H-4a) 2.03 (1 H, m, H-5) 1.87 (1 H, dddd, J = 12.2, 6.1, 6.1, and 2.3 Hz, H-6), 1.62 (1 H, ddqd, $J_{4,3(trans)} = J_{4,4a} = 9.7$, $J_{4,Me} = 6.9$, and $J_{4,3(cis)} = 3.4$ Hz, H-4), 1.26 (1 H, m, H-5), 1.21 (3 H, d, J = 6.4 Hz, 7-Me), 1.17 (1 H, m, H-5), and 1.00 (3 H, d, J = 6.9 Hz, 4-Me); ^{13}C-NMR ($CDCl_3$) δ 174.73 (s), 72.91 (t), 49.28 (d), 44.86 (d), 38.85 (d), 35.22 (d), 34.41 (t), 31.87 (t), 20.29 (q), and 15.76 (q); exact mass found m/z 168.1158, calcd for $C_{10}H_{16}O_2$ M, 168.1150. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.33; H, 9.22.

Acknowledgment. We thank Dr. Tsutomu Sakai of the Suntory Institute for Bio-organic Research, for copies of the spectra of dihydronepetalactone and isodihydronepetalactone.

A Novel Vinyl Anion Equivalent. An Extremely Short Synthesis of 2-Substituted 2-Cycloalkenones and Prostaglandin Key Intermediates via Destannylselenenylation

Shinya Kusuda, Yoshihiko Watanabe, Yoshio Ueno, and Takeshi Toru*

Department of Applied Chemistry, Nagoya Institute of Technology, Gokiso, Showa-ku, Nagoya 466, Japan

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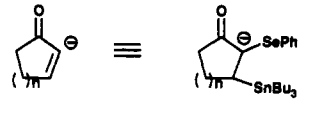
The preparation of a novel vinyl anion equivalent and a new destannylselenenylation procedure are described. The conjugate addition of (tributylstannyl)lithium to 2-(phenylseleno)-2-cycloalkenones, followed by the trapping of the resulting enolates with allylic halides, and subsequent destannylselenenylation gives 2-substituted 2-cycloalkenones in high yields, in a one-pot procedure. The destannylselenenylation can be successfully performed under a variety of conditions: treatments with fluoride, bases, Lewis acids, or silica gel as well as thermal or photochemical treatments are effective. Following the described method, chiral prostaglandin E_2 key intermediates were obtained in one pot from chiral 4-[(*tert*-butyldimethylsilyl)oxy]-2-(phenylseleno)-2-cyclopentenone.

Considerable attention has been paid to the preparation of 2-substituted 2-cycloalkenones because they can give rise to 2,3-disubstituted cycloalkanones, which are potential intermediates in many natural product syntheses.[1] For instance, a protected 4-hydroxy-2-alkyl-2-cyclopentenone is a reasonable starting point for the construction of the prostaglandin skeleton.[2] However, there are practical problems with the preparation of 2-substituted cyclopentenone intermediates. The known methods[3] for the preparation of such enones are neither simple nor versatile, and few methods for the synthesis of the chiral intermediate have been reported.[4] We now report a general procedure for the convenient synthesis of 2-substituted 2-cyclopentenones and 2-cyclohexenones using a novel vinyl anion equivalent. We also describe a very concise synthesis of protected or unprotected 4-hydroxy-2-[6-(methoxycarbonyl)-2(*Z*)-hexenyl]-2-cyclopentenones (optically active PG intermediates) starting from chiral 4-[(*tert*-butyldimethylsilyl)oxy]-2-(phenylseleno)-2-cyclopentenone.[5]

Results and Discussion

Synthesis of 2-Substituted 2-Cycloalkenones. One of the most efficient routes to 2-substituted 2-cycloalkenones is undoubtedly the direct alkylation of the vinyl anion 1. Rather than by this elusive vinyl anion, we envisioned the synthesis of these cycloalkenones via a new vinyl anion equivalent—the enolate 2, which carries adjacent stannyl and seleno groups (eq 1). The sequence



1 2 (1)

entails (1) conjugate addition of (tributylstannyl)lithium to the 2-(phenylseleno)-2-cycloalkenone, (2) regiospecific alkylation of the resulting enolate, and (3) β-elimination of the tributylstannyl group and the phenylseleno group. One of the advantages of this method is that it can be performed in one pot. Furthermore, regiospecific forma-

(1) For recent review of PG syntheses, see: (a) Baxter, A. D.; Roberts, S. M. *Chem. Ind.* **1986**, 510. (b) Pike, J. E.; Morton, D. R. *Chemistry of Prostaglandins and Leukotrienes*; Raven: New York, 1985. (c) Tayler, R. J. K. *Synthesis* **1985**, 364. (d) Noyori, R.; Suzuki, M. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 847. (e) Roberts, S. M.; Scheinmann, F. *New Synthetic Routes to Prostaglandins and Thromboxanes*; Academic: New York, 1982. For polyquinane syntheses, see: (f) Paquette, L. A. *Recent Synthetic Developments in Polyquinanes Chemistry*; Springler-Verlag: New York, 1984. (g) Ramaiah, M. *Synthesis* **1984**, 529. For steroid syntheses, see: (h) Kametani, T. *Pure Appl. Chem.* **1979**, *51*, 747. (i) Oppolzer, W. *Synthesis* **1978**, 793. (j) Funk, R. L.; Vollhardt, K. P. C. *Helv. Chim. Acta* **1978**, *61*, 1945.

(2) For example, see: (a) Sih, C. J.; Salomon, R. G.; Price, P.; Sood, R.; Peruzzotti, G. P. *J. Am. Chem. Soc.* **1975**, *97*, 857. (b) Sih, C. J.; Heather, J. B.; Sood, R.; Price, P.; Peruzzotti, G. P.; Hsu Lee, L. F.; Lee, S. S. *Ibid.* **1975**, *97*, 865. (c) Heather, J. B.; Sood, R.; Price, P.; Peruzzotti, G. P.; Lee, S. S.; Hsu Lee, L. F.; Sih, C. J. *Tetrahedron Lett.* **1973**, 2313. (d) Sih, C. J.; Heather, J. B.; Peruzzotti, G. P.; Price, P.; Sood, R.; Hsu Lee, L. F. *J. Am. Chem. Soc.* **1973**, *95*, 1676. (e) Kluge, A. F.; Untch, K. G.; Fried, J. H. *Ibid.* **1972**, *94*, 7827. (f) Sih, C. J.; Price, P.; Sood, R.; Salomon, R. G.; Peruzzotti, G. P.; Casey, M. *Ibid.* **1972**, *94*, 3643. (g) Dygos, J. H.; Aamek, J. P.; Babiak, K. A.; Behling, J. R.; Medich, J. R.; Ng, J. S.; Wieczorek, J. J. *J. Org. Chem.* **1991**, *56*, 2549. See also refs 1a–e.

(3) For recent developments of the preparation of 2-substituted 2-cycloalkenones, see: (a) Minami, I.; Nisar, M.; Yuhara, M.; Shimizu, I.; Tsuji, J. *Synthesis* **1987**, 992. (b) Boga, C.; Savoia, D.; Trombini, C.; Umani-Ronchi, A. *Synthesis* **1986**, 212. (c) Dalcanale, E.; Foa, M. *Synthesis* **1986**, 492. (d) Miller, D. D. *Tetrahedron Lett.* **1983**, *24*, 555. (e) Baraldi, P. G.; Barco, A.; Benetti, S.; Pollini, G. P.; Zanirato, V. *Tetrahedron Lett.* **1984**, *25*, 4291. (f) Ono, N.; Miyake, H.; Kaji, A. *Synthesis* **1981**, 1003. For the *dl* PGE_2 intermediate, see: (g) Levin, J. I. *Tetrahedron Lett.* **1989**, *30*, 13. (h) Lee, T. *Tetrahedron Lett.* **1979**, 2297. (i) Novak, L.; Rothaly, J.; Kajtar, M.; Czantay, C. S. *Acta Chim. Acad. Sci. Hung.* **1979**, *102*, 91. (j) Floyd, M. B. *J. Org. Chem.* **1978**, *43*, 1641. (k) Kobayashi, M.; Kurozumi, S.; Toru, T.; Ishimoto, S. *Chem. Lett.* **1976**, 1341. (l) Stork, G.; Kowalski, C.; Garcia, G. *J. Am. Chem. Soc.* **1975**, *97*, 3258. (m) Floyd, M. B. *Synth. Commun.* **1974**, *4*, 317. (n) Gruber, L.; Tomoskozi, T.; Major, E.; Kovacs, G. *Tetrahedron Lett.* **1974**, 3729. See also ref 2.

(4) For syntheses of the chiral PG enone intermediate, see: (a) Okamoto, S.; Kobayashi, Y.; Kato, H.; Hori, K.; Takahashi, T.; Tsuji, J.; Sato, F. *J. Org. Chem.* **1988**, *53*, 5590. (b) Stork, G.; Kowalski, C.; Garcia, G. *J. Am. Chem. Soc.* **1975**, *97*, 3258. See also ref 2b.

(5) Kusuda, S.; Watanabe, Y.; Ueno, Y.; Toru, T. *Tetrahedron Lett.* **1991**, *32*, 1325.

