Phenyl 2-(Trimethylsilyl)ethynyl Sulfone as a New Vinyl Cation Synthon

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Phenyl 2-(trimethylsilyl)ethynyl sulfone ($PhSO_2C{\equiv}CSiMe_3$, **1**) is provided as a new vinyl cation synthon for an efficient introduction of the vinyl group to a variety of carbanionic nucleophiles (see Table I), including a highly hindered one, **29**, an important precursor for the synthesis of *Aspidosperma* alkaloids. Another attractive feature of this reagent, which can be easily prepared in a large scale, is particularly demonstrated by its utility under rather strong basic conditions such as NaH, *t*-BuOK, KF, etc.

The efficient introduction of a vinyl substituent to the α-carbon of various carbonyl groups is an urgent need of organic synthesis, since such vinyl products are available as valuable precursors for Cope and oxy-Cope rearrangements. These methods could be further applicable to the synthesis of the medium-sized ring system[1] and, moreover, could be extended to the synthesis of many natural products having vinyl substituents. Recently, a number of vinylation methods of enolizable compounds have been developed by several groups.[2,3] We report here on the utility of remarkably reactive phenyl 2-(trimethylsilyl)-ethynyl sulfone (**1**, PTES),[4] which is readily available in

$$\underset{\mathbf{1}}{PhSO_2C{\equiv}CSiMe_3} \approx \text{“}C{=}C^{+}\text{”}$$

large amounts, as a vinyl cation equivalent for vinylation at the α-carbon of carbonyl groups.

The general outline for the introduction of a vinyl group into the anion **2** is shown in Scheme I, where the Michael reaction of PTES with **2** under mild basic conditions proceeded smoothly to afford the silyl intermediate **3**, which without isolation was immediately treated with acetic acid to yield the vinyl sulfone **4**.

Depending upon the substrate **2**, two procedures for desulfurization of the vinyl sulfones **4** were necessary for generation of **6**. Namely, with diesters **8** and **11**, diketone **26**, and enone **30**, the direct desulfurization method classified as "method A" was available, in which the sulfone **4** was treated with aluminum amalgam at room temperature[5] to afford the vinyl products **6** (see Table I). However, with β-keto esters (**14**, **18**, and **22**), the above direct desulfurization gave the unidentified products instead of the desired **6**.[6] Therefore, in these cases, the sulfones **4** were first converted into the masked cyanohydrins by treatment with trimethylsilyl cyanide (Me_3SiCN), and these were easily desulfurized with aluminum amalgam to give the compounds **5**. The silyl products **5** were then deprotected by using silver fluoride to furnish the final vinyl derivatives **6** (except **15**). This indirect desulfurization procedure is designated as "method B" (see Table I).

As a representative example of method A, addition of PTES (1.1 equiv) to the diester **7** with a catalytic amount of sodium hydride in THF–Me_2SO (10:1) at −80 °C gave exclusively the *Z* isomer **8** (80% yield) after purification by silica gel chromatography.[7] Desulfurization of **8** was conducted by aluminum amalgam in 5% aq CH_3CN to afford **9**[8,9] (81%) as a colorless oil.

In a typical procedure (i.e., method B), the keto group of the Michael adduct **18** was protected with trimethylsilyl cyanide (5 equiv) in the presence of a catalytic amount of ZnI_2 in CH_2Cl_2 to afford the cyanosilylated product,[10a] which was readily desulfurized with aluminum amalgam to give **19**. Removal of the cyanosilyl group from **19** proceeded instantaneously on treatment with silver fluoride (1 equiv)[10b] in THF–H_2O (10:1) at 40 °C to generate the β-keto ester **20**.

Treatment of **15** with silver fluoride under the same reaction conditions as described above produced ethyl tiglate (**16**), accompanied by elimination of acetaldehyde silylhydrin. The expected ethyl 2-methyl-2-vinylacetoacetate was not detected.

Compound **18** was treated with a large excess of triethyl orthoformate in ethanol under acidic conditions to give the ring-opened product **32** as a mixture of olefinic isomers. Desulfurization with aluminum amalgam furnished diethyl 2-vinyladipate (**33**) and its isomer **34** (7:3 by ^1H NMR

(1) (a) Rhoads, S. J.; Raulins, N. R. *Org. React.* **1975**, *22*, 1. (b) Bruhn, J.; Heimgartner, H.; Schmid, H. *Helv. Chim. Acta* **1979**, *62*, 2630.

(2) (a) Oishi, T.; Takechi, H.; Ban, Y. *Tetrahedron Lett.* **1974**, 3757. (b) Koppel, G. A.; Kinnick, M. D. *J. Chem. Soc., Chem. Commun.* **1975**, 473. (c) Metcalf, B. W.; Bonilavri, E. J. *Ibid.* **1978**, 914. (d) Hori, I.; Oishi, T. *Tetrahedron Lett.* **1979**, 4087. (e) Steglich, W.; Wegmann, H. *Synthesis* **1980**, 481. (f) Chang, T. C. T.; Rosenblum, M.; Samuels, S. B. *J. Am. Chem. Soc.* **1980**, *102*, 5930. (g) Kowalski, C. J.; Dung, J.-S. *Ibid.* **1980**, *102*, 7950. (h) Clive, D. L. J.; Russel, C. G. *J. Chem. Soc., Chem. Commun.* **1981**, 434. (i) Hudrlik, P. F.; Kulkarni, A. K. *J. Am. Chem. Soc.* **1981**, *103*, 6251. (j) Kende, A. S.; Fludzinski, P. *Tetrahedron Lett.* **1982**, 2373.

