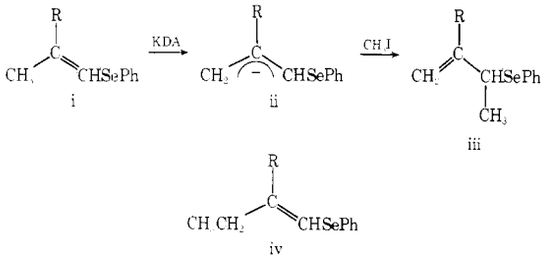
and H. Niederprum, *Chem. Ber.*, **94**, 1540 (1961); (b) G. Stork, J. O. Gardner, R. K. Boeckman, Jr., and K. A. Parker, *J. Am. Chem. Soc.*, **95**, 2014 (1973); (c) C. A. Brown, *J. Org. Chem.*, **39**, 3913 (1974); (d) C. A. Brown, *Synthesis*, 427 (1974).

(5) (a) Reaction of 2-methyl-1-(phenylseleno)alkenes (i, R = H or CH_3) with KDA leads to allylic deprotonation rather than α-deprotonation; the resulting selenium-stabilized allyl carbanions (ii) react with methyl iodide to give mixtures (4:1) of α and γ alkylation products, iii and iv, respectively.



(b) For the formation and alkylation of selenium-stabilized allyl carbanions from the corresponding allyl phenylselenides, see: H. J. Reich, *J. Org. Chem.*, **40**, 2570 (1975).

(6) 1-(Phenylseleno)alkenes are easily prepared from the corresponding alkenes: S. Raucher, *J. Org. Chem.*, **42**, 2950 (1977).

(7) Attempts to deprotonate **1** with alkyllithiums led to other reactions,[8] including carbon–selenium bond cleavage: H. Gilman and F. J. Webb, *J. Am. Chem. Soc.*, **71**, 4062 (1949).

(8) S. Raucher and G. A. Koolpe, submitted for publication.

(9) The ability of KDA to deprotonate weakly acidic compounds that are uneffected by LDA is undoubtedly a *kinetic* rather than a *thermodynamic* effect; thus, quantitative deprotonation of compounds which are intrinsically less acidic than diisopropylamine under equilibrium conditions should not be expected. Attempts to deprotonate 1-butyl phenyl selenide with KDA (THF, −78 °C, 30 min; or hexane, 0 °C, 4 h) were unsuccessful.

(10) (a) L. Lochmann, J. Pospisil, and D. Lim, *Tetrahedron Lett.*, 257 (1966); (b) M. Schlosser and J. Hartmann, *Angew. Chem., Int. Ed. Engl.*, **12**, 508 (1973); (c) M. Schlosser, *J. Organomet. Chem.*, **8**, 9 (1967). See also: (d) E. Weiss and G. Sauerman, *Chem. Ber.*, **103**, 265 (1970); (e) G. Thirase and E. Weiss, *J. Organomet. Chem.*, **81**, C1 (1974).

(11) L. Lochmann and D. Lim, *J. Organomet. Chem.*, **28**, 153 (1971).

(12) (a) Potassium diisopropylamide–lithium *tert*-butoxide is stable in hexane at 0 °C for at least 1 h; KDA decomposes rapidly at 0 °C in THF. (b) After the initial portion of this research was completed, Professor D. Seebach informed us that he has utilized potassium diisopropylamide–lithium *tert*-butoxide, prepared in a similar manner, for the deprotonation of nitrosamines.

(13) Formation of $PhSe^-$, presumably by α-elimination, occurs to some extent at −78 °C if the carbanions are not utilized immediately.

(14) (a) A typical experimental procedure for the synthesis of **2a** follows. To a solution of potassium *tert*-butoxide (168 mg, 1.50 mmol) and diisopropylamine (152 mg, 1.50 mmol) in THF (4 mL) cooled to −78 °C under an atmosphere of argon was added *n*-butyllithium in hexane (2.4 M, 0.50 mL, 1.2 mmol) over 30 s. The mixture was stirred for 10 min at −78 °C, and a solution of (phenylseleno)ethene (183 mg, 1.00 mmol) in THF (1.5 mL) was added over 1 min. The reaction mixture was stirred at −78 °C for 1 min,[13] a solution of methyl iodide (213 mg, 1.50 mmol) in THF (0.5 mL) was added over 5 s, and stirring at −78 °C was continued for 10 min. The reaction was quenched with methanol (0.5 mL) and poured into saturated aqueous NH_4Cl (4 mL), the THF was removed in vacuo, and the residue was extracted with hexane. Evaporation of the hexane, and purification by evaporative distillation (85 °C, 0.5 mm) gave 2-(phenylseleno)propene (194 mg, 98%): ^1H NMR (CCl_4) δ 2.07 (d, J = 1 Hz, 3 H), 5.08 (s, 1 H), 5.43 (q, J = 1 Hz, 1 H), 7.2–7.7 (m, 5 H). (b) All new compounds were fully characterized by spectroscopic methods. Yields are given for isolated, purified compounds. (c) Additional data: Anal. $C_9H_{10}Se$ (**2a**) *m/e* calcd 197.9948, found 197.9940; $C_{15}H_{22}OSe$ (**2l**) *m/e* calcd 298.0836, found 298.0824; $C_{10}H_{12}OSe$ (**2j**) *m/e* calcd 228.0053, found 228.0066.

