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Tandem Sakurai-Aldol Addition Reactions as a Route to Structurally Complex Carbocycles

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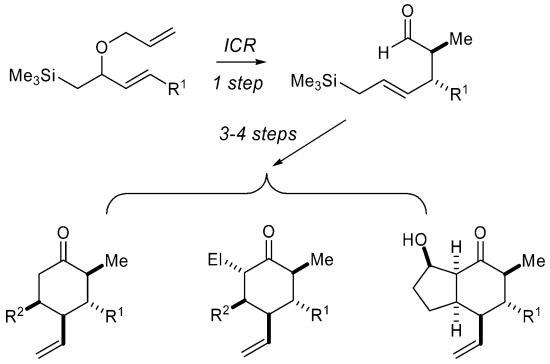
Received February 4, 2005



Tandem intramolecular Sakurai-aldol reactions provide a concise and highly diastereoselective route to substituted cyclohexenone derivatives. The cyclization substrates are readily obtained using olefin isomerization−Claisen rearrangement (ICR) reactions to prepare the key chiral allyl silane precursors. The Claisen reaction products are elaborated to the chiral Sakurai-aldol substrates by an efficient two-step sequence involving vinyl organometallic-aldehyde addition and oxidation of the resulting alcohol. The reaction of the resulting enones with $TiCl_4$ elicits a highly stereoselective allyl silane conjugate addition to produce a trichlorotitanium enolate as the reaction intermediate; intermolecular trapping of the enolate with an aldehyde provides pentasubstituted cyclohexanone derivatives in which the annulation reaction establishes four stereocenters and two new C−C bonds. A fully intramolecular variant of the Sakurai-aldol reaction that creates four stereocenters, two new C−C bonds, and establishes two new carbocyclic rings is also described.

Introduction

The potential for rapidly generating molecular complexity in the form of C−C bond networks, cyclic structures, or complex stereochemical relationships routinely characterizes the most salient organic synthesis methodologies.[1] Indeed, the enduring utility of Diels−Alder cycloadditions can be traced to their ability to rapidly and selectively generate structural complexity in the form of two new C−C σ-bonds and a new carbocyclic ring decorated with up to four contiguous stereocenters. Efforts to mimic similar efficiency in generating structural complexity have resulted in synthesis strategies that merge multiple transformations into a single operation becoming increasingly important in both target-directed and diversity-oriented synthesis activities.[2] We were attracted to the chiral allylic silanes **1** as templates for tandem reaction development (Figure 1) with the goal

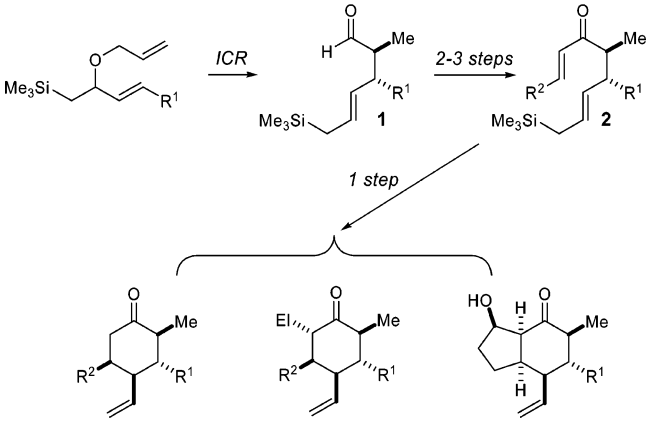


FIGURE 1. Allyl silane templates for stereochemically rich carbocycle construction.

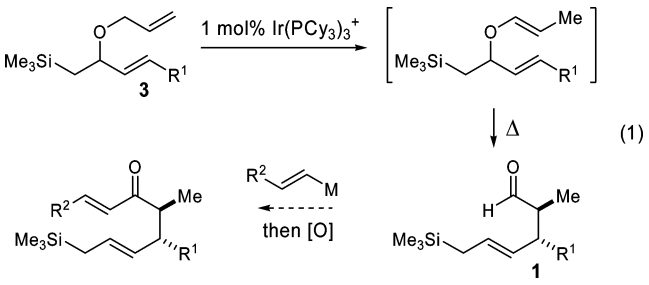
of developing new methodologies providing similar opportunities for multiple stereocontrolled C−C bond con-

(1) For a review, see: Nicolaou, K. C.; Montagnon, T.; Snyder, S. A. *Chem. Commun.* **2003**, 551−564.