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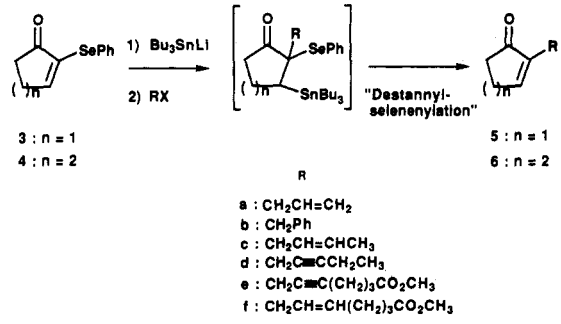
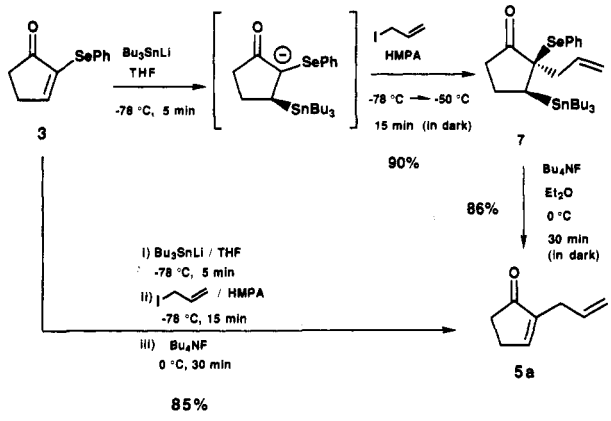
Scheme I



Scheme II



tion of the endocyclic enones can be achieved by destannylselenenylation (Scheme I).[6]

We first studied the preparation of several 2-substituted 2-cyclopentenones and 11-deoxy-PG intermediates from **3**.[7] The procedure was as follows. A solution of **3** was treated at −78 °C with (tributylstannyl)lithium (1.1 equiv) formed in situ from bis(tributylstannane) and *n*-butyllithium.[8] Then allyl iodide (2.0 equiv) and hexamethylphosphoramide (HMPA) (3.0 equiv) were added. After confirming the completion of the allylation by TLC, a THF solution of tetrabutylammonium fluoride (2.0 equiv) was added and the mixture was allowed to warm to room temperature to complete the destannylselenenylation. The reaction mixture was applied directly to a silica-gel column to give 2-(2-propenyl)-2-cyclopentenone (**5a**) in 85% yield (Scheme II). Results of the full study are shown in Table I. Allylic, propargylic, and benzylic iodides or bromides can be used in this reaction; however, alkyl halides such as methyl iodide and hexyl iodide do not produce the alkylated products in good yields. Reactions of the selenocyclopentenone **3** with methyl 7-iodo-5-heptynoate and methyl (*Z*)-7-iodo-5-heptenoate[9] gave respectively the 11-deoxy-5-dehydro-PGE_2 and 11-deoxy-PGE_2 intermediates (**5e** and **5f**) in high yield. Selenocyclohexenone **4** also gave various 2-substituted cyclohexenones **6** in moderate to high yields.

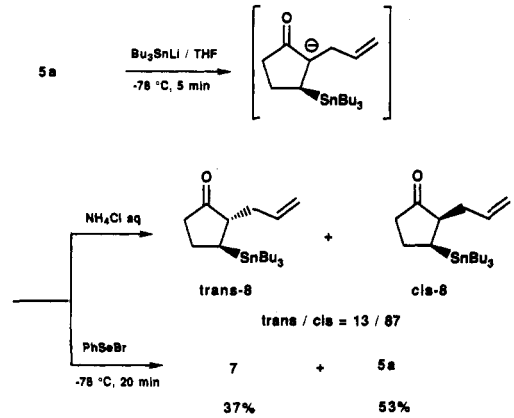
Destannylselenenylation. For investigation of the destannylselenenylation[10] under various conditions, **7** was needed in pure form. However, **7** proved difficult to isolate without decomposition. If purification was attempted before the addition of tetrabutylammonium fluoride without special precaution, the allylated product **7** was isolated in 56% yield together with the enone **5a** (36%). After several isolation attempts, it became clear that **7** is extremely light-sensitive (see the photochemical destannylselenenylation described below), but it could be isolated in 90% yield by careful operation in the dark

Table I. One-Pot Preparation of 2-Alkyl-Substituted 2-Cycloalkenones from 2-(Phenylseleno)cycloalkenones[a]

	reaction conditions of alkylation			product	
substr	RX (equiv)	temp, °C	time, h	no.	yield,[b] %
3	CH_2=$CHCH_2I$ (1.5)	−78	0.2	**5a**	85
3	CH_2=$CHCH_2Br$ (5.0)	−78	1.0	**5a**	97
3	$PhCH_2I$ (3.0)	−78 → −30	1.5	**5b**	94
3	$PhCH_2Br$ (5.0)	−78 → −20	2.5	**5b**	95
3	CH_3CH=$CHCH_2Br$[b] (4.8)	−78	0.8	**5c**	80
3	CH_3CH_2C≡CCH_2I (2.0)	−78	0.1	**5d**	90
3	$CH_3O_2C(CH_2)_3C$≡CCH_2I (1.5)	−78	0.3	**5e**	84
3	$CH_3O_2C(CH_2)_3CH$= $CHCH_2I$[c] (1.5)	−78	0.1	**5f**	90
4	CH_2=$CHCH_2I$ (1.7)	−78	0.2	**6a**	85
4	CH_2=$CHCH_2Br$ (3.0)	−78	0.8	**6a**	55
4	$PhCH_2I$ (3.0)	−78 → −40	1.0	**6b**	59
4	CH_3CH_2C≡CCH_2I (2.0)	−78 → −50	0.6	**6d**	85
4	$CH_3O_2C(CH_2)_3C$≡CCH_2I (2.0)	−78 → −10	0.3	**6e**	84
4	$CH_3O_2C(CH_2)_3CH$= $CHCH_2I$[c] (2.0)	−78 → −60	0.8	**6f**	78

[a] All reactions were carried out by treatment of **3** or **4** with (tributylstannyl)lithium and subsequent alkylation (conditions shown above) followed by treatment with tetrabutylammonium fluoride; see Experimental Section. [b] Isolated yields. [c] The cis isomer was used.

Scheme III



(6) We have observed the low regioselectivity of the deselenenylation of 2-allyl-2-(phenylseleno)cyclopentanone through oxidation with hydrogen peroxide at 0 °C, giving a 81:19 mixture of exocyclic and endocyclic enones. See also: (a) Liotta, D.; Barnum, C. S.; Saindane, M. *J. Org. Chem.* **1981**, *46*, 4301. (b) Zima, G.; Barnum, C. S.; Liotta, D. *Ibid.* **1980**, *45*, 2736.

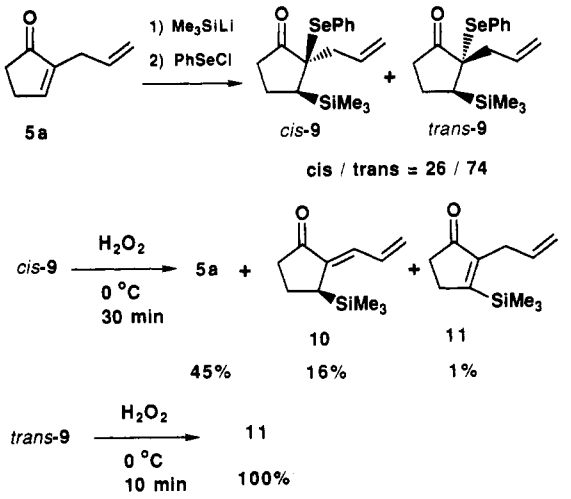
(7) (a) Zima, G.; Liotta, D. *Synth. Commun.* **1979**, *9*, 697. (b) Liotta, D.; Saindane, M.; Barnum, C.; Zima, G. *Tetrahedron* **1985**, *41*, 4881.

(8) Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836.

(9) Johnson and Penning have pointed out the formation of the undesired *trans*-alkene besides the *cis*-alkene on the catalytic hydrogenation of 7-hydroxy-5-heptynoate, see: Johnson, C. R.; Penning, T. D. *J. Am. Chem. Soc.* **1988**, *110*, 4726. We here recommend hydrogenation of the tetrahydropyranyl-protected hydroxyheptynoate with Lindlar's catalyst in ethyl acetate prior to the deprotection, which was found to give the *cis*-alkene without significant contamination of the trans isomer (^{1}H NMR and HPLC). The iodo compound was then prepared by the following sequence: deprotection with camphorsulfonic acid–methanol, bromination with carbon tetrabromide and triphenylphosphine in acetonitrile, and iodination with sodium iodide in acetone. See also: Donaldson, R. E.; Soddler, J. C.; Byrn, S.; McKenzie, A. T.; Fuchs, P. L. *J. Org. Chem.* **1983**, *48*, 2167.

(10) Destannylsulfurization has been reported; see (a) Pearlman, B. A.; Putt, S. R.; Fleming, J. A. *J. Org. Chem.* **1985**, *50*, 3622 and 3625. (b) Ochiai, M. Ukita, T.; Fujita, E.; Tada, S. *Chem. Pharm. Bull.* **1984**, *32*, 1829. (c) Ochiai, M.; Sumi, K.; Fujita, E.; Tada, S. *Chem. Pharm. Bull.* **1983**, *31*, 3346. (d) Ochiai, M.; Tada, S.; Sumi, K.; Fujita, E. *Tetrahedron Lett.* **1982**, *23*, 2205. See also: (e) Pereyre, M.; Quintard, J. P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987.