(3) The following examples were effected by direct vinylation at the α-carbon of carbonyl groups by utilizing organometallic complexes. (a) Millard, A. A.; Rathke, M. W. *J. Am. Chem. Soc.* **1977**, *99*, 4833. (b) Hegedus, L. S.; Williams, R. E.; McGuire, M. A.; Hayashi, T. *Ibid.* **1980**, *102*, 4973.

(4) Bhattacharya, S. N.; Josiah, B. M.; Walton, D. R. M. *Organomet. Chem. Synth.* **1971**, *1*, 145. According to the literature, the reaction of commercially available bis(trimethylsilyl)acetylene with preformed benzenesulfonyl chloride–aluminum chloride complex was carried out in methylene chloride at room temperature to furnish PTES [65% yield, slightly hygroscopic colorless crystals (mp 64–65 °C) from petroleum ether]. PTES is very sensitive to alkaline or acidic conditions which generate ethynyl phenyl sulfone ($PhSO_2C{\equiv}CH$).

(5) (a) Pascali, V.; Umani-Ronchi, A. *J. Chem. Soc., Chem. Commun.* **1973**, 351. (b) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1345.

(6) The following reductions of **14** were examined: lithium–ethylamine and potassium–graphite (Savoia, D.; Trombini, C.; Umani-Ronchi, A. *J. Chem. Soc., Perkin Trans. 1* **1977**, 123); sodium amalgam (Trost, B. M.; Arndt, H.-C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, 3477); sodium–naphthalene (Clossen, W. D.; Wriede, P.; Bank, S. *J. Am. Chem. Soc.* **1966**, *88*, 1581). All of them resulted in failure.

(7) The yields of the Michael adducts are dependent upon the dropping rate of PTES into the reaction solution. Therefore, the solution of PTES was slowly added dropwise to the anions over a period of 1 h in all of the present work.

(8) Heyl, D.; Cope, A. C. *J. Am. Chem. Soc.* **1943**, *65*, 669. The α-vinylation method for the carbonyl group was first reported, with 1,2-dibromoethylene being used.

(9) To confirm this structure, hydrogenation of **9** was carried out to give ethyl malonate.

(10) (a) Evans, D. A.; Truesdale, L. K.; Carroll, G. L. *J. Chem. Soc., Chem. Commun.* **1973**, 55. (b) Evans, D. A.; Hoffman, J. M.; Truesdale, L. K. *J. Am. Chem. Soc.* **1973**, *95*, 5822.

(11) Compound **12** was rearranged on heating at 170 °C into ethyl 4-pentenylidenemalonate.[8]

0022-3263/82/1947-4713$01.25/0

Scheme I

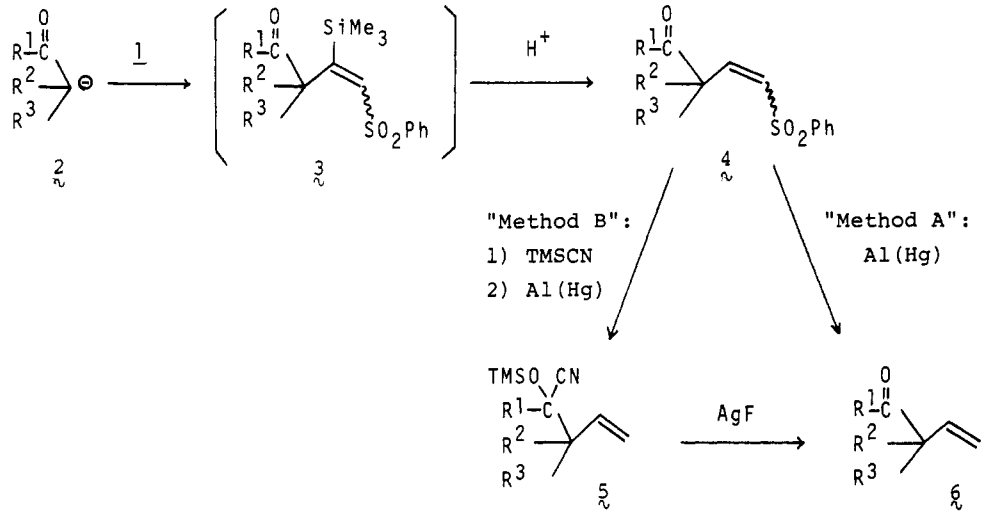
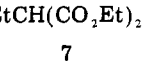
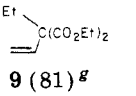
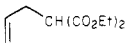
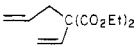
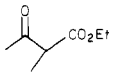
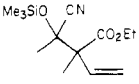
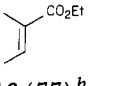
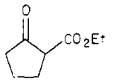
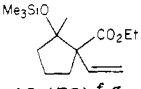
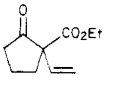
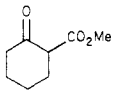
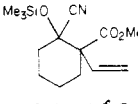
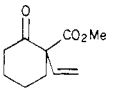
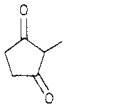
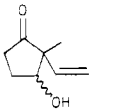
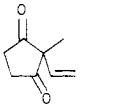
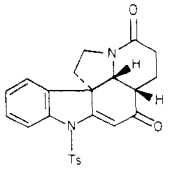
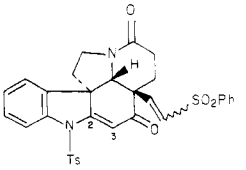
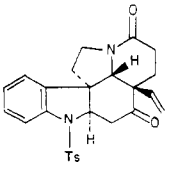