10.1021/jo050225y CCC: $30.25
Published on Web 04/27/2005

structions, carbocyclic ring formation, or establishing multiple stereogenic centers. The elaboration of these aldehydes to the corresponding enone **2** would present intramolecular allyl silane conjugate addition as a conduit to structurally complex and stereochemically rich carbocyclic products. Herein, we describe the facile access to the stereodefined allyl silane templates using olefin isomerization−Claisen rearrangement (ICR) reactions and the utility of these intermediates as platforms for the stereocontrolled synthesis of tri-, tetra-, and pentasubstituted carbocycles.[3]

Our interest in the allyl silane-based strategy for complex carbocycle construction originated from the ready availability of the requisite chiral allyl silanes from the catalyzed olefin ICR methodology developed in our laboratories. The ICR methodology makes easily prepared di(allyl) ether **3** the direct progenitor of aliphatic Claisen rearrangements producing 2,3-disubstituted 4-pentenal derivative **1** with high syn diastereoselection. Moreover, the aliphatic Claisen rearrangements accessed through the ICR sequence produce aldehyde functionalities that can be readily transformed to the targeted enone annulation precursors.



(1)

After elaborating the ICR-derived allyl silanes to the enone annulation precursor **2**, we anticipated that the ensuing allyl silane conjugate addition would proceed through a synclinal boatlike transition state orienting the C_2/C_3 substituents in the pseudoequatorial positions (Figure 2).[4,5] As a result, the C_2 and C_3 stereocenters established in the preceding Claisen rearrangement would be effectively translated to the incipient stereocenters arrayed about the trans,trans,cis-tetrasubstituted cyclohexanone product **3**.[6] Further functionalization of the putative carbocycles could then be accomplished by derivatization of the cyclohexanone-derived enolate or nucleophilic addition to the ketone functionality.

Results and Discussion

The di(allyl) ether ICR substrates were prepared from allylic alcohols (±)-**4a**−**c** which differ in the identity of the β substituent (R^1 = Me, ^{i}Pr, Ph) (Scheme 1). Alcohol

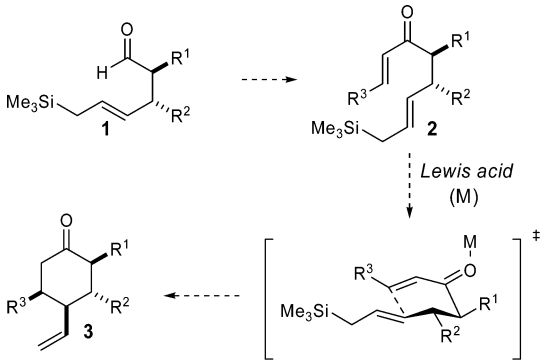
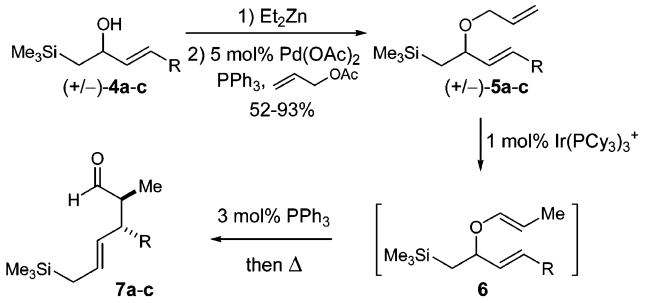


FIGURE 2. Sakurai annulation process.

SCHEME 1



R	*syn*:*anti* **7** (% yield from **5**)
Me (**7a**)	93:7 (98)
Ph (**7b**)	92:8 (100)
^{i}Pr (**7c**)	91:9 (100)

allylation proceeded by Pd(0)-catalyzed *O*-allylation of the corresponding zinc alkoxide to produce the di(allyl) ether ICR substrates (±)-**5a**−**c** (52−93%).[7,8] The di(allyl) ethers (±)-**5a**−**c** were subjected to the standard ICR reaction conditions (1 mol % $Ir(PCy_3)_3^+$ and then 3 mol % PPh_3, Δ) which produced the desired syn-2,3-disubstituted pentenals **7a**−**c** (98−100% unpurified).[9,10] In each case, the crude Claisen-derived aldehydes were sufficiently pure to use directly in subsequent transformations after filtration to remove the isomerization catalyst.