Scheme IV



throughout the reaction, purification, and separation sequence (Scheme II). The trans stereochemistry was assigned to **7** on the basis of the following NOE study.[11] The *cis*- and *trans*-2-allyl-3-(tributylstannyl)cyclopentanones *cis*-**8** and *trans*-**8** were first prepared. The 1,4-conjugate addition of (tributylstannyl)lithium to 2-allyl-2-cyclopentenone (**5a**) gave a trans/cis (13:87) mixture of **8**, which was readily isomerized to a trans/cis (94:6) equilibrium mixture by treatment with K_2CO_3 in methanol at room temperature (Scheme III). The ^{119}Sn chemical shift of **7** was −20.710 ppm, whereas the ^{119}Sn resonance of *trans*-**8** and *cis*-**8** appeared at −13.907 and −16.643 ppm, respectively. The ^{119}Sn signal for *cis*-**8** showed a significantly negative NOE (41%) upon irradiation at the allylic methylene resonance frequencies, whereas no appreciable NOE was observed between ^{119}Sn and the allylic methylene protons in *trans*-**8**. The magnitude of NOE in **7** (−31%) was comparable to that of *cis*-**8**.

Although the trans stereochemistry was first assigned on the basis of these NOE data, further investigation dictated assignment of the cis stereochemistry to **7**. An attempt to prepare the other stereoisomer by trapping the enolate with benzeneselenenyl bromide afforded **7** (37%), together with enone **5a** (53%) (Scheme III).[12] In contrast, reaction of **5a** with (trimethylsilyl)lithium followed by treatment with benzeneselenenyl chloride gave a cis/trans mixture of the silyl analogues *cis*-**9** and *trans*-**9** (74%) in a 26:74 ratio (Scheme IV). The stereochemistry of these compounds is assigned on the basis of the following evidence. Both isomers were separately treated with H_2O_2 in CH_2Cl_2 at 0 °C. The cis isomer, after 30 min, gave enone **5a**, 3-(trimethylsilyl)cyclopentanone **10**, and 3-(trimethylsilyl)cyclopentenone **11** in 45, 16, and 1% yields, respectively, whereas *trans*-**9**, after 10 min afforded **11** quantitatively. Since a syn orientation is expected in the selenoxide elimination,[13] these results demonstrate that the stereochemistry of the minor and major isomers are *cis*-**9** and *trans*-**9**, respectively.

The ^{29}Si NMR signal (2.45 ppm) for *cis*-**9** showed a negative NOE (5%) upon irradiation at the allylic methylene resonance frequencies, whereas an appreciable negative NOE (11%) was observed between ^{29}Si and one of the allylic protons. An examination of molecular models

Scheme V

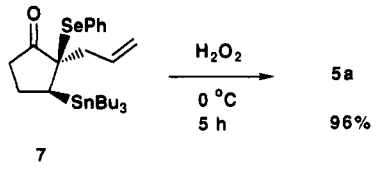


Table II. Destannylselenenylation to 5a

entry	reagent	equiv	reactn temp	reactn time	products, 5a	yield,[c] % 8
1	Bu_4NF[a]	2.0	rt	15 min	85	
2	Bu_4NF	1.5	0 °C	30 min	86[d]	
3	CsF/18C6	4.0	rt	3.5 h	68	
4	Bu_3SnLi	0.3	rt	5 min	86[d]	8[d]
5	PhSeLi	0.2	rt	10 min	87[d]	8[d]
6	*t*-BuOK	0.2	0 °C	15 min	44[d]	4[d]
7	*n*-BuLi	0.2	0 °C	15 min	26[d]	3[d]
8	$TiCl_4$[a]	2.0	−78 °C	5 min	81	
9	$SnCl_4$	1.0	rt	10 h	87[d]	
10	$BF_3{\cdot}Et_2O$[a]	2.0	rt	1 h	51	24
11	$MgCl_2$	1.0	rt	48 h	74[d]	16[d]
12	SiO_2	excess	45 °C	38 h	58	25
13	*a,b*		reflux	2 h	78	
14			reflux	2 h	92[d]	
15	*hν*		rt	1 min	99[d]	
16	*hν*[a]		rt	1.5 h	68	

[a] Elimination was performed on the reaction mixture obtained from a one-pot reaction starting with **3**; all other reactions were run with isolated **7**. [b] The reaction mixture was heated under reflux to effect destannylselenenylation, without further additives. [c] Isolated yields; yields are based on **3** unless otherwise noted. [d] Yield based on **7**.

indicates that the repulsive interaction between the phenylseleno and tributylstannyl (or trimethylsilyl) groups of **7** (or *cis*-**9**) causes significant distortions in the cyclopentanone ring.[14] In the distorted conformations the allyl methylene is located near the stannyl group and, therefore, a significant NOE is observed between ^{119}Sn (or ^{29}Si) and the allylic protons. The cis stereochemistry of **7** was further confirmed by treatment with H_2O_2 (0 °C, 5 h). This reaction gave **5a** exclusively (96%), which should be derived from the cis isomer[15] (Scheme V).

Given the deduced cis configuration of **7**, the elimination by fluoride ion of the vicinally positioned tributylstannyl and phenylseleno groups must have occurred in a syn fashion. After treatment of the reaction mixture of the selenocyclopentenone **3** and allyl iodide with tetrabutylammonium fluoride, tributylstannyl fluoride, allyl phenyl selenide, and diphenyl diselenide were isolated in 100%, 64%, and 6% yields, respectively, in addition to the allylcyclopentenone **5a**. Therefore, attack of fluoride ion at the stannane formed tributylstannyl fluoride. The subsequent elimination generated a selenenyl anion which reacted with excess allyl iodide to form allyl phenyl selenide and a small amount of diphenyl diselenide (eq 2 and Table II).

Furthermore, it was found that reflux of the reaction mixture for 2 h without any additives also led to destannylselenenylation to give the allylcyclopentenone **5a** in 78% yield (entry 13 in Table II). When the isolated, allylated product **7** was heated in THF for 2 h, tributyl-

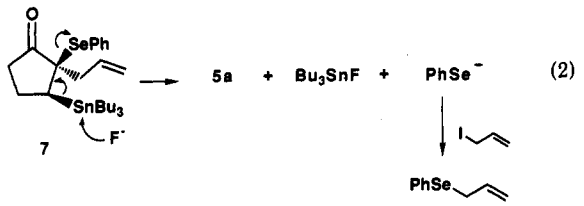
(11) Homogeneity of the cis product **7**, which was isolated by HPLC, was confirmed by ^1H, ^{13}C, and ^{119}Sn NMR spectra.

(12) The trans isomer once formed in this reaction might be too unstable to be isolated, owing to rapid elimination to enone **5a**.

(13) Kingsbury, C. A.; Cram, D. J. *J. Am. Chem. Soc.* **1960**, *82*, 1810.

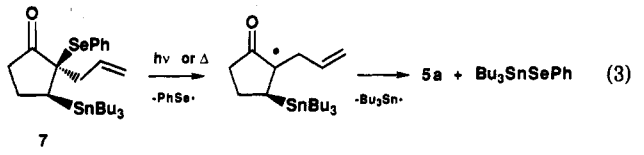
(14) The phenylseleno group may be located in a quasi axial position, and, therefore, the tributylstannyl group is equatorial; for the axial seleno group in cyclohexanones, see: Zervos, M.; Wartski, L. *J. Org. Chem.* **1986**, *51*, 1293.

(15) Treatment of **3** with (trimethylsilyl)lithium followed by the trapping of the enolate with allyl iodide gave a cis/trans (86:14) mixture of *cis*-**9** and *trans*-**9** in 86% yield. The predominant formation of the cis isomer in this reaction is also in accordance with the stereochemical assignments given.



(2)

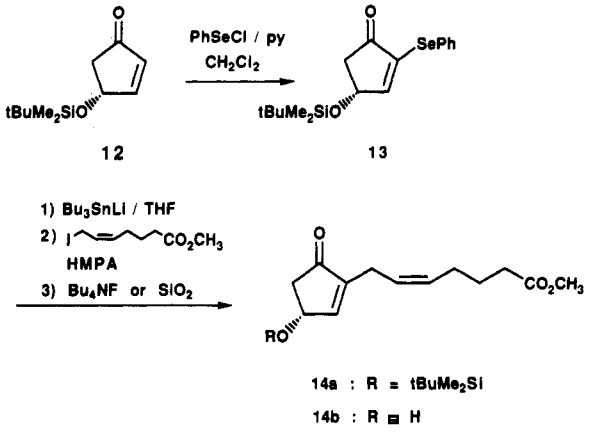
(phenylseleno)stannane was isolated in 87% yield along with **5a** (92%) (entry 14). Surprisingly, on irradiation of **7** in benzene with a 400-W high-pressure mercury lamp, instantaneous destannylselenenylation occurred (within 1 min) to give **5a** and tributyl(phenylseleno)stannane, both in 99% yields (entry 15). These photochemical and thermal destannylselenenylations were not substantially inhibited by the addition of 10 mol % or even 200 mol % of hydroquinone to the reaction mixture (Table III). The addition of 10 mol % of galvinoxyl retarded the formation of **5a** in both the photoinduced and thermal destannylselenenylation; almost 50% conversions were observed on irradiation for 1 h and on heating for 2 h, showing that the photoinduced elimination was inhibited more effectively by galvinoxyl than was the thermal reaction. Furthermore, 10 mol % of AIBN or hexabutyldistannane accelerated the thermal elimination so that the destannylselenenylation was almost complete within 15 min. These results suggest that radical intermediates are involved in both destannylselenenylations and that the elimination proceeds (almost wholly in the photoinduced reaction and at least partly in the thermal reaction) via a radical process other than a chain process. It is not so surprising that the radical scavenger did not inhibit the elimination completely, because an intramolecular radical process (unlike an intermolecular chain process)[16] would be unaffected by a radical scavenger and would cause the destannylselenenylation. The photoinduced or thermal cleavage of the carbon–selenium bond followed by subsequent respective β-elimination of the stannyl radical can undergo spontaneous destannylselenenylation (eq 3).

