Synthesis of PGB_1 Analogues by Radical Chain Substitution Reaction

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PGB_1 analogues with functionalized or sulfur atom-containing α-side chains have been synthesized in several steps from 1,3-cyclopentanedione. Introduction of α- and ω-side chains into the PGB_1 cyclopentenone skeleton has been accomplished by replacement of an allylic sulfonyl group in 3-substituted 2-[(phenylsulfonyl)methyl]-2-cyclopenten-1-one by stabilized carbanions or thiolate ions and Pd(0)-catalyzed cross-coupling reaction between the vinylic iodide moiety in 2-substituted 3-iodo-2-cyclopenten-1-ones and a vinyltin reagent or an alkyne, respectively. The former substitution reaction with stabilized carbanions has been confirmed to proceed via a radical chain mechanism of $S_{RN}1$ type by investigating the effects of a radical scavenger and by the ESR studies. Further, comparison of the reduction potentials of substrates with those of products supports a single electron transfer mechanism.

Introduction

Nucleophilic substitution reaction ($RX + Nu^- \rightarrow RNu + X^-$) proceeding via single electron transfer–radical chain mechanism ($S_{RN}1$) is controlled mainly by two factors: (i) the presence of an appropriate LUMO level of substrate RX so as to accept an electron for generation of its radical anion $RX^{\bullet-}$ in both the initiation and propagation steps and (ii) the degree of SOMO–HOMO or SOMO–LUMO interaction between the free-radical intermediate $R^\bullet$ and the nucleophile Nu^- in the propagation step to allow them to easily couple ($R^\bullet + Nu^- \rightarrow RNu^{\bullet-}$).[1] By taking advantage of these properties it should be possible to design highly chemo- and regioselective $S_{RN}1$ type reactions by judicious choice of reactants.[2] We have recently found a novel $S_{RN}1$ type reaction and reported its mechanistic aspect, where the radical-anion intermediate $NuR^{\bullet-}$ has been detected for the first time by ESR and UV–vis spectroscopy.[3] Its intriguing photochemical behavior shows that the coupling reaction between $R^\bullet$ and Nu^- should be the rate-determining step in the dark.[3] Here we describe an application of this reaction to selective introduction of functionalized or sulfur atom-containing α-side chains in the synthesis of several PGB_1 analogues and discuss the reaction mechanism.

During the past decade, it has been shown that oligomers synthesized chemically (by an alkaline treatment) from a PGB_1 derivative,[4] 15-dehydro-PGB_1 methyl ester, have wide-ranging biological protective and restorative effects in vivo in animals such as protection against ischemia.[5] Further, it has been recently demonstrated that the PGB_1 oligomers serve as potent inhibitors of a wide spectrum of mammalian phospholipases A_2 in vitro[6] as well as agonist-stimulated intracellular phospholipase A_2 activities in human cells.[7,8] It is noteworthy that the biologically less active, chemically stable, monomeric PGB_1 derivative exhibited such a dramatic increase in biological activity upon oligomerization. This discovery spurred the interest in the synthesis of monomeric PGB_1 derivaties with a veiw to supplying precursors of biologically active oligomers.[9] The majority of the reported synthetic methods of monomeric PGB_1 derivatives involve simultaneous elaboration of a cyclopentenone skeleton and an α-side chain by means of either of condensation with succinic acid derivatives or intramolecular cyclization as the key reaction, followed by introduction or manipulation of an

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(1) For reviews on mechanism, see: (a) Savéant, J.-M. *Adv. Phys. Org. Chem.* **1990**, *26*, 1. (b) Bowman, W. R. *Chem. Soc. Rev.* **1988**, *17*, 283. (c) Russell, G. A. *Adv. Phys. Org. Chem.* **1987**, *23*, 271.

(2) For reviews on synthetic aspect of $S_{RN}1$ reaction, see: (a) Kornblum, N. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 734. (b) Bunnet, J. F. *Acc. Chem. Res.* **1975**, *11*, 413. (c) Kornblum, N. *Aldrichimica Acta* **1990**, *23*, 71. For intramolecular cyclization, see: (d) Wolfe, J. F.; Sleevi, M. C.; Goehring, R. R. *J. Am. Chem. Soc.* **1980**, *102*, 3646. For rare examples of synthetic application to natural products: (e) Semmelhack, M. F.; Chong, B. P.; Stauffer, R. D.; Rogerson, T. D.; Chong, A.; Jones, L. D. *J. Am. Chem. Soc.* **1975**, *97*, 2507. (f) Semmelhack, M. F.; Barger, T. *Ibid.* **1980**, *102*, 7765.

(3) (a) Tamura, R.; Yamawaki, K.; Azuma, N. *J. Org. Chem.* **1991**, *56*, 5743. (b) Azuma, N.; Ozawa, T.; Yamawaki, K.; Tamura, R. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2860.

(4) For synthesis and purification, see: (a) Polis, B. D.; Kwong, S.; Polis, E.; Nelson, G.; Shmukler, H. W. *Physiol. Chem. Phys.* **1979**, *11*, 109. For structure elucidation studies, see: (b) Martin, I.; Anvelt, J.; Pehk, T.; Lille, O. *Tetrahedron* **1991**, *47*, 3999. (c) Nelson, G. L.; Verdine, G. L. *Tetrahedron Lett.* **1982**, *23*, 1967. (d) Nelson, G. L.; Verdine, G. L. *Ibid.* **1983**, *24*, 991.

(5) (a) Polis, D. B.; Miller, P.; Grandizio, A. M. *Physiol. Chem. Phys.* **1974**, *6*, 287. (b) Polis, D. B.; Polis, E. *Ibid.* **1976**, *8*, 429. (c) Polis, D. B.; Polis, E. *Ibid* **1979**, *11*, 3. (d) Polis, B. D.; Polis, E.; Kwong, S. *Proc. Natl. Acad. Sci. U.S.A.* **1979**, *76*, 1598. (e) Angelakos, E. T.; Riley, R. L.; Polis, B. D. *Physiol. Chem. Phys.* **1980**, *12*, 81. (f) Kolata, R. J.; Polis, B. D. *Ibid.* **1980**, *12*, 545. (g) Shmukler, H. W.; Soffer, E.; Zawryt, M. G.; Polis, E.; Freely, W. M.; Kwong, S. F.; Cope, F. W. *Ibid.* **1982**, *14*, 445. (h) Kumashiro, R.; Devlin, T. M.; Kholoussy, M.; Matsumoto, T. *Int. Surg.* **1985**, *70*, 247.

(6) Franson, R. C.; Rosenthal, M. D. *Biochim. Biophys. Acta* **1989**, *1006*, 272.

(7) Rosenthal, M. D.; Franson, R. C. *Ibid.* **1989**, *1006*, 278. This inhibition of cellular arachidonic acid mobilization by the PGB_1-oligomers may help to explain their diverse pharmacological effects.

(8) Similarly, an oligomer derived from PGE_1 exhibited membrane protection during ischemia and phospholipase A_2 and trypsin inhibition in vitro, see: Ohnishi, S. T.; Katsuoka, M.; Hidaka, S. *Cell Biochem. Funct.* **1989**, *7*, 51.