Homologating the ICR-derived allyl silanes to the enone annulation precursors exploited the electrophilicity of the aldehyde function emerging from the aliphatic Claisen rearrangement (Scheme 2). Enones **8a** and **8b** were obtained by vinylmagnesium bromide addition to aldehydes **7a** and **7b** followed by oxidation (SO_3·pyr or Dess−Martin periodinane (DMP)) of the intervening allylic alcohol (43−45% from **7**). The β-methyl-substituted

(2) For reviews, see: (a) Neuschuetz, K.; Velker, J.; Neier, R. *Synthesis* **1998**, 227−255. (b) Wipf, P. *Pharm. News* **2002**, *9*, 157−169.

(3) Nelson, S. G.; Bungard, C. J.; Wang, K. *J. Am. Chem. Soc.* **2003**, *125*, 13000−13001.

(4) Hosomi, A.; Sakurai, H. *J. Am. Chem. Soc.* **1977**, *99*, 1673−1675.

(5) For reviews of intramolecular allyl silane additions, see: (a) Hosomi, A. *Acc. Chem. Res.* **1988**, *21*, 200−206. (b) Schinzer, D. *Synthesis* **1988**, 263−273. (c) Sakurai, H. *Synlett* **1989**, 1−8. (d) Schinzer, D.; Langkopf, E. *Chem. Rev.* **1995**, *95*, 1375−1408. (e) Majetich, G.; Defauw, J. *Tetrahedron* **1988**, *44*, 3833 and references therein.

(6) For a related cyclization of Claisen-derived allyl silanes, see: Wilson, S. R.; Price, M. F. *J. Am. Chem. Soc.* **1982**, *104*, 1124−1126.

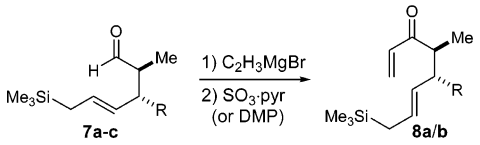
(7) Kim, H.; Lee, C. *Org. Lett.* **2002**, *4*, 4369−4371.

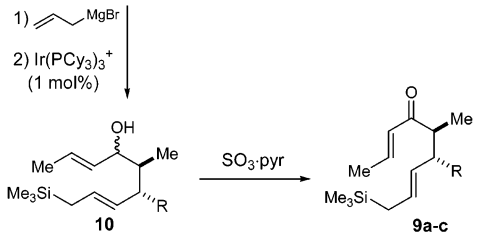
(8) The attempted allylation under typical Williamson etherification conditions (NaH or KH then allyl bromide) resulted in considerable Peterson elimination of the β-silyl alkoxide intermediates. See: Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780−784.

(9) The Ir(I) isomerization catalyst was prepared by reacting $[IrCl(C_8H_{14})_2]_2$, $NaBPh_4$ (2 equiv), and PCy_3 (6 equiv) (see Supporting Information for full procedural details). The resulting catalyst is formulated as the $Ir(PCy)_3^+$ complex on the basis of reaction stoichiometry and is not necessarily intended to represent the reactive catalyst complex that may be accessed by reversible phosphine dissociation. See ref 3.

(10) For certain substrates, Claisen reaction times were accelerated considerably by conducting the thermal sigmatropic rearrangement under microwave irradiation (see Supporting Information for full procedural details).

SCHEME 2

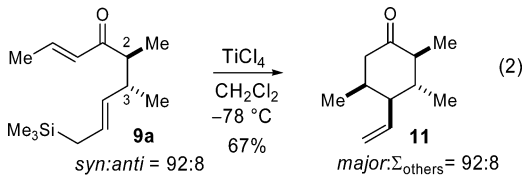




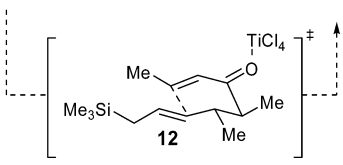
Enone	R	% yield (from **7**)
8a	Me	43
8b	Ph	45
9a	Me	51
9b	Ph	31
9c	^{i}Pr	46

enones **9a**−**c** were obtained by allylmagnesium bromide addition to aldehydes **7a**−**c** followed by Ir(I)-catalyzed olefin isomerization to the epimeric *E* allylic alcohols **10a**−**c** (50−59% from **7**). The resulting mixture of diastereomeric allylic alcohols was oxidized to the requisite enone cyclization precursors **9a**−**c** (62−86%).