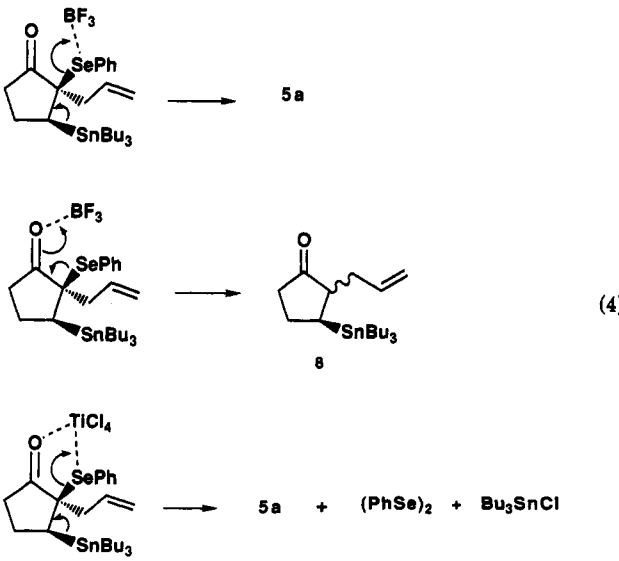


(3)

In contrast to the destannylselenenylation of the isolated allylated product **7**, neither the photoinduced nor thermal destannylselenenylation of the reaction mixture derived from cyclopentenone **3** gave tributyl(phenylseleno)stannane. This indicates that radical intermediates are not involved under these conditions and that the elimination can be accelerated by the action of certain bases or salts in the reaction mixture. In fact, a catalytic amount of (tributylstannyl)lithium was found to be effective for the destannylselenenylation. Thus, treatment of the isolated **7** with 0.3 equiv of (tributylstannyl)lithium yielded **5a** (86%) and the deselenenylated product **8** (8%), which might have been formed via the 1,4-addition of the stannyllithium to **5a** (entry 4). Benzeneselenolate ion formed via attack of the stannyl anion on the stannyl group might play a major role in this destannylselenenylation. Indeed, this was borne out by the following experiment. Treatment of **7** with 0.2 equiv of (benzeneselenenyl)lithium at −78 °C for 10 min did not cause the isomerization of the phenylseleno group on the cyclopentanone ring as reported by Liotta and his collaborators[6b] but resulted in destannylselenenylation to give **5a** in 87% yield (entry 5). Other bases such as potassium *tert*-butoxide and *n*-butyllithium were also effective but gave lower yields of **5a** (entries 6 and 7). Lewis acids such as $TiCl_4$, $BF_3{\cdot}Et_2O$, and $MgCl_2$ were also found to be capable of effecting the β-elimination; the allylcyclopentenone **5a** was obtained in 80% yield by treatment of the isolated allylated compound **7** with $TiCl_4$ at −78 °C for 5 min (entry 8). The reaction with $BF_3{\cdot}Et_2O$, $MgCl_2$, or silica gel gave the deselenenylated product **8** in 24%, 16%, or 25% yield, respectively, in addition to the allylcyclopentenone **5a** (51%, 74%, or 58%) (entries 10, 11, and 12). The mechanism of formation of **8** under the acidic conditions is different from that with stannyllithium mentioned above. The deselenenylation with Lewis acids presumably proceeds by formation of an enolate, encouraged by Lewis acid activation of the carbonyl.[17] Coordination of the Lewis acid to the selenium would have caused destannylselenenylation instead (eq 4).

Scheme VI





(4)

Preparation of PG Key Intermediates. The present method was applied to the synthesis of chiral PG key intermediates. Conjugate addition of (tributylstannyl)lithium[8] to the chiral selenocyclopentenone[18] **13**, obtained

(16) Greene, F. D.; Adam, W.; Cantrill, J. E. *J. Am. Chem. Soc.* 1961, *83*, 3461.

(17) We observed the high-yield formation of aldol condensation products in the reaction of 2-(phenylseleno)cyclopentanone or 2-methyl-2-(phenylseleno)cyclopentanone with an aldehyde such as benzaldehyde in the presence of a Lewis acid such as $TiCl_4$ or $BF_3{\cdot}Et_2O$.

(18) Toru, T.; Yamada, Y.; Ueno, T.; Maekawa, E.; Ueno, Y. *J. Am. Chem. Soc.* 1988, *110*, 4815.

from the chiral cyclopentenone[19] **12**, occurred virtually instantaneously at −78 °C. After alkylation with methyl (*Z*)-7-iodo-5-heptenoate, exposure of the reaction mixture to excess tetrabutylammonium fluoride (3 equiv) removed both the silyl and stannyl groups and gave the hydroxycyclopentenone **14b** in 79% yield (Scheme VI). Careful addition (2 equiv in 4 portions) of tetrabutylammonium fluoride afforded the PG intermediate **14a** in 67% yield, indicating that the tributylstannane–carbon bond is more readily cleaved by fluoride ion than the (*tert*-butyldimethylsilyl)oxy moiety.[20] A more effective, selective destannylselenenylation was achieved using silica gel. The reaction mixture was treated with a large excess of silica gel at 45 °C for 2 h, giving **14a** in 86% yield.[21]

In summary, the present method offers an exceptionally rapid, convenient, and efficient synthesis of 2-substituted 2-cycloalkenones through a novel vinyl anion equivalent. Destannylselenenylation can be effected by numerous reagents, which can be selected to suit the substrate. In particular, a chiral PGE_2 key intermediate bearing a silyl protecting group has been prepared in high yield via destannylselenenylation with silica gel. Thus, the present method provides a practical, convenient synthesis of the PG skeleton.

Experimental Section

General Procedures. ^1H NMR spectra were recorded at 60, 200, or 400 MHz. ^{119}Sn NMR chemical shifts are reported in δ from Me_4Sn.

All reactions were performed using oven- and flame-dried glassware under Ar. Air- and moisture-sensitive reagents and solvents were transferred via syringe or cannula and were introduced into reaction vessels through rubber septa. All reactions were monitored by TLC carried out on 0.25-mm E. Merck silica gel plates (60F-254). TLC plates were visualized with UV light and 7% phosphomolybdic acid in ethanol/heat. Column chromatography was carried out with a pressure-resisting column packed with Fuji Davison silica gel BW-200, equipped with FMI Lab Pump RPG150 and a FMI Pulse Damper PD-60LF, normally at a pressure at 1–2 kg cm^{-2}.

Representative Procedures for the Preparation of 2-Substituted 2-Cycloalken-1-ones. 2-(2-Propenyl)-2-cyclopenten-1-one (5a). Method A. Alkylation with Allyl Iodide. A solution of bis(tributylstannane) (135 mg, 0.23 mmol) in THF (0.5 mL) was stirred and cooled at −20 °C as *n*-butyllithium (1.6 M, 0.145 mL, 0.23 mmol) in hexane was added. After being stirred for 30 min, the reaction mixture was cooled to −78 °C and a solution of 2-(phenylseleno)-2-cyclopenten-1-one[7] (**3**) (50 mg, 0.21 mmol) in THF (0.3 mL and 0.1 mL for rinse) was added. The mixture was stirred for an additional 5 min, when the Michael addition was completed as judged by TLC. Then allyl iodide (40 μL, 75 mg, 0.45 mmol) and HMPA (0.12 mL, 0.69 mmol) were added. After 15 min at −78 °C, completion of the allylation was confirmed by TLC. A solution of tetrabutylammonium fluoride (1.0 M, 0.42 mL, 0.42 mmol) in THF was added at −78 °C, the cooling bath was removed, and the mixture was stirred at rt for 15 min, when the β-elimination was completed. The reaction mixture was then directly subjected to column chromatography (silica gel, 30 g, 80:20 petroleum ether/ethyl ether) to give **5a**[22] (22 mg, 85% yield): ^1H NMR (CCl_4) δ 2.15–2.69 (4 H, m), 2.84 (2 H, d, J = 7.5 Hz), 4.78–5.23 (2 H, m), 5.44–6.19 (1 H, m), 7.01–7.24 (1 H, m); IR (neat) 1698, 1638 cm^{-1}. In a separate experiment starting with 100 mg (0.422 mmol) of **3**, the resultant solution was evaporated under reduced pressure. Ethyl acetate was added to the residue and the precipitate was filtered to give tributylstannyl fluoride (253 mg, 99% yield). The filtrate was evaporated to leave an oil, which was purified by column chromatography to give allyl phenyl selenide[23] (53 mg, 64% yield) and diphenyl diselenide (4 mg, 6% yield) together with **5a**.