Table I [a]

substrate	vinyl sulfone of the general formula 4 (% yield, E/Z ratio) [b]	silylcyanohydrin of the general formula 5 or hydroxy ketone (yield, %)	final product (yield, %)	desulfurization method
$EtCH(CO_2Et)_2$ 7	 8 (80, 0:100) [d]		 9 (81) [g]	A
 10	11 (93, 1:5) [d]		 12[11] (70) [g]	A
 13	14 (73, 0:100) [d]	 15 (66) [f,g]	 16 (77) [h]	B
 17	18 (85, 1:8) [e]	 19 (73) [f,g]	 20 (82) [h]	B
 21	22 (79, 1:7) [e]	 23 (74) [f,g]	 24 (85) [h]	B
 25	26 (51, 0:100) [d]	 27 (47) [g]		A
 29[12]	 30 (74, 1:1) [c]		 31 (41) [g]	A

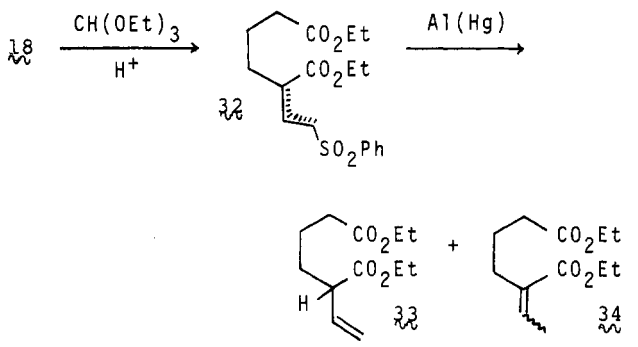
[a] The table indicates the isolated yields of all products after purification by silica gel chromatography. [b] The ratio of E and Z isomers was determined by the integration of olefinic protons in the NMR spectrum. [c] t-BuOK/THF-Me_2SO/−80 °C → room temperature. [d] NaH/THF/−80 °C → room temperature. [e] KF/18-crown-6 catalyst/−80 °C. [f] Me_3SiCN/ZnI_2 catalyst/CH_2Cl_2/room temperature. [g] Al(Hg)/2% aqueous THF/0 °C → room temperature. [h] AgF/10% aqueous THF/40 °C. [i] PCC/CH_2Cl_2/room temperature.

spectrum) in 90% overall yield from 18 (Scheme II).

The Michael addition of β-diketone **25** with **1** gave only the Z isomer **26**, whose desulfurization was performed by aluminum amalgam to give the hydroxy ketone **27**. This hydroxy ketone was converted into the vinyl diketone **28** by PCC oxidation.

Finally, the pentacyclic enone **29** which was synthesized in this laboratory[12] as a versatile intermediate for the

Scheme II



synthesis of *Aspidosperma* alkaloids, was reacted with **1**, affording the vinyl sulfone **30** as a 1:1 mixture of *E* and *Z* isomers. Desulfurization of **30** was directly accomplished by aluminum amalgam to give the vinyl ketone **31** in a moderate yield accompanied by reduction at the C(2)–C(3) olefinic bond.

Thus, it is apparent that PTES (**1**) is extremely reactive as a convenient reagent for vinylation of various enolizable compounds (Scheme I) in high or moderate overall yields (Table I). It is also noteworthy that the reagent **1** can be used for Michael reactions under basic conditions (e.g., NaH, *t*-BuOK, or KF), which is often not the case for the other vinylating reagents.

Studies are in progress to apply this method to other carbonyl systems, where Cope or oxy-Cope rearrangements would lead to the synthesis of natural products.

Experimental Section

General Procedure for Michael Addition of Substrates (7, 10, 13, 25) with Sodium Hydride as Base. Into a stirred suspension of sodium hydride (0.6 equiv, 50% oil dispersion prewashed with *n*-pentane under argon) in dry THF was added the substrate in dry THF under argon at room temperature. After the mixture was stirred at room temperature for 1 h, the reaction vessel was cooled to −80 °C. Then, the solution of PTES[4] (1.1 equiv) in dry THF was slowly added dropwise over a period of 1 h. The reaction mixture was allowed to stand at −80 °C under an argon balloon for 2–4 h and subsequently at room temperature overnight. After the reaction mixture was acidified with glacial acetic acid, the solvent was concentrated in vacuo to give the oily residue which was diluted with CH_2Cl_2, washed with water, and dried over $MgSO_4$. Evaporation of the solvent in vacuo gave the crude product, which was chromatographed on a silica gel column or a preparative-layer plate.

Diethyl Ethyl[(*Z*)-2-(phenylsulfonyl)vinyl]malonate (8). Addition of PTES (74 mg, 0.31 mmol) in dry THF (10 mL) to diethyl ethylmalonate (**7**; 53 mg, 0.28 mmol) in dry THF (5 mL) with 50% sodium hydride (8 mg, 0.17 mmol) in dry THF (5 mL) gave the *Z* isomer **8** (80 mg, 80%) as a colorless oil after silica gel preparative chromatography [CH_2Cl_2–*n*-hexane (2:1)]: ^{1}H NMR ($CDCl_3$) δ 0.89 (t, 3, *J* = 7 Hz), 1.29 (t, 6, *J* = 7 Hz), 2.50 (q, 2, *J* = 7 Hz), 4.27 (q, 4, *J* = 7 Hz), 6.32 (d, 1, *J* = 12 Hz), 6.98 (d, 1, *J* = 12 Hz), 7.5–8.1 (m, 5); IR (neat) 1730, 1610, 1310, 1150 cm^{-1}; mass spectrum, *m/e* 309 (M$^+$ − 45), 213 (base peak).