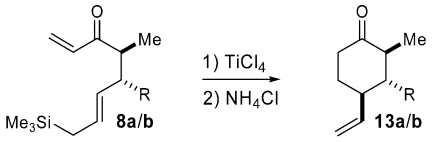
Access to the enone annulation templates provided the opportunity to evaluate the ability of the C_2 and C_3 stereocenters established in the Claisen rearrangement and to define stereoselectivity during the allyl silane conjugate addition. The efficiency of the Lewis acid-promoted enone cyclizations proved to be strongly dependent on the identity of the requisite Lewis acid. Reacting enone **9a** with $TiCl_4$ (1.2 equiv) at −78 °C promoted rapid conjugate addition to produce the tetrasubstituted cyclohexanone **11** in a 67% yield (major/Σ_{others} = 92:8) (eq 2).[11] Other Lewis acid promoters possessing attenuated Lewis acidity relative to $TiCl_4$ eroded cyclization efficiency considerably; rapid enone cyclization mediated by a strong Lewis acid is believed to eliminate competing reaction pathways such as enone oligomerization. Sakurai annulation diastereoselection is directly reflective of the diastereomer ratio emerging from the ICR sequence used to prepare the cyclization substrates; this suggests that stereocontrol derived from preexisting enone chirality is complete. The veracity of this assertion was unambiguously established by the $TiCl_4$-mediated cyclization of diastereometrically pure **9a**, obtained by HPLC separation, that produced cyclohexanone **11** as a single diastereomer.



(2)



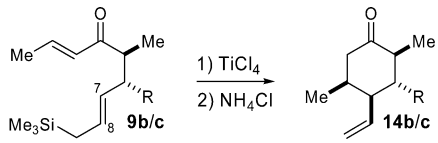
The relative stereochemistry about Sakurai-derived cyclohexanone **11** was consistent with annulation proceeding through a synclinal transition state **12** with the C_2 and C_3 alkyl substituents occupying pseudoequatorial orientations.[12] Adherence to this transition state was predicted to be independent of allyl silane geometry;[13] thus, minor amounts of the *Z* allyl silane converge with the same cyclohexanone diastereomer derived from the predominant *E* allyl silane. In accordance with this model, the diastereoselectivity in the remaining enone cyclizations reflected the original Claisen diastereomer ratios and proved to be independent of any allyl silane isomers. Thus, acryloyl enones **8a** [syn/anti = 90 (6.5:1 *E*/*Z*):10] and **8b** [syn/anti = 92 (10.5:1 *E*/*Z*):8] produced the trans,trans-2,3,4-trisubstituted cyclohexanones **13a** (major/Σ_{others} = 90:10, 59%) and **13b** (major/Σ_{others} = 93:7, 82%), respectively (eq 3).



(3)

R	*syn:anti* **8** (*syn E*:*Z*)	% yield **13** (major:Σ_{others})
Me (**8a**)	90:10 (6.5:1)	59 (90:10) (**13a**)
Ph (**8b**)	93:7 (10.5:1)	82 (93:7) (**13b**)

The *E* enones **9b** [syn/anti = 92 (4.3:1 E/Z_{C7-8}):8] and **9c** [syn/anti = 91 (8.1:1 E/Z_{C7-8}):9] also cyclized to the trans,-trans,cis-tetrasubstituted cyclohexanones **14b** (major/Σ_{others} = 95:5, 82%) and **14c** (major/Σ_{others} = 89:11, 87%), respectively, with faithful translation of chirality (eq 4).



(4)

R	*syn:anti* **9** (*syn E*:Z_{C7-8})	% yield **14** (major:Σ_{others})
Ph (**9b**)	92:8 (14.3:1)	82 (95:5) (**14b**)
^{i}Pr (**9c**)	91:9 (8.1:1)	87 (89:11) (**14c**)

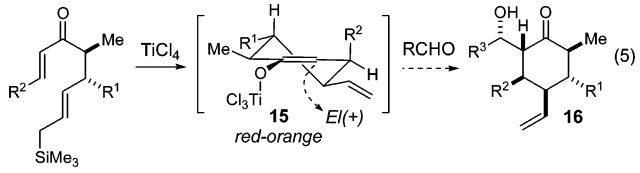
Analyzing the Lewis acid-promoted Sakurai reaction mechanisms revealed an opportunity for accessing fully substituted cyclohexanone derivatives by merging the annulation process with the ensuing stereoselective enolate functionalization. Provided that the putative Ti(IV) cyclohexanone enolate **15**, emerging from the conjugate

(11) Huang, X.; Pi, J. *Synlett* **2003**, 481−484.