Method B. Alkylation with Allyl Bromide. To the reaction mixture obtained from bis(tributylstannane) (135 mg, 0.23 mmol) and **3** (50 mg, 0.21 mmol) as above were added allyl bromide (55 μL, 77 mg, 0.64 mmol) and HMPA (0.11 mL, 0.63 mmol) at −78 °C. The reaction mixture was stirred at the same temperature for 30 min, but the allylation was not completed. Allyl bromide (18 μL, 0.21 mmol) and HMPA (73 μL, 0.42 mmol) were added and then after 15 min another portion of allyl bromide and HMPA were added. Stirring for an additional 15 min completed the allylation. A THF solution of tetrabutylammonium fluoride (1.0 M, 0.42 mL, 0.42 mmol) was then added at −78 °C, the cooling bath was removed, and the mixture was stirred for 15 min, when the completion of β-elimination was confirmed by TLC. The reaction mixture was directly subjected to column chromatography (silica gel 30 g, 95:5 and then 90:10 hexane/ethyl acetate) to give **5a** (25 mg, 97% yield).

2-Benzyl-2-cyclopenten-1-one (5b). Method A. Alkylation with Benzyl Iodide. To the reaction mixture obtained from bis(tributylstannane) (135 mg, 0.23 mmol) and **3** (50 mg, 0.21 mmol) as described for **5a** were added a THF (0.2 mL) solution of benzyl iodide (137 mg, 0.62 mmol) and HMPA (0.13 mL, 0.75 mmol). The mixture was stirred for 1.5 h, during which time the bath temperature was allowed to increase gradually to −30 °C. A THF solution of tetrabutylammonium fluoride (1.0 M, 0.42 mL, 0.42 mmol) was then added, the cooling bath was removed, and the mixture was stirred for 15 min, when the completion of β-elimination was confirmed by TLC. The reaction mixture was directly subjected to column chromatography (silica gel 36 g, 90:10 and then 80:20 hexane/ethyl acetate) to give **5b**[24] (34 mg, 94% yield): ^1H NMR (CCl_4) δ 2.15–2.64 (4 H, m), 3.31–3.47 (2 H, m), 6.83–7.36 (6 H, m); IR (neat) 1698, 1628 cm^{-1}.

Method B. Alkylation with Benzyl Bromide. To the reaction mixture obtained from bis(tributylstannane) (135 mg, 0.23 mmol) and **3** (50 mg, 0.21 mmol) as described for **5a** were added benzyl bromide (0.125 mL, 180 mg, 1.05 mmol) and HMPA (0.18 mL, 1.05 mmol). The mixture was stirred for 2.5 h, during which time the temperature of the bath was allowed to gradually increase to −20 °C. β-Elimination and purification were identical with those described above to give **5b** (34.5 mg, 95% yield).

The following compounds were prepared according to the representative procedures described above. The alkyl halide (amount), reaction time and temperature, chromatography solvent(s), and product yield are given in this abbreviated format.

2-(2-Butenyl)-2-cyclopenten-1-one (5c): 1-bromo-2-butene (0.11 mL, 144 mg, 1.02 mmol), 45 min at −78 °C, 95:5 and then 90:10 hexane/ethyl acetate, yield 23 mg (80%); ^1H NMR (CCl_4) δ 1.57–1.78 (3 H, m), 2.18–2.70 (4 H, m), 2.70–3.00 (2 H, m), 5.30–5.66 (2 H, m), 7.13–7.30 (1 H, m); IR (neat) 1690, 1628 cm^{-1}; MS *m/e* 136 (M^+, 11), 109 (100), 95 (20), 81 (41), 79 (29), 77 (28), HRMS calcd for $C_9H_{12}O$ 136.0888, found 136.0955.

2-(2-Pentynyl)-2-cyclopenten-1-one (5d):[25] 1-iodo-2-pentyne[26] (82 mg, 0.42 mmol), 5 min at −78 °C, hexane and then 90:10

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(20) The high affinity of fluoride ion for stannane relative to silicon has been observed, see: Gibbs, R. A.; Okamura, W. H. *Tetrahedron Lett.* **1987**, *28*, 6021. See also ref 9a.

(21) Destannylation of a vinylstannane with silica gel has been reported: Stork, G.; Mook, R., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 2829.

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hexane/ethyl acetate, yield 28 mg (90%); ^{1}H NMR (CCl_4) δ 1.12 (3 H, t, J = 7.5 Hz), 1.87–3.01 (8 H, m), 7.15–7.51 (1 H, m); IR (neat) 2220, 1690, 1632 cm^{-1}.

Methyl 7-(5-oxo-1-cyclopentenyl)-5-heptynoate (5e):[27] methyl 7-iodo-5-heptynoate[9] (85 mg, 32 mmol), 15 min at −78 °C, 90:10 and then 70:30 hexane/ethyl acetate, yield 39 mg (84%); ^{1}H NMR (CCl_4) δ 1.60–2.78 (10 H, m), 2.78–3.03 (2 H, m), 3.60 (3 H, s), 7.30–7.46 (1 H, m); IR (neat) 1733, 1695, 1637 cm^{-1}.

Methyl (*Z*)-7-(5-oxo-1-cyclopentenyl)-5-heptenoate (5f):[27] methyl (*Z*)-7-iodo-5-heptenoate[9] (85 mg, 0.32 mmol), 90:10, 85:15, and then 80:20 hexane/ethyl acetate, yield 42 mg (90%); ^{1}H NMR (CCl_4) δ 1.59–2.68 (10 H, m), 2.68–2.93 (2 H, m), 3.58 (3 H, s), 5.28–5.49 (2 H, m), 7.05–7.18 (1 H, m); IR (neat) 1735, 1700, 1630 cm^{-1}.

Compounds **6a–f** were prepared according to the representative procedures using 2-(phenylseleno)-2-cyclohexenone[7] (4).

2-(2-Propenyl)-2-cyclohexen-1-one (6a).[28] **Method A**: allyl iodide (30 μL, 56 mg, 0.34 mmol), 15 min at −78 °C, 95:5 and then 90:10 hexane/ethyl acetate, yield 23 mg (85%); ^{1}H NMR (CCl_4) δ 1.73–2.60 (6 H, m), 2.86 (2 H, d, J = 7 Hz), 4.73–5.16 (2 H, m), 5.32–6.10 (1 H, m), 6.41–6.67 (1 H, m); IR (neat) 1670, 1640 cm^{-1}. **Method B**: allyl bromide (52 μL, 73 mg, 0.60 mmol), 1 h at −78 °C, yield 19 mg (55%).

2-Benzyl-2-cyclohexen-1-one (6b):[29] benzyl iodide (130 mg, 0.60 mmol), 1 h at −78 °C and then −40 °C, 95:5 and then 90:10 hexane/ethyl acetate, yield 22 mg (59%); ^{1}H NMR (CCl_4) δ 1.60–2.54 (6 H, m), 3.36–3.50 (2 H, m), 6.32–6.47 (1 H, m), 7.03–7.33 (5 H, m); IR (neat) 1670 cm^{-1}.

2-(2-Pentynyl)-2-cyclohexen-1-one (6d): 1-iodo-2-pentyne (62 mg, 0.32 mmol), 40 min at −78 °C and then −50 °C, hexane and then 95:5 hexane/ethyl acetate, yield 22 mg (85%); ^{1}H NMR (CCl_4) δ 1.13 (3 H, t, J = 7.5 Hz), 1.74–2.63 (8 H, m), 2.84–3.10 (2 H, m), 6.81–7.06 (1 H, m); IR (neat) 2220, 1662 cm^{-1}; MS m/e 162 (M^+, 85), 147 (100), 133 (8), 128 (7), 119 (13), 91 (79), 77 (22); HRMS calcd for $C_{11}H_{14}O$ 162.1045, found 162.1041.

Methyl 7-(6-oxo-1-cyclohexenyl)-5-heptynoate (6e): methyl 7-iodo-5-heptynoate (102 mg, 0.38 mmol), 1 h at −78 °C and then −10 °C, 90:10 and then 80:20 hexane/ethyl acetate, yield 39 mg (84%); ^{1}H NMR (CCl_4) δ 1.57–2.62 (12 H, m), 2.88–3.11 (2 H, m), 3.58 (3 H, s), 6.82–7.04 (1 H, m); IR (neat) 1734, 1670 cm^{-1}; MS m/e 234 (M^+, 50), 203 (27), 174 (14), 161 (69), 147 (100), 133 (38), 117 (17), 105 (22), 91 (42), 79 (15), 77 (28); HRMS calcd for $C_{14}H_{18}O_3$ 234.1256, found 234.1245.

Methyl (*Z*)-7-(6-oxo-1-cyclohexenyl)-5-heptenoate (6f): methyl (*Z*)-1-iodo-2-heptenoate (111 mg, 0.41 mmol), 45 min at −78 °C and then at −60 °C, hexane and then 85:15 hexane/ethyl acetate, yield 38 mg (78%); ^{1}H NMR (CCl_4) δ 1.27–2.53 (12 H, m), 2.70–2.91 (2 H, m), 3.57 (3 H, s), 5.20–5.44 (2 H, m), 6.40–6.63 (1 H, m); IR (neat) 1728, 1662 cm^{-1}; MS m/e 236 (M^+, 66), 205 (32), 187 (16), 176 (23), 163 (19), 149 (58), 135 (100), 121 (29), 105 (22), 91 (46), 79 (44), 77 (30); HRMS calcd for $C_{14}H_{20}O_3$ 236.1412, found 236.1421.

