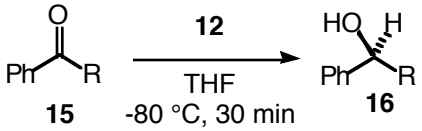


	R^1	R^2	R^3	yield (%)	ee (%)	recovery of **6**
6a	Me	H	Bu^t	31	>99[b]	53
6b	*i*-Pr	H	Bu^t	55	>99[b]	4
6c	*c*-C_6H_{11}	H	Bu^t	55	>99[b]	32
6d	*c*-C_3H_5	H	Bu^t	68	>99[b]	13
6k	-$(CH_2)_3$-		Ph	63	>99[c]	37
6l	-$(CH_2)_4$-		Ph	55	>99[c]	41
6m	-$(CH_2)_5$-		Ph	61	>99[c]	34

[a] Absolute configuration was assigned by analogy with **13**.
[b] Enantiomeric purity was determined by chiral HPLC assay (Daicel Chiralcel-OD and Chiralcel-OJ). [c] Enantiomeric purity was determined by ^1H NMR spectra after conversion into the corresponding Mosher's esters

This method was applicable to benzoylsilanes **15a**-**b** and nonenolizable phenyl ketones **15c**-**d**, albeit in lower chemical and optical yields.

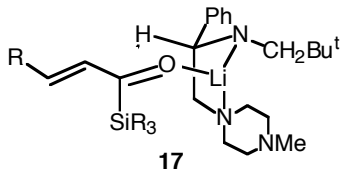
Table 4



	R	yield (%)	ee (%)[a]
15a	$SiMe_3$	64	81[b]
15b	$SiMe_2Bu^t$	37	53[c]
15c	CF_3	65	23[b]
15d	β-naphthyl	43	33[b]

[a] Enantiomeric purity was determined by chiral HPLC assay (Daicel Chiralcel-OD and Chiralcel-OJ). [b] Absolute configuration was assigned by comparison of the sign of optical rotation with reported value.[14,15] [c] Absolute configuration was assigned by analogy with **16a**. [d] Commercially available.

Although the enantioselectivity can be interpreted as being the result of a process via a six-membered transition state **17** in which the silyl and the chelated piperazinylmethyl groups occupy an axial position, the precise mechanism is not known and is now under investigation.[16]



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In conclusion, we have found that the lithium amide of chiral secondary am[17]ines can serve as the chiral source in the enantioselective reduction of a carbonyl group, especially α,β-unsaturated acylsilanes. In this method, α-silylalcohols can be obtained in an optically pure form even if the chemical yield is not so good because, in most cases, the α-silylalcohol is only a product and can be easily separated from the recovered acylsilanes. Investigation of the potential application, especially the use of acryloylsilanes as a chiral homoenolate equivalent using a tandem reaction sequence involving enantioselective reduction, and Brook and allylic rearrangements is underway.

Acknowledgment This research was partially supported by a grant-in-aid for Scientific Research (No. 10671986) from the Japanese Ministry of Education, Sciences, Sports and Culture, and the Ciba-Geigy Foundation (Japan) for the Promotion of Science.

Supporting Information Available: Full experimental details and characterization data for all new compounds described in the text (7 pages, PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(5) The formation of 1,2- and/or 1,4-adducts of the amide to the α,β-unsaturated acylsilanes leading to the recovery of the starting material cannot be ruled out. (a) Kowalski, C.; Creary, X.; Rollin, A. J.; Burke, M. C. *J. Org. Chem.* **1978**, *43*, 2601-2608. (b) Herrmann, J. L.; Kieczykowski, G. R.; Schlessinger, R. H. *Tetrahedron Lett.* **1973**, 2433-2436.

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Enantioselective Reduction of α,β-Unsaturated Acylsilanes by Chiral Lithium Amides

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Supporting Information

Experimental Section

General: IR spectra were recorded on a Perkin-Elmer FT1640 spectrometer. ^{1}H NMR spectra were taken on Varian UnityPlus 500 (500 MHz) in $CDCl_3$ with reference to $CHCl_3$ (δ 7.26). ^{13}C NMR spectra were measured with Varian UnityPlus 500 (125 MHz) in $CDCl_3$ with reference to the $CDCl_3$ triplet (δ 77.2). Resonance patterns were described as s = singlet, d = doublet, t = triplet, m = multiplet, and br = broad. Low-and high-resolution mass spectra (EI-MS) were obtained with a JEOL JMS-D-300 spectrometer combined with a JEOL JMA-2000 data processing system. For chromatography, the following adsorbents were used: Fuji-Davison silica gel BW-200 (150-325 mesh) for column chromatography; Merck precoated silica gel 60 F-254 plates for analytical thin-layer chromatography. All moisture sensitive reactions were performed under a positive pressure of nitrogen. Anhydrous $MgSO_4$ was used for drying all organic solvent extracts in workup, and the removal of the solvents was performed with a rotary evaporator. Dry solvents and reagents were obtained by using standard procedures. Melting points (uncorrected) were determined by using a Yanagimoto micro-melting point apparatus. Elemental combustion analysis was performed at the Microanalysis Laboratory of this University.

(*E*)-*tert*-Butyldimethylsilyl 2-(Methyldiphenylsilyl)ethenyl Ketone (6h) This compound was prepared according to the procedure for 2-trimethylsilyl derivative by Reich.[1] yellow oil, R_f = 0.30 (hexane-AcOEt = 20 : 1). IR (film) 1600 cm^{-1}. ^{1}H NMR δ 0.24 (6H, s, $SiMe_2$), 0.70 (3H, s, SiMe), 0.93 (9H, s, *t*-Bu), 6.76 (1H, d, *J* = 19.0 Hz), 7.14 (1H, d, *J* = 19.0), 7.34-7.52 (10H, m, Ar). ^{13}C NMR δ -5.8 ($SiMe_2$), -4.0 (SiMe), 16.9 (CMe_3), 26.8 (*t*-Bu), 128.1, 129.8, 134.9, 134.9, 135.0, 140.5 and 150.0 (Ar), 236.5 (C=O). Anal. calcd for $C_{22}H_{30}OSi_2$: C, 72.07; H, 8.25, found: C, 71.72; H, 8.42.

(*E*)-*tert*-Butyldimethylsilyl 2-(Triphenylsilyl)ethenyl Ketone (6i) This compound was prepared according to the procedure for 2-trimethylsilyl derivative. yellow needles, R_f = 0.26 (hexane-AcOEt = 30

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: 1). IR (KBr) 1595 cm^{-1}. ^1H NMR δ 0.23 (6H, s, $SiMe_2$), 0.92 (9H, s, *t*-Bu), 6.78 (1H, d, *J* = 19.0 Hz), 6.28 (1H, d, *J* = 19.0), 7.37-7.53 (15H, m, Ar). ^{13}C NMR δ -5.8 ($SiMe_2$), 16.9 (CMe_3), 26.8 (*t*-Bu), 128.3, 130.2, 133.1 and 136.1 (Ar), 138.4 (C-3), 151.1 (C-2), 236.5 (C=O). MS, *m/e*, 428 (M^+), 259 (base peak). Anal. calcd for $C_{27}H_{32}OSi_2$: C, 75.64; H, 7.52, found: C, 75.40; H, 7.45.

***tert*-Butyldimethylsilyl Ethenyl Ketone (6j)** This compound was prepared according to the procedure for trimethylsilyl derivative. colorless oil, IR (film) 1600 cm^{-1}. ^1H NMR δ 0.24 (6H, s, $SiMe_2$), 0.93 (9H, s, *t*-Bu), 5.77 (1H, dd, *J* = 10.8, 1.3 Hz, H-3a), 6.03 (1H, dd, *J* = 17.7, 1.3 Hz, H-3b), 6.57 (1H, dd, *J* = 17.7, 10.8 Hz, H-2). ^{13}C NMR δ -5.9 ($SiMe_2$), 16.8 (CMe_3), 26.7 (*t*-Bu), 126.8 (C-3), 141.7 (C-2), 237.3 (C=O). HRMS calcd for $C_9H_{19}OSi$ (M^++1) 171.1205 found 171.1204.

Cycloheptenecarbonyl(dimethyl)phenylsilane (6m) To a mixture of cycloheptanone (15.0 g, 0.134 mol) and Me_3SiCN (17.3g, 23.2 mL, 0.174 mol) in benzene (50 mL) was added zinc iodide (1.00 g, 3.13 mmol). After the reaction mixture was stirred at room temperature for 1 h, $POCl_3$ (60.0 g, 0.991 mol) and pyridine (200 mL) were added, and then the mixture was refluxed for 5 h. The cooled dark solution was poured into ice-10% hydrochloric acid (900 mL), and extracted with ether (800 mL x 3). The combined organic phases were washed with saturated brine (800 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 400g; elution with hexane-AcOEt = 20:1) to give 1-cyano-1-cycloheptene (12.9 g, 79 %) as a colorless oil.

To a cooled (0 °C) solution of 1-cyano-1-cycloheptene (10 g, 85.2 mmol) in Et_2O (200 mL) was added dropwise diisobutylaluminium hydride (0.94 M hexane solution, 100 mL, 94 mmol) over 20 min. After the reaction mixture was stirred for 1 h, the reaction was quenched by addition of MeOH (100 mL) followed by stirring at room temperature for 1 h. The mixture was filtered through a plug of Celite, and the filtrate was concentrated *in vacuo*. The residual oil was diluted with THF (300 mL), and then oxalic acid (10 % aqueous solution, 300 mL) was added at 0 °C. After stirring at room temperature for 20 min, the mixture was poured into H_2O (600 mL), and extracted with ether (600 mL x 3). The combined organic phases were washed with saturated brine (400 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 500g; elution with hexane-AcOEt = 20:1) to give 1-cycloheptenecarboxaldehyde (6.8 g, 64 %, as a colorless oil).

To a cooled (-80°C) solution of $PhMe_2SiLi$[2] (0.37 M in THF, 164 mL, 60.7 mmol) in Et_2O (300 mL) was added dropwise 1-cycloheptenecarboxaldehyde (6.8 g, 54.8 mmol). The solution was allowed to warm to 0 °C over 2 h, and then quenched by saturated aqueous NH_4Cl solution (300 mL). The mixture was diluted with water (200 mL), and then extracted with Et_2O (500 mL x 3). The combined organic

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phases were washed with saturated brine (500 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 400g; elution with hexane-AcOEt = 20:1) to give cycloheptenyl(dimethylphenylsilyl)methanol (12.6 g, 88 % as an yellow oil). R_f = 0.17 (hexane-AcOEt = 30 : 1). IR (film) 3455 cm^{-1}. ^1H NMR δ 0.35 and 0.37 (each 3H, s, $SiMe_2$), 1.33-1.48 (4H, m, H-4 and H-6), 1.67-1.75 (2H, m, H-5), 1.90-1.99 (2H, m, H-7), 2.06-2.21 (2H, m, H-3), 4.02 (1H, s, C*H*OH), 5.63 (1H, t, *J* = 6.6 Hz, H-2), 7.35-7.42 (3H, m, Ar-H), 7.58-7.64 (2H, m, Ar). ^{13}C NMR δ -5.0 and -4.5 ($SiMe_2$), 27.0 (C-4), 27.5 (C-6), 28.5 (C-3), 31.5 (C-7), 32.8 (C-5), 72.3 (CHOH), 123.7 (C-2), 127.9, 129.4, 134.3 and 137.2 (Ar), 146.6 (C-1). HRMS calcd for $C_{16}H_{24}OSi$ 260.1596 found 260.1604.

A solution of cycloheptenyl(dimethylphenylsilyl)methanol (6.0 g, 23.0 mmol) in CH_2Cl_2 (9 mL) was added at -60 °C over 10 min to a solution of chloro(dimethyl)sulfonium chloride, which was prepared by dropwise addition of solution of DMSO (3.6 g, 3.27 mL, 46.1 mmol) in CH_2Cl_2 (6 mL) to a cooled (-70 °C) solution of oxalyl chloride (3.2 g, 2.2 mL, 25.2 mmol) in CH_2Cl_2 (9 mL) over 5 min, followed by stirring at -60 to -70 °C for 30 min. After stirring at ca. -65 °C for 30 min, triethylamine (11.6 g, 16 mL, 1.15 mmol) was added. The solution was allowed to warm to room temperature over 30 min. The mixture was diluted with water (100 mL), and extracted with CH_2Cl_2 (75 mL x 2). The combined organic phases were washed with saturated brine (75 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 550g; elution with hexane-AcOEt = 30:1) to give cycloheptenecarbonyl(dimethyl)phenylsilane (5.8 g, 98 %) as an yellow oil, which solidified on keeping in a refrigerator. Yellow prisms, mp 62-64 °C (hexane). R_f = 0.33 (hexane-AcOEt = 30 : 1). IR (KBr) 1575 cm^{-1}. ^1H NMR δ 0.52 (6H, s, $SiMe_2$), 1.38-1.43 (2H, m, H-6), 1.46-1.51 (2H, m, H-4), 1.79-1.76 (2H, m, H-5), 2.25-2.30 (2H, m, H-3), 2.36-2.40 (2H, H-7), 6.92 (1H, t, *J* = 6.4 Hz, H-2), 7.34-7.54 (3H, m, Ar-H), 7.50-7.54 (2H, m, Ar). ^{13}C NMR δ -2.2 ($SiMe_2$), 23.9 (C-7), 25.9 (C-6), 26.1 (C-4), 29.4 (C-3), 32.0 (C-5), 127.9, 129.3, 133.7 and 136.9 (Ar), 151.8 (C-2), 152.0 (C-1), 232.6 (C=O). Anal. calcd for $C_{16}H_{22}OSi$: C, 74.36; H, 8.58, found: C, 74.27; H, 8.65.

General Procedure for LDA reduction To a cooled (-80 °C) solution of β-*t*-butylacryloylsilane **6e** (96 mg, 0.424 mmol) in THF (4.2 mL) was added dropwise a solution of lithium diisopropylamide (LDA), prepared from diisopropylamine (77.2 μL, 55.8 mg, 0.551 mmol) and *n*-BuLi (1.46 M in hexane, 378 μL, 0.551 mmol) in THF (0.8 mL). After the solution was stirred at -80 °C for 30 min, a solution of acetic acid (33 mg, 0.55 mmol) in THF (2 mL) was added rapidly in one portion. The reaction mixture was poured into half saturated aqueous NH_4Cl solution, and extracted with Et_2O (30 mL x 3). The combined organic phases were washed with saturated brine (30 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 10 g; elution with hexane-AcOEt = 30:1) to give corresponding alcohol **7e** (90.0 mg, 93%).

7a (X = Me) colorless oil, R_f = 0.22 (hexane-AcOEt = 30 : 1). IR (film) 3450 cm^{-1}. ^1H NMR δ -0.06 and 0.01 (each 3H, s, $SiMe_2$), 0.94 (9H, s, *t*-Bu), 1.71 (3H, dt, *J* = 6.4, 1.5 Hz, H-4), 4.05 (1H, ddq, *J* = 7.1, 1.5, 1.5 Hz, H-1), 5.50 (1H, dqd, *J* = 15.3, 6.4, 1.5 Hz, H-3), 5.65 (1H, ddq, *J* = 15.3, 7.1, 1.5 Hz, H-2). ^{13}C NMR δ -8.7 and-7.5 ($SiMe_2$), 17.1 (CMe_3), 18.1 and 27.1 (*t*-Bu), 67.1 (C-1), 122.5 (C-3), 133.4 (C-2). HRMS calcd for $C_{10}H_{22}OSi$ 186.1440 found 186.1424.

7b (X = *i*-Pr) colorless oil, R_f = 0.22 (hexane-AcOEt = 28 : 1). IR (film) 3455 cm^{-1}. ^1H NMR δ -0.06 and 0.00 (each 3H, s, $SiMe_2$), 0.94 (9H, s, *t*-Bu), 0.98 and 0.99 (6H, d, *J* = 1.5 Hz), 2.31 (1H, m, H-4), 4.06 (1H, ddd, *J* = 0.9, 1.5, 6.8 Hz, H-1), 5.45 (1H, ddd, *J* = 1.5, 6.6, 15.4 Hz, H-3), 5.59 (1H, ddd, *J* = 1.1, 6.8, 15.4 Hz, H-2). ^{13}C NMR δ -8.7 and-7.5 ($SiMe_2$), 17.2 (CMe_3), 22.8 and 27.2 (*t*-Bu), 31.2 (C-4), 67.0 (C-1), 129.3 (C-2), 134.9 (C-3). HRMS calcd for $C_{12}H_{25}OSi$ 213.1675(M^+ -1) found 213.1665.

7c (X = *c*-C_6H_{11}) colorless oil, R_f = 0.32 (hexane-AcOEt = 30 : 1). IR (film) 3455 cm^{-1}. ^1H NMR δ -0.07 and -0.01 (each 3H, s, $SiMe_2$), 0.94 (9H, s, *t*-Bu), 0.95-1.28 and 1.62-1.73 (10H, m, *c*-C_6H_{11}), 1.97 (1H, m, H-4), 4.06 (1H, br d, *J* = 6.8, H-1), 5.43 (1H, ddd, *J* = 15.4, 6.6, 1.5 Hz, H-3), 5.58 (1H, ddd, *J* = 15.4, 6.8, 1.3 Hz, H-2). ^{13}C NMR δ -8.7 and-7.4 ($SiMe_2$), 17.2 (CMe_3), 27.2 (*t*-Bu), 26.4 and 33.4 (*c*-C_6H_{11}), 40.8 (C-4), 67.1 (C-1), 129.7 (C-2), 133.7 (C-3). HRMS calcd for $C_{15}H_{30}OSi$ 254.2066 found 254.2063.