Diethyl Allyl[2-(phenylsulfonyl)vinyl]malonate (11). Addition of PTES (281 mg, 1.18 mmol) in dry THF (10 mL) to diethyl allylmalonate (**10**; 210 mg, 1.05 mmol) in dry THF (10 mL) with 50% sodium hydride (33 mg, 0.68 mmol) in dry THF (5 mL) gave the *E* isomer (58 mg, 15%; colorless oil) and the *Z* isomer (301 mg, 78%; colorless oil) after separation by silica gel column chromatography [CH_2Cl_2–*n*-hexane (25:1)]. For the *E* isomer: ^{1}H NMR (CCl_4) δ 1.22 (t, 6, *J* = 7 Hz), 2.74 (d, 2, *J* = 7 Hz), 4.18 (q, 4, *J* = 7 Hz), 4.9–5.7 (m, 3), 6.36 (d, 1, *J* = 16 Hz), 7.16 (d, 1, *J* = 16 Hz), 7.4–8.0 (m, 5); IR (neat) 1735, 1635, 1620, 1315, 1140 cm^{-1}; mass spectrum, *m/e* 366 (M$^+$), 225 (base peak). For the *Z* isomer: ^{1}H NMR (CCl_4) δ 1.30 (t, 6, *J* = 7 Hz), 3.13 (d, 2, *J* = 7 Hz), 4.24 (q, 4, *J* = 7 Hz), 4.9–5.8 (m, 3), 6.20 (d, 1, *J* = 12 Hz), 6.81 (d, 1, *J* = 12 Hz), 7.5–8.0 (m, 5); IR (neat) 1735, 1635, 1620, 1315, 1140 cm^{-1}; mass spectrum, *m/e* 366 (M$^+$) 225 (base peak).

Ethyl 2-Methyl-3-oxo-2-[(*Z*)-2-(phenylsulfonyl)vinyl]butanoate (14). Addition of PTES (2.00 g, 8.38 mmol) in dry THF (25 mL) to ethyl 2-methylacetoacetate (**13**; 1.00 g, 6.94 mmol) in dry THF (10 mL) with 50% sodium hydride (267 mg, 5.54 mmol) in dry THF (5 mL) gave the *Z* isomer **14** (1.57 g, 73%) as a colorless oil after silica gel column chromatography [AcOEt–*n*-hexane (2:1)]: ^{1}H NMR (CCl_4) δ 1.31 (t, 3, *J* = 7 Hz), 1.78 (s, 3), 2.33 (s, 3), 4.25 (q, 2, *J* = 7 Hz), 6.14 (d, 1, *J* = 12 Hz), 6.86 (d, 1, *J* = 12 Hz), 7.4–8.0 (m, 5); IR (neat) 1730, 1710, 1615, 1300, 1130 cm^{-1}; mass spectrum, *m/e* 268 (M$^+$ − 42), 99 (base peak).

2-Methyl-2-[(*Z*)-2-(phenylsulfonyl)vinyl]-1,3-cyclopentanedione (26). Addition of PTES (4.46 g, 18.7 mmol) in dry THF (40 mL) to 2-methyl-1,3-cyclopentanedione (**25**; 1.75 g, 15.6 mmol) in dry THF (60 mL) with 50% sodium hydride (600 mg, 12.5 mmol) in dry THF (20 mL) at room temperature for 2 days and then at 50 °C for 1 day gave **26** (2.21 g, 51%) as colorless crystals after silica gel column chromatography [AcOEt–*n*-hexane (1:1)]: mp 164–165 °C (AcOEt–*n*-hexane); ^{1}H NMR ($CDCl_3$) δ 1.51 (s, 3), 2.98 (s, 4), 6.11 (d, 1, *J* = 12 Hz), 6.38 (d, 1, *J* = 12 Hz), 7.4–8.0 (m, 5); IR (Nujol) 1720, 1610, 1290, 1140 cm^{-1}; mass spectrum, *m/e* 278 (M$^+$), 109 (base peak). Anal. Calcd for $C_{14}H_{14}O_4S$: C, 60.42; H, 5.07; S, 11.52. Found: C, 60.27, H, 5.01; S, 11.61.

General Procedure for Michael Addition of Substrates (17, 21) with Potassium Fluoride as Base. To a stirred solution of the substrate in dry THF were added anhydrous potassium fluoride (0.6 equiv) and a chip of 18-crown-6 ether at room temperature under argon. After stirring at room temperature for 1 h, the reaction vessel was cooled to −50 °C. Then, the solution of PTES (1.1 equiv) in dry THF was slowly added dropwise over a period of 1 h. The reaction mixture was allowed to stand at −50 °C for 2 h and subsequently at room temperature overnight. After the reaction mixture was quenched with glacial acetic acid, the solvent was concentrated in vacuo to give the crude product, which was chromatographed on a silica gel column to separate the *E* and *Z* isomers.

Ethyl 2-Oxo-1-[2-(phenylsulfonyl)vinyl]cyclopentanecarboxylate (18). Addition of PTES (1.26 g, 5.3 mmol) in dry THF (30 mL) to ethyl 2-oxo-cyclopentanecarboxylate (**17**; 753 mg, 4.8 mmol) in dry THF (20 mL) with anhydrous potassium fluoride (168 mg, 2.9 mmol) and a chip of 18-crown-6 ether gave a mixture of *E* and *Z* isomers **18** (1:8 by ^{1}H NMR spectrum) as a colorless oil (1.33 g, 85%) after silica gel column chromatography [CH_2Cl_2–EtOH (30:1)]. A part of this oil was further separated on a silica gel preparative-layer plate [CH_2Cl_2–*n*-hexane (2:1)] to give the pure *E* and *Z* isomers, respectively. For the *E* isomer **18**: ^{1}H NMR (CCl_4) δ 1.18 (t, 3, *J* = 7 Hz), 1.8–2.7 (m, 6), 4.10 (q, 2, *J* = 7 Hz), 6.44 (d, 1, *J* = 16 Hz), 7.00 (d, 1, *J* = 16 Hz), 7.4–8.0 (m, 5); IR (neat) 1755, 1725, 1615, 1310, 1140 cm^{-1}; mass spectrum, *m/e* 322 (M$^+$), 181. For the *Z* isomer **18**: ^{1}H NMR (CCl_4) δ 1.26 (t, 3, *J* = 7 Hz), 1.9–2.8 (m, 6), 4.18 (q, 2, *J* = 7 Hz), 6.11 (d, 1, *J* = 12 Hz), 6.70 (d, 1. *J* = 12 Hz), 7.4–8.0 (m, 5); IR (neat) 1755, 1725, 1620, 1305, 1140 cm^{-1}; mass spectrum, *m/e* 322 (M$^+$), 181.