(9) (a) Stille, J. K.; Sweet, M. P. *Organometallics* **1990**, *9*, 3189. (b) Moorthy, B. K.; Miller, D. D. *Indian J. Chem., Sect. B* **1990**, *29B*, 1084. (c) Naora, H.; Ohnuki, T.; Nakamura, A. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2401. (d) Naora, H.; Ohnuki, T.; Nakamura, A. *Ibid.* **1988**, *61*, 2859. For classical synthetic procedure, see: (e) Miyano, M. *J. Org. Chem.* **1970**, *35*, 2314. (f) Yura, Y.; Ide, J. *Chem. Pharm. Bull.* **1969**, *17*, 408. (g) Katsube, J.; Matsui, M. *Agr. Biol. Chem.* **1969**, *33*, 1078. (h) Klok, R.; Pabon, H. J. J.; van Dorp, D. A. *Recl. Trav. Chim. Pays-Bas* **1967**, *87*, 813. (i) Collins, P.; Jung, C. J.; Pappo, R. *Isr. J. Chem.* **1968**, *6*, 839.

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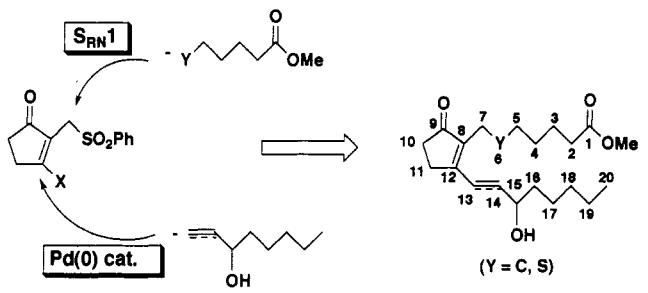
Scheme I

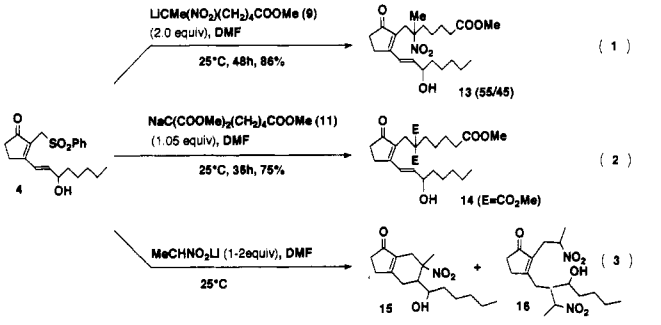


ω-side chain.[9] With the aim of obtaining PGB_1 analogues with functionalized or heteroatom-containing α-side chains, we utilized $S_{RN}1$ reaction of 3-substituted 2-[(phenylsulfonyl)methyl]-2-cyclopenten-1-ones with carbon and sulfur nucleophiles for introduction of α-side chains and Pd(0)-catalyzed coupling reaction with a vinyltin reagent or an alkyne for an ω-side chain as shown in Scheme I. This methodology is of special value because there has been no report using commercially available 1,3-cyclopentanedione (1)[10] as a starting material for synthesis of PGB_1 derivatives due to considerable limitation of selective mono-C-alkylation of 1 for elaboration of α-side chains.[11] Further, to date no PGB_1 analogues containing a sulfur atom in place of C(6) in the α-side chain or functionalized α-side chains as described herein have been synthesized.

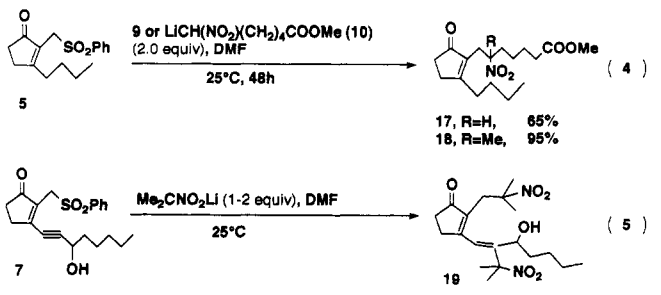
Results and Discussion

Preparation of Various 3-Substituted 2-[(Phenylsulfonyl)methyl]-2-cyclopenten-1-ones. Requisite sulfonyl enones were obtained in good to excellent yields by general synthetic methods from 3-hydroxy-2-[(phenylsulfonyl)methyl]-2-cyclopenten-1-one (2), which was derived from 1 by applying a reported phenylsulfonylmethylation procedure (Scheme II).[12] Attempted direct replacement of vinylic hydroxy group of 2 by a halogen atom using dihalophosphoranes[13] failed to give 3 or the corresponding bromo compound. Since 2 can form a stable ammonium salt with Et_3N at 25 °C, desired iodination was accomplished by successive trifluoromethanesulfonylation of the salt with Tf_2O and addition–elimination reaction with LiI to afford 3 in 96% yield.[14] Subsequently, sulfonyl dienone 4 was produced by Pd(0)-catalyzed coupling reaction between 3 and a vinyltin reagent.[14,15] Pd(0)- and CuI-catalyzed coupling reaction between 3 and 1-octyn-3-ol[15] in the presence of Et_3N in DMF gave sulfonyl ynenone 7 in 72% yield.[16]

Initial Introduction of an ω-Side Chain Followed by an α-Side Chain. Sulfonyl dienone 4 was allowed to react with tertiary stabilized carbanions such as 9 and 11 at 25 °C, the former of which was derived from 2-nitrocyclohexanone derivatives,[17] giving the regioselective substitution products 13 as a mixture of diastereomers (55/45) and 14 in 82% and 75% yields, respectively (eqs 1 and 2). Less reactive nitronate anion 9 needed longer reaction time (48 h) for completion of the reaction than malonate anion derivative 11 (36 h), albeit the yield (82%) of 13 was better than that (75%) of 14.



Reaction of 4 with secondary nitronate 10 failed to give the desired substitution product, instead giving a mixture of unidentified products which no longer contain a carbon–carbon double bond in the ω-side chain. Since 5 was reacted with 10 and 9 smoothly to afford 17 and 18, respectively (eq 4), it was anticipated that the dienone moiety in 4 was susceptible to 1,6-addition by 10. Therefore, reaction of 4 with $MeCHNO_2Li$ was carefully examined to identify the reaction products (eq 3). As a consequence, it was found by HPLC and NMR analyses that six major products lacking olefinic protons were produced in almost comparable proportions. Although purification and identification of each product was infeasible, mass spectral analysis (Cl) of the product mixture showed that quasi-molecular ion (M + 1) and fragment ($M - NO_2$, $M - NO_2 - H_2O$) peaks corresponding to intra- and intermolecular 1,6-adducts (15 and 16) were detected.[18] Probably a mixture of respective diastereomers of 15 and 16 should be produced, although their structures are still tentative. Neither careful selection of reaction conditions nor the use of the sterically congested sulfonyl dienone 8 could prevent the undesired 1,6-addition. Sulfonyl ynenone 7 also underwent both substitution and intermolecular 1,6-addition even by Me_2CNO_2Li, due to the high reactivity of the ynenone moiety in 7 comparable to that of the activated allylic sulfonyl group, producing 19 as the sole isolable product with the recovery of 7 (eq 5). These results suggest that initial introduction of the α-side chain followed by the ω-side chain seems desirable (see the following section).



Although analogous substitution and 1,6-addition were expected to occur in the reaction of 4 with thiolate ions,

(10) For the synthetic procedures, see: (a) Fuchs, R.; McGarrity, J. F. *Synthesis* **1992**, 373. (b) Merenyi, F.; Nilsson, M. *Organic Syntheses*; Wiley: New York, 1988; Vol. 6, p 28. (c) Tajima, K. *Chem. Lett.* **1987**, 1319. (d) Lick, C.; Schrank, K. *Chem. Ber.* **1978**, *111*, 2461.

(11) Schick, H.; Eichhorn, I. *Synthesis* **1989**, 477.

(12) Hellman, H.; Müller, K. *Chem. Ber.* **1965**, *98*, 638.

(13) Piers, E.; Grierson, J. R.; Lau, C. K.; Nagakura, I. *Can. J. Chem.* **1982**, *60*, 210.