7d (X = *c*-C_3H_5) colorless oil, R_f = 0.23 (hexane-AcOEt = 30 : 1).IR (film) 3455 cm^{-1}. ^1H NMR δ -0.06 and 0.00 (each 3H, s, $SiMe_2$), 0.33 and 0.68(each 2H, m, *c*-C_3H_5), 0.94 (9H, s, *t*-Bu), 1.38 (1H, m, H-4), 4.04 (1H, dd, *J* = 1.5, 7.2, H-1), 5.06 (1H, ddd, *J* = 1.5, 8.5, 15.3 Hz, H-3), 5.69 (1H, dd, *J* = 7.2, 15.3 Hz, H-2). ^{13}C NMR δ -8.7 and-7.5 ($SiMe_2$), 6.8 and 6.9 (*c*-C_3H_5), 13.7 (C-4), 17.2 (CMe_3), 27.2 (*t*-Bu), 67.0 (C-1), 129.9 (C-2), 131.7 (C-3). HRMS calcd for $C_{12}H_{25}OSi$ (M^+ + 1) 213.1675 found 213.1673.

7e (X = *t*-Bu) colorless oil, R_f = 0.32 (hexane-AcOEt = 30 : 1). IR (film) 3848 cm^{-1}. ^1H NMR δ -0.07 and -0.01 (each 3H, s, $SiMe_2$), 0.94 (9H, s, *t*-Bu), 4.07 (1H, d, *J* = 5.7 Hz, H-1), 5.50 (1H, d, *J* = 15.8 Hz, H-3), 5.54 (1H, dd, *J* = 5.7, 15.8 Hz, H-2). ^{13}C NMR δ -8.6 and-7.5 ($SiMe_2$), 17.2 (CMe_3), 27.2 and 30.0 (*t*-Bu), 33.0 (C-4), 67.1 (C-1), 127.0 (C-2), 134.9 (C-3). HRMS calcd for $C_{13}H_{27}OSi$ (M^+ - 1) 227.1831 found 227.1829.

7f (X = $SiMe_3$) colorless oil, R_f = 0.39 (hexane-AcOEt = 30 : 1). IR (film) 3435 cm^{-1}. ^1H NMR δ -0.05 and -0.02 (each 3H, s, $SiMe_2$), 0.06 (9H, s, $SiMe_3$), 0.95 (9H, s, *t*-Bu), 4.21 (1H, dd, *J* = 2.1, 4.7 Hz, H-1), 5.67 (1H, dd, *J* = 2.1, 18.8 Hz, H-3), 6.28 (1H, dd, *J* = 4.7, 18.8 Hz, H-2). ^{13}C NMR δ -8.8 and-7.4 ($SiMe_2$), -0.9 ($SiMe_3$), 17.3 (CMe_3), 27.1 (*t*-Bu), 69.6 (C-1), 122.9 (C-3), 133.4 (C-2). HRMS calcd for $C_{12}H_{28}OSi_2$ 244.1679 found 244.1654.

7g (X = $SiMe_2Ph$) colorless oil, R_f = 0.31 (hexane-AcOEt = 30 : 1). IR (film) 3430 cm^{-1}. ^1H NMR δ -0.05 and -0.01 (each 3H, s, Me of $SiMe_2Bu^t$), 0.34 (6H, s, Me of $SiMe_2Ph$), 0.95 (9H, s, *t*-Bu), 4.26 (1H,

br, H-1), 5.82 (1H, dd, *J* = 2.1, 18.8 Hz, H-3), 6.35 (1H, dd, *J* = 4.5, 18.8 Hz, H-2), 7.26-7.53 (5H, m, Ar-H). ^{13}C NMR δ -8.8 and-7.3 (Me of $SiMe_2Bu^t$), -2.2 (Me of $SiMe_2Ph$), 17.3 (CMe_3), 27.1 (*t*-Bu), 69.6 (C-1), 120.4 (C-3), 127.9, 129.1 and 134.7 (Ar), 150.7 (C-2). HRMS calcd for $C_{17}H_{30}OSi_2$ 306.1835 found 306.1859.

7h (X = SiMePh$_2$) colorless oil, R_f = 0.13 (hexane-AcOEt = 35 : 1). IR (film) 3455 cm^{-1}. ^{1}H NMR δ -0.05 and 0.02 (each 3H, s, $SiMe_2$), 0.64 (3H, s, SiMe), 0.95 (9H, s, *t*-Bu), 4.31 (1H, dd, *J* = 2.2, 4.3 Hz, H-1), 6.03 (1H, dd, *J* = 2.2, 18.8 Hz, H-3), 6.38 (1H, dd, *J* = 4.3, 18.8 Hz, H-2) 7.34-7.55 (10H, m, Ar-H). ^{13}C NMR δ -8.8 ($SiMe_2$), -3.3 (SiMe), 17.2 (CMe_3), 27.1 and 27.2 (*t*-Bu), 69.7 (C-1), 118.1 (C-3), 128.0, 129.4, 134.9 and 135.0 (Ar), 153.1 (C-2). HRMS calcd for $C_{22}H_{32}OSi_2$ 368.1992 found 368.1965.

7i (X = SiPh$_3$) colorless oil, R_f = 0.29 (hexane-AcOEt = 15 : 1). IR (film) 3490cm^{-1}. ^{1}H NMR δ -0.10and 0.01 (each 3H, s, $SiMe_2$), 0.92 (9H, s, *t*-Bu), 4.34 (1H, br, H-1), 6.26 (1H, dd, *J* = 2.1, 18.7Hz, H-3), 6.38 (1H, dd, *J* = 3.8, 18.7 Hz, H-2) 7.34-7.65 (15H, m, Ar-H). ^{13}C NMR δ -12.4 ($SiMe_2$), 13.7 (CMe_3), 23.6 (*t*-Bu), 66.3 (C-1), 112.5 (C-3), 124.5, 126.1, 131.6 and 132.6 (Ar), 151.7 (C-2). HRMS calcd for $C_{27}H_{34}OSi_2$ 430.2148 found 430.2156.

7j (X = H) colorless oil, R_f = 0.29 (hexane-AcOEt = 30 : 1). IR (film) 3390 cm^{-1}. ^{1}H NMR δ -0.04 and 0.00 (each 3H, s, $SiMe_2$), 0.96 (9H, s, *t*-Bu), 1.28 (1H, br, OH), 4.18 (1H, m, H-1), 4.99 (1H, ddd, *J* = 1.6, 3.0, 10.7 Hz, H-3a), 5.08 (1H, ddd, *J* = 1.6, 2.1, 17.0 Hz, H-3b), 6.07 (1H, ddd, *J* = 5.3, 10.7, 17.0 Hz, H-2). ^{13}C NMR δ -9.0 and -9.0 (each $SiMe_2$), 17.2 (CMe_3), 27.1 (*t*-Bu), 67.7 (C-1), 109.5 (C-3), 140.9 (C-2). HRMS calcd for $C_9H_{19}OSi$ 171.1205(M^+-1) found 171.1194.

General Procedure for Asymmetric Reduction by Chiral Lithium Amides The following procedure for **6e** is representative: To a cooled (-80°C) solution of **6e** (104 mg, 0.459 mmol) in THF (4.5 mL) was added dropwise a solution of lithium amide of **12**, prepared from **12** (159 mg, 0.549 mmol) and *n* -BuLi (1.45 M in hexane, 379 μL, 0.549 mmol) in THF (0.9 mL). After the reaction mixture was stirred at -80 °C for 30 min, the reaction was quenched by acetic acid (33 mg, 0.55mmol) in THF (2 mL). The mixture was poured into half saturated aqueous NH_4Cl solution (20 mL) and then extracted with Et_2O (30 mL x 3). The combined organic phases were washed with saturated brine (30 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 10 g; elution with hexane-AcOEt = 30:1) to give **13** (92.1 mg, 88%).

14k ($R_1 = R_2 = -(CH_2)_3-$) colorless oil, R_f = 0.21 (hexane-AcOEt = 30 : 1). IR (film) 3435 cm^{-1}. ^{1}H NMR δ 0.37 and 0.39 (each 3H, s, $SiMe_2$), 1.79 -2.39 (6H, m, $(CH_2)_3$), 4.28 (1H, m, H-1), 5.44 (1H, m, H-3), 7.36-7.61 (5H, m, Ph). ^{13}C NMR δ -5.2 and -5.1 (each $SiMe_2$), 23.8, 32.3, 34.0 ($(CH_2)_3$), 67.3 (C-1), 121.9 (C-3), 147.0 (C-2), 127.9, 129.5, 134.2, 147.0 (Ph). HRMS calcd for $C_{14}H_{20}OSi$ 232.1283 found 232.1283.

14l ($R_1 = R_2 = -(CH_2)_4-$) colorless oil, R_f = 0.24 (hexane-AcOEt = 30 : 1). IR (film) 3455 cm^{-1}. ^1H NMR δ 0.35 and 0.36 (each 3H, s, $SiMe_2$), 1.34 -2.05 (8H, m, $(CH_2)_4$), 3.96 (1H, br, H-1), 5.50 (1H, m, H-3), 7.36-7.60 (5H, m, Ph). ^{13}C NMR δ -5.0 and -4.8 (each $SiMe_2$), 22.9, 22.9, 25.2, 27.3 ($(CH_2)_4$), 71.0 (C-1), 119.5 (C-3), 137.2 (C-2), 127.9, 134.2, 134.3, 137.2 (Ph). HRMS calcd for $C_{15}H_{22}OSi$ 246.1440 found 246.1142.

14m ($R_1 = R_2 = -(CH_2)_5-$) yellow oil, R_f = 0.17 (hexane-AcOEt = 30 : 1). IR (film) 3455 cm^{-1}. ^1H NMR δ 0.35 and 0.37 (each 3H, s, $SiMe_2$), 1.33-1.48 (4H, m, H-4,6), 1.67-1.75 (2H, m, H-5), 1.93-1.95 (2H, m, H-7), 2.06-2.21 (2H, m, H-3), 4.02 (1H, s, CHSi), 5.63 (1H, t, J = 6.6 Hz, H-2), 7.35-7.61 (5H, m, Ar-H). ^{13}C NMR δ -5.0 and -4.5 ($SiMe_2$), 27.0 (C-4), 27.5 (C-6), 28.5 (C-3), 31.5 (C-7), 32.8 (C-5), 72.3 (CHSi), 123.7 (C-2), 127.9, 129.4, 134.3 and 137.2 (Ar), 146.6 (C-1). HRMS calcd for $C_{16}H_{24}OSi$ 260.1596 found 260.1604.

Enantiomeric Purity Assays of 13, 14 and 16.[a]

				retention times (min)		$[\alpha]_D$ ($CHCl_3$)
	HPLC column[b]	eluent (hexane:*i*-PrOH)	flow rate (mL/min)	*R*	*S*	*S*
13	OD	200 :1	0.3	17.0	14.8	-41.1 ° (c = 1.13)
14a	OD	200 :1	0.3	19.9	19.0	-36.7 ° (c = 0.65)
14b	OJ	200 :1	0.3	14.3	12.1	-38.8 ° (c = 1.90)
14c	OD	200 :1	0.3	17.2	16.1	-37.6 ° (c = 1.05)
14d	OD	200 :1	0.5	13.1	12.4	-39.1 ° (c = 1.20)
14k	-	-	-	-	-	-49.8 ° (c = 0.44)[c]
14l	OD	20 :1	0.3	16.5, 15.9[c]		-8.2 ° (c = 1.07)
14m	-	-	-	-	-	-21.2 ° (c = 1.03)[c]
16a	OD	20 : 1	1.0	12.5	7.0	-79.7 ° (c = 1.08)
16b	OD	20 : 1	1.0	8.6, 16.5[c]		-43.5 ° (c = 0.51)
16c	OD	20 : 1	1.0	15.5	12.8	+7.0 ° (c = 0.56)
16d	OD	20 : 1	1.3	8.6, 16.5[c]		-4.0 ° (c = 1.35)

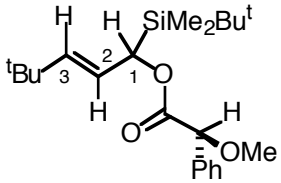
[a] In the case of **16c** and **16d**, (*R*)-**12** was used. [b] OD: Daicel Chiralcel-OD ; OJ: Daicel Chiralcel-OJ. [c] The absolute configuration was not determined.

Determination of the Absolute Configuration of 13.

The MTPA esters of **13** and the *O*-methylmandelates of **13** and *ent*-**13** were prepared by conventional manner.

		^{1}H chemical shift, δ (ppm)		$\Delta\delta = \delta_S - \delta_R$	assigned configuration
		(*S*)-MTPA	(*R*)-MTPA		
MTPA esters	H-1	5.55	5.44	+0.11	*S*
of **13**	H-2	5.46	5.34	+0.12	
	H-3	5.68	5.57	+0.11	

SiMe	-0.03	0.00	-0.03
SiMe	-0.04	-0.02	-0.02
t-Bu	0.86	0.89	-0.03



(*S*)-*O*-methylmandelates of **6e** and *ent*-**13**

	^{1}H chemical shift, δ (ppm)		$\Delta\delta = \delta_{\mathbf{6e}} - \delta_{ent\text{-}\mathbf{6e}}$	assigned configuration
	15	*ent*-**15**		
H-1	5.29	5.29	0	
H-2	5.17	5.35	-0.18	
H-3	4.88	5.42	-0.54	
SiMe	-0.07	-0.26	+0.19	*S*
SiMe	-0.07	-0.26	+0.19	
t-Bu	0.77	0.72	+0.05	

Facile Construction of a Tricyclo[5.3.0.0^{1,4}]decenone Ring System by the Brook Rearrangement-Mediated [3 + 4] Annulation

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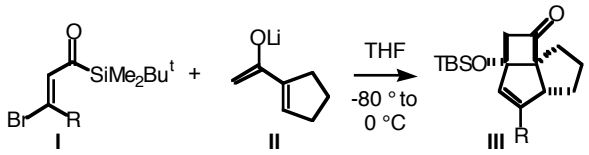
Abstract

Reaction of 3-alkyl-3-haloacryloylsilanes Ⅰ with the lithium enolate of 1-acetyl-1-cyclopentene Ⅱ afforded tricylco[5.3.0.0^{1,4}]decenone derivatives Ⅲ via Brook rearrangement-mediated [3 + 4] annulation.

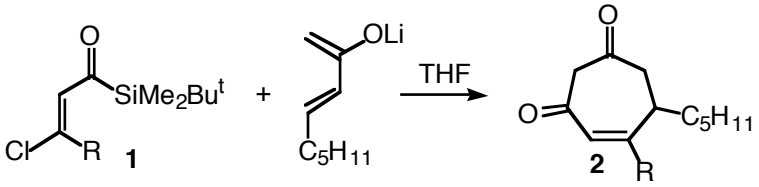


Recently, we have reported that the reaction of β,β-dichloroacryloylsilane with ketone enolates proceeds smoothly at lower temperatures to afford 3-alkyl-3-chloro-4-hydroxy-2-cyclopentenone derivatives via Brook rearrangement-mediated [3 + 2] annulation followed by dechlorosilylation.[1,2] Herein, we describe the direct formation of tricyclo[5.3.0.0^{1,4}]decenone ring system from the reaction of β-alkyl-β-haloacryloylsilane with the lithium enolate of 1-acetyl-1-cyclopentene which was found during an extension of the [3 + 2] annulation for the formation of cycloheptenedione derivatives by the [3 + 4] annulation[3] using enolates of alkenyl methyl ketones.

Our initial attempt to react β-chloro-β-methylacryloylsilane **1a**[4] with the lithium enolate of 3-nonen-2-one, produced the corresponding [3 + 4] annulation-dechlorosilylation product **2a** in 75% yield (Scheme 1). Additional examples using acyclic enone enolates are given in Scheme 1.

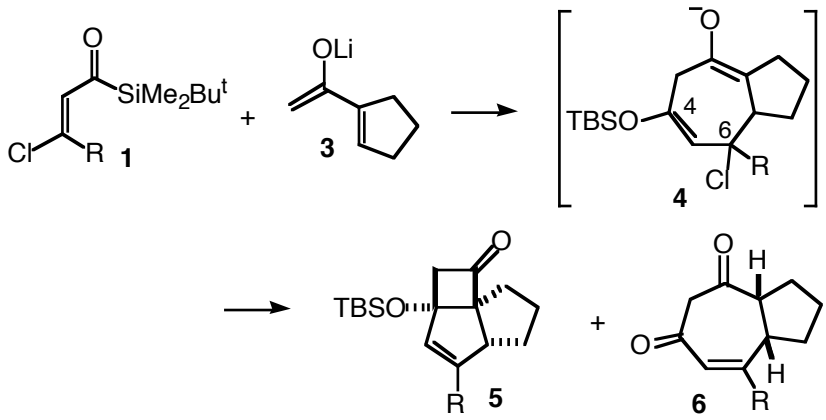
In sharp contrast to these results, reaction of **1** with the enola[5]te of 1-acetyl-1-cyclopentene (**3**) produced tricyclo[5.3.0.0^{1,4}]decenone derivatives **5**[6] in yields dependent upon the β-substituent of **1**, in addition to **6**, a [3 + 4] annulation-dechlorosilylation product. The formation of **5** can be understood in terms of an S_N'-like intramolecular attack of the enolate at C-4 position in the intermediate **4**.

Scheme 1



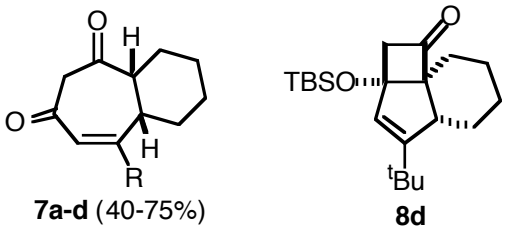
	R	conditions	yield (%)
a	CH_3	-80 ° to 0 °C	75
b	*n*-Bu	-80 ° to 0 °C	41
c	*n*-hexyl	-80 ° to 0 °C	33
d	*t*-Bu	rt	54

Scheme 2



			yield (%)	
	R	conditions	**5**	**6**
a	CH_3	-80 ° to 0 °C	25	35
b	*n*-Bu	-80 ° to 0 °C	48	11
c	*n*-hexyl	-80 ° to 0 °C	22	31
d	*t*-Bu	rt	4	43

In the reactions with enolates of 1-acetyl-1-cyclohexene, **7** was the only product except for R = *t*-Bu where the corresponding tricyclic compound **8d** was obtained in 9% yield (50% yield of **7d**).