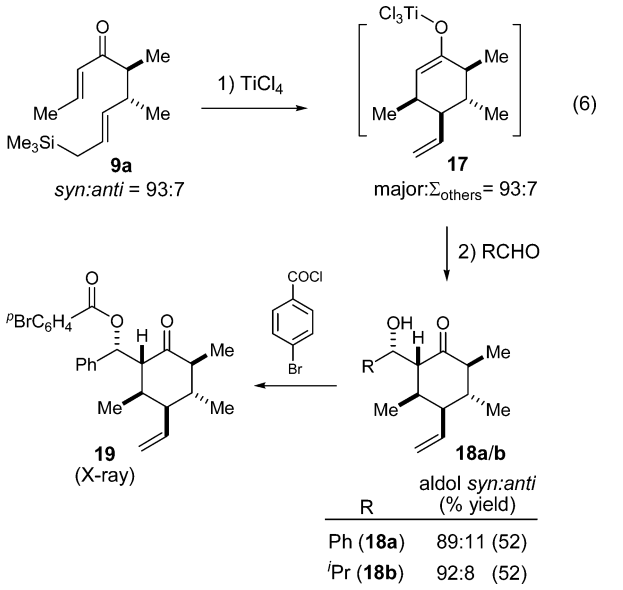
(12) Related allyl silane-enone additions exhibit a similar preference for reaction via the synclinal transition state. The competing *anti*-allyl silane-enone orientation in **12** suffers a developing *syn*-pentane interaction. For a discussion of competing transition states in related intramolecular Hosomi-Sakuari reactions, see: (a) Schinzer, D.; Solyom, S.; Becker, M. *Tetrahedron Lett.* **1985**, *26*, 1831−1834. (b) Majetich, G.; Hull, K.; Defauw, J.; Desmond, R. *Tetrahedron Lett.* **1985**, *26*, 2747−2750.

(13) Tokoroyama, T.; Tsukamoto, M.; Asada, T.; Iio, H. *Tetrahedron Lett.* **1987**, *28*, 6645−6648.

addition, was sufficiently long-lived, the addition of a suitable electrophile should lead to stereoselective C_6 bond construction (eq 5).[14,15]

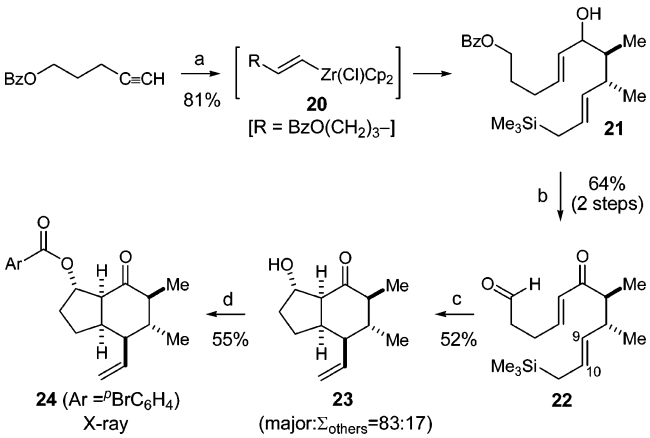


Indeed, the reaction of the enone cyclization substrates with $TiCl_4$ (CH_2Cl_2, −78 °C) was accompanied by the appearance of a red-orange color, characteristic of Ti(IV)-enolates, that persisted until the reaction was quenched. Considering the utility of Ti(IV) enolates in aldol addition reactions, we elected to examine the potential for developing a tandem Sakurai annulation-aldol sequence for stereodefined pentasubstituted cyclohexanone **16**. Thus, enone **9a** was reacted with $TiCl_4$ (1 equiv) to generate cyclohexanone enolate **17**; the addition of benzaldehyde quenched the resulting red-orange color and, after workup, provided the pentasubstituted cyclohexanone derivative **18a** in a 52% yield (89:11 syn/anti aldol diastereoselectivity) (eq 6).