(14) Stille, J. K.; Sweet, M. P. *Tetrahedron Lett.* **1989**, *30*, 3645. Also see ref 9a.

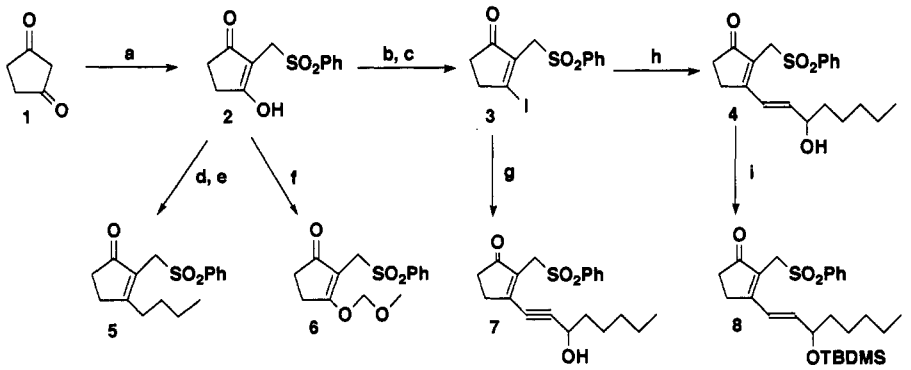
(15) (±)-1-Octyn-3-ol and its derivative (±)-$Bu_3SnCH{=}CHCH(OH)(CH_2)_4Me$ were employed in the present study. For the synthesis of (−)-(*S*)-1-octyn-3-ol, see: Kang, S.; Lee, D.; Lee, J. *Synlett* **1990**, 591 and references cited therein.

(16) (a) Stephans, R. D.; Castro, C. E. *J. Org. Chem.* **1963**, *28*, 3313. (b) Sonogashira, Y.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467. (c) Cassar, L. *J. Organomet. Chem.* **1975**, *93*, 253. (d) Dieck, H. A.; Heck, R. F. *Ibid.* **1975**, *93*, 259.

(17) Bhattacharjya, A.; Mukhopadhyay, R.; Pakrashi, S. C. *Synthesis* **1985**, 886.

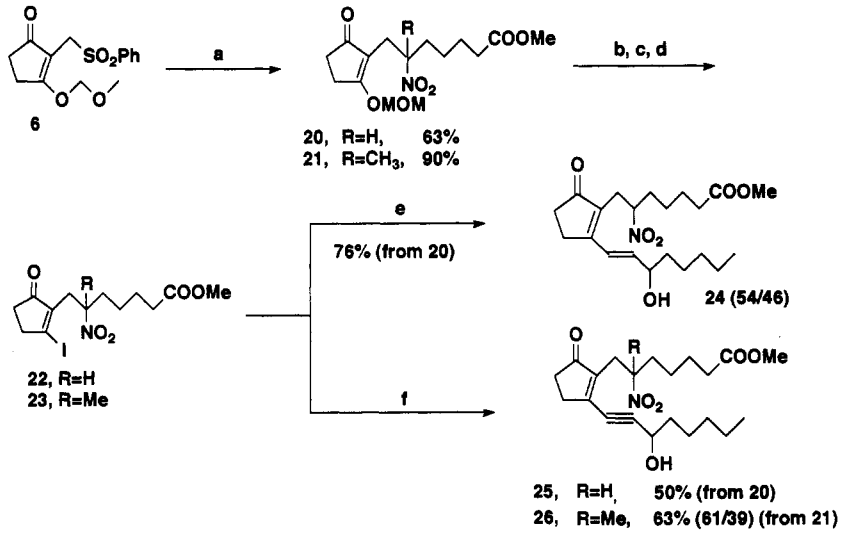
(18) Measured at 70 eV using CH_4 as a carrier gas.

Scheme II[a]



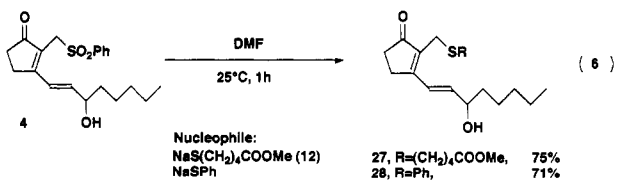
[a] (a) $(CH_2O)_n$, $PhSO_2Na$, AcOH, reflux, 5 h (85%); (b) $(CF_3O_2)_2O$, Et_3N, CH_2Cl_2, 0 °C, 1 h (95%); (c) LiI, THF, reflux, 1 h (100%); (d) AcCl, Et_3N, CH_2Cl_2, 0 °C, 15 min (99%); (e) *n*-Bu_2CuLi-BF_3 (1.5 equiv), ether/THF = 4/1, −78 °C, 3 h (65%); (f) $MeOCH_2Cl$, Et_3N, CH_2Cl_2, 0 °C, 30 min (100%); (g) octyn-3-ol (1.5 equiv), $(PPh_3)_2PdCl_2$ (0.05 equiv), CuI (0.1 equiv), Et_3N (1.2 equiv), DMF, 25 °C, 2 h (72%); (h) $Bu_3SnCH{=}CHCH(OH)(CH_2)_4Me$ (1.2 equiv), $(MeCN)_2PdCl_2$ (0.05 equiv), DMF, 25 °C, 2 h (86%); (i) TBDMSCl, imidazole, DMF, 25 °C, 48 h (85%).

Scheme III[a]



[a] (a) **9** or **10** (2 equiv), DMF, 25 °C, 72 h; (b) aq HCl, MeOH, 25 °C, 5 min; (c) Tf_2O, Et_3N, CH_2Cl_2, 0 °C, 30 min; (d) LiI, THF, reflux, 1 h; (e) $Bu_3SnCH{=}CHCH(OH)(CH_2)_4Me$ (1.2 equiv), $(MeCN)_2PdCl_2$ (0.05 equiv), DMF, 25 °C, 3 h; (f) octyn-3-ol (1.5 equiv), $(PPh_3)_2PdCl_2$ (0.05 equiv), CuI (0.1 equiv), Et_3N (1 equiv), DMF, 25 °C, 24 h.

selective substitution took place by slow addition of an equimolar amount of the thiolate ion dissolved in DMF to **4** at ambient temperature (eq 6). Sodium alkanethiolate **12** and PhSNa afforded **27** and **28**, respectively, whereas the less nucleophilic sodium salt of methyl thioglycolate failed to react with **4**.



(6)

Initial Introduction of an α-Side Chain Followed by an ω-Side Chain. As shown in Scheme III, β-protected sulfonyl enone **6** was subjected to $S_{RN}1$-type substitution by nitronate anions **10** and **9**, giving substitution products **20** and **21** in 63% and 90% yields, respectively, although a longer reaction time compared to **4** was required. Further manipulation of the α-side chain by taking advantage of the unique properties of the secondary and tertiary nitro group is possible at this stage.[19] After deprotection of the methoxymethyl group of **20** and **21**, the vinylic hydroxy group was converted to the desired vinyl iodide through a vinyl triflate. Subsequent Pd(0)-catalyzed coupling reaction with a vinyltin or an alkyne afforded desired **24** (diastereomeric ratio: 54/46), **25** (undetermined), and **26** (61/39) in good overall yields from **20** and **21** (Scheme III).

Thus, by using either of two successive side-chain elaborative methods described above, desired PGB_1 analogues have been synthesized in several steps from **1**.