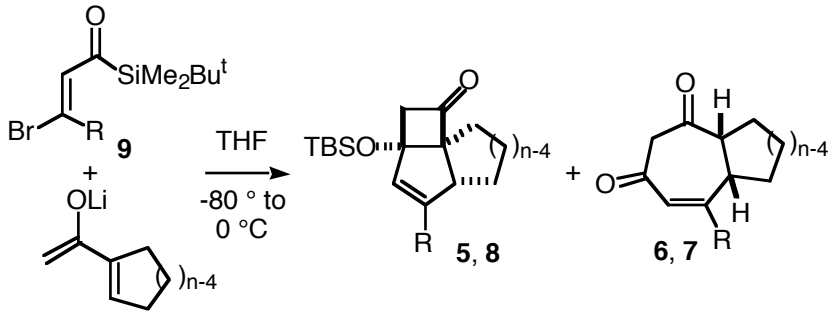


7a-d (40-75%) **8d**

Figure 1.

These results suggest that small structural changes in **1** and the enolates significantly affect the product distributions, and led us to consider replacing the chlorine atom with a better leaving group. When the β-bromo derivative **9**[4] was reacted with **3** under the same conditions as those for the β-chloroderivative **1**, **5** was obtained as a sole product in all cases except for **9d** (R = *t*-Bu) where 7% of **6** was isolated. The same reaction with the enolate of 1-acetyl-cyclohexene afforded the corresponding tricyclic compounds **8** in moderate yield, in sharp contrast to the reaction with **1** in which only substrate **1d** afforded a tricyclic product (**8d**).

Scheme 3



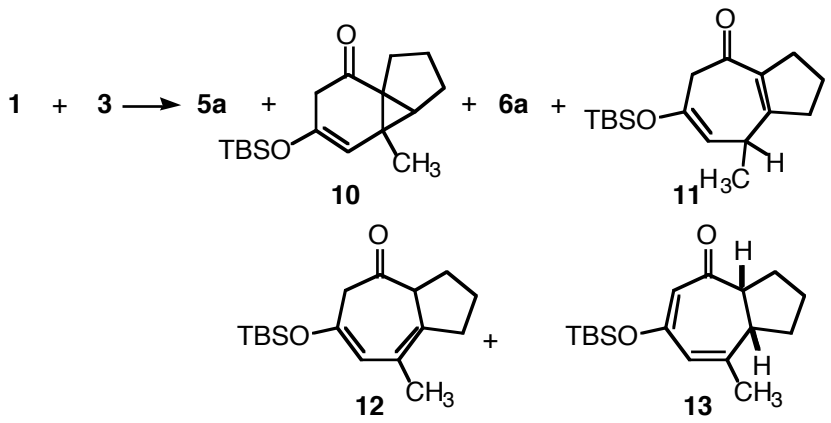
		yield (%), n = 5		yield (%), n = 6	
	R	**5**	**6**	**8**	**7**
a	CH_3	68	0	27	45
b	*n*-Bu	49	0	27	14
c	*n*-hexyl	41	0	35	17
d	*t*-Bu	51	7	58	14
e	*c*-C_3H_5	56	0	39	32

A low-temperature quenching experiment was carried out using **1a** to gain information on the reaction path for the formation of the tricyclic compound **5** and the cycloheptenedione **6** (Scheme 4). Tricyclic compound **10**,[7] an intramolecular alkylation product of the enolate at C-6 position in **4**, and **11** and

its double bond isomers **12** and **13** were isolated. The yield of **6a** increased at the expense of **10** with rising temperature, whereas that of **5a** was relatively constant, suggesting that the major pathway involves the initial formation of **5a** and **10** by way of intramolecular alkylation of the enolate in **4** followed by transformation of **10** to **6a** via **11**-**13**. In fact, in order to duplicate the conditions present when LDA was used to generate the enolates, treatment of **10** with LiCl and diisopropylamine in THF at –80 ° to 0 °C afforded **6a** (56%) and **13** (14%), while in the case of **5a**, no reactions occurred under the same conditions.

In conclusion, we have developed a rapid and efficient route for the synthesis of a tricyclo[5.3.0.$0^{1,4}$]decenone ring system, which is a potentially useful intermediate for synthesizing a variety of biologically significant compounds, but which is difficult to make by other approaches.[8]

Scheme 4



	yield (%)						
conditions	**5a**	**10**	**6a**	**11**	**12**	**13**	**1**
-80 °C, 1h	3	5	0	3	0	0	59
-80 ° to -50 °C	22	14	12	3	4	0	20
-80 ° to -30 °C	21	1	15	2	6	23	12
-80 ° to -15 °C	27	0	43	5	0	3	3

Acknowledgment This research was partially supported by a grant-in-aid for Scientific Research (No. 10671986) from the Japanese Ministry of Education, Sciences, Sports and Culture, and the Ciba-Geigy Foundation (Japan) for the Promotion of Science.

Supporting Information Available: Full experimental details and characterization data for all new compounds described in the text (7 pages).

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(3) (a) Takeda, K.; Takeda, M.; Nakajima, A.; Yoshii, E. *J. Am. Chem. Soc*. **1995**, *117*, 6400-6401. (b) Takeda, K.; Nakajima, A.; Yoshii, E. *Synlett* **1996**, 753-754. (c) Takeda, K.; Nakajima, A.; Takeda, M.; Okamoto, Y.; Sato, T.; Yoshii, E.; Koizumi, T.; Shiro, M. *J. Am. Chem. Soc.* **1998**, *120*, 4947-4959. (d) Takeda, K.; Nakajima, A.; Takeda, M.; Yoshii, E. *Org. Synth*. **1999**, *76*, 199-213.

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(6) The structures were assigned on the basis of their IR spectra, which showed a peak at 1775 cm^{-1}, and confirmed by a X-ray analysis of **5a** after derivatization.

(7) The structure of **10** was assigned on the basis of its ^{13}C NMR spectrum that showing peaks assinged as a quatanary carbon at 34.2 and 49.7 ppm, and IR absorption at 1685 cm^{-1} which is indicative of the cyclopropyl carbonyl moiety with an siloxyvinyl group, see: Lyle, T. A.; Frei, B. *Helv. Chim. Acta*. **1981**, *64*, 2598-2605.

(8) For preparation of tricyclo[5.3.0.$0^{1,4}$]decenone ring system using α-oxycyclopropylcarbinol-cyclobutanone rearrangement, see: (a) Wenkert, E.; Arrhenius, T. S. *J. Am. Chem. Soc*. **1983**, *105*, 2030-2033. For preparation by photochemical reaction, see: (b) Exon, C.; Nobbs, M.; Magnus, P. *Tetrahedron* **1981**, *37*, 4515-4519, (c) Wiesner, K. *Tetrahedron* **1975**, *31*, 1655-1658, and ref. 6.

Facile Construction of a Tricyclo[5.3.0.0^{1,4}]decenone Ring System by the Brook Rearrangement-Mediated [3 + 4] Annulation

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Supporting Information

General: IR spectra were recorded on a Perkin-Elmer FT1640 spectrometer. ^{1}H NMR spectra were taken on Varian UnityPlus 500 (500 MHz) in $CDCl_3$ with reference to $CHCl_3$ (δ 7.26) unless otherwise noted. ^{13}C NMR spectra were measured with Varian UnityPlus 500 (125 MHz) in $CDCl_3$ with reference to the $CDCl_3$ triplet (δ 77.2) unless otherwise noted. Resonance patterns were described as s = singlet, d = doublet, t = triplet, m = multiplet, and br = broad. Low- and high-resolution mass spectra (EI-MS) were obtained with a JEOL JMS-D-300 spectrometer combined with a JEOL JMA-2000 data processing system. For routine chromatography, the following adsorbents were used: Fuji-Davison silica gel BW-200 (150-325 mesh) for column chromatography; Merck precoated silica gel 60 F-254 plates for analytical thin-layer chromatography. All moisture sensitive reactions were performed under a positive pressure of nitrogen. Anhydrous $MgSO_4$ was used for drying all organic solvent extracts in workup, and the removal of the solvents was performed with a rotary evaporator. Dry solvents and reagents were obtained by using standard procedures. Melting points (uncorrected) were determined by using a Yanagimoto micro-melting point apparatus. Elemental combustion analysis was performed at the Microanalysis Laboratory of this University.

1-(*tert*-Butyldimethylsilyl)-3-alkyl-3-chloro-2-propen-1-one (1). The following procedure for **1a** (R = Me) is representative: These compounds were prepared by a modified procedure of Cunico as described for the the corresponding trimethylsilyl derivative. A solution of (1-(ethoxy)ethenyl)-*tert*-butyldimethylsilane (6.00 g, 32.2 mmol), $BrCCl_3$ (6.30 mL, 64.4 mmol), and DBU (4.80 mL, 32.2 mmol) in CCl_4 (21 mL) was irradiated with a sunlamp for 4 h before addition of H_2O (20 mL). The mixtue was extracted with pentane (20 mL x 3). The combined organic phases were successively washed with hydrochloric acid (0.1N) and saturated brine, and concentrated. The residual oil was filtered through a pad of Florisil (pentane), and then subjected to column chromatography (silica gel, 200 g; elution with 5:1 pentane-CH_2Cl_2) to give **1** (R = Cl) (6.56 g, 85%). a red oil. R_f = 0.23 (hexane : CH_2Cl_2 = 5 : 1). IR (film) 1630

cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.21 (6H, s, Si*Me*$_2$), 0.94 (9H, s, Si*tBu*), 7.01 (1H, s, H-2). ^{13}C-NMR (125 MHz, $CDCl_3$) δ -7.14 (Si*Me*$_2$), 17.1 (Si*C*), 26.6 (Si-*tBu*), 128.7 (C-2), 130.0 (C-3), 231.9 (C-1). HRMS calcd for $C_9H_{16}OCl_2Si$ 238.0347, found 238.0336.

To a cooled (-80 °C) suspension of anhydrous CuCN (1.34 g, 14.7 mmol) in THF (120 mL) was added dropwise a solution of MeLi (1.0 M in Et_2O, 14.7 mL, 14.7 mmol). The reaction mixture was allowed to warm to –20 °C. After the mixture became a clear solution, the solution was cooled to –80 °C. To this solution was added dropwise a solution of **1** (R = Cl) (2.50 g, 10.5 mmol) in THF (175 mL). The reaction mixture was allowed to warm to –30 °C before addition of AcOH (0.86 mL, 14.7 mmol) in THF (5 mL). The mixture was diluted with H_2O (200 mL), and then extracted with pentane (150 mL x 3). The combined organic phases were washed with saturated brine, dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 120 g; elution with 19:1 hexane-Et_2O) to give **1a** (R = Me) (1.84 g, 80%).

1a (R = Me): an yellow oil. R_f = 0.42 (hexane : CH_2Cl_2 = 5 : 1). IR (film) 1635 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.19 (3H, s, Si*Me*), 0.19 (3H, s, Si*Me*), 0.93 (9H, s, Si*tBu*), 2.47 (3H, s, H-4), 6.88 (1H, q, *J* = 0.4 Hz, H-2). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-7.1 (Si*Me*$_2$), 17.1 (Si*C*), 24.6 (C-4), 26.7 (Si*tBu*), 129.4 (C-2), 147.7 (C-3), 234.8 (C-1). HRMS calcd for $C_{10}H_{19}OClSi$, 218.0894, found 218.0925.

1b (R = *n*-Bu): an orange oil. R_f = 0.48 (hexane : CH_2Cl_2 = 6 : 1). IR (film) 1630 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.18 (6H, s, Si*Me*$_2$), 0.90 (3H, t, *J* = 7.5 Hz, H-7), 0.92 (9H, s, Si*tBu*), 1.34 (2H, m, H-5), 1.56 (2H, m, H-6), 2.81 (2H, t, *J* = 7.7 Hz, H-4), 6.86 (1H, s, H-2). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-7.1 (Si*Me*$_2$), 14.0 (C-7), 17.0 (SiC), 22.2 (C-6), 26.7 (Si*tBu*), 30.2 (C-5), 36.4 (C-4), 129.4 (C-2), 152.7 (C-3), 234.5 (C-1). HRMS calcd for $C_{13}H_{25}ClOSi$ 260.1363, found 260.1368.

1c (R = *n*-hexyl): a yellow oil. R_f = 0.38 (hexane : CH_2Cl_2 = 9 : 1). IR (film) 1640 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.19 (6H, s, Si*Me*$_2$), 0.87 (3H, t, *J* = 7.5, H-9), 0.93 (9H, s, Si*tBu*), 1.25-1.35 (6H, m), 1.54-1.59 (2H, m), 2.81 (2H, t, *J* = 7.5 Hz, H-4), 6.86 (1H, s, H-2). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-7.0 (Si*Me*$_2$), 14.2 (C-7),17.1 (Si*C*), 22.7, 26.7 (Si*tBu*), 28.1, 28.7, 31.7, 36.6 (C-4), 129.5 (C-2), 152.7 (C-3), 234.5 (C-1). HRMS calcd for 288.1676, found 288.1673.

1d (R = *t*-Bu): an yellow oil. R_f = 0.38 (hexane : CH_2Cl_2 = 9 : 1). IR (film) 1630 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.20 (6H, s, Si*Me*$_2$), 0.94 (9H, s, Si*tBu*), 1.19 (9H, s, *t*-Bu), 6.43 (1H, s, H-2). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-6.6 (Si*Me*$_2$), 17.0 (Si*C*), 26.6 (Si*tBu*), 30.1 (*t*-Bu), 40.4 (C-4), 133.4 (C-2), 151.1 (C-3), 238.8 (C-1). HRMS calcd for $C_9H_{16}OClSi$ (M^+ - C_4H_9), 203.0659, found 203.0629.

General Procedure for the [3 + 4] Annulation Leading to Cycloheptenediones 2: Reaction of 1a with Lithium Enolate of 3-Nonen-2-one. To a cooled (-80°C) solution of lithium diisopropylamide (LDA), prepared from diisopropylamine (0.100 mL, 80 mg, 0.789 mmol) and *n*-BuLi (1.41 M in hexane, 0.55 mL, 0.775 mmol) in THF (0.8 mL) was added dropwise a solution of 3-nonen-2-one (130 δL, 109 mg, 0.775 mmol) in THF (0.8 mL). After stirring at -80 °C for 30 min, the solution was added dropwise via a cannula to a cooled (-80 °C) solution of **1a** (150 mg, 0.686 mmol) in THF (31 mL). The reaction mixture was allowed to warm to 0 °C, and then quenched by addition of AcOH (46 δL, 0.789 mmol). The mixture was diluted with saturated aqueous NH_4Cl solution, and extracted with Et_2O (50 mL x 3). The combined organic phases were washed with saturated brine, dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 40 g; elution with 1:2 hexane-Et_2O) to give **2a** (106 mg, 75%).

2a (R = Me): a pale yellow oil. R_f = 0.16 (hexane : Et_2O = 5 : 1). IR (film) 1655 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.85 (3H, t, *J* = 6.8 Hz, H-5'), 1.21-1.31 (5H, br m), 1.42-1.47 (2H, br m), 1.67-1.72 (1H, br m), 2.00 (3H, d, *J* = 1.3 Hz, CH_3), 2.57-2.62 (1H, br m, H-6), 2.67 (1H, dd, *J* = 15.3, 6.6 Hz, H-7), 2.78 (1H, dd, *J* = 15.3, 3.2 Hz, H-7), 3.62 (1H, d, *J* = 16.7, H-2), 3.71 (1H, d, *J* = 16.7, H-2), 5.96 (1H, s, H-4). ^{13}C-NMR (125 MHz, $CDCl_3$) δ14.1 (C-5'), 22.5, 25.9 (CH_3), 27.5, 31.6, 32.0, 41.0 (C-6), 46.1 (C-7), 60.7 (C-2), 129.0 (C-4), 161.5 (C-5), 193.4 (C-3), 203.6 (C-1). HRMS calcd for $C_{13}H_{20}O_2$, 208.1463, found 208.1494.

2b (R = *n*-Bu): a colerless oil. R_f = 0.23 (hexane : Et_2O = 1 : 2). IR (film) 1650, 1575 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.85 (3H, t, *J* = 6.8, H-5"), 0.89 (3H, t, *J* = 7.3, H-4'), 1.21-1.38 (7H, br m), 1.39-1.49 (4H, m), 1.67 (1H, m), 2.20 (2H, t, *J* = 8.1 Hz), 2.53 (1H, m, H-6), 2.74 (2H, app d, *J* = 4.7 Hz, H-7), 3.58 (1H, dd, *J* = 16.8, 0.9 Hz, H-2), 3.76 (1H, d, *J* = 16.8 Hz, H-2), 5.94 (1H, d, *J* = 0.9, H-4). ^{13}C-NMR (125 MHz, $CDCl_3$) δ14.0 (C-5"), 14.1 (C-4'), 22.5, 27.6, 30.4, 30.5, 31.6, 32.4, 38.7, 40.0 (C-6), 46.3 (C-7), 60.9 (C-2), 127.9 (C-4), 165.6 (C-5), 193.7 (C-3), 203.6 (C-1). HRMS calcd for $C_{16}H_{26}O_2$ 250.1933, found 250.1929.

2c (R = *n*-hexyl): olorless oil. R_f = 0.21 (hexane : Et_2O = 1 : 1). IR (film) 1650, 1575 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.89 (6H,m, H-6'and H-5"), 1.23-1.36 (11H, m), 1.43-1.55 (4H, m), 1.67-1.71 (1H, m), 2.23 (2H, t, *J* = 7.0 Hz, H-1'), 2.54-2.59 (1H, m, H-6), 2.78 (2H, app d, *J* = 7.1 Hz, H-7), 3.62 (1H, dd, *J* = 16.9, 1.0 Hz, H-2), 3.80 (d, *J* = 16.9 Hz, 1H, H-2), 5.98 (1H, d, *J* = 1.0 Hz, H-4). ^{13}C-NMR (125 MHz, $CDCl_3$) δ14.1 (C-5"), 14.2 (C-6'), 22.6, 22.7, 27.7, 28.4, 29.2, 31.7, 32.5, 39.1 (C-1'), 40.1 (C-6), 46.4 (C-7), 61.0 (C-2), 128.0 (C-4), 165.7 (C-5), 193.9 (C-3), 203.7 (C-1). HRMS calcd for $C_{18}H_{30}O_2$ 278.2246, found 278.2232.