As expected, the intrinsic Sakurai diastereoselection was retained in these tandem reactions with enolate facial selectivity ensured by chirality established during the allyl silane addition. While the Ti(IV) enolate expressed a strong facial bias in establishing the C_6 stereocenter, some erosion in aldehyde facial selectivity was observed which resulted in an 89:11 syn/anti mixture of aldol adducts. The use of isobutyraldehyde to trap the intervening Ti(IV) enolate similarly leads to the pentasubstituted cyclohexanone **18b** as a 92:8 syn/anti mixture of aldol products (52%). The relative stereoselection of the tandem Sakurai-aldol reactions was unambiguously

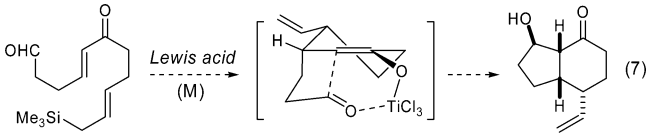
SCHEME 3[a]



[a] (a)(i) $Cp_2Zr(H)Cl$, (ii) 5 mol % $AgAsF_6$, **9a**; (b) (i) NaOH, (ii) Dess−Martin periodinane; (c) $TiCl_4$, CH_2Cl_2, −78 °C; and (d) 4-BrC_6H_4COCl, DMAP, $^iPr_2NEt$.

confirmed by X-ray structure determination of the *p*-bromobenzoate ester **19** derived from **18a**, thereby confirming the predictive value of the proposed transition states for both the Sakurai annulation and aldol addition events.

The potential strategic value of the tandem Sakurai-aldol reactions became apparent when we considered the potential for executing the tandem reactions in a fully intramolecular manifold. Tethering the aldehyde electrophile to the allyl silane provided an opportunity for a tandem Sakurai-aldol annulation process establishing two new C−C σ-bonds, four new stereocenters, and two new carbocycles in a single operation (eq 7).



To investigate the feasibility of the proposed bicyclization reaction, we required efficient access to the aldehyde-tethered enone, preferably via a synthesis sequence paralleling that previously developed for preparing the simple enones (Scheme 3). Thus, the benzoate ester of 5-pentynol was subjected to alkyne hydrozirconation,[16] and the resulting alkenyl zirconium complex **20** was directly engaged in $AgAsF_6$-catalyzed[17] addition to the Claisen-derived aldehyde **9a** to produce the allylic alcohol **21** as an inconsequential mixture of alcohol epimers (81%). After the benzoate protecting group was removed, the Dess−Martin periodinane oxidation of the resulting diol provided the tandem cyclization precursor in the form of keto aldehyde **22** [64%, syn/anti = 94 (14.7:1 $E/Z_{C9,10}$):6]. In accordance with previous results, the $TiCl_4$-induced cyclization of enone **22** led to the hydrindane derivative **23** (52%, major/Σ_{others} = 83:17) resulting from intramolecular allyl silane conjugate addition and the ensuing intramolecular aldol annulation (90:10 anti/syn aldol diastereoselectivity). The relative stereochemistry of the major cycloadduct diastereomer was con-

(14) For a related tandem annulation-enolate derivatization reaction, see ref 11.

(15) For aldol additions involving chlorotitanium enolates, see: Evans, D. A.; Rieger, D. L.; Bilodeau, M. T.; Urpi, F. *J. Am. Chem. Soc.* **1991**, *113*, 1047−1049.

(16) Schwartz, J.; Labinger, J. A. *Angew. Chem.* **1976**, *88*, 402−409.

(17) Suzuki, K.; Hasegawa, T.; Imai, T.; Maeta, H.; Ohba, S. *Tetrahedron* **1995**, *51*, 4483−4494.

firmed by X-ray structure determination of the C_7 *p*-bromobenzoate ester **24**.

Conclusion

Merging the ICR methodology with the tandem Sakurai-aldol annulation process provides a concise and highly stereoselective entry to highly substituted cyclohexanones. Considerable structural complexity emerges from the tandem annulation process with two new C−C bonds, one or two new carbocyclic rings, and up to four new stereocenters established in a single transformation. The ability to elaborate simple precursors to structurally complex and stereochemically rich carbocycles provided by the tandem Sakurai-aldol process is expected to be useful in both diversity- and target-oriented synthesis.