***cis*-3-(Tributylstannyl)-2-(phenylseleno)-2-(2-propenyl)-1-cyclopentanone (7).** To a solution of bis(tributylstannane) (1.38 g, 2.38 mmol) in THF (10 mL) was added *n*-butyllithium (1.58 M/hexane, 1.50 mL, 2.37 mmol) at −20 °C and the mixture was stirred for 30 min during which time the reaction was warmed to −10 °C. To a recooled (−78 °C) mixture was added a solution of **3** (510 mg, 2.15 mmol) in THF (2 mL and 0.5 mL for rinse), and the mixture was stirred for 5 min. Then allyl iodide (712 mg, 4.24 mmol) and HMPA (1.15 mL, 6.45 mmol) were added successively. The bath temperature was allowed to increase to −50 °C over 30 min. The reaction mixture was poured into a mixture of hexane (50 mL), ethyl ether (15 mL), and 1 N acetic acid aqueous solution (30 mL) with ice in a 200-mL Erlenmeyer flask wrapped with aluminum foil. The mixture was stirred for 5 min. The organic layer was separated and then the aqueous solution was extracted with ethyl ether (3 × 20 mL). The combined extracts were washed with saturated aqueous NaCl and dried ($MgSO_4$). The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (silica gel 90 g, 95:5 hexane/ethyl acetate) to give **7** (1.10 g, 90% yield), which was shown to contain less than 5% of contamination by HPLC (Nacalai Finepak SIL; eluent 95:5 hexane/ethyl acetate; flow speed 1.0 mL/min; t_R 6.27 min for the major product and 5.52 min for the minor component overlapped with another contamination which was detectable by the refractive index detector but not by the UV detector). Preparative HPLC afforded the pure cis isomer: ^{1}H NMR ($CDCl_3$) δ 0.93 (9 H, t, J = 7.3 Hz), 0.99–1.14 (6 H, m), 1.38 (6 H, tq, J = 7.3, 6.8 Hz), 1.48–1.67 (6 H, m), 1.97–2.38 (4 H, m), 2.47 (1 H, dd, J = 13.8, 5.8 Hz), 2.58 (1 H, dd, J = 13.8, 9.0 Hz), 2.66–2.83 (1 H, m), 4.95–5.08 (2 H, m), 5.42 (1 H, dddd, J = 18.0, 9.0, 9.0, 5.8 Hz), 7.29–7.48 (3 H, m), 7.50–7.61 (2 H, m); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 10.32 (t), 13.54 (q), 23.72 (t), 27.38 (t), 29.11 (t), 32.09 (d), 36.78 (t), 38.67 (t), 63.66 (s), 118.21 (t), 126.48 (s), 128.66 (d), 129.24 (d), 134.24 (d), 137.60 (d), 210.25 (s), ^{119}Sn NMR ($CDCl_3$) δ −20.710; IR (neat) 1713, 1634 cm^{-1}; MS m/e 513 (M^+ − Bu, ^{120}Sn, ^{80}Se, 1), 448 (6), 391 (69), 335 (4), 277 (48), 201 (22), 179 (21), 122 (58), 79 (100). Anal. Calcd for $C_{26}H_{42}OSeSn$: C, 54.95; H, 7.45. Found: C, 54.98; H, 7.70.

3-(Tributylstannyl)-2-(2-propenyl)-1-cyclopentanone (8). To a solution of (tributylstannyl)lithium, prepared from bis(tributylstannane) (570 mg, 0.98 mmol) as described in the general procedure, was added a solution of **5a** (100 mg, 0.82 mmol) in THF (1 mL and 0.5 mL for rinse) at −78 °C. After stirring for 5 min, saturated NH_4Cl (3 mL) and ethyl ether (3 mL) were added. The organic layer was separated and the aqueous layer was extracted with ethyl ether (3 × 10 mL). The combined extracts were washed successively with water and brine, dried over $MgSO_4$, and filtered. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (silica gel 40 g, 97:3 hexane/ethyl acetate) to give **8** (275 mg, 81% yield), which was shown to be a 13:87 mixture of *trans*-**8** and *cis*-**8** by HPLC (Nacalai Finepak SIL; eluent 99:1 hexane/ethyl acetate; flow speed 1.0 mL/min; t_R 17.16 min for *trans*-**8** and 18.19 min for *cis*-**8**). Preparative HPLC afforded each pure isomer. ***trans*-8**: ^{1}H NMR ($CDCl_3$) δ 0.89 (6 H, t, J = 8.5 Hz), 0.90 (9 H, t, J = 7.0 Hz), 1.32 (6 H, tq, J = 7.0, 8.0 Hz), 1.40–1.59 (6 H, m), 1.71–2.54 (8 H, m), 4.99–5.11 (2 H, m), 5.72 (1 H, ddt, J = 7.0, 10.5, 17.0 Hz); ^{119}Sn NMR ($CDCl_3$) δ −13.907; IR (neat) 1735, 1638 cm^{-1}; MS m/e 373 (M^+ − $CH_2CH{=}CH_2$, ^{120}Sn, 13), 357 (100), 291 (49), 177 (77). Anal. Calcd for $C_{20}H_{38}OSn$: C, 58.13; H, 9.27. Found: C, 58.21; H, 9.55. ***cis*-8**: ^{1}H NMR ($CDCl_3$) δ 0.86 (6 H, t, J = 7.1 Hz), 0.90 (9 H, t, J = 7.0 Hz), 1.31 (6 H, tq, J = 7.0, 7.6 Hz), 1.39–1.56 (6 H, m), 1.79–2.67 (8 H, m), 4.99–5.14 (2 H, m), 5.87 (1 H, ddt, J = 6.5, 10.0, 17.0 Hz); ^{119}Sn NMR ($CDCl_3$) δ −16.643; IR (neat) 1735, 1638 cm^{-1}; MS m/e 373 (15), 357 (100), 291 (43), 177 (98). Anal. Calcd for $C_{20}H_{38}OSn$: C, 58.13; H, 9.27. Found: C, 57.84; H, 9.57.

Isomerization of 8. To a 13:87 mixture of *trans*-**8** and *cis*-**8** (106 mg, 0.26 mmol) in methanol (5 mL) was added K_2CO_3 (35 mg), and the mixture was stirred at rt for 1 day. After usual workup column chromatography gave an oil (90 mg, 85% yield), which was shown to be a 94:6 mixture of *trans*-**8** and *cis*-**8** by HPLC.

***cis*- and *trans*-3-(Trimethylsilyl)-2-(phenylseleno)-2-(2-propenyl)-1-cyclopentanone (9).** To an ice-cooled solution of bis(trimethylsilane) (204 mg, 1.39 mmol) in THF–HMPA (4:1, 5.0 mL) was added methyllithium (1.1 M/ethyl ether, 1.0 mL, 1.10 mmol), and the resulting red solution was stirred for 15 min. To a recooled (−78 °C) solution was added a THF (0.8 mL) solution of **5a**, and the mixture was stirred for 5 min. A THF (1.0 mL) solution of benzeneselenenyl chloride (241 mg, 1.26 mmol) was added and the mixture was stirred for 5 min. Then NH_4Cl aqueous solution (5 mL) and ethyl ether (10 mL) were added. The usual workup afforded a crude oil, which was purified by column chromatography (silica gel 40 g, 95:5 hexane/ethyl acetate) to give **9** (271 mg, 74% yield). The trans/cis ratio was determined by ^{1}H NMR and HPLC (Nacalai Finepak SIL; eluent 95:5 hexane/ethyl acetate; flow speed 1.0 mL/min; t_R 8.72 min for *trans*-**9** and 9.46 min for *cis*-**9**). Preparative HPLC afforded each pure isomer. ***cis*-9**: ^{1}H NMR ($CDCl_3$) δ 0.23 (9 H, s), 1.60–1.68 (1 H, m), 1.95–2.16 (3 H, m), 2.61 (2 H, d, J = 7.3 Hz), 2.67–2.78 (1 H, m), 4.98–5.04 (2 H, m), 5.35 (1 H, ddt, J = 9.5, 17.7, 7.3 Hz), 7.26–7.32 (2 H, m), 7.36–7.41 (1 H, m), 7.46–7.51 (2 H, m); ^{13}C NMR ($CDCl_3$) δ −0.33 (q), 20.89 (t), 32.37 (d), 36.20 (t), 38.75 (t), 62.12 (s), 118.59 (t), 125.75 (s), 128.72 (d), 129.42 (d), 134.43 (d), 138.19 (d), 210.25 (s); ^{29}Si NMR ($CDCl_3$) δ 2.45 (J_{Si-Se} = 7.5 Hz,