2d (R = *t*-Bu): an amorphous solid, R_f = 0.21 (hexane : Et_2O = 1 : 2). IR (film) 1640, 1575 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.86 (3H, t, *J* = 7.1 Hz, H-5'), 1.15 (9H, s, tBu), 1.19-1.29

(5H, m, H-2', H-3', and H-4'), 1.46-1.53 (2H, m, H-1' and H-2'), 1.59-1.63 (1H, m, H-1'), 2.65-2.72 (2H, m, H-6 and H-7), 2.90 (1H, dd, J = 15.6, 4.3 Hz, H-7), 3.62 (1H, d, J = 16.6 Hz, H-2), 3.89 (1H, d, J = 16.6 Hz, H-2), 6.03 (1H, s, H-4). ^{13}C-NMR (125 MHz, $CDCl_3$) δ14.1 (C-5'), 22.6 (C-2'), 27.9 (C-3'), 28.6 (tBu), 35.2 (C-1'), 35.3 (C-6), 38.9 (CMe$_3$), 45.6 (C-7), 61.3 (C-2), 125.3 (C-4), 171.6 (C-5), 194.9 (C-3), 203.4 (C-1). HRMS calcd for $C_{16}H_{26}O_2$ 250.1933 found 250.1936

Reaction of 1 with Lithium Enolate of 1-Acetyl-1-cyclopentene. Reaction was carried out in the same way as described for the [3 + 4] annulation leading to cycloheptenediones **2**.

5a (R = CH_3): a pale yellow oil, R_f = 0.41 (hexane : Et_2O = 12 : 1). IR (film) 1775 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.09 (3H, s, Si*Me*), 0.10 (3H, s, Si*Me*), 0.89 (9H, s, Si*tBu*), 1.43-1.53 (2H, br m, H-8 and H-10), 1.64-1.71 (3H, br m, H-8, H-9, and H-10), 1.72 (3H, d, J = 0.9 Hz, CH_3), 2.18-2.22 (m, 1H, H-9), 2.98 (1H, br d, H-7), 3.02 (1H, d, J = 17.7 Hz, H-3), 3.08 (1H, d, J = 17.7 Hz, H-3), 5.50 (1H, s, H-5). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-3.0 (Si*Me*), -2.6 (Si*Me*), 15.7 (6-CH_3), 18.2 (Si*C*), 25.9 (Si*tBu*), 26.5 (C-8), 28.8 (C-9), 30.4 (C-10), 57.9 (C-7), 60.2 (C-3), 81.0 (C-4), 82.3 (C-1), 129.2 (C-5), 145.7 (C-6), 215.9 (C-2). In order to obtain a crystaline derivative for an X-ray analysis, this compound was transformed into 4-(*tert*-butyldimethylsiloxy)-6-methyltricyclo[5.4.0.0^{1,4}]undec-5-en-2-yl 3,5-dinitrobenzoate by the following sequence: (1) DIBAL, Et_2O (2) 3,5-dinitrobenzoyl chloride, pyridine (3) 5% HF-MeCN (4) separation of the diastereomers (5) Ac_2O, NEt_3, CH_2Cl_2. X ray; monoclinic $P2_1/a$(#14), a = 10.629(1), b = 10.277(1), c = 18.411(1) Å, δ = 96.535(7)°, V = 1998.0(3) Å^3, Z = 4, D_{calc} = 1.384 g/cm^3, R = 3.9 for 2996 reflections. Diffraction data were collected on a Rigaku AFC7R diffractometer with graphite monochromated Mo-Ka radiation and rotating anode generator. The structure was solved by the direct methods and expanded using Fourier techniques.

5b (R = *n*-Bu): a colorless oil. R_f = 0.44 (hexane : Et_2O = 19 : 1). IR (film) 1775 cm^{-1}. ^{1}H-NMR (500 MHz , $CDCl_3$) δ0.09 (3H, s, Si*Me*), 0.11 (3H, s, Si*Me*), 0.89 (9H, s, Si*tBu*), 0.90 (3H, t, J = 7.5 Hz, H-4'), 1.25-1.43 (4H, m, H-2' and H-3'), 1.43-1.52 (2H, m, H-9, and H-10), 1.63-1.72 (3H, m, H-8, H-9, and H-10), 1.96-2.02 (1H, m, H-1'), 2.06-2.13 (1H, m, H-1'), 2.16-2.21 (1H, m, H-8), 3.03 (1H, br m, H-7), 3.03 (1H, d, J = 18.0 Hz, H-3), 3.07 (1H, d, J = 18.0 Hz, H-3), 5.50 (1H, d, J = 0.8 Hz, H-5). ^{13}C-NMR (125 MHz, $CDCl_3$) ; -3.0 (Si*Me*), -2.6 (Si*Me*), 14.1 (C-4'), 18.2 (Si*C*), 22.7 (C-3'), 25.9 (Si*tBu*), 26.6 (C-10), 28.6 (C-8), 29.6 (C-1'), 30.1 (C-2'), 30.8 (C-9), 56.7 (C-7), 60.3 (C-3), 80.8 (C-4), 81.8 (C-1), 127.7 (C-5), 150.4 (C-6), 216.0 (C-2). HRMS calcd for $C_{20}H_{34}O_2Si$ 334.2328, found 334.2306

5c (R = *n*-hexyl): a yellow oil. R_f = 0.43 (hexane : Et_2O = 15 : 1). IR (film) 1775 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.09 (3H, s, Si*Me*), 0.11 (3H, s, Si*Me*), 0.87 (3H, t, J = 6.4 Hz, H-

6'), 0.89 (9H, s, Si*tBu*), 1.24-1.34 (6H, m, H-2', H-3', H-4', and H-5'), 1.44-1.52 (2H, m, H-9 and H-10), 1.64-1.72 (3H, m, H-8, H-9, and H-10), 1.96-2.01 (1H, m, H-1'), 2.04-2.11 (1H, m, H-1'), 2.14-2.21 (1H, m, H-8), 3.03 (1H, br s, H-7), 3.03 (1H, d, *J* = 17.8 Hz, H-3), 3.07 (1H, d, *J* = 17.8 Hz, H-3), 5.50 (1H, d, *J* = 1.1 Hz, H-5). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-3.0 (Si*Me*), -2.6 (Si*Me*), 14.3 (C-6'), 18.2 (Si*C*), 22.8 (C-5'), 25.9 (Si*tBu*), 26.6 (C-10), 26.7 (C-8), 27.8 (C-1'), 28.6 (C-9), 29.3, 29.9, 30.8, 56.7 (C-7), 60.3 (C-3), 80.8 (C-4), 81.8 (C-1), 127.7 (C-5), 150.4 (C-6), 216.0 (C-2). HRMS calcd for $C_{22}H_{38}O_2Si$ 362.2641, found 362.2651.

5d (R = *t*-Bu): colorless oil, R_f = 0.38 (hexane : Et_2O = 19 : 1). IR (film) 1775 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 0.09 (3H, s, Si*Me*), 0.11 (3H, s, Si*Me*), 0.90 (9H, s, Si*tBu*), 1.08 (9H, s, tBu), 1.37-1.44 (1H, m, H-8), 1.64-1.77 (3H, m, H-9 and H-10), 1.91 (1H, m, H-8), 2.11 (1H, m, *J* = 6.4 Hz, H-10), 3.06 (1H, d, *J* = 7.5 Hz, H-3), 3.09 (1H, d, *J* = 7.5 Hz, H-3), 3.12 (1H, t, *J* = 8.3, H-7), 5.54 (1H, s, H-5). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ-2.8 (Si*Me*), -2.5 (Si*Me*), 18.2 (Si*C*), 25.9 (Si*tBu*), 27.4 (C-10), 28.2 (C-9), 30.5 (C*Me*$_3$), 34.4 (C-8), 55.6 (C-7), 60.8 (C-3), 79.3 (C-4), 81.3 (C-1), 126.1 (C-5), 159.2 (C-6), 216.2 (C-2). HRMS calcd for $C_{20}H_{34}O_2Si$ 334.2328, found 334.2299

6a (R = CH_3): a colorless prism, mp 105-107 °C. R_f = 0.12 (hexane : Et_2O = 2 : 1). IR (KBr) 1715, 1655 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ1.48-1.65 (2H, m, H-8 and H-9), 1.74-1.88 (2H, m, H-9 and H-10), 2.04 (3H, s, CH_3), 2.20-2.26 (2H, m, H-8 and H-10), 2.72-2.78 (1H, ddd, *J* = 13.8, 10.0, 10.0 Hz, H-1), 2.89-2.95 (1H, m, H-7), 3.53 (1H, dd, *J* = 16.0, 1.5 Hz, H-3), 3.90 (1H, d, *J* = 16.0 Hz, H-3), 6.06 (1H, m, H-3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ23.2 (C-9), 24.4 (CH_3), 25.3 (C-8), 32.2 (C-10), 48.0 (C-7), 57.3 (C-1), 60.0 (C-3), 129.8 (C-5), 160.3 (C-6), 194.4 (C-4), 204.3 (C-2). Anal. calcd for $C_{11}H_{14}O_2$ C 74.33, H 7.92. found C 74.13, H 7.92.

6b (R = *n*-Bu): a colerless oil. R_f = 0.20 (hexane : Et_2O = 3 : 1). IR (film) 1715, 1655 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.93 (1H, s, H-4'), 1.31-1.42 (2H, m, H-3'), 1.43-1.64 (4H, br m, H-2', H-9, and H-10), 1.72-1.87 (2H, m, H-8 and H-9), 2.21-2.29 (3H, m, H-1', H-8, and H-10), 2.34-2.40 (1H, m, H-1'), 2.75-2.81 (1H, m, H-7), 2.90-2.96 (1H, m, H-1), 3.55 (1H, dd, *J* = 16.2, 1.5 Hz, H-3), 3.88 (1H, d, *J* = 16.2 Hz, H-3), 6.05 (1H, s, H-5). ^{13}C-NMR (125 MHz, $CDCl_3$) δ14.1 (C-4'), 22.7 (C-3'), 23.2 (C-9), 25.3 (C-10), 30.6 (C-2'), 32.0 (C-8), 37.2 (C-1'), 47.6 (C-7), 57.5 (C-1), 59.9 (C-3), 128.6 (C-5), 164.0 (C-6), 195.1 (C-4), 204.4 (C-2). HRMS calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1450.

6c (R = *n*-hexyl): a colorless oil. R_f = 0.21 (hexane : Et_2O = 2 : 1). IR (film) 1715, 1655 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.89 (3H, t, *J* = 6.8 Hz, H-6'), 1.25-1.40 (7H, m), 1.40-1.67 (4H, m), 1.75-1.87 (2H, m, H-8 and H-10), 2.20-2.30 (3H, m, H-8, H-10, and H-1'), 2.32-2.40 (1H, m, H-1'), 2.74-2.81 (1H, m, H-1), 2.89-2.96 (1H, m, H-7), 3.36 (1H, dd, *J* = 16.2, 1.5 Hz,

H-3), 3.99 (1H, d, J = 16.2 Hz, H-3), 6.05 (1H, app q, J = 1.3 Hz, H-5). ^{13}C-NMR (125 MHz, $CDCl_3$) δ14.2 (C-6'), 22.7, 23.2, 25.3 (C-8), 28.5, 29.3, 31.8 (C-10), 32.0, 37.5 (C-1'), 47.7 (C-1), 57.5 (C-7), 59.9 (C-3), 128.6 (C-5), 163.9 (C-6), 195.0 (C-4), 204.4 (C-2). HRMS calcd for $C_{16}H_{24}O_2$ 248.1776, found 248.1797.

6d (R = *t*-Bu): colorless oil, R_f = 0.11 (hexane : CH_2Cl_2 = 1 : 1). IR (film) 1710, 1655 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ1.11 (9H, s, C*Me*$_3$), 1.74-1.85 (2H, m, H-8 and H-10), 1.91-1.97 (1H, m, H-9), 2.00-2.04 (1H, m, H-10), 2.18-2.27 (2H, m, H-8 and H-9), 2.91-2.99 (2H, m, H-1 and H-7), 3.32 (1H, dt, J = 15.8, 1.7 Hz, H-3), 4.05 (1H, d, J = 15.8 Hz, H-3), 5.97 (1H, s, H-3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ25.8 (C-10), 28.4 (C*Me*$_3$), 30.3 (C-9), 37.4 (C-8), 43.2 (C-7), 54.9 (C-1), 56.5 (C-3), 125.1 (C-5), 170.2 (C-6), 194.2 (C-4), 206.1 (C-2). HRMS calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1461

Reaction of 1 with Lithium Enolate of 1-Acetyl-1-cyclohexene. Reaction was carried out in the same way as described for the [3 + 4] annulation leading to cycloheptenediones **2**.

8d (R = *t*-Bu): a pale yellow oil, R_f = 0.41 (hexane : Et_2O = 19 : 1). IR (film) 1775 cm^{-1}. ^{1}H-NMR (500 MHz, C_6D_6) δ 0.08 (3H, s, Si*Me*), 0.10 (3H, s, Si*Me*), 1.01 (9H, m, Si*tBu*), 1.03 (9H, s, tBu), 1.10-1.17 (1H, m, H-10), 1.50-1.65 (2H, m, 2H, H-9 and H-11), 1.80-1.83 (1H, m, H-10), 1.85-1.89 (1H, m, H-11), 1.90-1.94 (2H, m, H-8 and H-9), 2.27 (1H, dddd, J = 12.4, 12.4, 12.4, 3.4 Hz, H-8), 2.63 (1H, ddd, J = 12.4, 3.0, 3.0 Hz, H-7), 2.87 (1H, d, J = 15.8 Hz, H-3), 3.28 (1H, d, J = 15.8 Hz, H-3), 5.46 (1H, d, J = 3.0 Hz, H-5). ^{13}C-NMR (C_6D_6, 125 MHz) δ -2.8 (Si*Me*), -2.7 (Si*Me*), 18.2 (Si*C*), 22.7 (C-11), 26.0 (Si*tBu*), 26.9 (C-9), 27.0 (C-8), 27.2 (C-9), 28.7 (C*Me*$_3$), 33.9 (*C*Me$_3$), 53.9 (C-7), 59.9 (C-3), 73.8 (C-4), 77.9 (C-1), 125.3 (C-5), 159.7 (C-6), 210.7 (C-2). HRMS calcd for $C_{21}H_{36}O_2Si$ 348.2485 found 348.2475.

7a (R = CH_3): a colorless prism, mp 96-98 °C, R_f = 0.27 (hexane : Et_2O = 1 : 1). IR (KBr): 1655, 1570 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ1.39-1.46 (3H, m, H-9 and H-10), 1.50-1.58 (2H, m, H-8 and H-11), 1.79-1.84 (1H, m, H-9), 1.93-1.97 (1H, br dm, J = 12.9 Hz, H-11), 2.03 (3H, d, J = 1.3 Hz, CH_3), 2.24-2.27 (1H, br m, H-8), 2.57 (1H, ddd, J = 11.8, 7.1, 7.1 Hz, H-1), 2.73-2.74 (1H, m, H-7), 3.63 (1H, dd, J = 14.9, 1.5 Hz, H-3), 3.90 (1H, dd, J = 14.9, 0.6 Hz, H-3), 6.03 (1H, dq, J = 1.3 Hz, H-5). ^{13}C-NMR (125 MHz, $CDCl_3$) δ22.4 (C-11), 26.6 (C-10), 26.6 (CH_3), 27.8 (C-9), 28.4 (C-8), 46.6 (C-1), 50.6 (C-7), 62.1 (C-3), 129.3 (C-5), 161.1 (C-6), 192.6 (C-4), 204.7 (C-2). Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39, found C, 75.28; H, 8.30.

7b (R =*n*-Bu): a colorless oil. R_f = 0.20 (hexane : Et_2O = 2 : 1). IR (film) 1705, 1660 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl^3$) δ0.92 (3H, t, J = 7.3 Hz, H-4'), 1.29-1.60 (9H, m), 1.84-1.86 (1H, m), 1.94 (1H, br d, J = 13.4 Hz), 2.23 (2H, t, J = 8.3 Hz, H-1'), 2.35 (1H, br d, J = 13.4 Hz), 2.52 (1H, dt, J = 12.1, 3.2 Hz, H-1), 2.70 (1H, br s, H-7), 3.63 (1H, dd, J = 15.0, 1.7 Hz, H-3),

4.00 (1H, d, J = 15.0 Hz, H-3), 6.02 (1H, s, H-5). ^{13}C-NMR (125 MHz, $CDCl_3$) δ14.0 (C-4'), 22.2, 22.6, 26.9, 28.1, 29.2, 30.7, 39.1, 45.9 (C-1), 50.4 (C-7), 62.5 (C-3), 128.2 (C-5), 165.6 (C-6), 192.8 (C-4), 205.0 (C-2). HRMS calcd for $C_{15}H_{22}O_2$ 234.1620, found 234.1611.

7c (R =*n*-hexyl): a colorless oil. R_f = 0.16 (hexane : Et_2O = 3 : 1). IR (film) 1705, 1660 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.87 (3H, t, J = 4.0 Hz, H-6'), 1.27-1.60 (13H, m), 1.84-1.87 (1H, br m), 1.92-1.95 (H-1, br d, J = 13.3 Hz), 2.23 (2H, m, H-1'), 2.35 (1H, br d, J = 11.3 Hz), 2.50-2.54 (1H, dt, J = 12.4, 3.9 Hz, H-1), 2.69 (1H, br s, H-7), 3.63 (1H, dd, J = 14.9, 1.5 Hz, H-3), 3.99 (1H, d, J = 14.9 Hz, H-3), 6.01 (1H, d, J = 0.9 Hz, H-5). ^{13}C-NMR (125 MHz, $CDCl_3$) δ14.2 (C-6'), 22.2, 22.7, 26.9, 28.1, 28.5, 29.1, 29.2 29.2, 31.7, 39.4 (C-1'), 45.9 (C-1), 50.4 (C-7), 62.5 (C-3), 128.2 (C-5), 165.6 (C-6), 192.7 (C-4), 205.0 (C-2).