Experimental Section

Representative Procedure for Sakurai Annulation Reactions. Preparation of *R-(2*S*,3*R*,4*S*,5*S*)-2,3,5-Trimethyl-4-vinylcyclohexanone (11).** A solution of 0.10 g (0.42 mmol) of enone **9a** (82.5:7.9:9.7 syn/anti/*Z*) in 10 mL of CH_2Cl_2 was slowly added to 1.2 mL (1.2 mmol) of a vigorously stirred solution of $TiCl_4$ in CH_2Cl_2 (1.0 M) at −78 °C to produce a deep red reaction mixture. The syringe and flask were washed with an additional 1 mL of CH_2Cl_2, and this rinse was added to the reaction vessel. After the mixture was stirred for 15 min at −78 °C, the reaction was quenched with saturated aqueous NH_4Cl, and the resulting mixture was warmed to ambient temperature. The aqueous layer was extracted with CH_2Cl_2 (3×), and the combined organic extracts were dried (Na_2SO_4) and filtered through a fine glass frit; the filter cake was washed with Et_2O. The evaporation of the solvents produced the crude product mixture that was purified by flash chromatography on SiO_2 (20:1 pentane/Et_2O) to yield 46 mg of **11** (67%) as a colorless volatile oil. The separation of the diastereomers by GC−MS [HP-1 (12 m × 0.20 mm), pressure 21 kPa, 70 °C for 2.00 min, ramp at 10 °C/min to 300 °C, hold for 60 min] provided the diastereomer ratio: 91.7% (trans, trans, cis T_r = 6.49), 8.3% (T_r = 6.99); IR (thin film) 3076, 2969, 1713, 1638, 915 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.67 (dt, J = 18.0, 9.3 Hz, 1H), 5.11−5.06 (m, 2H), 2.63 (dd, J = 13.0, 5.0 Hz, 1H), 2.37−2.18 (m, 3H), 2.02 (dqd, J = 12.9, 6.5, 0.7 Hz, 1H), 1.60−1.46 (m, 1H), 1.04 (d, J = 6.5 Hz, 3H), 0.98 (d, J = 6.5 Hz, 3H), 0.83 (d, J = 6.9 Hz. 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.8, 13.9, 19.2, 36.9, 38.8, 48.6, 50.6, 52.2, 116.2, 140.6, 212.2; MS (EI) *m/z* 166 (M^+), 138, 96, 68; HRMS (EI) *m/z* calcd for $C_{11}H_{18}O$ 166.1358, found 166.1357.

General Procedure F for Tandem Intermolecular Sakurai-Aldol Reactions. Preparation of *R-(2*R*,3*R*,4*R*,-5*R*,6*S*)-2-((*S*)-1-Hydroxy-2-methylpropyl)-3,5,6-trimethyl-4-vinylcyclohexanone (18b).** A solution of 0.050 g (0.21 mmol) of enone **9a** (82.5:7.9:9.7 syn/anti/*Z*) in 5 mL of CH_2Cl_2 was slowly added to 0.6 mL (0.6 mmol) of a vigorously stirred solution of $TiCl_4$ in CH_2Cl_2 (1.0 M) at −78 °C to produce a deep red reaction mixture. The syringe and flask were washed with an additional 0.5 mL of CH_2Cl_2, and this rinse was added to the reaction vessel. After the mixture was stirred for 15 min at −78 °C, 23 μL (18 mg, 0.25 mmol) of isobutyraldehyde was added, and the reaction mixture was stirred for 60 min at −78 °C. The reaction was quenched with saturated aqueous NH_4Cl, and the resulting mixture was warmed to ambient temperature. The aqueous layer was extracted with CH_2Cl_2 (3×), and the combined organic extracts were dried (Na_2SO_4) and filtered through a fine glass frit; the filter cake was washed with Et_2O. The evaporation of the solvents produced the crude product mixture that was purified by flash chromatography on SiO_2 (5:1 hexanes/EtOAc) to yield 26 mg of **18b** (52%) as a clear oil. The diastereomer ratio was determined by 500 MHz ^1H NMR (C***H***OH): 85% (**18b**, δ 3.88), 8% (**18b** anti aldol, δ 3.98), 7% (Sakurai minor diastereomer/syn aldol, δ 3.32); IR (thin film) 3454, 3076, 2965, 1704, 1639, 999, 914 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.67 (ddd, J = 16.8, 10.4, 9.0 Hz, 1H), 5.10 (dm, J = 10.3 Hz, 1H), 5.07 (dm, J = 16.8 Hz, 1H), 3.92−3.86 (m, 1H), 2.38−2.28 (m, 3H), 2.12 (qdd, J = 7.1, 4.3, 3.1 Hz, 1H), 1.90 (pd, J = 6.9, 3.5 Hz, 1H), 1.63−1.52 (m, 1H), 1.51 (d, J = 7.8 Hz, 1H), 1.08 (d, J = 6.5 Hz, 3H), 1.04 (d, J = 6.9 Hz, 3H), 1.01 (d, J = 6.4 Hz, 3H), 0.89 (d, J = 7.2 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.4, 14.7, 15.1, 19.2, 20.1, 30.5, 37.9, 38.6, 48.1, 48.4, 61.2, 75.7, 116.4, 140.4, 214.7; MS (EI) *m/z* 220 ($M^+ - H_2O$), 205, 195, 166, 98, 68; HRMS (EI) *m/z* calcd for $C_{15}H_{24}O$ ($M^+ - H_2O$) 220.1827, found 220.1835.