Methyl 2-Oxo-1-[2-(phenylsulfonyl)vinyl]cyclohexanecarboxylate (22). Addition of PTES (597 mg, 2.51 mmol) to methyl 2-oxocyclohexanecarboxylate (**21**; 357 mg, 2.28 mmol) gave a mixture of *E* and *Z* isomers (1:7 by ^{1}H NMR spectrum) as a colorless oil (595 mg, 81%) after silica gel column chromatography [Et_2O–*n*-hexane (1:2)]. A part of this oil was further separated on a silica gel preparative-layer plate [CH_2Cl_2–*n*-hexane (2:1)] to give the pure *E* and *Z* isomers, respectively. For the *E* isomer **22**: ^{1}H NMR (CCl_4) δ 1.5–2.7 (m, 8), 3.73 (s, 3), 6.40 (d, 1, *J* = 16 Hz), 7.21 (d, 1, *J* = 16 Hz), 7.4–8.0 (m, 5); IR (neat) 1745, 1710, 1615, 1310, 1140 cm^{-1}; mass spectrum, *m/e* 322 (M$^+$), 181. For the *Z* isomer **22**: ^{1}H NMR (CCl_4) δ 1.6–2.8 (m, 8), 3.75 (s, 3), 6.12 (d, 1, *J* = 12 Hz), 6.62 (d, 1, *J* = 12 Hz), 7.4–8.0 (m, 5); mass spectrum, *m/e* 322 (M$^+$), 181.

Δ^2,Δ^{20}-*N*-Tosyl-4,8-dioxo-21-(phenylsulfonyl)aspidospermidine (30). To a stirred solution of the enone **29**[12] (81 mg, 0.19 mmol) in dry THF (5 mL)–Me_2SO (1 mL) at −80 °C under argon was added 1.3 mL of a 0.1 M solution of KO-*t*-bu in dry *t*-

(12) Ban, Y.; Ounuma, T.; Nagai, M.; Sendo, Y.; Oishi, T. *Tetrahedron Lett.* **1972**, 5023.

BuOH–THF (1:4), and the mixture was allowed to stand at −80 °C for 1 h. After a solution of PTES (53 mg, 0.22 mmol) in dry THF (7 mL) was slowly added dropwise over a period of 1 h, the cooling bath was removed and the reaction mixture was stirred at room temperature overnight. The reaction mixture was acidified with glacial acetic acid, concentrated in vacuo, and diluted with CH_2Cl_2. The organic layer was washed with water and dried over $MgSO_4$, and evaporation of the solvent in vacuo gave the crude oil which was purified on a silica gel column chromatography to give a 1:1 mixture (by ^1H NMR spectrum) of *E* and *Z* isomers **30** as a brown oil: 83 mg (74%); ^1H NMR ($CDCl_3$) δ 1.4–4.0 (m, 8), 2.30 and 2.36 (each s, 3), 4.21 and 5.14 (each s, 1), 5.33 (d, 0.5, J = 12 Hz), 6.00 (d, 0.5, J = 15 Hz), 5.67 (d, 0.5, J = 12 Hz), 6.53 (d, 0.5, J = 15 Hz), 6.48 and 6.54 (each s, 1), 7.0–8.2 (m, 13); IR ($CHCl_3$) 1660, 1640, 1375, 1170 cm^{-1}; mass spectrum, m/e 434 (M^+ − 166).

General Desulfurization Method A. Aluminum amalgam was prepared from aluminum foil and 2% aqueous $HgCl_2$ according to the Corey's method.[5b] To a solution of the vinyl sulfone (**8**, **11**, **26**, or **30**) in 2% aqueous THF or 5% aqueous CH_3CN at 0 °C under argon was added aluminum amalgam, and the mixture was stirred vigorously at room temperature under an argon balloon for 2 days. The reaction mixture was filtered with suction to remove the inorganic solids and washed with Et_2O or CH_2Cl_2. The combined filtrates were washed with brine, dried over $MgSO_4$, and evaporated in vacuo to give the crude oil which was chromatographed on a silica gel column or a preparative-layer plate.

Diethyl Ethylvinylmalonate (9). A solution of the sulfone **8** (57 mg, 0.16 mmol) in 5% aqueous CH_3CN (20 mL) was submitted to desulfurization with aluminum amalgam (aluminum, 200 mg, 7.4 mmol). The crude oil was chromatographed on a silica gel preparative-layer plate [CH_2Cl_2–*n*-hexane (2:1)], which gave **9** as a colorless oil: 28 mg (81%); ^1H NMR (CCl_4) δ 0.82 (t, 3, J = 7 Hz), 1.25 (t, 6, J = 7 Hz), 2.01 (q, 2, J = 7 Hz), 4.16 (q, 4, J = 7 Hz), 5.16 (d, 1, J = 17 Hz), 5.23 (d, 1, J = 10 Hz), 6.30 (dd, 1, J = 10, 17 Hz); IR (neat) 1730, 1635 cm^{-1}; mass spectrum, m/e 214 (M^+), 149 (base peak).