Mechanism. In a previous paper, we described mechanistic details on the analogous $S_{RN}1$-type reaction using six-membered sulfonyl enone homologues.[3] Experimental data described in the present paper showed distinct radical character consistent with the previous results.[3] (1) The reaction with bulky tertiary stabilized carbanions proceeded smoothly, showing the preference of stabilized

(19) For recent reviews for C–C bond formation and substitution reactions using aliphatic nitro compounds as the nucleophile and electrophile, see: (a) Tamura, R.; Kamimura, A.; Ono, N. *Synthesis* **1991**, 423. (b) Ono, N. In *Nitro Compounds; Recent Advances in Synthesis and Chemistry*; Feuer, H., Nielsen, A. T., Ed.; VCH Publishers: New York, 1990; p1. (c) Rosini, G.; Ballini, R. *Synthesis* **1988**, 833. (d) Ono, N.; Kaji, A. *Synthesis* **1986**, 693.

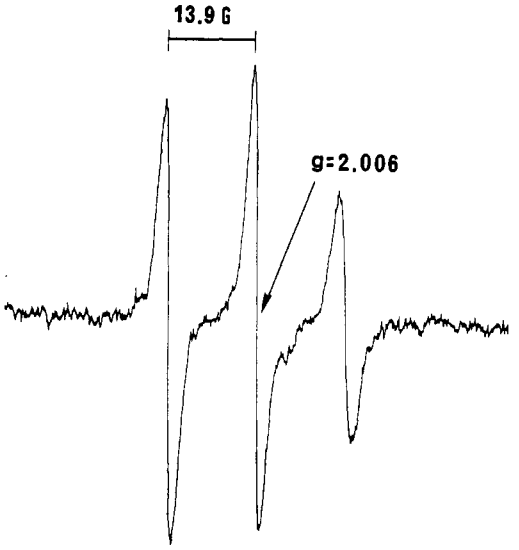
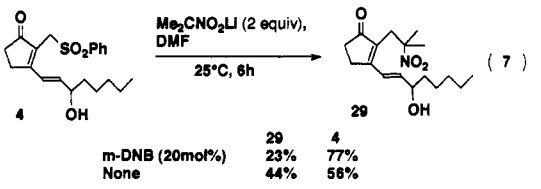


Figure 1. ESR spectrum of radical intermediate **30** formed during reaction of **4** (1.0 M) and Me_2CNO_2Li (2.0 M) in DMF at 25 °C (eq 7).

carbanions with higher HOMO level.[1] (2) Selective C-alkylation with nitronate anions was observed.[2] (3) The initial red-orange color development on mixing starting materials was uniformly observed, indicating the formation of the charge-transfer complex between the reactants. (4) Addition of 20 mol % of *m*-dinitrobenzene (m-DNB) as a radical scavenger decreased the reaction rate between **4** and Me_2CNO_2Li with high reproducibility as shown in eq 7, although dead time was not observed, implying a radical chain mechanism. (5) An ESR spectrum corresponding to nitroxide radical-anion intermediate **30** was detected during the reaction of **4** and Me_2CNO_2Li in DMF at 25 °C (eq 7 and Figure 1), which disappeared on



completion of the reaction through a steady state.[20] A typical radical chain mechanism of $S_{RN}1$-type reaction applied to our system is shown in Scheme IV.[1,2] The observed intermediate **30** must correspond to a radical-anion resulting from the coupling reaction between a free radical and an anion shown in step c.[3] In general, the ability of the substrate to accept an electron from a nucleophile in step a and from a radical-anion in step d as well as the coupling reaction rate between a free radical and a nucleophile in step c determine the nature of the

(20) The analogous radical-anion intermediate **31** formed by the coupling reaction between the corresponding allyl free radical and nitronate ion has been detected by ESR and UV–vis spectroscopy; see ref 3a. It has been shown in ref 3a that **31** is the actual reaction intermediate in the $S_{RN}1$ type reaction. The same radical species as **31** was produced by one-electron reduction of **32**. The structure of **31** was supported by the X-ray analysis of the precursor **32**; see ref 3b. The details concerning generation, isolation, and structural confirmation of **31** will be reported in a separate paper.

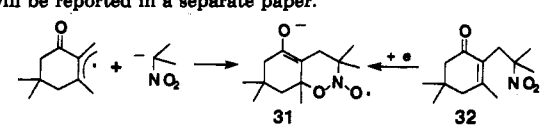
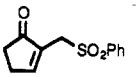
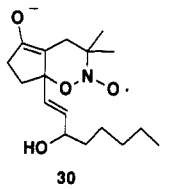


Table I. Reduction Potential of Substrates and Products by Polarography[a]

compound	$E_{1/2}^{red}$ (V vs SCE)	compound	$E_{1/2}^{red}$ (V vs SCE)
	−1.68	**13**	−1.57
4	−1.56	**14**	−1.79
6	−2.05	**24**	−1.60
7	−1.51	**27**	−1.71

[a] Measurement conditions, see ref 21.

individual $S_{RN}1$-type reaction. In this context, the rare detection of radical-anion intermediate **30** implies that step d is rate-determining in the reaction of eq 7. In order



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to evaluate the feasibility of intermolecular SET processes, the reduction potential of various substrates and products were measured by polarography.[21] Results are shown in Table I. Comparison of the reduction potential of the substrate **4** (−1.56 V vs SCE) with those of the products **13** (−1.57 V), **14** (−1.79 V), and **27** (−1.71 V) indicates that intermolecular single-electron transfer from the radical anion of **13**, **14**, or **27** to substrate **4** (step d in Scheme IV) is possible. Therefore, although mechanistic evidence concerning the reaction with thiolate anions shown in eq 6 has not been obtained yet, it is possible that this reaction also proceeds by a $S_{RN}1$ mechanism.[22] Higher reduction potential (−2.05 V) of **6** than that of **4** (−1.56 V) might be responsible for the slower reaction rate with nucleophiles (eq 1 and Scheme III), if step d in Scheme IV is again the rate-determining stage.

Conclusions

Methodology described herein provides easy access to a new class of PGB_1 analogues with functionalized or sulfur atom-containing α-side chains and with an alkenyl or alkynyl ω-side chain, which are promising synthetic precursors of biologically active oligomers of PGB_1 derivatives. By using either of two successive side chain elaborative methods, i.e., (a) introduction of an α-side chain into the PGB_1 cyclopentenone skeleton by using $S_{RN}1$-type substitution reaction followed by that of an ω-one by Pd(0)-catalyzed cross-coupling reaction or (b) ω followed by α, several PGB_1 analogues have proved to be obtained in several steps from 1,3-cyclopentanedione. Mechanistic studies suggest that the substitution reaction proceeds by a radical chain mechanism involving SET processes.

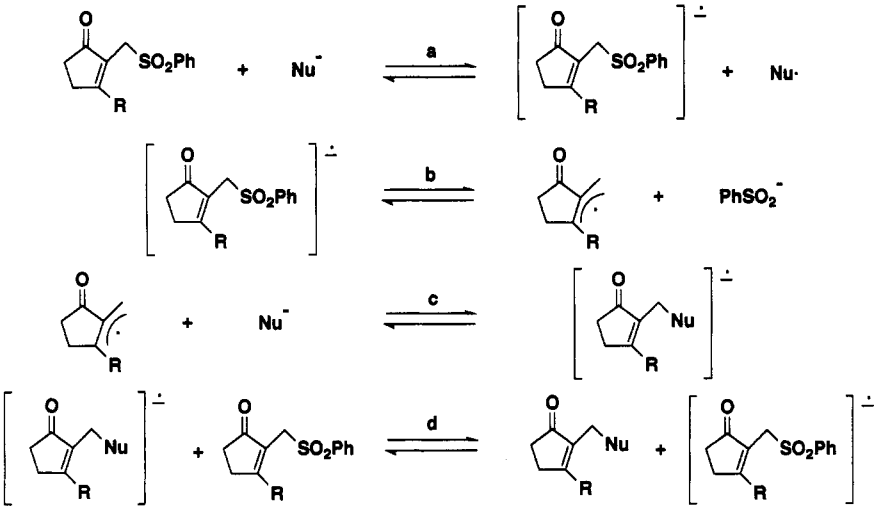
Experimental Section

Infrared spectra were recorded as liquid films on NaCl plates or as KBr pellets. ^1H NMR spectra were recorded at 270 MHz, and ^{13}C NMR were recorded at 67.8 MHz. HPLC analyses were

(21) Measured in DMF at 25 °C in the concentration of (0.5–2.0) × 10^{-3} of organic compounds in the presence of *n*-Bu_4NClO_4 (1.0 × 10^{-3} M) as the supporting electrolyte by using Pt wire as the counter electrode. SCE was used as the reference electrode.