Tandem Intramolecular Sakurai-Aldol Reactions. *R-(3a*S*,5*S*,6*R*,7*R*,7a*R*)-Octahydro-3-hydroxy-5,6-dimethyl-7-vinylinden-4-one (23).** A 1.0 M CH_2Cl_2 solution of $TiCl_4$ (0.28 mL, 0.28 mmol) was added to a −78 °C solution of 65 mg (23 mmol) of keto aldehyde **22** (87.8:6.1:6.1 syn/anti/*Z*) in 4.6 mL of CH_2Cl_2. After the mixture was stirred for 20 min at −78 °C, the reaction was quenched with 5 mL of saturated aqueous NH_4Cl, and the biphasic mixture was warmed to ambient temperature. The aqueous layer was extracted with CH_2Cl_2 (3×), and the combined organic extracts were dried (Na_2SO_4) and filtered through a fine glass frit; the filter cake was washed with Et_2O. The solvent was evaporated, and the resulting crude product mixture was purified by flash chromatography on SiO_2 (2:1 hexanes/EtOAc) to yield 25 mg of **23** (52%) as a clear viscous oil. The diastereomeric ratio was determined by GC−MS [HP-1 (12 m × 0.20 mm), pressure 21 kPa, 70 °C for 2.00 min, ramp at 10 °C/min to 300 °C, hold for 60 min]: 5.8% (T_r = 10.15), 6.1% (**23** syn aldol, T_r = 10.42), 5.3% (T_r = 11.63), 83% (**23**, T_r = 11.95); IR (thin film) 3400, 3075, 2969, 1706, 1639, 998, 913 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.59 (dt, J = 17.1, 9.8 Hz, 1H), 5.12 (dd, J = 17.0, 1.9 Hz, 1H), 5.09 (dd, J = 9.9, 1.9 Hz, 1H), 4.83 (dd, J = 6.4, 2.3 Hz, 1H), 2.85−2.73 (m, 2H), 2.48 (td, J = 10.3, 4.7 Hz, 1H), 2.20−2.09 (m, 2H), 1.81−1.71 (m, 1H), 1.58−1.40 (m, 3H), 1.26−1.09 (m, 1H), 1.03 (d, J = 6.5 Hz, 3H), 0.99 (d, J = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.7, 18.7, 23.7, 33.1, 39.4, 46.6, 49.2, 50.1, 61.2, 72.3, 116.2, 140.5, 212.2; MS (EI) *m/z* 208 (M^+), 190, 140, 122, 68; HRMS (EI) *m/z* calcd for $C_{13}H_{20}O_2$ 208.1463, found 208.1468.

Acknowledgment. Support from the National Institutes of Health (P50 GM067082) for the University of Pittsburgh Center for Chemical Methodologies and Library Development, the Merck Research Laboratories, and Eli Lilly & Co. is gratefully acknowledged.

Supporting Information Available: Experimental procedures, characterization data, proton and carbon NMR spectra, and X-ray diffraction data. This material is available free of charge via the Internet at http://pubs.acs.org.

JO050225Y