7d (R =*t*-Bu): colorless prism, mp 152-155 °C, R_f = 0.08 (hexane : CH_2Cl_2 = 1 : 1). IR (KBr) 1650, 1575 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ1.15 (9H, s, Si*tBu*), 1.24-1.34 (1H, m, H-9), 1.39-1.48 (1H, m, H-10), 1.61-1.68 (2H, m, H-8 and H-9), 1.77 (1H, ddd, J = 12.7, 4.1, 4.1 Hz, H-11), 1.89 (2H, br m, H-10 and H-11), 2.30 (1H, br d, J = 11.6 Hz, H-8), 2.64 (1H, br s, H-7), 2.71 (1H, ddd, J = 12.4, 4.3, 4.3, H-1), 3.68 (1H, dd, J = 16.4, 1.1 Hz, H-3), 4.23 (1H, d, J = 16.5 Hz, H-3), 6.08 (1H, s, H-5). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ21.8 (C-9), 26.4 (C-10), 28.5 (CH_3), 30.3 (C-11), 31.5 (C-8), 39.2 (CMe$_3$), 39.9 (C-7), 50.2 (C-1), 62.5 (C-3), 126.2 (C-5), 172.2 (C-6), 193.7 (C-4), 207.4 (C-2). Anal. $C_{15}H_{22}O_2$ calcd for C 76.88, H 9.46, found C 77.02, H 9.80.

7e (R = *c*-C_3H_5): a pale yellow needle. mp = 92-94 °C, R_f = 28 (hexane : Et_2O = 1 : 1). IR (KBr) 1655, 1555 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.59-0.64 (1H, m, H-2'), 0.69-0.75 (1H, m, H-3'), 0.88-1.00 (2H, m, H-2' and H-3'), 1.34-1.51 (4H, m, H-1', H-8, H-9, and H-10), 1.54-1.64 (2H, m, H-9, 11), 1.83-1.88 (1H, m, H-10), 2.04-2.09 (1H, br d, J = 13.7 Hz, H-11), 2.30-2.33 (1H, br d, J = 13.7, H-8), 2.62-2.66 (1H, dt, J = 12.0, 3.4 Hz, H-1), 2.70-2.71 (1H, br m, H-7), 3.61 (1H, dd, J = 15.2, 1.7 Hz, H-3), 3.94 (1H, d, J = 15.2, H-3), 5.74 (1H, d, J = 1.7 Hz, H-5). ^{13}C-NMR (125 MHz, $CDCl_3$) δ8.69 (C-2'), 10.8 (C-3'), 19.3 (C-1'), 22.2 (C-9), 26.7 (C-10), 28.5 (C-8), 28.9 (C-11), 46.5 (C-1), 50.5 (C-7), 62.2 (C-3), 123.5 (C-5), 167.7 (C-6), 192.4 (C-4), 204.9 (C-2). Anal. calcd for $C_{14}H_{18}O_2$ C 77.03, H 8.31, found C 77.23, H 8.60.

1-(*tert*-Butyldimethylsilyl)-3-alkyl-3-bromo-2-propen-1-one (9). The following procedure for **9a** (R = Me) is representative: These compounds were prepared by a modified procedure of Cunico as described for the corresponding trimethylsilyl derivative. A solution of (1-(ethoxy)ethenyl)-*tert*-butyldimethylsilane (10.00 g, 53.7 mmol), CBr_4 (35.5 g, 107 mmol), and pyridine (1.7 mL, 21.5 mmol) in CCl_4 (45 mL) was irradiated with a sunlamp for 8 h before addition of H_2O (40 mL). The mixtue was extracted with pentane (50 mL x 3). The

combined organic phases were washed with H_2O, and concentrated. The residual oil was subjected to column chromatography (silica gel, 240 g; elution with 6:1 pentane-CH_2Cl_2) to give **9** (R = Br) (9.03 g, 51%). red oil. R_f = 0.31 (hexane:CH_2Cl_2 = 5 : 1). IR (film) 1630 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.20 (6H, s, Si*Me*$_2$), 0.94 (9H, s, Si*tBu*), 7.62 (1H, s, H-2). ^{13}C-NMR (125 MHz, $CDCl_3$) δ -7.2 (Si*Me*$_2$), 17.2 (Si*C*), 26.6 (Si*tBu*), 97.9 (C-2), 136.7 (C-3), 232.6 (C-1). HRMS calcd for $C_9H_{16}OBr_2Si$ 329.9337, found 329.9298.

To a cooled (-80 °C) suspension of anhydrous CuCN (455 mg, 4.98 mmol) in THF (42 mL) was added dropwise a solution of MeLi (1.25 M in Et_2O, 4.0 mL, 4.98 mmol). The reaction mixture was allowed to warm to –20 °C. After the mixture became a clear solution, the solution was cooled to –80 °C. To this solution was added dropwise a solution of **9** (R = Br) (1.50 g, 3.32 mmol) in THF (66 mL). The reaction mixture was stirred at the same temperature for 1 h, and then allowed warm to –30 °C before addition of AcOH (0.29 mL, 4.98 mmol) in THF (8 mL). The mixture was diluted with H_2O (100 mL), and then extracted with pentane (100 mL x 3). The combined organic phases were washed with saturated brine, dried, and concentrated. The residual oil was filtered through a pad of Florisil (pentane), and then subjected to column chromatography (silica gel, 100 g; elution with 19:1 hexane-Et_2O) to give **9a** (R = Me) (730 mg, 57%).

9a (R = Me): a yellow oil, R_f = 0.32 (hexane : CH_2Cl_2 = 5 : 1). IR (film) 1640, 1560 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.19 (6H, s, Si*Me*$_2$), 0.93 (9H, s, Si*tBu*), 2.67 (3H, t, *J* = 1.1 Hz, H-4), 7.11 (1H, q, *J* = 1.1, H-2). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-7.1 (Si*Me*$_2$), 17.1 (Si*C*), 26.6 (Si*tBu*), 27.3 (C-4), 133.6 (C-2), 139.8 (C-1), 234.7 (C-1). Anal. Calcd. for $C_{10}H_{19}OBrSi$,: C, 45.63; H, 7.27, found C, 45.44; H, 7.52.

9b (R = *n*-Bu): a yellow oil. R_f = 0.38 (hexane : CH_2Cl_2 = 7 : 1). IR (film) 1645, 1555 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.18 (3H, s, Si*Me*$_2$), 0.18 (3H, s, Si*Me*$_2$), 0.90 (3H, t, *J* = 10.5, H-7), 1.33 (2H, sex, *J* = 7.7 Hz, H-6), 1.55 (2H, m, H-5), 2.92 (2H, t, *J* = 7.7 Hz, H-4), 7.11 (1H, t, *J* = 0.4 Hz, H-2). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-6.8 (Si*Me*$_2$), 14.3 (C-7), 17.3 (SiC), 22.3 (C-6), 26.9 (Si*tBu*), 31.3 (C-5), 38.8 (C-4), 133.9 (C-2), 146.8 (C-3), 234.5 (C-1). HRMS calcd for $C_{13}H_{25}O^{81}BrSi$ 306.0837, found 306.0833.

9c (R = *n*-hexyl): an yellow oil. R_f = 0.50 (hexane : CH_2Cl_2 = 6 : 1). IR (film) 1645, 1550 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.18 (6H, s, Si*Me*$_2$), 0.87 (3H, t, *J* = 7.5, H-9), 0.92 (9H, s, Si*tBu*), 1.25-1.32 (6H, m, H-5), 1.54-1.58 (2H, m), 2.92 (2H, t, *J* = 7.5, H-4), 7.11 (1H, s, H-2). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-7.1 (Si*Me*$_2$), 14.2 (C-9),17.1 (Si*C*), 22.7, 26.7 (Si*tBu*), 28.6, 28.9, 31.7, 38.7 (C-4), 133.7 (C-2), 146.5 (C-3), 234.3 (C-1). HRMS calcd for $C_{15}H_{29}OBrSi$, 332.1171, found 332.1211.

9d (R = *t*-Bu): an yellow oil. R_f = 0.37 (hexane : CH_2Cl_2 = 6 : 1). IR (film) 1640, 1620 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.20 (6H, s, Si*Me*$_2$), 0.94 (9H, s, Si*tBu*), 1.19 (9H, s, *t*-Bu), 6.62 (1H, s, H-2). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-6.6 (Si*Me*$_2$), 17.0 (Si*C*), 26.6 (Si*tBu*), 30.8 (*t*-Bu), 41.3 (C-4), 138.1 (C-2), 144.8 (C-3), 239.4 (C-1). HRMS calcd for $C_{13}H_{25}O^{81}BrSi$ 306.0837, found 306.0848.

9e (R = *c*-C_3H_5): an yellow oil. R_f = 0.33 (hexane : CH_2Cl_2 = 5 : 1). IR (film) 1535 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.20 (6H, s, Si*Me*$_2$), 0.84 (2H, m), 0.87 (9H, s, Si*tBu*), 1.10 (2H, m), 3.21 (m, 1H), 7.18 (1H, s, H-2). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-6.8 (Si*Me*$_2$), 10.9, 17.4, 17.9, 26.9 (Si*tBu*), 133.2 (C-2), 151.8 (C-3), 234.0 (C-1). HRMS calcd for $C_{13}H_{21}BrO$ 272.0776, found $C_{13}H_{22}{}^{79}BrO$ 273.0857.

Reaction of 9 with Lithium Enolate of 1-Acetyl-1-cyclopentene. Reaction was carried out in the same way as described for the reaction of the corresponding derivative **2**.

5e (R = *c*-C_3H_5): a yellow oil. R_f= 0.33 (hexane : Et_2O = 16 : 1). IR (film) 1775 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.06 (s, 3H, Si*Me*), 0.08 (3H, s, Si*Me*), 0.42-0.49 (2H, m, H-2' and H-3'), 0.66-0.74 (1H, m, H-2'), 0.74-0.78 (1H, m, H-3'), 0.87 (9H, s, Si*tBu*), 1.23-1.28 (1H, m, H-1'), 1.48-1.52 (1H, m, H-10), 1.58-1.73 (4H, m, H-8, H-9, and H-10), 2.15-2.19 (1H, m, H-9), 3.00 (1H, d, *J* = 17.6 Hz, H-3), 3.04 (1H, d, J = 17.6 Hz, H-3), 3.04 (1H, m, H-7), 5.33 (1H, s, H-5). ^{13}C-NMR (125 MHz, $CDCl_3$) δ -3.0 (Si*Me*), -2.6 (Si*Me*), 7.0 (C-2'), 7.9 (C-3'), 10.8 (C-1'), 18.1 (Si*C*), 25.8 (Si*tBu*), 26.6 (C-8), 28.5 (C-9), 31.4 (C-10), 56.5 (C-7), 60.3 (C-3), 80.4 (C-4), 81.9 (C-1), 124.8 (C-5), 152.4 (C-6), 215.6 (C-2). HRMS calcd for $C_{19}H_{30}O_2Si$ 318.2015, found 318.2036.

Reaction of 9 with Lithium Enolate of 1-Acetyl-1-cyclohexene. Reaction was carried out in the same way as described for the reaction of the chloro derivative **2**.

8a (R = Me): colerless oil, R_f = 0.31 (hexane : Et_2O = 12 : 1). IR (film) 1780 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.09 (3H, s, Si*Me*), 0.11 (3H, s, Si*Me*), 0.89 (9H, s, Si*tBu*), 0.86-0.95 (1H, m, H-8), 1.12-1.20 (1H, m, H-9), 1.30-1.38 (1H, m, H-10), 1.46-1.52 (1H, ddd, *J* = 13.7, 13.7, 4.7 Hz, H-11), 1.62-1.65 (2H, br d, *J* = 10.7, H-9 and H-10), 1.69 (3H, s, CH_3), 1.99-2.05 (1H, m, H-8), 2.18-2.22 (1H, br d, *J* = 13.7 Hz, H-11), 2.34 (1H, dd, *J* = 11.1, 6.6 Hz, H-7), 2.93 (1H, d, *J* = 16.4 Hz, H-4), 3.28 (1H, d, *J* = 16.4 Hz, H-4), 5.43 (1H, s, H-6). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-2.8 (Si*Me*), -2.5 (Si*Me*), 15.6 (CH_3), 18.3 (SiC), 26.1 (Si*tBu*), 23.1 (C-10), 23.9 (C-9), 24.7 (C-11), 26.1 (CH_3), 30.6 (C-8), 47.7 (C-7), 59.0 (C-3), 73.1 (C-4), 81.0 (C-1), 127.6 (C-5), 150.2 (C-6), 215.5 (C-2). HRMS : calcd for $C_{18}H_{30}O_2Si$ 306.5151, found 306.2007.

8b (R = *n*-Bu): a colorless oil. R_f = 0.40 (hexane : Et_2O = 19 : 1). IR (film) 1780 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.11 (3H, s, Si*Me*), 0.13 (3H, s, Si*Me*), 0.89 (3H, t, *J* = 7.0, C-4'),

0.90 (9H, s, Si*tBu*), 1.14-1.48 (7H, m), 1.49-1.55 (1H, m, H-11), 1.63-1.65 (2H, m), 1.96-2.10 (3H, m, H-3'and H-8), 2.21 (1H, d, *J* = 13.7 Hz, H-11), 2.42 (1H, dd, *J* = 11.4, 6.6 Hz, H-7), 2.93 (1H, d, *J* = 16.4 Hz, H-3), 3.30 (1H, d, *J* = 16.4 Hz, H-3), 5.44 (1H, s, H-5). ^{13}C-NMR (125 MHz, $CDCl_3$) δ -3.1 (Si*Me*), -2.7 (Si*Me*), 14.1 (C-4'), 18.1, 22.6, 22.9, 23.9, 24.6, 25.9 (Si*tBu*), 26.7, 29.1, 29.8, 30.7, 46.1 (C-7), 58.9 (C-3), 72.5 (C-4), 80.5 (C-1), 126.0 (C-5), 154.7 (C-6), 215.7 (C-2). HRMS calcd for $C_{21}H_{36}O_2Si$ 348.2485, found 248.2470.

8c (R = *n*-hexyl): a pale yellow oil. R_f = 0.35 (hexane : CH_2Cl_2 = 3 : 1). IR (film) 1780 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.09 (3H, s, Si*Me*), 0.11 (3H, s, Si*Me*), 0.87 (3H, t, *J* = 7.0 Hz, H-6'), 0.90 (9H, s, Si*tBu*), 1.11-1.21 (1H, m, H-11), 1.22-1.32 (8H, br m, H-2', H-3', H-4', and H-5'), 1.33-1.41 (2H, m), 1.46-1.53 (1H, ddd, *J* = 15.3, 13.2, 4.2 Hz), 1.63-1.66 (2H, m), 1.95-2.08 (3H, m, H-8 and H-1'), 2.20 (1H, d, *J* = 3.7 Hz), 2.40 (1H, dd, *J* = 11.1, 6.6 Hz, H-7), 2.92 (1H, d, *J* = 6.6 Hz, H-3), 3.29 (1H, d, *J* = 6.6 Hz, H-3), 5.43 (1H, s, H-5). ^{13}C-NMR (125 MHz, $CDCl_3$) δ -3.1 (Si*Me*), -2.7 (Si*Me*), 14.3 (C-6'), 18.0 (Si*C*), 22.8, 22.9, 23.8, 24.5, 25.8 (Si*tBu*), 27.6, 29.2, 29.4, 30.7, 31.8, 46.1 (C-7), 58.9 (C-3), 72.5 (C-4), 80.5 (C-1), 126.0 (C-5), 154.7 (C-6), 215.2 (C-2). HRMS calcd for $C_{19}H_{31}O_2Si$ (M^+ - C_4H_9) 319.2093, found 319.2084.

8e (R = *c*-C_3H_5): a yellow oil. R_f = 0.35 (hexane : Et_2O = 16 : 1). IR (film) 1780 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.06 (3H, s, Si*Me*), 0.09 (3H, s, Si*Me*), 0.43-0.45 (2H, m, H-2' and H-3'), 0.65-0.68 (1H, m, H-2'), 0.72-0.76 (1H, m, H-3'), 0.88 (9H, s, Si*tBu*), 0.98-1.03 (1H, dddd, *J* = 11.1, 11.1, 11.1, 3.4 Hz, H-8), 1.15-1.26 (2H, m, H-9 and H-1'), 1.31-1.39 (1H, m, H-10), 1.46-1.53 (1H, ddd, *J* = 13.0, 13.0, 4.1 Hz, H-11), 1.60-1.66 (2H, m, H-9 and H-10), 2.06-2.12 (1H, br d, H-8), 2.18-2.23 (1H, br d, *J* = 13.7 Hz, H-11), 2.46 (1H, dd, *J* = 11.1, 6.4 Hz, H-7), 2.89 (1H, d, *J* = 16.3 Hz, H-3), 3.27 (1H, d, *J* = 16.3 Hz, H-3), 5.24 (1H, d, *J* = 0.7 Hz, H-5). ^{13}C-NMR (125 MHz, $CDCl_3$) δ -3.1 (Si*Me*), -2.7 (Si*Me*), 6.9 (C-3'), 8.3 (C-2'), 10.6 (C-1'), 18.0 (Si*C*), 22.9 (C-10), 23.8 (C-9), 24.5 (C-11), 25.8 (Si*tBu*), 31.3 (C-8), 47.0 (C-7), 58.9 (C-3), 72.6 (C-4), 80.2 (C-1), 122.9 (C-5), 156.7 (C-6), 214.9 (C-2). HRMS calcd for $C_{20}H_{32}O_2Si$ 332.2172, found 332.2143.

Low-temperature Quenching of the raction of 1a with 3. Reaction was carried out in the same way as described for the above reaction of **1** with **3** except the quenching temperature.