(22) This displacement may involve two consecutive S_N2' substitutions, see: (a) Tamura, R.; Katayama, H.; Watabe, K.; Suzuki, H. *Tetrahedron* **1990**, *46*, 7557. (b) Houwen-Claassen, A. A. M.; Klunder, A. J. H.; Kooy, M. G.; Steffann, J.; Zwanenburg, B. *Ibid* **1989**, *45*, 7109.

Scheme IV



carried out by using a silica gel stationary-phase column (YMC-Pack SIL-06, 0.46 cm × 30 cm) and UV–vis spectrometer (254 nm) as the detector. All solvents were distilled before use. All reactions were run under Ar.

Preparation of 2. A mixture of 1,3-cyclopentanedione (1.00 g, 10.2 mmol), paraformaldehyde (0.351 g, 11.7 mmol), and $PhSO_2Na$ (2.04 g, 10.2 mmol) in glacial AcOH (10 mL) was heated at reflux for 5 h. After cooling to 25 °C, water (30 mL) was added. The resultant pale orange solid was collected by filtration and washed with three portions of ether (10 mL) to give 2.20 g (86%) of **2**, whose solubility in ordinary organic solvents was quite low. Therefore, the NMR spectrum was not available. **2**: mp 235 °C dec; IR (KBr) 1600, 1542, 1442, 1335, 1302, 1237, 1158 cm^{-1}. Anal. Calcd for $C_{12}H_{12}O_4S$: C, 57.13; H, 4.79. Found: C, 57.42; H, 4.55.

Preparation of 3. To a suspension of **2** (2.90 g, 8.0 mmol) in CH_2Cl_2 (40 mL) was added Et_3N (0.99 g, 9.8 mmol) at 0 °C. The suspension turned to a solution after 15 min. Then Tf_2O (2.71 g, 9.6 mmol) was added. The reaction mixture was stirred for 1 h at 0 °C. Aqueous 5% $NaHCO_3$ solution (30 mL) was added, and the aqueous mixture was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phase was washed with water (30 mL), dried over $MgSO_4$, and concentrated in vacuo. The residual brown solid was purified by column chromatography on silica gel to give 2.92 g (95%) of the triflate of **2**. Anal. Calcd for $C_{13}H_{11}O_6S_2F_3$: C, 40.63; H, 2.88. Found: C, 40.55; H, 2.80.

To a solution of anhydrous LiI (3.08 g, 23 mmol) in THF (80 mL) was added the triflate (7.6 mmol). The solution was heated at reflux for 1 h, diluted with CH_2Cl_2 (200 mL), washed with brine (50 mL) and water (2 × 50 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was triturated with ether to give 2.75 g (100%) of **3** in a high state of purity as a pale yellow solid. **3**: mp 170 °C dec; IR (KBr) 1698, 1598, 1300, 1132, 740, 690 cm^{-1}; ^1H NMR δ 7.91–7.53 (m, 5 H), 4.12 (s, 2H), 3.09 (m, 2H), 2.49 (m, 2H); ^{13}C NMR δ 199.7, 140.9, 140.4, 138.9, 134.1, 129.6, 128.5, 54.4, 40.3, 36.1. Anal. Calcd for $C_{12}H_{11}O_3SI$: C, 39.79; H, 3.06. Found: C, 40.14; H, 2.93.

Preparation of 4. To a mixture of **3** (1.81 g, 5.0 mmol) and $PdCl_2(CH_3CN)_2$ (0.065 g, 0.25 mmol) in DMF (30 mL) was added $Bu_3SnCH{=}CHCH(OH)(CH_2)_4Me$ (2.50 g, 6.0 mmol). The reaction mixture was stirred for 2 h at 25 °C. Aqueous 10% NH_3 solution (30 mL) was added, and the aqueous mixture was extracted with ether (3 × 50 mL). The combined organic phase was washed with brine (3 × 30 mL) and water (2 × 30 mL), dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel to provide 1.56 g (86%) of **4** as a white solid. **4**: mp 96–97 °C; IR (KBr) 3400, 1698, 1642, 1598, 1310, 1142, 742, 688 cm^{-1}; ^1H NMR δ 7.85–7.48 (m, 5H), 6.95 (d, J = 15.9 Hz, 1H), 6.46 (dd, J = 5.5, 15.9 Hz, 1H), 4.35 (br m, 1H), 4.17 (s, 2H) for CH_2SO_2, 2.76 (m, 2H), 2.68 (br m, 1H), 2.32 (m, 2H), 1.60 (m, 2H), 1.49–1.31 (m, 6H), 0.90 (t, J = 6.7 Hz, 3H); ^{13}C NMR δ 205.9, 167.0, 144.5, 138.6, 134.0, 129.1, 128.5, 127.5, 123.2, 72.0, 50.6, 36.9, 33.1, 31.7, 26.2, 25.1, 22.6, 14.0. Anal. Calcd for $C_{20}H_{26}O_4S$: C, 66.27; H, 7.23. Found: C, 65.99; H, 7.02.

Preparation of 5. To a suspension of **2** (2.90 g, 8.0 mmol) in CH_2Cl_2 (40 mL) was added Et_3N (0.99 g, 9.8 mmol) at 0 °C. Then acetyl chloride (1.26 g, 16.0 mmol) was added, and the reaction solution was stirred for 30 min at 0 °C. A 5% $NaHCO_3$ solution (30 mL) was added. The aqueous mixture was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic phase was washed with water (100 mL), dried over $MgSO_4$, and concentrated in vacuo. The residual solid was triturated with ether to give 2.33 g (99%) of the acetate of **2**.

To a solution of *n*-BuCuLi (3.0 mmol) in ether (40 mL) was added dropwise $BF_3{\cdot}OEt_2$ (45 mmol) at −78 °C. After the mixture was stirred for 15 min at −78 °C, a solution of the acetate (3.0 mmol) in THF (10 mL) was added. The reaction mixture was stirred for 3 h at −78 °C and then worked up by addition of saturated NH_4Cl solution (15 mL). The aqueous phase was extracted with ether (2 × 30 mL). The combined organic phase was washed with brine (30 mL) and water (30 mL), dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel to give 0.57 g (65%) of **5** as a white solid. **5**: mp 64–65 °C; IR (KBr) 1698, 1638, 1305, 1140 cm^{-1}; ^1H NMR δ 7.86–7.49 (m, 5H), 4.06 (s, 2H) for CH_2SO_2, 2.62 (m, 2H), 2.28 (m, 2H), 1.60–1.36 (m, 6H), 0.95 (t, J = 7.3 Hz, 3H); ^{13}C NMR δ 206.2, 182.5, 138.8, 133.8, 129.0, 128.4, 128.1, 50.6, 33.5, 31.8, 29.7, 29.2, 22.9, 13.8. Anal. Calcd for $C_{16}H_{20}O_3S$: C, 65.73; H, 6.89. Found: C, 66.00; H, 6.57.