Diethyl Allylvinylmalonate (12). A solution of the sulfone **11** (113 mg, 0.31 mmol) in 2% aqueous THF (30 mL) was desulfurized with aluminum amalgam (aluminum, 590 mg, 21.9 mmol). Purification on a silica gel preparative-layer plate [CH_2Cl_2–*n*-hexane (4:1)] gave **12** as a colorless oil: 49 mg (70%); ^1H NMR (CCl_4) δ 1.24 (t, 6, J = 7 Hz), 2.72 (d, 2, J = 7 Hz), 4.15 (q, 4, J = 7 Hz), 4.9–6.6 (m, 6); IR (neat) 1730, 1635 cm^{-1}; mass spectrum, m/e 226 (M^+), 79 (base peak).

2-Methyl-2-vinyl-1,3-cyclopentanedione (28). A solution of the sulfone **26** (206 mg, 0.74 mmol) in 2% aqueous THF (50 mL) was desulfurized with aluminum amalgam (aluminum, 1.00 g, 37.0 mmol). Purification on a silica gel preparative-layer plate [Et_2O–*n*-hexane (1:1)] gave a mixture of the diastereoisomers **27** (by ^1H NMR spectrum) as a colorless oil: 49 mg (47%); ^1H NMR ($CDCl_3$) δ 1.15 (s, 1.2), 1.16 (s, 1.8), 1.5–2.5 (m, 5), 4.08 (m, 0.6), 4.28 (m, 0.4), 5.0–6.1 (m, 3); IR (neat) 3440, 1730, 1630 cm^{-1}; mass spectrum, m/e 140 (M^+), 81 (base peak). To a stirred suspension of pyridinium chlorochromate (104 mg, 0.48 mmol) with Celite (No. 545, 500 mg) in dry CH_2Cl_2 (5 mL) was added a solution of the alcohol **27** (45 mg, 0.32 mmol) in dry CH_2Cl_2 (3 mL). After being stirred at room temperature for 2 h, the reaction mixture was filtered with suction to remove Celite and washed with CH_2Cl_2. The filtrate was concentrated in vacuo to afford a crude oil, which was chromatographed on a silica gel column to give **28** as a colorless oil: 41 mg (93%); ^1H NMR ($CDCl_3$) δ 1.23 (s, 3), 2.79 (m, 4), 5.16 (dd, 1, J = 0.7, 17 Hz), 5.24 (dd, 1, J = 0.7, 10 Hz), 5.64 (dd, J = 10, 17 Hz); IR (neat) 1720, 1625 cm^{-1}; mass spectrum, m/e 138 (M^+), 110, 95 (base peak).

Δ^{20}-*N*-Tosyl-4,8-dioxoaspidospermidine (31). A solution of the sulfone **30** (43 mg, 0.07 mmol) in 5% aqueous CH_3CN (11 mL) was desulfurized with aluminum amalgam (aluminum, 58 mg, 2.15 mmol). Purification on a silica gel preparative-layer plate [CH_2Cl_2–AcOEt–MeOH (8:12:1)] gave **31** as a brown oil: 14 mg (41%); ^1H NMR ($CDCl_3$) δ 2.38 (s, 3), 4.10 (dd, 1, J = 7, 15 Hz), 4.10 (s, 1), 4.80 (dd, 1, J = 4, 10 Hz), 4.93 (dd, 1, J = 4, 15 Hz), 5.45 (dd, 1, J = 10, 15 Hz), 7.0–7.8 (m, 8); IR ($CHCl_3$) 1710, 1625 cm^{-1}; mass spectrum, m/e 462 (M^+).

General Desulfurization Method B. To a solution of the vinyl sulfone (**14**, **18**, or **22**) in dry CH_2Cl_2 were added trimethylsilyl cyanide (Me_3SiCN, 5 equiv) and a catalytic amount of ZnI_2 under argon, and the mixture was stirred at room temperature for 4 days. The reaction mixture was washed with water, dried over $MgSO_4$, and concentrated in vacuo to give the cyanosilylated product. This was submitted to desulfurization by method A. Finally, the general procedure for deprotection of the cyanosilyl group of the desulfurized products is as follows. To a stirred solution of the cyanosilyl compound (**15**, **19**, or **23**) in 10% aqueous THF was added AgF (1.1 equiv), and then the mixture was heated at 40 °C for 5 h. After cooling at room temperature, the reaction mixture was diluted with CH_2Cl_2, washed with water, and dried over $MgSO_4$. Evaporation of the solvent gave the crude product, which was purified by silica gel column chromatography (Et_2O–*n*-hexane).