10: a pale yellow oil, R_f = 0.17 (hexane : Et_2O = 19 : 1). IR (film) 1685 cm^{-1}. ^{1}H-NMR (500 MHz, C_6D_6) δ0.08 (6H, s, $SiMe_2$), 0.95 (9H, s, Si*tBu*), 0.96 (3H, s, CH_3), 1.24-1.32 (1H, m, H-9), 1.43-1.57 (2H, m, H-9 and H-10), 1.62-1.74 (2H, m, H-8), 1.75 (1H, d, J = 5.6 Hz, H-7), 288 (1H, dd, *J* = 21.4, 2.4 Hz, H-3), 297 (1H, d, *J* = 21.4 Hz, H-3), 3.04-3.12 (1H, m, H-10), 5.13 (1H, d, *J* = 2.4 Hz, H-5). ^{13}C-NMR (125 MHz, C_6D_6) δ-4.5 (Si*Me*), -4.5 (Si*Me*), 14.7 (CH_3), 18.1 (Si*C*), 24.1 (C-10), 25.7 (Si*tBu*), 26.2 (C-9), 27.0 (C-8), 34.2 (C-1), 42.5 (C-3),

48.1 (C-7), 49.7 (C-1), 111.8 (C-5), 144.7 (C-4), 203.4 (C-2). HRMS calcd for $C_{17}H_{28}O_2Si$ 292.1859, found 292.1859.

11: a pale yellow oil, R_f = 0.24 (hexane : Et_2O = 15 : 1). IR (film) 1655 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.12 (6H, s, Si*Me*$_2$), 0.91 (9H, s, Si*tBu*), 1.27 (3H, d, *J* = 7.5 Hz, CH_3), 1.70-1.82 (2H, m, H-9), 2.50-2.68 (3H, m, H-8 and H-10), 2.71-2.80 (1H, m, H-10), 3.14-3.22 (1H, m, H-5), 3.35 (1H, dd, *J* = 15.1, 1.1 Hz, H-2), 3.43 (1H, d, *J* = 15.1 Hz, H-2), 5.02 (1H, d, *J* = 6.0 Hz, H-4). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-4.4 (Si*Me*), -4.4 (Si*Me*), 18.1 (Si*C*), 18.5 (CH_3), 20.8 (C-10), 25.8 (Si*tBu*), 33.2 (C-8), 39.2 (C-10), 51.0 (C-3), 112.5 (C-5), 136.7 (C-7), 148.0 (C-1), 164.9 (C-4), 192.9 (C-2). HRMS calcd for $C_{17}H_{28}O_2Si$ 292.1859, found 292.1850.

12: pale yellow oil, R_f = 0.45 (hexane : Et_2O = 15 : 1). IR (film) 1715 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.16 (3H, s, Si*Me*), 0.18 (3H, s, Si*Me*), 0.93 (9H, s, Si*tBu*), 1.65-1.75 (3H, m, H-9 and H-10), 1.76 (3H, d, *J* = 1.2 Hz, CH_3), 2.25-2.29 (1H, m, H-8), 2.32-2.38 (2H, m, H-8 and H-10), 3.03 (1H, dd, *J* = 18.6, 0.9 Hz, H-3), 3.17-3.22 (2H, m, H-3 and H-1), 5.49 (1H, s, H-3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-4.5 (Si*Me*), -4.2 (Si*Me*), 18.2 (Si*C*), 20.0 (CH_3), 25.8 (Si*tBu*), 26.6, 31.2, 50.3 (C-3), 57.0 (C-1), 114.2 (C-5), 125.4 (C-4), 133.9, 146.8, 208.3 (C-2). HRMS: calcd for $C_{17}H_{28}O_2Si$ 292.1859, found 292.1866.

13: a pale yellow oil, R_f = 0.14 (hexane : Et_2O = 15 : 1). IR (film) 1640 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ0.21 (6H, s, Si*Me*$_2$), 0.94 (9H, s, Si*tBu*), 1.43-1.45 (1H, m, H-9), 1.60-1.68 (1H, m, H-8), 1.70-1.77 (2H, m, H-10 and H-9), 1.96-2.02 (1H, m, H-8), 2.02 (3H, dd, *J* = 1.3, 1.1 Hz, CH_3), 2.25-2.33 (1H, m, H-10), 2.52-2.58 (1H, m, H-1), 2.64-2.72 (1H, m, H-7), 5.63 (1H, d, *J* = 1.7 Hz, H-3), 5.75 (1H, dq, *J* = 1.7 Hz, H-5). ^{13}C-NMR (125 MHz, $CDCl_3$) δ-4.4 (Si*Me*), -4.2 (Si*Me*), 18.3 (Si*C*), 24.9 (CH_3), 25.5 (C-9), 25.7 (C-10), 25.7 (Si*tBu*), 30.8 (C-8), 44.8 (C-7), 53.5 (C-1), 113.6 (C-3), 124.3 (C-5), 154.7 (C-6), 163.9 (C-4), 200.2 (C-2). HRMS calcd for $C_{17}H_{28}O_2Si$ 292.1859, found 292.1858.

Synthesis of the Tricyclic Skeleton of Cyathins Using Brook Rearrangement-Mediated [3 + 4] Annulation

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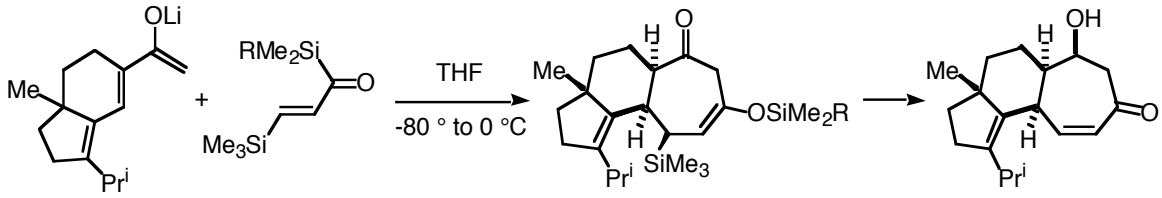
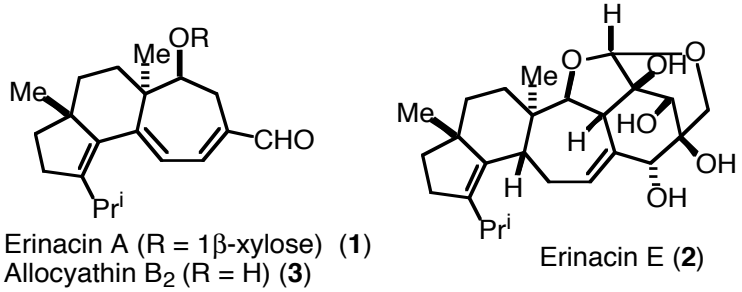
Abstract The tricyclic core of cyathins has been synthesized using a Brook rearrangement-mediated [3 + 4] annulation that we previously developed.



Cyathins,[1] isolated from bird nest fungi, and other members[2,3,4] of this family, including erinacins (**1**, **2**)[5], which are collectively called cyathins, continue to be of interest because of their unusual 5-6-7 tricyclic ring system coupled with their important biological activities (Figure 1). Recently, erinacine E (**2**), one of the complex members of the cyathin family, has been shown to have potent nerve growth factor (NGF) synthesis-stimulating activity[5] and to be a κopioid receptor agonist.[6] Synthetic efforts have been described by several groups,[7] and two total syntheses of allocyathin B_2 (**3**) have been reported.[8,9]

Figure 1

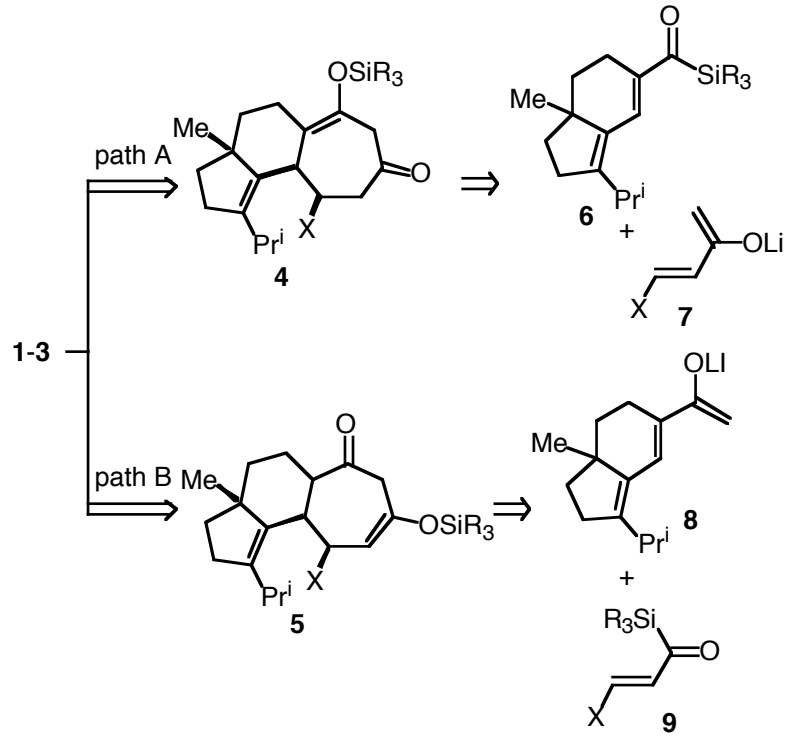


Erinacin A (R = 1β-xylose) (**1**)
Allocyathin B_2 (R = H) (**3**)

Erinacin E (**2**)

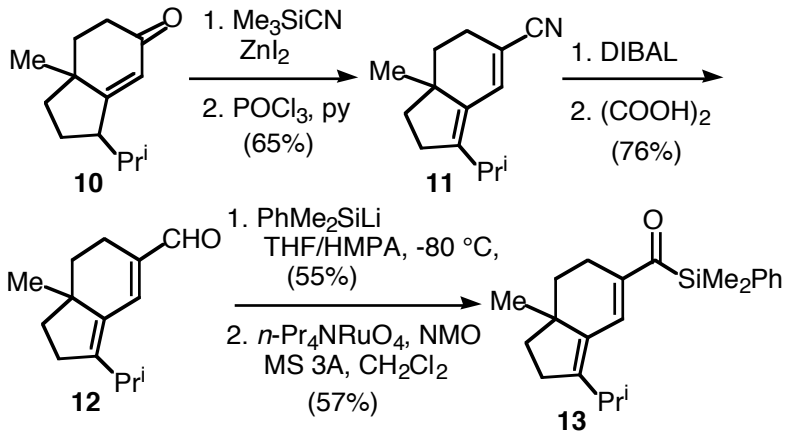
We have recently developed a Brook rearrangement-mediated [3 + 4] annulation for the stereoselective synthesis of seven-membered carbocycles by the reaction of α,β–unsaturated acylsilanes with lithium enolate of alkenyl methyl ketones.[10] To demonstrate the effectiveness of the methodology for the synthesis of functionalized cycloheptenones, we decided to apply this method to the synthesis of the tricyclic skeleton of the cyathin ring system. As a target we selected the tricyclic compounds **4** and **5** bearing the appropriate functionalities necessary for their conversion to natural products, and we addressed two retrosynthetic pathways defined as A and B that use the 5-6 ring systems **6** and **8** as three-carbon and four-carbon units in the key [3 + 4] annulation, respectively (Scheme 1).

Scheme 1



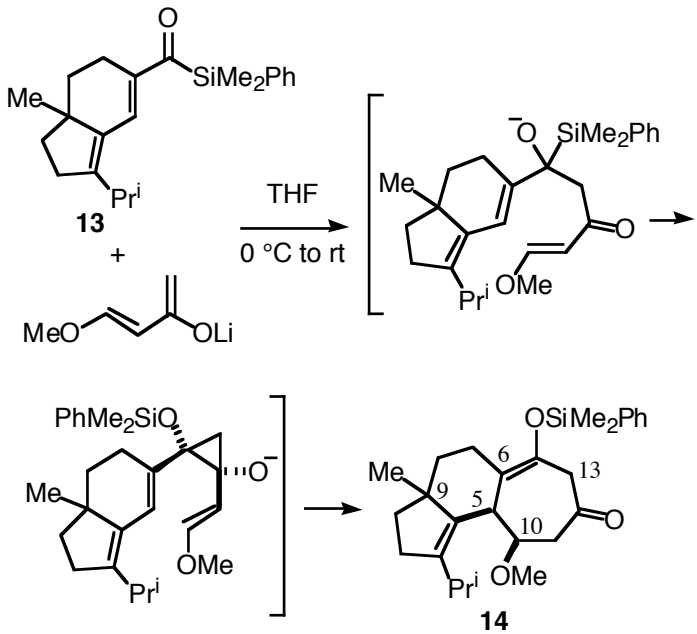
Path A. Acylsilane **13** was prepared by a four-step sequence starting with known enone **10**[11] (Scheme 2). When **10** was reacted with Me_3SiCN in the presence of ZnI_2 followed by elimination of silanol with $POCl_3$,[12] unsaturated nitrile **11** was obtained in 65% yield. Reduction of **11** with DIBAL followed by an acid quench afforded aldehyde **12** in 76% yield. Conversion of **12** into acylsilane **13** was carried out by reaction with dimethyl(phenyl)silyllithium[13] followed by oxidation of the generated α-silylalcohol. Oxidation with DMSO/$(COCl)_2$, PCC, and MnO_2 resulted in a low yield of **14** with the concomitant formation of **12**. The best result was obtained when 1 equiv. of *n*-Pr_4NRuO_4 (TPAP)[14] was used to provide **13** in 57% yield along with 14% of **12**. The use of a catalytic amount of TPAP and/or a longer reaction time resulted in increased formation of **12**.

Scheme 2



As a four-carbon unit in the [3 + 4] annulation, we initially examined several vinyl methyl ketone derivatives **7** which have a leaving group such as phenylthio, phenylsulfonyl groups at the β-position, anticipating that facile elimination of LiX would occur to lead to an enone derivative in the annulation product. Not unexpectedly, significant decomposition of the substrate occurred during the formation of the enolate. Next, we turned to the use of lithium enolate of 4-methoxy-3-buten-2-one. When the lithium enolate was added to a THF solution of **13** at 0 °C and the solution was then warmed to room temperature, tricycliclic ketone **14** was obtained as an epimeric mixture at C(9) in 47% yield along with recovery of **13** (14%) (Scheme 3).

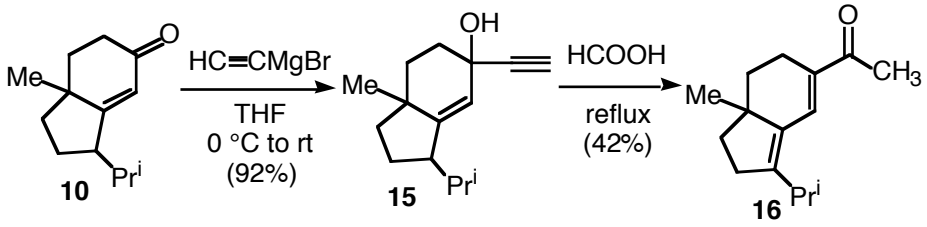
Scheme 3



The structures were assigned by analogy with structurally related compounds,[10c] and the 5,10-cis stereochemistry of **14** was based on the $J_{5,10}$ (ca. 0 Hz for both isomers) and NOESY experiments.

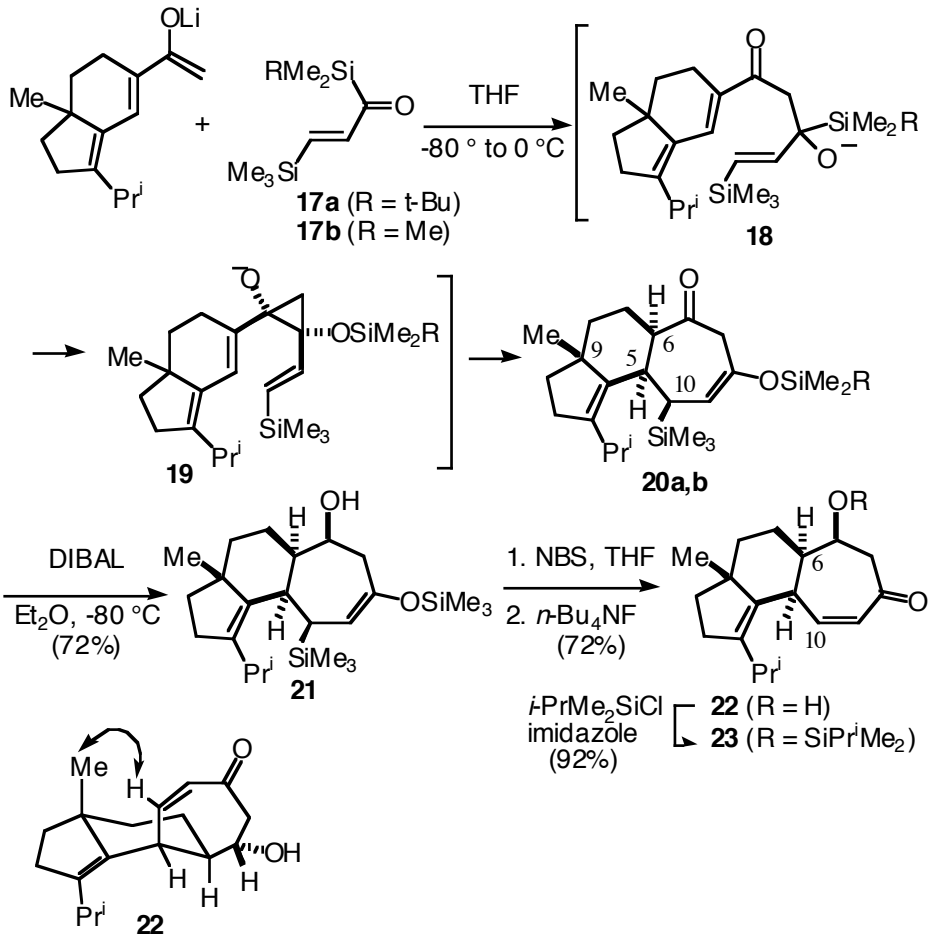
Path B. Bicyclic methyl ketone **16** was prepared from **10** via a two-step sequence: (1) addition of ethynylmagenisum bromide, and (2) Rupe rearrangement[15] (Scheme 4).