Preparation of 6. To a suspension of **2** (3.62 g, 10 mmol) in CH_2Cl_2 (10 mL) was added Et_3N (1.06 g, 10.5 mmol) at 0 °C. Chloromethyl methyl ether (1.61 g, 20 mmol) was added dropwise, and the reaction mixture was stirred for 30 min at 0 °C. A 5% $NaHCO_3$ solution (30 mL) was added. The aqueous mixture was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phase was washed with water (30 mL), dried over $MgSO_4$, and concentrated in vacuo. The residual solid was tritulated with ether to provide 2.96 g (100%) of **6** as a white solid. **6**: mp 214 °C dec; IR (KBr) 1695, 1628, 1545, 1426, 1352, 1300, 1237, 1144 cm^{-1}; ^1H NMR δ 8.16–7.83 (m, 2H), 7.79–7.53 (m, 3H), 5.32 (s, 2H) for OCH_2O, 4.10 (s, 2H) for CH_2SO_2, 3.60 (s, 3H), 2.83 (m, 2H), 2.40 (m, 2H). Anal. Calcd for $C_{14}H_{16}O_5S$: C, 56.74; H, 5.44. Found: C, 56.64; H, 5.63.

Preparation of 7. To a mixture of $PdCl_2(PPh_3)_2$ (0.24 g, 0.34 mmol) and CuI (0.13 g, 0.68 mmol) in DMF (5 mL) was added successively 1-octyn-3-ol (0.86 g, 6.8 mmol), a solution of **3** (1.66 g, 4.6 mmol) in DMF (20 mL), and Et_3N (0.56 g, 5.5 mmol). The reaction mixture was stirred for 20 h at 25 °C. Saturated NH_4Cl solution (30 mL) was added, and the aqueous mixture was extracted with ether (3 × 30 mL). The combined organic phase was washed with brine (3 × 30 mL) and water (2 × 30 mL), dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel to give 1.24 g (75%) of **7** as an orange oil. **7**: IR (neat) 3480, 2210, 1704, 1348, 1140, 734 cm^{-1}; ^1H NMR δ 7.88–7.35 (m, 5H), 4.61 (t, J = 6.7 Hz, 1H), 4.16 (s, 2H) for CH_2SO_2, 2.85 (br m, 1H), 2.72 (m, 2H), 2.36 (m, 2H), 1.78 (m, 2H), 1.56–1.28 (m, 6H), 0.90 (t, J = 6.8 Hz, 3H); ^{13}C NMR δ 205.0, 156.6, 138.8, 134.7, 129.1, 128.4, 110.7, 79.6,

62.8, 60.4, 52.0, 37.1, 33.4, 31.4, 30.8, 30.0, 22.5, 14.0. Anal. Calcd for $C_{20}H_{24}O_4S$: C, 66.64; H, 6.71. Found: C, 66.87; H, 6.96.

Preparation of 8. A mixture of **4** (0.081 g, 0.22 mmol), imidazole (0.038 g, 0.56 mmol), and TBDMSCl (0.041 g, 0.27 mmol) in DMF (3 mL) was stirred for 24 h at 25 °C. Addition of another portion of imidazole (0.56 mmol) and TBDMSCl (0.27 mmol) in DMF (3 mL) together with additional stirring (24 h) at 25 °C was necessary for completion of the reaction. The reaction mixture was diluted with ether (100 mL), washed with brine (3 × 30 mL) and water (30 mL), dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography on Florisil to give 0.091 g (85%) of **8** as an yellow oil. **8**: ^{1}H NMR (60 MHz) δ 7.87–7.06 (m, 5H), 6.77 (d, J = 15.0 Hz, 1H), 6.22 (dd, J = 5.6, 15.0 Hz, 1H), 4.17 (br m, 1H), 3.96 (s, 2H) for CH_2SO_2, 2.63 (m, 2H), 2.14 (m, 2H), 1.70–1.00 (m, 8H), 1.04 (s, 9H), 0.95 (br, 3H), 0.0 (s, 6H).

General Procedure for Reaction of Sulfonyl Enones (4–7) with Stabilized Carbanions (9–11, $MeCHNO_2Li$, and Me_2CNO_2Li). To the carbanion (1.0–2.0 mmol) in DMF (3 mL) was added a DMF (3 mL) solution of the sulfonyl enone (1.0 mmol) at 25 °C. After being stirred at 25 °C for the stated period of time, the reaction mixture was partitioned between ether (30 mL) and water (30 mL), and the aqueous phase was extracted with ether (3 × 30 mL). The combined organic phase was washed with brine (3 × 30 mL) and water (30 mL), dried over $MgSO_4$, and concentrated in vacuo. The crude product obtained in this manner could be purified by column chromatography on Florisil. The diastereomeric ratio of **13** was determined to be 55/45 by HPLC analysis (9:1 n-hexane/2-propanol).

13 (86%): IR (neat) 1738, 1698, 1640, 1540, 1370 cm^{-1}; ^{1}H NMR δ 6.68 (d, J = 15.9 Hz, 1H), 6.34 (dd, J = 5.5, 15.9 Hz, 1H), 4.32 (br m, 1H), 3.67 (s, 3H), 3.00 (d, J = 13.7 Hz, 1H), for H-C(7), 2.86 (d, J = 13.7 Hz, 1H) for H-C(7), 2.72 (m, 2H), 2.46 (m, 2H), 2.31 (t, J = 7.6 Hz, 2H), 2.10 (m, 2H), 1.88-1.12 (m, 13H), 1.454 and 1.447 (s, 3H) for CH_3-C(6), 0.91 (t, J = 6.7 Hz, 3H); ^{13}C NMR δ 208.7, 173.8, 167.74 and 167.71, 142.70 and 142.67, 134.5, 122.77 and 122.74, 91.32 and 91.29, 72.0, 51.57 and 51.54, 39.21 and 39.09, 36.93 and 36.88, 33.58 and 33.51, 33.43 and 33.38, 31.7, 26.0, 25.0, 24.66 and 24.64, 23.5, 22.5, 21.50 and 21.48, 21.4, 14.0 Anal. Calcd for $C_{22}H_{35}NO_6$: C, 64.52; H, 8.61; N, 3.42. Found: C, 64.87; H, 8.43; N, 3.39.

14 (75%): IR (neat) 3480, 1740, 1700, 1642 cm^{-1}; ^{1}H NMR δ 6.84 (d, J = 15.6 Hz, 1H), 6.39 (dd, J = 5.5, 15.6 Hz, 1H), 4.37 (m, 1H), 3.76 (s, 6H), 3.72 (s, 3H), 2.99 (s, 2H) for CH_2(7), 2.73 (m, 2H), 2.44 (m, 2H), 2.37 (t, J = 7.3 Hz, 2H), 1.98 (br m, 1H), 1.78–1.21 (m, 14H), 0.95 (t, J = 6.4 Hz, 3H); ^{13}C NMR δ 208.7, 174.4, 171.5, 166.3, 142.1, 135.7, 123.0, 71.9, 57.2, 52.5, 52.3, 33.8, 31.7, 28.4, 26.8, 26.6, 25.7, 25.1, 25.0, 24.4, 23.9, 22.5, 14.0. Anal. Calcd for $C_{25}H_{38}O_8$: C, 64.36; H, 8.21. Found: C, 64.52; H, 7.99.