Ethyl Tiglate (16). According to method B, addition of **14** (200 mg, 0.64 mmol) with Me_3SiCN (0.3 mL, 3.2 mmol) in dry CH_2Cl_2 (2 mL) gave ethyl 3-cyano-2-methyl-2-[(*Z*)-2-(phenylsulfonyl)vinyl]-3-(trimethylsiloxy)butanoate as colorless crystals: 218 mg (83%); mp 125–127 °C (*n*-hexane); ^1H NMR δ 0.28 (s, 9), 1.35 (t, 3, J = 7 Hz), 1.67 (s, 3), 1.81 (s, 3), 4.31 (q, 2, J = 7 Hz), 6.22 (d, 1, 12 Hz), 6.50 (d, 1, J = 12 Hz), 7.5–8.1 (m, 5); IR (Nujol) 2220, 1730, 1615, 1310, 1140 cm^{-1}. Anal. Calcd for $C_{19}H_{27}NO_5SSi$: C, 55.72; H, 6.64; N, 3.42. Found: C, 55.26; H, 6.67; N, 3.40. Desulfurization of the above sulfone (108 mg, 0.26 mmol) with aluminum amalgam (aluminum, 350 mg, 13.0 mmol) in 2% aqueous THF (20 mL) gave the crude oil, which was chromatographed on a silica gel preparative-layer plate [Et_2O–*n*-hexane (1:2)] to afford a 1:1 mixture of diastereoisomers **15** as a colorless oil: 60 mg (80%); ^1H NMR (CCl_4) δ 0.22 (s, 9), 1.29 (t, 1.5, J = 7 Hz), 1.30 (t, 1.5, J = 7 Hz), 1.34 (s, 1.5), 1.42 (s, 1.5), 1.56 (s, 1.5), 1.60 (s, 1.5), 4.15 (q, 2, J = 7 Hz), 5.0–6.4 (m, 3); IR (neat) 2150, 1720, 1620 cm^{-1}; mass spectrum, m/e 254, 100 (base peak). Deprotection of the cyanosilyl group of **15** (82 mg, 0.30 mmol) in 10% aqueous THF (5 mL) with AgF (42 mg, 0.33 mmol) gave ethyl tiglate (**16**) as a colorless oil (30 mg, 77%) whose spectral data (^1H NMR and IR) were identical with those of the authentic sample.

Ethyl 2-Oxo-1-vinylcyclopentanecarboxylate (20). Addition of **18** (100 mg, 0.31 mmol) with Me_3SiCN (0.16 mL, 1.55 mmol) in dry CH_2Cl_2 (1 mL) gave ethyl 2-cyano-1-[(2-phenylsulfonyl)vinyl]-2-(trimethylsiloxy)cyclopentanecarboxylate as a colorless oil (123 mg, 94%). Desulfurization of the above sulfone (105 mg, 0.25 mmol) with aluminum amalgam (aluminum, 350 mg, 13.0 mmol) in 2% aqueous THF (20 mL) gave the crude oil, which was chromatographed on a silica gel preparative-layer plate [Et_2O–*n*-hexane (2:1)] to afford **19** as a colorless oil: 55 mg (78%); ^1H NMR (CCl_4) δ 0.22 (s, 9), 1.31 (t, 3, J = 7 Hz), 1.8–2.3 (m, 6), 4.15 (q, 2, J = 7 Hz), 5.1–6.5 (m, 3); IR (neat) 2230, 1735, 1625 cm^{-1}; mass spectrum, m/e 281 (M^+), 235 (base peak).

Deprotection of the cyanosilyl group of **19** (100 mg, 0.36 mmol) in 10% THF (5 mL) with AgF (54 mg, 0.43 mmol) gave **20** as a colorless oil: 53 mg (82%); ^1H NMR ($CDCl_3$) δ 1.26 (t, 3, J = 7 Hz), 1.9–2.5 (m, 4), 2.5–2.7 (m, 2), 4.22 (q, 2, J = 7 Hz), 5.24 (d, 1, J = 17 Hz), 5.34 (d, 1, J = 11 Hz), 6.11 (dd, 1, J = 11, 17 Hz); IR (neat) 1750, 1725, 1635 cm^{-1}; mass spectrum, m/e 182 (M^+), 154 (base peak), 137.

Methyl 2-Oxo-1-vinylcyclohexanecarboxylate (24). Addition of **22** (550 mg, 1.71 mmol) with Me_3SiCN (0.80 mL, 8.55 mmol) in dry CH_2Cl_2 (4 mL) gave methyl 2-cyano-1-[(2-(phenylsulfonyl)vinyl]-2-(trimethylsiloxy)cyclohexanecarboxylate as a colorless oil (666 mg, 93%). Desulfurization of the above sulfone (101 mg, 0.24 mmol) with aluminum amalgam (aluminum, 350 mg, 13.0 mmol) in 2% aqueous THF (20 mL) gave the crude oil, which was chromatographed on a silica gel preparative-layer plate [Et_2O–*n*-hexane (1:1)] to afford **23** as a colorless oil: 54 mg (80%); ^1H NMR ($CDCl_3$) δ 0.22 (s, 9), 1.4–2.2 (m, 8), 3.66 (s, 3), 5.1–6.4 (m, 3); IR (neat) 2240, 1735, 1630 cm^{-1}; mass spectrum, m/e 281 (M^+), 266 (base peak), 249. Deprotection of the cyanosilyl group of **23** (84 mg, 0.30 mmol) in 10% aqueous THF (5 mL) with AgF (42 mg, 0.33 mmol) gave **24** as a colorless oil: 46 mg (85%); ^1H NMR ($CDCl_3$) δ 1.6–2.8 (m, 8), 3.75 (s, 3), 5.12 (d, 1, J = 17 Hz), 5.29 (d, 1, J = 11 Hz), 6.27 (dd, 1, J = 11, 17 Hz); IR (neat) 1740, 1715, 1635 cm^{-1}; mass spectrum, m/e 182 (M^+), 150, 123 (base peak).