Scheme 4



The key [3 + 4] annulation proceeded smoothly when **16** was added to a solution of acryloylsilane **17a** at –80 °C and allowed to warm to 0 °C to afford **20a** as a single diastereomer in 60% yield (Scheme 5). The 6,5,10-cis stereochemistry was assigned on the basis of $J_{5,6}$ = 7.3 Hz, $J_{5,10}$ = 6.6 Hz and of a NOESY correlation between H-6 and H-10. The relative stereochemisty of Me-15 was tentatively assigned as trans to H-5 and H-6 since no NOESY correlation between the 9-Me and H-5 was observed. The observed stereoselectivity can be rationalized by a concerted pathway of the anionic oxy-Cope rearrangement of the *cis*-1,2-divinylcyclopropanediolate intermediate **19** which was stereoselectively derived from the 1,2-adduct **18** by the Brook rearrangement, followed by internal trapping of the generated carbanion by the ketone carbonyl.[10c] The stereoselectivity, which is different from that in the reaction of **13**, remains unclear at the present time. Although the trimethylsilyl group at C-10 could be removed by exposure to NBS followed by *n*-Bu_4NF to give an enone derivative,[10c] the reaction turned out to produce a low yield and to have poor reproducibility. We then decided to use trimethylsilyl derivative **17b**, anticipating a more facile conversion into the enone derivative. The [3 + 4] annulation using **17b** proceeded in a similar manner to give **20b** as a single isomer in 50% yield. Oxidative desilylation of **20b** was realized after DIBAL reduction to alcohol **21** to afford enone **22** in 79% yield. The configuration of 9-Me was assigned on the basis of a NOESY correlation between 9-Me and H-10 and of comparison of ^{1}H NMR of its *O*-silylated derivative **23** with that of 6-methyl derivative of **23**, which is known.[8b]

Scheme 5



In summary, we have demonstrated the synthetic utility of our Brook rearrangement-mediated [3 + 4] annulation by application to the synthesis of the tricyclic ring system of cyathins.

Acknowledgment This research was partially supported by a grant-in-aid for Scientific Research (No. 10671986) from the Japanese Ministry of Education, Sciences, Sports and Culture.

Supporting Information Available: Full experimental details and characterization data for all new compounds described in the text (5 pages).

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Synthesis of the Tricyclic Skeleton of the Cyathin Diterpene Using the Brook Rearrangement-Mediated [3 + 4] Annulation

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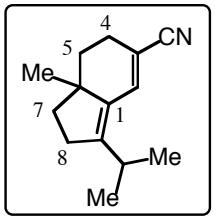
Supporting Information

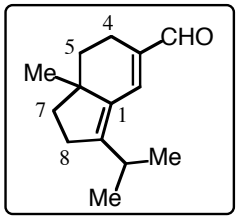
General: IR spectra were recorded on a Perkin-Elmer FT1640 spectrometer. ^{1}H NMR spectra were taken on Varian UnityPlus 500 (500 MHz) in $CDCl_3$ with reference to $CHCl_3$ (δ 7.26) unless otherwise noted. ^{13}C NMR spectra were measured with Varian UnityPlus 500 (125 MHz) in $CDCl_3$ with reference to the $CDCl_3$ triplet (δ 77.2) unless otherwise noted. Resonance patterns were described as s = singlet, d = doublet, t = triplet, sep = septet, m = multiplet, and br = broad. The assignment of ^{1}H and ^{13}C NMR spectra is based on H-H decoupling and HMQC experiments. Low- and high-resolution mass spectra (EI-MS) were obtained with a JEOL JMS-D-300 spectrometer combined with a JEOL JMA-2000 data processing system. For routine chromatography, the following adsorbents were used: Fuji-Davison silica gel BW-200 (150-325 mesh) for column chromatography; Merck precoated



silica gel 60 F-254 plates for analytical thin-layer chromatography. All moisture sensitive reactions were performed under a positive pressure of nitrogen. Anhydrous $MgSO_4$ was used for drying all organic solvent extracts in workup, and the removal of the solvents was performed with a rotary evaporator. Dry solvents and reagents were obtained by using standard procedures. Melting points (uncorrected) were determined by using a Yanagimoto micro-melting point apparatus. Elemental combustion analysis was performed at the Microanalysis Laboratory of this University.

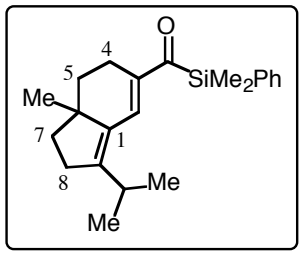
6-Methyl-9-(1-methylethyl)bicyclo[4.3.0]nona-2,9-diene-3-carbonitrile (11)

To a solution of **10** (1.84 g, 9.54 mmol) in benzene (4 mL) was added Me_3SiCN (1.65mL,



12.4 mmol) and ZnI_2 (75 mg) at room temperature. The solution was stirred at room temperature for 1 h before addition of pyridine (15 mL) and $POCl_3$ (2.59 mL, 28.6 mmol). After being stirred at the same temperature for 1 h, the mixure was poured into Et_2O-ice-satd. $NaHCO_3$ solution. Phases were separted, and the organic phase was extracted with

Et_2O. Combined organic phase was successively washed with H_2O and saturated brine, then dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 30 g; elution with 2:1 hexane-AcOEt) to give **11** (1.24 g, 65%). colorless needles (hexane), R_f = 0.41 (hexane:AcOEt = 15:1). mp 60 °C. IR (KBr) 2195 cm^{-1}. ^{1}H-NMR δ 0.90 (3H, s, Me),



1.00 (3H, d, *J* = 6.8 Hz, CH*Me*), 1.03 (3H, d, *J* = 6.8Hz, CH*Me*), 1.38 -1.51 (2H, m, H-5 and H-7), 1.76-1.82 (2H, m, H-5 and H-7), 2.27-2.34 (2H, m, H-4 and H-8), 2.39-2.51 (2H, m, H-4 and H-8), 2.81 (1H, sep, *J* = 6.8 Hz, C*H*Me_2), 7.02 (1H, d, *J* = 2.4 Hz, H-2). ^{13}C NMR δ21.2, 21.7, and 21.8 (CHMe_2 and 6-Me), 25.7 and 29.2 (C-5 and C-7), 27.2 (*C*HMe_2) 34.9 and 38.8 (C-4 and C-8), 107.8 (C-1, C-3, and C-9), 121.1 (CN), 134.9 (C-2), 135.4 and 152.4 (C-1 and C-9). HRMS calcd for $C_{14}H_{19}N$ 201.1517, found 201.1519.

6-Methyl-9-(1-methylethyl)bicyclo[4.3.0]nona-2,9-diene-3-carboaldehyde (12)

To an ice-cooled solution of **11** (0.42 g, 2.1 mmol) in Et_2O (12 mL) was added DIBAL (0.94 M hexane solution, 2.68 mL, 2.52 mmol). After being stirred at the same temperature for 1 h, the reaction mixture was quenced with addtion of MeOH, and filtered through a pad of Celite and concentrated. The residue was dissolved in THF (10 mL) in ice-water bath, and 10% aqueous $(COOH)_2$ (10 mL) solution was added. The mixture was stirred at the same temperature for 30 min, and poured into Et_2O-water. Phases were separated, and the aqueous phase was extracted with Et_2O. Combined organic phases were successively washed with water and saturated brine, dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 15 g; elution with 2:1 hexane-AcOEt) to give **12** (326 mg, 76%). a pale yellow oil, R_f = 0.41 (hexane:AcOEt = 12:1). IR (film) 2955, 2920, 1675 cm^{-1}. ^{1}H-NMR δ 0.91 (3H, s, Me), 1.05 (3H, d, *J* = 6.8 Hz, CH*Me*), 1.07 (3H, d, *J* = 6.8 Hz, CH*Me*), 1.34 (1H, ddd, *J* = 12. 6, 12.6, 5.6 Hz, H-5), 1.52 (1H, ddd, *J* = 10.6, 10.6, 10.6 Hz, H-7), 1.79-1.86 (2H, m, H-5 and H-7), 2.20-2.29 (1H, m, H-4), 2.38 (1H, dd, *J* = 17.7, 9.0 Hz, H-8), 2.49-2.57 (1H, m, H-4), 2.49-2.57 (1H, m, H-8), 2.96 (1H, sep, *J* = 6.8 Hz, C*H*Me_2), 7.16 (1H, d, *J* =2.1 Hz, H-2), 9.49 (1H, s, CHO). ^{13}C NMR δ 20.2, 21.3, 21.8, 22.0, 27.5, 29.7, 34.8, 39.0, 45.6, 137.7, 137.9, 139.3, 155.0, 194.5. HRMS calcd for $C_{14}H_{20}O$ 204.1514, found 204.1498.

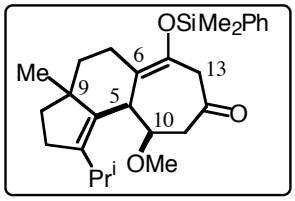
6-Methyl-9-(1-methylethyl)bicyclo[4.3.0]nona-2,9-diene-1-carbonyl(dimethyl)phenylsilane (13)

To a cooled (-80 °C) solution of $PhMe_2SiLi$ (0.62 M in THF, 11.8 mL, 7.32 mmol) in THF (19 mL) was added dropwise **12** (1.00 g, 4.89 mmol). The solution was stirred at the same temperature for 1 h, and then quenched by saturated aqueous NH_4Cl solution. The mixture

was extracted with Et_2O, and the combined organic phases were washed with saturated brine, dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 100 g; elution with 20:1 hexane-AcOEt) to give silylcarbinol (775 mg, 47%).

This material was dissoolved in CH_2Cl_2 (20 mL) and *N*-methylmorpholine-*N*-oxide (399 mg, 3.4 mmol) and TPAP (800 mg, 2.28 mmol). The reaction mixture was stirred at room temperature for 5 min, filtered through a pad of silica gel (45 g) eluting with hexane-AcOEt (24:1), and the solvent was concentrated. The residual oil was subjected to column chromatography (silica gel, 50 g; elution with 25:1 hexane-AcOEt) to give **13** (440 mg, 46%). a pale yellow needles, R_f = 0.47 (hexane:AcOEt = 12:1). ^{1}H-NMR δ 1.25 (1H, ddd, *J* = 12.7, 12.7, 5.6 Hz, H-5), 1.42 (1H, ddd, *J* = 10.5, 10.5, 10.5 Hz, H-7), 1.70-1.78 (2H, H-5 and H-7), 2.09-2.18 (1H, m, H-4), 2.25 (1H, dd, *J* = 17.8, 8.8 Hz, H-8), 2.32 (1H, sep, *J* = 6.8 Hz, C*H*Me$_2$), 2.38-2.47 (1H, m, H-8), 2.46-2.52 (1H, m, H-4), 7.14 (1H, d, *J* = 2.4 Hz, H-2), 7.36-7.40 (3H, m, Ph), 7.59 (2H, m, Ph). ^{13}C NMR δ -2.6 and –2.7 (SiMe$_2$), 20.3 (C-4), 21.2, 21.8, and 22.0 (6-Me, CH*Me*$_2$), 27.2 (*C*HMe$_2$), 29.7 (C-8), 35.1 (C-5), 39.0 (C-7), 45.0 (C-6), 128.3, 129.6, 134.1, 136.4 (C-2), 137.6, 138.1, 142.0, 153.6, 233.8 (C=O). HRMS calcd for $C_{22}H_{30}OSi$ 338.2066, found 338.2057.

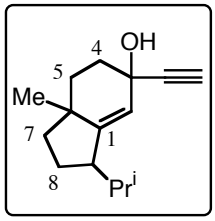
[3 + 4] annulation of 13 with lithium enolate of 4-methoxy-3-buten-2-one



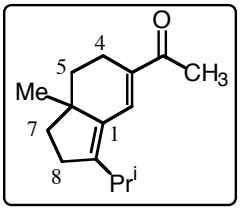
To a stirred and cooled (-80°C) solution of lithium diisopropylamide (LDA) prepared from diisopropylamine (216 μL, 156 mg, 1.54 mmol) and *n*-BuLi (1.47 M in hexane, 1.05 mL, 1.54 mmol) in THF (1 mL) was added dropwise a solution of 4-methoxy-3-buten-2-one (130 μL, 128 mg, 1.28 mmol) in THF (1 mL). After stirring at -80 °C for 30 min, the solution was added dropwise via a cannula to a cooled (-80 °C) solution of **13** (440 mg, 1.30 mmol) in THF (3.8 mL). The reaction mixture was allowed to warm to room temperature over 1 h, and then quenched by addition of AcOH (88 μL) in THF (1 mL). The mixture was concentrated, and the residue was subjected to column chromatography (silica gel, 80 g; elution with 12:1 hexane-AcOEt) to give **14** (265 mg, 47%) as a 1:1 mixture of diastereomers along with **13** (62 mg, 14%). The mixture could be separated by subjecting MPLC (elution with 12:1 hexane-AcOEt) to give **14a** (less polar) and **14b** (more polar). **14a**: a colorless oil, R_f = 0.36 (hexane:AcOEt=12:1). IR (film) 1710 cm^{-1}. ^{1}H-NMR δ 0.47 (3H, s, SiMe), 0.48 (3H, s, SiMe), 0.94 (3H, d, *J* = 6.8 Hz, CH*Me*), 0.94 (3H, d, *J* = 6.8 Hz, CH*Me*), 1.06 (3H, s, 9-CH$_3$), 1.01 (1H, dm, H-1 or H-2), 1.38 (1H, (1H. ddd. *J* = 11.1, 11.1, 11.1 Hz, H-8), 1.64 (1H, ddd, *J* = 12.4. 3.6, 3.6 Hz, H-1 or H-2), 1.72 (1H, dd, *J* = 11.1, 3.6 Hz, H-8), 2.05-2.16 (2H, m, H-7 and H-1 or H-2), 2.24-2.32 (1H, m, H-7), 2.48 (1H, sep, *J* = 6.8 Hz, C*H*Me$_2$), 2.68 (1H, dd, *J* = 10.8, 6.6 Hz, H-11), 2.74 (1H, dd, *J* = 10.8, 6.6Hz, H-11), 2.76 (1H, d, *J* = 19.0 Hz, H-

13), 3.18 (1H, s, H-5), 3.19 (3H, s, OCH_3), 3.47 (1H, dd, *J* = 19.0, 3.4 Hz, H-13), 3.55 (1H, ddd, *J* = 6.6, 6.6, 2.8 Hz, H-10), 7.36-7.43 (3H, m, ArH), 7.59-7.61 (2H, m, ArH). ^{13}C NMR δ -0.86 and –0.66 ($SiMe_2$), 21.2, 21.7, and 21.8 (9-Me and CH*Me*$_2$), 23.0 (C-1 or C-2), 26.9 (*C*HMe_2), 27.1 (C-7), 38.9 (C-1 or C-2), 40.5 (C-5), 41.9 (C-8), 45.9 (C-9), 47.2 (C-11), 50.2 (C-13), 57.6 (OCH_3), 86.0 (C-10), 119.9 (C-6), 128.2, 130.1, 133.6, 137.2, 137.8, 138.9, 142.4 (C-14), 207.0 (C-12). HRMS calcd for $C_{27}H_{38}O_3Si$ 438.2590, found 438.2574. **14b**: a colorless oil, R_f = 0.36 (hexane:AcOEt = 12:1). IR (film) 1710 cm^{-1}. ^{1}H-NMR δ 0.48 (6H, s, $SiMe_2$), 0.71 (3H, s, CH_3), 0.90 (3H, d, *J* = 6.8 Hz, CH*Me*), 1.00 (3H, d, *J* = 6.8Hz, CH*Me*), 1.38 (1H, br ddd, *J* = 10.9, 10.9, 10.9 Hz, H-8), 1.51 (1H, ddd, *J* = 12.1, 6.2, 1.7 Hz, H-1 or H-2), 1.54-1.64 (2H, m, H-8 and H-1 or H-2), 2.07 (1H, ddd, *J* = 15.4, 8.5, 1.5 Hz, H-7), 2.25-2.32 (1H, m, H-7), 2.35-2.48 (2H, m, H-1 or H-2), 2.52 (1H, sep, *J* = 6.8 Hz, C*H*Me_2), 2.68 (1H, dd, *J* = 10.5, 7.1 Hz, H-11), 2.73 (1H, dd, *J* = 10.5, 7.1 Hz, H-11), 2.75 (1H, d, *J* = 19.5 Hz, H-13), 3.20 (3H, s, OCH_3), 3.26 (1H, s, H-5), 3.42 (1H, ddd, *J* = 19.5, 3.0, 3.0 Hz, H-13), 3.81 (1H, ddd, *J* = 7.1, 7.1, 2.6 Hz, H-10), 7.35-7.42 (3H, m, ArH), 7.60-7.62 (2H, m, ArH). ^{13}C NMR δ -0.68 and –0.4 ($SiMe_2$), 21.1, 21.4, and 21.9 (9-Me, CH*Me*$_2$), 23.4 (C-1 or C-2), 27.3 (C-7), 27.3 (*C*HMe_2), 32.7 (C-1 or C-2), 39.1 (C-8), 39.5 (C-5), 45.9 (C-9), 46.9 (C-11), 50.3 (C-13), 57.8 (OCH_3), 84.8 (C-10), 117.8 (C-6), 128.2, 130.2, 133.5, 137.4, 137.7, 138.8, 140.7 (C-14), 208.2 (C-12). HRMS calcd for $C_{27}H_{38}O_3Si$ 438.2590, found 438.2582.