17 (65%): IR (neat) 1738, 1698, 1640, 1552, 1362 cm^{-1}; ^{1}H NMR δ 4.78 (m, 1H) for H-C(6), 3.67 (s, 3H), 2.82 (dd, J = 10.1, 13.7 Hz, 1H) for H-C(7), 2.55 (m, 2H), 2.42 (dd, J = 7.8, 13.7 Hz, 1H) for H-C(7), 2.38 (m, 2H), 2.31 (t, J = 7.4 Hz, 2H), 2.01 (m, 2H), 1.83–1.57 (m, 4H), 1.53–1.20 (m, 6H), 0.93 (t, J = 7.0 Hz, 3H); ^{13}C NMR δ 209.3, 178.3, 173.6, 134.1, 86.3, 51.6, 34.0, 33.63, 33.59, 30.8, 29.8, 29.5, 28.5, 25.3, 24.2, 22.8, 13.9. Anal. Calcd for $C_{17}H_{27}NO_5$: C, 62.75; H, 8.36; N, 4.30. Found: C, 63.10; H, 7.97; N, 4.44.

18 (95%): IR (neat) 1740, 1700, 1637, 1539, 1352 cm^{-1}; ^{1}H NMR δ 3.67 (s, 3H), 2.88 (d, J = 13.7 Hz, 1H) for H-C(7), 2.75 (d, J = 13.7 Hz, 1H) for H-C(7), 2.54 (m, 2H), 2.38 (m, 2H), 2.36–2.22 (m, 3H), 2.05 (m, 1H), 1.82–1.50 (m, 4H), 1.50–1.20 (m, 6H), 1.43 (s, 3H) for CH_3-C(6), 0.94 (t, J = 7.0 Hz, 3H); ^{13}C NMR δ 209.1, 179.4, 173.6, 134.2, 91.3, 51.5, 39.2, 33.8, 33.5, 31.0, 29.7, 29.2, 24.6, 24.2, 23.4, 22.7, 21.3, 13.8. Anal. Calcd for $C_{18}H_{29}NO_5$: C, 63.69; H, 8.61; N, 4.13. Found: C, 63.99; H, 8.25; N, 4.01.

19: IR (neat) 3400, 1705, 1540, 1375 cm^{-1}; ^{1}H NMR δ 6.40 (s, 1H) for HC≡C, 4.10 (t, J = 4.5 Hz, 1H), 2.89 (d, J = 14.1 Hz, 1H), 2.79 (d, J = 14.1 Hz, 1H), 2.63 (m, 2H), 2.46 (m, 2H), 1.80–1.47 (m, 3H), 1.73 (s, 3H), 1.72 (s, 3H), 1.59 (s, 3H), 1.50 (s, 3H), 1.45–1.27 (m, 6H), 0.91 (t, J = 6.7 Hz, 3H); ^{13}C NMR δ 207.4, 171.6, 145.3, 136.3, 124.0, 90.5, 87.7, 71.4, 38.1, 34.8, 33.6, 31.6, 30.9, 26.9, 26.73, 26.70, 26.0, 25.0, 22.6, 14.0. Anal. Calcd for $C_{19}H_{30}N_2O_6$: C, 59.67; H, 7.91; N, 7.32. Found: C, 60.01; H, 7.59; N, 7.44.

20 (63%): IR (neat) 1738, 1698, 1640, 1550, 1360 cm^{-1}; ^{1}H NMR δ 5.20 (d, J = 13.4 Hz, 1H) for OCHO, 5.18 (d, J = 13.4 Hz, 1H) for OCHO, 4.75 (m, 1H), for H-C(6), 3.67 (s, 3H), 3.51 (s, 3H), 2.87 (dd, J = 9.2, 14.0 Hz, 1H) for H-C(7), 2.75 (m, 2H), 2.54 (dd, J = 4.9, 14.0 Hz, 1H) for H-C(7), 2.48 (m, 2H), 2.31 (t, J = 7.5 Hz, 2H), 1.98 (m, 1H), 1.75 (m, 1H), 1.63 (m, 2H), 1.35 (m, 2H); ^{13}C NMR δ 204.3, 184.8, 173.7, 116.1, 94.2, 86.0, 57.2, 51.6, 33.6, 33.5, 33.3, 26.5, 25.3, 24.7, 24.2. Anal. Calcd for $C_{15}H_{23}NO_7$: C, 54.70; H, 7.04; N, 4.25. Found: C, 55.05; H, 6.83; N, 4.55.

21 (90%): IR (neat) 1740, 1697, 1632, 1540, 1357 cm^{-1}; ^{1}H NMR δ 5.17 (d, J = 11.8 Hz, 1H) for OCHO, 5.14 (d, J = 11.8 Hz, 1H) for OCHO, 3.66 (s, 3H), 3.51 (s, 3H), 2.84 (d, J = 14.4 Hz, 1H), 2.78 (m, 2H), 2.73 (d, J = 14.4 Hz, 1H), 2.49 (m, 2H), 2.37 (m, 1H), 2.32 (t, J = 7.2 Hz, 2H), 2.10 (m, 1H), 1.80–1.56 (m, 2H), 1.47 (s, 3H) for CH_3-C(6), 1.45–1.10 (m, 2H); ^{13}C NMR δ 204.2, 185.4, 173.8, 116.2, 94.2, 91.1, 57.3, 51.5, 38.9, 33.6, 33.4, 32.4, 24.8, 24.5, 23.5, 21.7. Anal. Calcd for $C_{16}H_{25}NO_7$: C, 55.95; H, 7.34; N, 4.08. Found: C, 56.33; H, 7.05; N, 4.45.

29: IR (neat) 3420, 1698, 1640, 1538, 1372 cm^{-1}; ^{1}H NMR δ 6.69 (d, J = 15.3 Hz, 1H), 6.33 (dd, J = 5.8, 15.3 Hz, 1H), 4.32 (br m, 1H), 2.95 (s, 2H), 2.72 (m, 2H), 2.47 (m, 2H), 2.08 (br m, 1H), 1.60 (m, 2H), 1.56 (s, 6H), 1.45–1.18 (m, 6H), 0.89 (t, J = 6.7 Hz, 3H); ^{13}C NMR 208.7, 167.7, 142.6, 134.7, 122.9, 88.3, 72.2, 36.9, 33.8, 33.5, 31.7, 26.0, 25.9, 25.0, 22.6, 14.0. Anal. Calcd for $C_{17}H_{27}NO_4$: C, 65.99; H, 8.80; N, 4.53. Found: C, 66.33; H, 8.88; N, 4.72.

Preparation of 24–26. A mixture of **20** or **21** (1.0 mmol) and concd HCl (2 drops) in MeOH (8 mL) was stirred for 5 min at 25 °C. After removal of MeOH in vacuo, the residue was dissolved in $CHCl_3$ (40 mL). The $CHCl_3$ solution was washed with water (2 × 20 mL), dried over $MgSO_4$, and concentrated in vacuo, giving the corresponding deprotected enone quantitatively.

To the enone dissolved in CH_2Cl_2 (5 mL) were added successively Et_3N (1.2 mmol) and Tf_2O (1.1. mmol) at 0 °C. After the mixture was stirred for 30 min at 0 °C, 5% $NaHCO_3$ solution (20 mL) was added. The aqueous mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phase was washed with water (10 mL), dried over $MgSO_4$, and concentrated in vacuo to produce the corresponding triflate as a brown oil. Without purification the triflate was dissolved in THF (8 mL) containing LiI (3.0 mmol). The solution was heated at reflux for 30 min and cooled. It was diluted with CH_2Cl_2 (50 mL), washed with water (2 × 20 mL) and brine (20 mL), dried over $MgSO_4$, and concentrated in vacuo to give the crude **22** or **23** as a red brown oil almost quantitatively.