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J_{Si-C} = 47.7 Hz); IR (neat) 3060, 2950, 2900, 2825, 1720, 1635, 1245, 835 cm^{-1}; MS *m/e* 352 (M$^+$, ^{80}Se, 0.2), 337 (0.5), 314 (0.02), 230 (4), 215 (3), 195 (52), 157 (3), 73 (100). Anal. Calcd for $C_{17}H_{24}OSeSi$: C, 58.10; H, 6.88. Found: C, 58.24; H, 6.99. ***trans*-9**: ^{1}H NMR ($CDCl_3$) δ 0.08 (9 H, s), 1.65 (1 H, dd, J = 2.2, 8.4 Hz), 1.97 (1 H, dddd, J = 2.2, 2.2, 8.9, 13.3 Hz), 2.17 (1 H, ddd, J = 8.9, 8.9, 18.7 Hz), 2.37 (1 H, dddd, J = 2.2, 2.2, 4.4, 16.9 Hz), 2.47 (1 H, dddd, J = 8.4, 8.9, 9.3, 13.3 Hz), 2.57 (1 H, dd, J = 8.2, 16.9 Hz), 2.70 (1 H, ddd, J = 2.2, 9.3, 18.7 Hz), 5.03 (1 H, ddd, J = 2.0, 3.5, 17.3 Hz), 5.22 (1 H, ddd, J = 2.0, 3.5, 10.2 Hz), 6.00 (1 H, dddd, J = 4.4, 8.2, 10.2, 17.3 Hz), 7.24–7.30 (2 H, m), 7.34–7.39 (1 H, m), 7.45–7.50 (2 H, m); ^{13}C NMR ($CDCl_3$) δ −0.34 (q), 20.83 (t), 34.01 (d), 34.64 (t), 35.76 (t), 65.14 (s), 117.67 (t), 127.20 (s), 128.76 (d), 129.29 (d), 134.86 (d), 137.54 (d), 210.08 (s); ^{29}Si NMR ($CDCl_3$) δ 3.37 (J_{Si-Se} = 9.9 Hz, J_{Si-C} = 51.1 Hz); IR (neat) 3050, 2950, 2880, 1715, 1630, 1250, 850, 830 cm^{-1}; MS *m/e* 352 (M$^+$, ^{80}Se, 0.05), 337 (0.63), 314 (0.15), 230 (3), 215 (1), 195 (36), 73 (100). Anal. Calcd for $C_{17}H_{24}OSeSi$: C, 58.10; H, 6.88. Found: C, 58.02; H, 6.95.

Oxidation of *cis*-9. To an ice-cooled CH_2Cl_2 (1.0 mL) solution of *cis*-**9** (973 mg, 2.77 mmol) was added H_2O_2 (35%, 1.0 mL, 13.4 mmol) at 0 °C, and the mixture was stirred for 30 min. The mixture was washed with an aqueous $NaHCO_3$ solution (10 mL) and H_2O (10 mL) successively. The combined aqueous layers were extracted with ethyl ether (3 × 15 mL). The organic solution was dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel 40 g, 95:5 and then 93:7 hexane/ethyl acetate) to give **5a** (153 mg, 45%), **3-(trimethylsilyl)-2-(2-propenylidene)-1-cyclopentanone (10)** (86 mg, 16%), and **3-(trimethylsilyl)-2-(2-propenyl)-2-cyclopenten-1-one (11)** (6 mg, 1%). **10**: ^{1}H NMR ($CDCl_3$) δ 0.02 (9 H, s), 2.01–2.47 (4 H, m), 2.56–2.64 (1 H, m), 5.47 (1 H, d, J = 9.9 Hz), 5.58 (1 H, d, J = 16.1 Hz), 6.38 (1 H, ddd, J = 9.9, 11.7, 16.1 Hz), 6.84 (1 H, dd, J = 2.1, 11.7 Hz); IR (neat) 2945, 2880, 1705, 1615, 1580, 1245, 830 cm^{-1}; MS *m/e* 194 (M$^+$, 23), 179, (4), 73 (100). Anal. Calcd for $C_{11}H_{18}OSi$: C, 67.98; H, 9.33. Found: C, 67.85; H, 9.16. **11**: ^{1}H NMR ($CDCl_3$) δ 0.25 (9 H, s), 2.31–2.42 (2 H, m), 2.59–2.70 (2 H, m), 3.08 (2 H, d, J = 6.0 Hz), 4.90–5.07 (2 H, m), 5.84 (1 H, ddt, J = 6.0, 9.1, 16.7 Hz); IR (neat) 2950, 2900, 1690, 1633, 1245, 840 cm^{-1}; MS *m/e* 194 (M$^+$, ^{80}Se, 28), 179 (10), 149 (5), 123 (23), 104 (38), 73 (100). Anal. Calcd for $C_{11}H_{18}OSi$: C, 67.98; H, 9.33. Found: C, 67.90; H, 9.49.

Oxidation of *trans*-9. Treatment of *trans*-**9** (45 mg, 0.128 mmol) with H_2O_2 (35%, 0.1 mL, 1.34 mmol) at 0 °C for 10 min afforded **11** (25 mg, 100%).

Oxidation of 7. Treatment of **7** (116 mg, 0.204 mmol) with H_2O_2 (35%, 0.2 mL, 2.69 mmol) in the dark at 0 °C for 5 h yielded **5a** (24 mg, 96%).

Destannylselenenylation of 7. (a) With Tetrabutylammonium Fluoride. To an ice-cooled solution of **7** (27 mg, 0.048 mmol) in ethyl ether (0.3 mL) was added a THF solution of tetrabutylammonium fluoride (1.0 M, 75 μL, 0.075 mmol). The colorless reaction mixture gave a yellow and white precipitate. The elimination was completed by stirring the mixture for 30 min under ice-cooling. The reaction mixture was subjected to column chromatography (silica gel 8 g, 80:20 petroleum ether/ethyl ether) to give **5a** (5 mg, 86% yield).

(b) With (Tributylstannyl)lithium. To a solution of **7** (103 mg, 0.181 mmol) in THF (1 mL) was added (tributylstannyl)-lithium (0.18 M/THF, 0.3 mL, 0.54 mmol) at −78 °C, and the mixture was stirred for 5 min at −78 °C and for an additional 5 min at room temperature. Purification by column chromatography gave **5a** (19 mg, 86% yield) and **8** (6 mg, 8% yield).

(c) With (Benzeneselenenyl)lithium. To a solution of benzeneselenol (13 mg, 0.08 mmol) in benzene (0.5 mL) was added *n*-butyllithium (1.58 M/hexane, 0.05 mL, 0.08 mmol) at room temperature, and the mixture was stirred for 10 min. To this was added a solution of **7** (250 mg, 0.44 mmol) in THF (0.5 mL and 0.2 mL for rinse). Immediately after the addition, the color of the solution turned to yellow and TLC showed completion of the destannylselenenylation. The usual workup and purification gave **5a** (47 mg, 87% yield) and **8** (15 mg, 8% yield).

(d) With $TiCl_4$. After confirming the formation of **7** by TLC, to the reaction mixture obtained from 50 mg (0.21 mmol) of **3** was added $TiCl_4$ (0.05 mL, 0.46 mmol) at −78 °C. Immediately after the addition, the color of the mixture turned to brown through yellow and finally a white precipitate was deposited. The reaction mixture was directly subjected to column chromatography (silica gel 30 g, 80:20 petroleum ether/ethyl ether) to give **5a** (21 mg, 81% yield).

(e) Photolytic Destannylselenenylation. A Pyrex glass tube containing a degassed benzene (1.5 mL) solution of **7** (88 mg, 0.155 mmol) was externally irradiated under argon at a distance of 15 cm from the mercury lamp. After 1 min the disappearance of **7** was confirmed by TLC. Benzene was evaporated under vacuum and the residual oil was purified by column chromatography to give **5a** (18.7 mg, 99%) and (phenylseleno)tributylstannane[30] (68.6 mg, 99%).

(f) Thermal Destannylselenylation. A THF (2 mL) solution of **7** (113 mg, 0.20 mmol) was heated under reflux for 2 h. After the mixture was cooled, THF was evaporated under vacuum and the residual oil was purified by chromatography (silica gel 8 g, 80:20 petroleum ether/ethyl ether) to give **5a** (22 mg, 92% yield) and (phenylseleno)tributylstannane (77 mg, 87% yield).

Methyl (*Z*)-7-[(3*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-5-oxo-1-cyclopentenyl]-5-heptenoate (14a). Method A. To a solution of bis(tributylstannane) (222 mg, 0.38 mmol) in THF (0.5 mL) was added *n*-butyllithium (1.4 M, 0.27 mL, 0.38 mmol) in hexane at −20 °C. After being stirred for 30 min, the reaction mixture was cooled to −78 °C and a solution of (4*R*)-4-[(*tert*-butyldimethylsilyl)oxy]-2-(phenylseleno)-2-cyclopenten-1-one[18] (**13**) (70 mg, 0.19 mmol) in THF (0.3 mL and 0.1 mL for rinse) was added. The mixture was stirred for additional 5 min, when the Michael addition was completed as judged by TLC. Then methyl (*Z*)-7-iodo-5-heptenoate (153 mg, 0.57 mmol) and HMPA (0.2 mL, 1.15 mmol) were added. The mixture was stirred for 1 h, during which time the bath temperature increased to −20 °C. Completion of the allylation was confirmed by TLC. A solution of tetrabutylammonium fluoride (1.0 M, 0.23 mL, 0.23 mmol) in THF was added at −20 °C, and the cooling bath was removed. Since the mixture was stirred at rt for 30 min, when the β-elimination was not completed, additional tetrabutylammonium fluoride (0.2 mL, 0.2 mmol) was added and stirring was continued for 1.5 h. The reaction mixture was then directly subjected to column chromatography (silica gel, 20 g, hexane and then 95:5 hexane/ethyl acetate) to give **14a**[4] (45 mg, 67% yield): $[\alpha]^{25}_D$ +15.5° (*c* 1.32, MeOH); ^{1}H NMR (CCl_4) δ 0.09 (6 H, s), 0.89 (9 H, s), 1.48–2.61 (8 H, m), 2.69–2.93 (2 H, m), 3.58 (3 H, s), 4.69–4.99 (1 H, m), 5.47–5.53 (2 H, m), 6.80–6.96 (1 H, m); IR (neat) 1740, 1714, 1640 cm^{-1}.