1-Ethynyl-6-methyl-9-(1-methylethyl)bicyclo[4.3.0]non-1-en-3-ol (15)



To an ice-cooled solution of ethynylmagnesium bromide (0.5 M in THF, 8.7 mL, 4.3 mmol) in THF (2 mL) was added 11 (695 mg, 3.60 mmol) in THF (1 mL). The mixture was stirred at room temperature for 20 h before quenching saturated aqueous $NaHCO_3$ solution (30 mL). The mixture was extracted with Et_2O. Combined organic phases were washed with saturated brine, dried, concentrated. The residual oil was distilled (150-200 °C/4 mmHg, bulb-to-bulb) to give **15** (625 mg, 79%) which solidfied after standing. a colorless needels, R_f = 0.34 (hexane:AcOEt = 5:1). IR (KBr) 3290, 2955, 2100 cm^{-1}. ^{1}H-NMR δ 0.73 and 0.96 (3H, d, *J* = 6.8 Hz, CH*Me*$_2$), 1.05 (3H, s, 6-Me), 1.16 (1H, br ddd, *J* = 11.2, 11.2, 11.2 Hz, H-7), 1.49-1.61 (2H, m, H-7 and H-4 or H-5), 1.67 (1H, ddd, *J* = 13.7, 13.7, 3. 0 Hz, H-8), 1.74-1.85 (2H, m, H-8 and H-4 or H-5), 1.97-2.06 (2H, m, C*H*Me_2 or H-4 or H-5), 2.07 (1H, s, HC≡C), 2.16 (1H, dm, *J* =



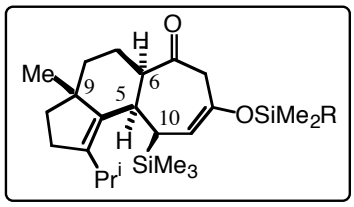
14.7 Hz, H-4 or H-5), 2.50 (1H, s, OH), 2.51-2.60 (1H, m, H-9), 5.23 (1H, br dd, *J* = 1.8, 1.8 Hz, H-2). ^{13}C NMR δ15.8 (CH*Me*), 22.2 (CH*Me*$_2$ and C-4 or C-5), 24.7 (6-Me), 29.1 (C*H*Me_2), 35.6 (C-8 and C-4 or C-5), 35.8 (H*C*≡C), 37.6 (), 40.1 (C-4, C-5), 42.4 (C-6), 44.9 (C-9), 68.3 (C-3), 71.8, 87.9 (HC≡*C*), 119.8 (C-2), 123, 6, 134.1, 152.2, 154.2. $C_{15}H_{22}O$ 218.34. Anal. calcd for

$C_{15}H_{22}O$: C: 82.52; H: 10.16 ; found: C, 82.70; H, 10.25.

3-Acetyl-6-methyl-9-(1-methylethyl)bicyclo[4.3.0]nona-2,9-diene (16)

Ethynylalcohol **15** (1.00 g, 4.60 mmol) was dissolved in HCOOH (10 mL) and refluxed for 15 min. The mixture was poured into saturated aqueous $NaHCO_3$, and extracted with pentane. Combined organic phases were succesively washed with saturated aqueous $NaHCO_3$ and saturated brine, dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 80 g; elution with 8:1 hexane-AcOEt) to give **16** (419 mg, 42%). a colorless plate, R_f = 0.47 (hexane:AcOEt = 5:1). mp 42-43 °C (hexane). IR (KBr) 1700, 1625 cm^{-1}. ^1H NMR δ 0.89 (3H, s, Me), 1.04 and 1.07 (each 3H, d, *J* = 6.8 Hz, CH*Me*$_2$), 1.32 (1H, dd, *J* = 12.6, 12.6, 5.6 Hz, H-5), 1.48 (1H, ddd, *J* =12.0, 9.2, 9.2 Hz, H-8), 1.79 (1H, dd, *J* = 12.0, 7.1 Hz, H-8), 1.82 (1H, ddd, *J* = 12.6, 5.8, 1.5 Hz, H-5), 2.21-2.32 (1H, m, H-4), 2.35 (3H, s, MeCO), 2.35 (1H, dd, *J* = 16.9, 9.6 Hz, H-7), 2.47-2.56 (1H, m, H-7), 2.58 (1H, dd, *J* = 18.6, 5.6 Hz, H-4), 2.94 (1H, sep, *J* = 6.8 Hz, C*H*Me$_2$), 7.29 (1H, br d, *J* = 2.4 Hz, H-2). ^{13}C NMR δ 21.3, 21.8, 21.9, and 22.1 (6-Me, C-4, CH*Me*$_2$), 25.7 (*Me*CO), 27.2 (*C*HMe$_2$), 29.6 (C-7), 35.3 (C-5), 39.0 (C-8), 44.7 (C-6), 130.3 (C-2), 136.4, 137.6, and 152.7 (C-1, C-3, and C-9), 199.7 (C=O). Anal. calcd for $C_{15}H_{22}O$ C: 82.52; H: 10.16. found: C, 82.63; H, 10.27.

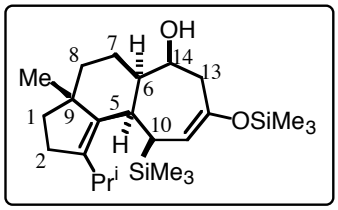
[3 + 4] annulation of 16 with acryloylsilanes (17a,b)



This procedure is representative of reactions of **16** with **17a**. To a stirred and cooled (-80°C) solution of LDA from diisopropylamine (86 μL, 62 mg, 0.62 mmol) and *n*-BuLi (1.61 M in hexane, 0.385 mL, 0.62 mmol) in THF (0.5 mL) was added dropwise a solution of **16** (122 mg, 0.56 mmol) in THF (1 mL). After stirring at -80 °C for 30 min, the solution was added dropwise via a cannula to a cooled (-80 °C) solution of **17a** (223 mg, 1.21 mmol) in THF (5.8 mL). The reaction mixture was allowed to warm to 0 °C, and then quenched by addition of saturated aqueous NH_4Cl solution (50 mL). The mixture was extracted with Et_2O. Combined organic phases were washed with saturated brine, dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 30 g; elution with 20:1 hexane-AcOEt) to give **20a** (155 mg, 60%). a pale yellow oil, R_f = 0.39 (hexane:AcOEt = 11:1). IR (film) 1700, 1645, 1250 cm^{-1}. ^1H NMR δ -0.03 (9H, s, $SiMe_3$), 0.11 and 0.15 (each, 3H, $SiMe_3$), 0.90 and 0.96 (each 3H, d, *J* = 6.8 Hz, $CHMe_2$), 0.91 (9H, s, *t*-Bu), 1.16-1.25 (1H, m, H-1), 1.18 (3H, s, 9-Me), 1.54-1.64 (4H, m, H-1, H-7, and H-8), 1.92 (1H, ddd, *J* = 8.1, 6.8, 0.7 Hz, H-10), 2.17 (1H, ddd, *J* = 16.0, 9.4, 6.4 Hz, H-2), 2.25 (1H, ddd, *J* = 16.0, 9.2, 6.0 Hz, H-2), 2.45 (1H, ddd, *J* = 13.2, 6.8, 4.3 Hz, H-6), 2.53 (1H, dddd, *J* = 13.2, 13.2, 13.2, 4.1 Hz, H-7), 2.74 (1H, sep, *J* = 6.8 Hz, C*H*Me$_2$), 2.98 (1H, d, *J* = 19.7 Hz,

H-13), 3.30 (1H, dm, J = 19.7 Hz, H-13), 3.43 (1H, ddm, J = 6.8, 6.8 Hz, H-5), 4.91 (1H, dd, J = 8.1, 2.1 Hz, H-11). ^{13}C NMR δ -4.47 and-3.61 ($SiMe_2$), -1.08 ($SiMe_3$), 18.1 (*C*-Bu^t), 20.4 and 22.1 ($CHMe_2$), 22.7 (C-7), 25.1 (9-Me), 25.8 (Bu^t), 27.0 ($CHMe_2$), 27.5 (C-2), 28.0 (C-10), 38.7 (C-8), 40.3 (C-1), 46.7 (C-9), 49.2 (C-13), 58.7 (C-6), 108.5 (C-11), 138.6 and 142.9 (C-3 and C-4), 148.5 (C-12), 214.7 (C-14). HRMS calcd for $C_{27}H_{48}O_2Si_2$ 460.3190, found 460.3180.

20b: colorless needles, R_f = 0.33 (hexane:Et_2O = 17:1), mp 103 °C. IR (KBr) 1700, 1630 cm^{-1}. ^{1}H-NMR δ -0.02 (9H, s, $SiMe_3$), 0.19 (9H, s, $OSiMe_3$), 0.90 (3H, d, J = 6.8 Hz, CHMe), 0.95 (3H, d, J = 6.8Hz, CH*Me*), 1.19 (3H, s, 9-CH_3), 1.17-1.22 (1H, m, H-8), 1.54-1.65 (4H, m, H-1, H-7, and H-8), 1.93 (1H, dd, J = 8.1, 6.6 Hz, H-10), 2.18 (1H, ddd, J = 16.0, 9.4, 6.4 Hz, H-2), 2.26 (1H, ddd, J = 16.0, 9.4, 6.0 Hz, H-2), 2.45 (1H, ddd, J = 13.3, 7.3, 4.7 Hz, H-6), 2.55 (1H, dddd, J = 13.3, 13.3, 13.3, 4.3 Hz, H-7), 2.75 (1H, sep, J = 6.8Hz, C*H*Me), 3.00 (1H, d, J = 19.7 Hz, H-13), 3.31 (1H, d, J = 19.7 Hz, H-13), 3.44 (1H, dd, J = 7.3, 6.6 Hz, H-5), 4.94 (1H, dd, J = 8.1, 2.1 Hz, H-11). ^{13}C NMR δ -1.1($SiMe_3$), 0.7 ($OSiMe_3$), 20.4 and 22.1

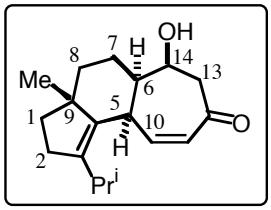


($CHMe_2$), 22.8 (C-7), 25.2 (9-Me), 27.0 ($CHMe_2$), 27.5 (C-10), 28.1 (C-2), 38.8 (C-5), 40.3 (C-1 and C-8), 46.8 (C-9), 49.2 (C-13), 58.7 (C-6), 108.7 (C-11), 138.6 and 142.9 (C-3 and C-4), 148.5 (C-12), 214.5 (C-14). HRMS calcd for $C_{24}H_{42}O_2Si_2$ 418.2723, found 418.2729.

21

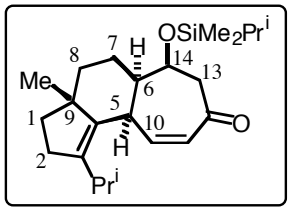
To an ice-cooled solution of **20b** (670 mg, 1.60 mmol) in Et_2O (14 mL) was added DIBAL (0.95 M in hexane, 2.02 mL, 1.92 mmol). After being stirred at the same temperature for 10 min, the reaction mixture was quenced with addtion of MeOH, and filtered through a pad of Celite and concentrated. The residual oil was subjected to column chromatography (silica gel, 40 g; elution with 2:1 hexane-Et_2O) to give **21** (488 mg, 72%). a colorless oil, R_f = 0.54 (hexane:Et_2O = 1:1). IR (film) 3395cm^{-1}. ^{1}H-NMR (substantial peak broadening was observed): δ 0.03 (9H, s, $SiMe_3$), 0.17 (9H, s, $OSiMe_3$), 0.93 (3H, d, J = 6.8 Hz, CH*Me*), 0.96 (3H, d, J = 6.8 Hz, CH*Me*), 1.11 (3H, s, 9-CH_3), 1.12-1.20 (1H, br m), 1.47-1.62 (3H, br m), 1.75 (1H, br s), 2.14 (1H, dm, J = 15.8 Hz, H-2), 2.24 (1H, ddd, J = 15.8, 8.6, 6.4 Hz, H-2), 2.45 (1H, dd, J = 18.2, 6.2 Hz, H-13), 2.60 (1H, dm, J = 18.2 Hz, H-13), 2.71-2.79 (1H, br s, $CHMe_2$), 3.32-3.27 (1H, br s, H-5), 3.95-4.08 (1H, br s, H-14), 4.92-4.96 (1H, br s, H-11). ^{13}C NMR δ 0.68, 20.9, 22.0, 24.2, 25.4, 26.9, 27.3, 41.4, 47.2, 48.5, 70.3 (C-14), 100.9 (C-11), 113.0, 135.3, 141.3 (C-12),. HRMS calcd for $C_{24}H_{44}O_2Si_2$ 420.7760, found 420.2871.

22



To an ice-cooled solution of **21** (329 mg, 0.782 mmol) in THF (8.3 mL) was added NBS (145.7 mg, 0.821 mmol). The reaction mixture was stirred at the same temperature for 10 min before addition of TBAF (1.0 M in THF, 782 μL, 0.782 mmol). After being stirred at the same temperature for 5 min, the mixture was poured into saturated aqueous $NaHCO_3$ solution. Phases were separated, and the aqueous phase was extracted with Et_2O. Combined organic phases were succesively washed with water and saturated brine, dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 25 g; elution with 1:2 hexane-Et_2O) to give **22** (169 mg, 79%). a yellow oil, R_f = 0.25 (hexane:Et_2O = 1:2). IR (film) 3430, 1650 cm^{-1}. ^{1}H-NMR δ 0.93 (3H, d, *J* = 6.8 Hz, CH*Me*), 0.97 (3H, d, *J* = 6.8 Hz, CH*Me*), 1.02 (3H, s, 9-CH_3), 1.29 (1H, ddd, *J* = 13.2, 13.2, 3.7 Hz, H-8), 1.46-1.59 (2H, m, H-1 and H-7), 1.64-1.73 (2H, m, H-1 and H-7), 1.77 (1H, ddd, *J* = 13.2, 3.2, 3.2 Hz, H-8), 1.80-1.86 (1H, m, H-6), 2.20 (1H, dd, *J* = 15.8, 8.8 Hz, H-2), 2.33 (1H, ddd, *J* = 15.8, 8.8, 2.1 Hz, H-2), 2.63 (1H, sep, *J* = 6.8 Hz, C*H*Me_2), 2.83 (1H, dd, *J* = 16.8, 1.5 Hz, H-13), 2.96 (1H, dd, *J* =16.8, 8.6 Hz, H-13), 3.87 (1H, ddd, *J* = 8.6, 8.6, 1.5 Hz, H-14), 3.92 (1H, m, H-5), 5.89 (1H, dd, *J* = 12.2, 2.6 Hz, H-11), 6.21 (1H, dd, *J* = 12.2, 3.9 Hz, H-10). ^{13}C NMR δ 21.6 (CH*Me*$_2$), 24.1 (CH*Me*$_2$), 25.0 (C-7), 26.5 (*C*HMe_2), 27.9 (C-2), 36.8 (C-5), 40.5 (C-1), 40.9 (C-8), 46.4 (C-6), 47.1 (C-9), 49.9 (C-13), 70.9 (C-14), 130.8 (C-11), 138.4 and 141.7 (C-3 and C-4), 150.6 (C-10), 201.5 (C-12). HRMS calcd for $C_{18}H_{26}O_2$ 274.1933, found 274.1946.

23



To an ice-cooled solution of **22** (62 mg, 0.226 mmol) in CH_2Cl_2 (1 mL) was added imidazole (77 mg, 1.13 mmol) and *i*-PrMe_2SiCl (39 μL, 0.248 mmol). The solution was stirred at the same temperature for 10 min, and poured into saturated aqueous $NaHCO_3$ solution. Phases were separated, the aqueous phase was extracted with Et_2O. Combined organic phases were succesively washed with water and saturated brine, dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 7 g; elution with 8:1 hexane-Et_2O) to give **23** (78 mg, 92%). a pale yellow oil, R_f = 0.33 (hexane:Et_2O = 8:1). IR (film) 1660 cm^{-1}. ^{1}H-NMR δ 0.05 and 0.06 (each 3H, s, SiMe), 0.79 (1H, sep, *J* = 7.3 Hz, SiHMe_2), 0.92-0.98 (12H, m, CH*Me*$_2$, SiCH*Me*$_2$), 1.01 (3H, s, 9-Me), 1.29 (1H, ddd, *J* = 12.8, 12.8, 3.7 Hz, H-8), 1.46-1.53 (2H, m, H-1 and H-7), 1.59 (1H, dddd, *J* = 13.3, 12.8, 12.8, 3.2 Hz, H-7), 1.71 (1H, ddd, *J* = 10.7, 7.7, 1.5 Hz, H-1), 1.79 (1H, ddd, *J* = 12.8, 3.2, 3.2 Hz, H-8), 1.79-1.86 (1H, m, H-6), 2.21 (1H, ddd, *J* = 15.8, 9.4, 1.3 Hz, H-2), 2.34 (1H, ddd, *J* =15.8, 8.5, 1.7 Hz, H-2), 2.65 (1H, sep, *J* = 6.8 Hz, C*H*Me_2), 2.79 (1H, dd, *J* = 16.6, 2.6 Hz, H-13), 2.85 (1H, dd, *J* = 16.6, 6.8 Hz, H-13), 3.90 (1H, ddd, *J* = 6.8, 6.6, 2.6 Hz, H-14), 3.95 (1H, ddd, *J* = 5.1, 3.0, 2.7

Hz, H-5), 5.88 (1H, dd, J = 12.5, 2.7 Hz, H-11), 6.10 (1H, dd, J =12.5, 3.0 Hz, H-10). ^{13}C NMR δ -3.8 and –3.5 ($SiMe_2$), 14.9, 17.0, 21.5, 21.6, 24.3 (C-7), 26.6 ($CHMe_2$), 28.0 (C-2), 37.5 (C-5), 40.5 (C-1), 41.4 (C-8), 47.0 (C-6), 47.5 (C-9), 49.4 (C-13), 71.1 (C-14), 130.5 (C-11), 139.2 and 140.8 (C-3 and C-4), 149.7 (C-10), 201.4 (C-12). HRMS calcd for $C_{23}H_{38}O_2Si$ 374.2641, found 374.2662.