A mixture of the crude **22** (ca. 1 mmol), $Bu_3SnCH{=}CHCH(OH)(CH_2)_4Me$ (1.2 mmol), and $PdCl_2(CH_3CN)_2$ (0.05 mmol) in DMF (6 mL) was stirred for 3 h at 25 °C. Saturated NH_4Cl solution (30 mL) was added. The aqueous mixture was extracted with ether (3 × 30 mL). The combined organic phase was washed with brine (3 × 30 mL) and water (30 mL), dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography on Florisil to give 0.300 g (76%) of **24** as an orange oil. The diastereomeric ratio was determined to be 54/46 by HPLC analysis (9:1 n-hexane/2-propanol).

24: IR (neat) 3420, 1740, 1698, 1642, 1552, 1360 cm^{-1}; ^{1}H NMR δ 6.75 (dd, J = 4.0, 15.6 Hz, 1H), 6.34 (dd, J = 5.8, 15.6 Hz, 1H), 4.75 and 4.33 (m, 1H) for H-C(6), 3.67 (s, 3H), 2.96 (dd, J = 9.8, 14.0 Hz, 1H) for H-C(7), 2.70 (m, 3H), 2.45 (m, 2H), 2.31 (t, J = 7.3 Hz, 2H), 2.00 and 1.78 (m, 2H), 1.62 (m, 4H), 1.33 (m, 8H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR δ 208.7, 173.7, 166.8, 142.7, 134.3, 122.49 and 122.46, 86.1, 72.11 and 72.07, 51.60 and 51.57, 37.0, 33.54 and 33.51, 31.7, 27.8, 26.8, 26.0, 24.97 and 24.95, 24.1, 22.5, 17.5, 13.98 and 13.96, 13.56. Anal. Calcd for $C_{21}H_{33}NO_6$: C, 63.78; H, 8.41; N, 3.54. Found: C, 64.03; H, 8.24; N, 3.92.

A mixture of the crude **23** or **24** (ca. 1 mmol), 1-octyn-3-ol (1.5 mmol), Et_3N (1.0 mmol), $PdCl_2(PPh_3)_2$ (0.05 mmol), and CuI (0.10 mmol) in DMF (10 mL) was stirred for 24 h at 25 °C. Saturated NH_4Cl solution (30 mL) was added. The aqueous mixture was extracted with ether (3 × 30 mL). The combined organic phase was washed with brine (3 × 30 mL) and water (2 × 30 mL), dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography on Florisil to give **25** or **26** as an orange oil. The diastereomeric ratio of **26** was determined to be 61/39 by HPLC analysis (9:1 n-hexane/2-propanol).

25 (50% from **20**): IR (neat) 3420, 2215, 1740, 1703, 1619, 1557, 1352 cm^{-1}; ^{1}H NMR δ 4.78 (m, 1H) for H-C(6), 4.63 (t, J

= 6.1 Hz, 1H), 3.67 (s, 3H), 3.00 (dd, J = 9.1, 14.3 Hz, 1H) for H-C(7), 2.72 (dd, J = 4.9, 14.3 Hz, 1H) for H-C(7), 2.67 (m, 2H), 2.46 (m, 2H), 2.32 (t, J = 7.3 Hz, 2H), 2.17 (s, 1H), 2.00 (m, 2H), 1.86–1.12 (m, 12H), 0.92 (t, J = 7.0 Hz, 3H); ^{13}C NMR δ 207.7, 173.8, 153.2, 142.27 and 142.23, 108.6, 85.5, 65.9, 62.9, 51.64 and 51.60, 37.2, 33.9, 33.52 and 33.46, 33.2, 31.4, 30.5, 29.69 and 29.64, 29.2, 25.1, 24.1, 22.5, 14.0. Anal. Calcd for $C_{21}H_{31}NO_6$: C, 64.10; H, 7.94; N, 3.56. Found: C, 63.78; H, 8.25; H, 3.33.

26 (63% from **21**): IR (neat) 3400, 2210, 1738, 1702, 1540, 1354 cm^{-1}; ^1H NMR δ 4.59 (br m, 1H), 4.43 (br m, 1H), 3.67 (s, 3H), 3.02 (d, J = 13.7 Hz, 1H) for H-C(7), 2.88 (d, J = 13.7 Hz, 1H) for H-C(7), 2.68 (m, 2H), 2.46 (m, 2H), 2.32 (t, J = 7.3 Hz, 2H), 2.19–2.02 (m, 2H), 1.84–1.20 (m, 13H), 1.71 and 1.46 (s, 3H) for CH_3-C(6), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C NMR δ 207.8, 173.8, 154.2, 142.35 and 142.34, 108.3, 90.68 and 90.64, 80.50, 62.87 and 62.83, 51.6, 39.0, 37.4, 37.12 and 37.10, 33.7, 33.6, 31.38 and 31.37, 30.5, 24.8, 24.7, 23.4, 22.54 and 22.50, 21.5, 14.0. Anal. Calcd for $C_{22}H_{33}NO_6$: C, 64.84; H, 8.16; N, 3.44. Found: C, 65.11; H, 7.88; N, 3.40.

General Procedure for Reaction of Sulfonyl Enones (4 and 6) with Sulfur Nucleophiles (12 and PhSNa). To the sulfonyl enone (1.0 mmol) in DMF (25 mL) was added dropwise a DMF (25 mL) solution of the sulfur nucleophile over 30 min at 25 °C. The reaction mixture was stirred for 1 h at 25 °C, and then saturated NH_4Cl solution (100 mL) was added. The aqueous mixture was extracted with ether (3 × 30 mL). The combined organic phase was washed with brine (3 × 30 mL) and water (2 × 30 mL), dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography on Florisil to give a pale yellow oil.

27: IR (neat) 3420, 1740, 1688, 1638, 1598 cm^{-1}; ^1H NMR δ 6.90 (d, J = 15.3 Hz, 1H), 6.35 (dd, J = 5.5, 15.3 Hz, 1H), 4.36 (m, 1H), 3.67 (s, 3H), 3.37 (s, 2H) for CH_2(7), 2.71 (m, 2H), 2.52–2.38 (m, 4H), 2.33 (t, J = 6.6 Hz, 2H), 1.78–1.54 (m, 5H), 1.5–1.2 (m, 8H), 0.90 (t, J = 6.7 Hz, 3H); ^{13}C NMR δ 208.0, 174.1, 164.8, 142.0, 137.3, 123.1, 72.0, 51.5, 37.1, 33.6, 33.5, 31.8, 31.7, 28.9, 25.7, 25.0, 24.1, 22.6, 22.5, 14.0. Anal. Calcd for $C_{20}H_{32}O_4S$: C, 65.18; H, 8.75. Found: C, 65.45; H, 8.39.

28: IR (neat) 3420, 1683, 1640, 1598 cm^{-1}: ^1H NMR δ 7.43–7.18 (m, 5H), 6.48 (d, J = 15.6 Hz, 1H), 6.20 (dd, J = 5.8, 15.6 Hz, 1H), 4.18 (m, 1H), 3.74 (s, 2H) for CH_2SPh, 2.65 (m, 2H), 2.45 (m, 2H), 1.8–1.2 (m, 9H), 0.92 (t, J = 6.7 Hz, 3H); ^{13}C NMR δ 207.5, 165.4, 141.5, 136.1, 135.7, 132.0, 128.8, 127.0, 123.1, 72.2, 37.0, 33.6, 31.7, 26.7, 25.6, 25.0, 22.5, 14.0. Anal. Calcd for $C_{20}H_{26}O_2S$: C, 72.69; H, 7.93. Found: C, 73.01; H, 7.55.

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