Method B. To the reaction mixture starting with 148 mg (0.40 mmol) of (4*R*)-4-[(*tert*-butyldimethylsilyl)oxy]-2-(phenylseleno)-2-cyclopenten-1-one (**13**), obtained as described above, was added silica gel (Fuji Davison BW-200, 6 g), and the vessel containing the mixture was rotated in the 45 °C water bath by the rotary evaporator. After 2 h all the stannylated compounds had disappeared. The mixture was put on the top of the silica gel (80 g) bed in column and eluted with hexane/ethyl acetate (90:10 and then 85:15) to give the product, which was contaminated with an unidentified stannane-derived compound. Repurification by column chromatography (silica gel 7 g, 80:20:0.1 hexane/ethyl acetate/triethylamine) gave **14a** (122 mg, 86% yield).

Methyl (*Z*)-7-[(3*R*)-3-Hydroxy-5-oxo-1-cyclopentenyl]-5-heptenoate (14b). To the reaction mixture obtained as described for **14a** was added a solution of tetrabutylammonium fluoride (1.0 M/THF, 0.57 mL, 0.57 mmol) at −20 °C, and the mixture was stirred for 30 min at rt. Purification gave **14b** (36 mg, 79% yield): $[\alpha]^{29}_D$ +12.6° (*c* 0.94, MeOH) [lit.[2b] $[\alpha]^{23}_D$ +12.4° (*c* 0.91, MeOH)]; ^{1}H NMR (CCl_4) δ 1.46–2.93 (10 H, m), 3.58 (3 H, s), 3.69 (1 H, br s), 4.63–4.95 (1 H, m), 5.31–5.56 (2 H, m), 7.00–7.13 (1 H, m); IR (neat) 3400, 1718, 1693, 1631 cm^{-1}.

Registry No. **3**, 71996-27-5; **4**, 57204-95-2; **5a**, 51557-85-8; **5b**, 22354-39-8; **5c**, 139462-03-6; **5d**, 29119-44-6; **5e**, 38698-55-4; **5f**, 38698-54-3; **6a**, 38019-50-0; **6b**, 13694-36-5; **6d**, 139462-04-7; **6e**, 132570-81-1; **6f**, 71098-29-8; *cis*-**7**, 139462-05-8; *trans*-**8**, 139462-06-9; *cis*-**8**, 139462-07-0; *cis*-**9**, 140110-71-0; *trans*-**9**, 140110-72-1; **10**, 140110-74-3; **11**, 140110-73-2; **13**, 115094-66-1; **14a**, 82542-42-5;

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14b, 42541-96-8; CH_2=$CHCH_2I$, 556-56-9; CH_2=$CHCH_2Br$, 106-95-6; $PhCH_2I$, 620-05-3; $PhCH_2Br$, 100-39-0; PhSeCl, 5707-04-0; CH_3CH=$CHCH_2Br$, 4784-77-4; CH_3CH_2C≡CH_2I, 34498-11-8; $CH_3O_2C(CH_2)_3C$≡CCH_2I, 31776-12-2; $CH_3O_2C(CH_2)_3CH$=$CHCH_2I$, 64493-06-7; (tributylstannyl)lithium, 4226-01-1.

Supplementary Material Available: ^1H NMR spectra for compounds 5c, 6d, 6e, and 6f (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Calixarenes. 28. Synthesis, Structures, and Conformations of Aroylates of Calix[6]arenes

Janet S. Rogers and C. David Gutsche*

Departments of Chemistry of Texas Christian University, Fort Worth, Texas 76129, and Washington University, St. Louis, Missouri 63130

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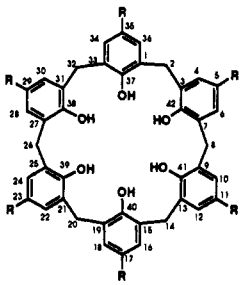
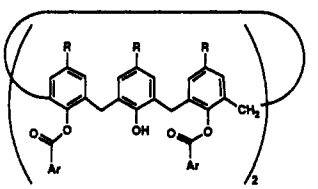
A study of the aroylation of calix[6]arenes under a variety of conditions has shown that the reaction often yields the 1,2,4,5-tetraester as a major product but that the outcome is dependent both on the aroylating agent and the calixarene. The best results have been obtained with *p*-nitrobenzoyl chloride which reacts with *p*-*tert*-butylcalix[6]arene (**1a**) to yield a separable mixture containing ca. 40% tetraester **2a** and 30% pentaester **3** when NaH is used as the base or up to 85% of the tetraester when 1-methylimidazole is used as the base. In comparable fashion benzoyl chloride and *p*-nitrobenzoyl chloride react with **1a** and **1b**, respectively, to yield the tetraesters **2b** and **2c**, whereas *p*-allylcalix[6]arene (**1c**) reacts under the same conditions to produce the hexaester **6**. With limiting amounts of *p*-nitrobenzoylating agent the diesters **4** and **5** have been isolated in low yields. 3,5-Dinitrobenzoyl chloride gives less satisfactory results, producing mixtures containing six or more esters from which only small amounts of the 1,2,4,5-tetraester **2d** have been isolated. The structure and conformation of the products have been established by elemental analysis, mass spectral measurements, and ^1H NMR techniques. In the case of **2a** this includes difference NOE and transient NOE determinations which show that the compound exists in a conformation in which two of the aroylated moieties are canted inward so that their *p*-*tert*-butyl groups occupy the two faces of the calix[6]arene cavity, thus self-complexing the compound and preventing intermolecular complexation.

The increasing attention currently being devoted to the [1_n]metacyclophanes known as calixarenes[1] is focusing principally on the calix[4]arenes, these members of the series possessing the minimum of functionality and conformational flexibility. Although the larger calixarenes have received a modicum of attention, their higher degree of functionality and greater conformational flexibility complicate their chemistry and make isolations and characterizations an often difficult task. The present work addresses this problem in the case of certain aromatic esters of *p*-*tert*-butylcalix[6]arene (**1a**), *p*-H-calix[6]arene (**1b**), and *p*-allylcalix[6]arene (**1c**).[2] First, the syntheses of these compounds are presented, followed by discussions of their structures, conformations, and complexing characteristics.



1a (R = *tert*-Butyl)
1b (R = H)
1c (R = CH_2CH=CH_2)



2a (R = *tert*-Butyl, Ar = $-C_6H_4-NO_2$)
2b (R = H, Ar = $-C_6H_5$)
2c (R = *tert*-Butyl, Ar = $-C_6H_3(NO_2)_2$)
2d (R = *tert*-Butyl, Ar = $-C_6H_3(NO_2)_2$)

Synthesis of Aroylates of Calix[6]arenes

3,5-Dinitrobenzoates. The work described in this paper had its inception in the hope that calix[6]arenes **1** could be selectively esterified with 3,5-dinitrobenzoylating agents in a manner analogous to the calix[4]arenes[3] and thus provide a starting material for the synthesis of double-cavity calix[6]arenes.[4] However, early attempts in the present investigation to isolate pure materials from reaction mixtures obtained by the action of 3,5-dinitrobenzoylating agents on *p*-*tert*-butylcalix[6]arene (**1a**) and *p*-H-calix[6]arene (**1b**) gave difficultly separable mixtures. For example, products containing from 6 to 10 or more components were obtained when **1a** was treated with 3,5-dinitrobenzoyl chloride in the presence of NaH or 1-methylimidazole or with 3,5-dinitrobenzoic acid in the presence of phenyl dichlorophosphate. Only late in the investigation was a compound obtained in low yield from one of these reaction mixtures that was identified as the tetraester **2d**.

(1) Gutsche, C. D. *Calixarenes*; Stoddart, F. J., Ed.; Monographs in Supramolecular Chemistry; The Royal Society of Chemistry: Cambridge, 1989, Vol. 1.

(2) The term "calixarene" is variously employed in different contexts. In colloquial usage (as employed in the Discussion), it implies the presence of hydroxyl groups as, for instance, in "*p*-*tert*-butylcalix[6]arene" for **1a** and "*p*-H-calix[6]arene" for **1b**. In the precise and complete specification of a compound (as used in the Experimental Section) it implies only the basic skeleton to which the substituents, including the OH groups, are attached at the positions that are designated by appropriate numbers.

(3) See, K. A.; Fronczek, F. R.; Watson, W. H.; Gutsche, C. D. *J. Org. Chem.* **1991**, *56*, 7256.

(4) Gutsche, C. D.; See, K. A. To be published.

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