Diethyl 2-Vinyladipate (33) and Diethyl 2-Ethylideneadipate (34). To a solution of the vinyl sulfone 18

(352 mg, 1.09 mmol) in dry EtOH (12 mL) were added triethyl orthoformate (1.7 mL, 10.3 mmol) and one drop of concentrated H_2SO_4, and the mixture was stirred at room temperature for 2 days. After addition of saturated $NaHCO_3$ (10 mL) to the reaction mixture, the solvent was concentrated in vacuo, and the residue was extracted with CH_2Cl_2. The extract was washed with water, dried over $MgSO_4$, and evaporated in vacuo to give a mixture of olefinic isomers **32** as a colorless oil (401 mg, 100%). According to method A, desulfurization of **32** (88 mg, 0.24 mmol) with aluminum amalgam (aluminum, 350 mg, 13.0 mmol) in 2% aqueous THF (20 mL) gave a 7:3 mixture (by ^1H NMR spectrum) of **33** and **34** as a colorless oil: 49 mg (90%); ^1H NMR ($CDCl_3$) δ 1.27 (t, 6, J = 7 Hz), 1.5–1.9 (m, 4), 1.83 (d, 0.9, J = 7 Hz), 2.2–2.4 (m, 2), 3.01 (m, 0.7), 4.16 (q, 2, J = 7 Hz), 4.18 (q, 2, J = 7 Hz), 5.1–6.0 (m, 2.1), 6.96 (q, 0.3, J = 7 Hz); IR (neat) 1730, 1635 cm^{-1}; mass spectrum, m/e 228 (M^+), 183, 81 (base peak).

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Registry No. **1**, 32501-93-2; **7**, 133-13-1; **8**, 83219-76-5; **9**, 63383-27-7; **10**, 2049-80-1; (*E*)-**11**, 83219-90-3; (*Z*)-**11**, 83219-77-6; **12**, 83219-78-7; **13**, 609-14-3; **14**, 83219-79-8; **15** (isomer 1), 83219-80-1; **15** (isomer 2), 83219-95-8; **16**, 5837-78-5; **17**, 611-10-9; (*E*)-**18**, 83219-91-4; (*Z*)-**18**, 83219-81-2; **19**, 83219-82-3; **20**, 63383-28-8; **21**, 41302-34-5; (*E*)-**22**, 83219-92-5; (*Z*)-**22**, 83219-83-4; **23**, 83219-84-5; **24**, 83219-85-6; **25**, 765-69-5; **26**, 83219-86-7; **27** (isomer 1), 83289-18-3; **27** (isomer 2), 83289-19-4; **28**, 71545-36-3; **29**, 83219-87-8; (*E*)-**30**, 83219-88-9; (*Z*)-**30**, 83219-89-0; **31**, 83231-98-5; **33**, 83219-93-6; **34**, 83219-94-7; Me_3SiCN, 7677-24-9; ethyl 3-cyano-2-methyl-2-[(*Z*)-2-(phenylsulfonyl)vinyl]-3-(trimethylsiloxy)butanoate, 83219-96-9; ethyl 2-cyano-1-[(2-phenylsulfonyl)vinyl]-2-(trimethylsiloxy)cyclopentanecarboxylate, 83219-97-0; methyl 2-cyano-1-[2-phenylsulfonyl)vinyl]-2-(trimethylsiloxy)cyclohexanecarboxylate, 83219-98-1.

Sequential (π-Allyl)palladium Alkylations

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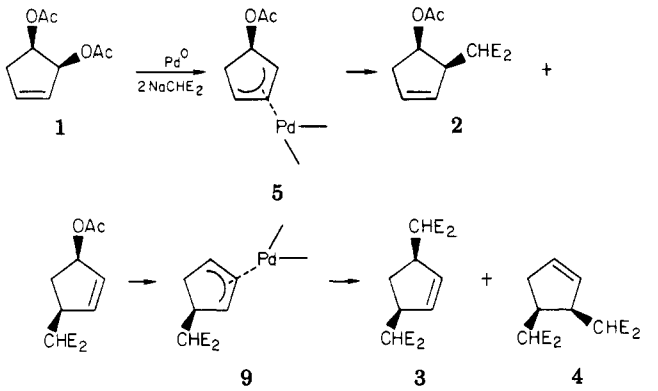
Sequential π-allyl alkylation reactions have been studied by using diallylic and allylic–homoallylic cyclopentenyl diesters as substrates. The regio- and stereochemistry of these reactions have been determined. The use of an acetate–pivalate diester allowed discrete addition of two different nucleophiles in this reaction.

We envisioned sequential π-allyl alkylation reactions as having the potential for considerable synthetic utility. To date, only a single example of such a process has been investigated, and it involved a discrete, two-step procedure for the construction of cyclopropanes.[1] Specifically, we sought the development and application of this methodology for the preparation of the five-membered ring containing antileukemic alkaloid cephalotaxine[2] as well as prostaglandin analogues.

The tandem π-allyl intermediates in this double alkylation process allow the two new bonds to be made with complete stereospecificity, their stereochemistry being dictated by the relative stereochemistry of the initial diallylic or allylic–homoallylic π-allyl precursor.[3] In addition, π-allyl alkylations are known[4] to tolerate a number of active electrophiles (e.g., carbonyl groups) in the key bond-forming steps, further widening the applicability of this process.

The use of a cyclopentene precursor to test the feasibility of this reaction, in addition to the indicated synthetic relevance, provides a particularly stringent challenge. This is based on our a priori analysis that the major competing reaction would be a base-induced elimination of HOR to give a diene, a process to which a cyclopentene substrate should be particularly susceptible.

Scheme I[a]



[a] E = $CO_2C_2H_5$.

Results and Discussion

Our investigation of sequential π-allyl alkylation reactions was initiated by using simple cyclopentene substrates in order to determine the viability of this process as well as to gain information regarding its regio- and stereochemistry.

The bis(π-allyl) substrate *cis*-3,4-diacetoxycyclopent-1-ene (**1**)[5] was prepared by acetylation of the corresponding diol.[6] In principle, three products (**2**–**4**, Scheme I) could

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