(15) (a) Hydrolyzed with $HgCl_2$ in CH_3CN/H_2O: E. J. Corey and J. I. Shulman, *J. Org. Chem.*, **35**, 777 (1970); (b) N. Petragnani, R. Rodrigues, and J. V. Comasseto, *J. Organomet. Chem.*, **114**, 281 (1976).

(16) (a) It is possible to deprotonate the more acidic $(PhSe)_2CH_2$ with LDA in THF at −30 °C. We have successfully alkylated the resulting carbanion with methyl iodide (98% yield), *n*-decyl bromide (95% yield), and benzyl bromide (92%) yield). It is noteworthy that $(PhSe)_2CH_2$ undergoes no detectable dialkylation even in the presence of excess LDA and alkylating agent. (b) Deprotonation of $(PhSe)_2CH_2$ with lithium diisobutylamide in THF at −78 °C, and subsequent reaction with benzophenone, methyl iodide, and D_2O has been reported: D. Seebach and N. Peleties, *Angew. Chem., Int. Ed. Engl.*, **8**, 450 (1969); D. Seebach and N. Peleties, *Chem. Ber.*, **105**, 511 (1972).

(17) Bis(phenylseleno) acetals are available either from the corresponding aldehydes and selenophenol–zinc chloride, or by the alkylation of bis(phenylseleno)methane: (a) W. Dumont and A. Krief, *Angew. Chem., Int. Ed. Engl.*, **16**, 540 (1977), and references cited therein; (b) ref 16.

(18) (a) A typical experimental procedure for the synthesis of **4e** follows. To a suspension of KDA prepared as above[14a] was added a solution of 1,1-bis(phenylseleno)ethane (340 mg, 1.00 mmol) in THF (1.5 mL) over 2 min. After 10 min at −78 °C, a solution of benzyl bromide (180 mg, 1.05 mmol) in THF (1.5 mL) was added over 15 s, and stirring at −78 °C was continued for 15 min. The reaction was quenched with methanol (0.5 mL) and poured into saturated aqueous NH_4Cl (4 mL), the THF was removed in vacuo, and the residue was extracted with hexane. Evaporation of the hexane gave a white solid which was crystallized from methanol to yield 1-phenyl-2,2-bis(phenylseleno)propane (**4e**): 380 mg (88%); mp 109–110 °C; ^1H NMR ($CDCl_3$) δ 1.48 (s, 3 H), 3.27 (s, 2 H), 7.0–7.8 (m, 15 H). (b) All new compounds were fully characterized by spectroscopic methods. Yields are given for chromatographically pure, isolated products. (c) Additional data: Anal. $C_{21}H_{20}Se_2$ (**4e**) *m/e* calcd 429.9903, found 429.9896; $C_{17}H_{20}OSe_2$ (**4h**) *m/e* calcd 397.9852, found 397.9902.

(19) For example, see: (a) ref 16; (b) D. Seebach and A. K. Beck, *Angew. Chem., Int. Ed. Engl.*, **13**, 806 (1974); (c) W. Dumont, P. Bayet, and A. Krief, *ibid.*, **13**, 804 (1974); (d) W. Dumont and A. Krief, *ibid.*, **14**, 350 (1975); (e) W. Dumont and A. Krief, *ibid.*, **15**, 161 (1976); (f) A. Anciaux, A. Eman, W. Dumont, D. Van Ende, and A. Krief, *Tetrahedron Lett.*, 1613 (1975); (g) A. Anciaux, A. Eman, W. Dumont, and A. Krief, *ibid.*, 1617 (1975); (h) J. N. Denis, W. Dumont, and A. Krief, *ibid.*, 453 (1976); (i) J. Remion, W. Dumont, and A. Krief, *ibid.*, 1385 (1976); (j) M. Sevrin, D. Van Ende, and A. Krief, *ibid.*, 2643 (1976).

(20) (a) T. Mukaiyama, K. Narasaka, and M. Furusato, *J. Am. Chem. Soc.*, **94**, 8641 (1972); (b) T. Mukaiyama, K. Narasaka, K. Maekawa, and M. Furusato, *Bull. Chem. Soc. Jpn.*, **44**, 2285 (1971).

(21) **Note Added in Proof:** Professor Seebach's research involving KDA has now been published: B. Renger, H. Hugel, W. Wykypiel, and D. Seebach, *Chem. Ber.*, **111**, 2630 (1978).

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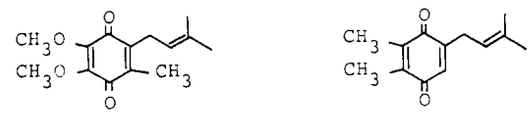
Allylation of Quinones with Allyltin Reagents. New Synthesis of Coenzyme Q_1 and Plastquinone-1[1]

Summary: Lewis-acid catalyzed allylation of *p*-benzoquinone with allyltributyltins is examined; coenzyme Q_1 and plastquinone-1 are prepared in good yields.

Sir: Prenylated quinones, which are widely distributed in nature, play an important role in the life of living things, e.g., in electron transport, oxidative phosphorylation, and blood clotting.[2] Regiospecific and direct introduction of the prenyl group into a quinone ring has been a challenging subject for organic chemists. So far, the direct introduction of an allyl or prenyl group into the quinone ring has met limited success,[4] though the successful allylation of protected quinones has been attained.[3]

In this communication, we wish to report on the successful direct introduction of the prenyl group into the quinone ring using allyltributyltin reagent. With our procedure regiospecific synthesis of coenzyme Q_1 (**4**) and plastquinone-1 (**5**) was



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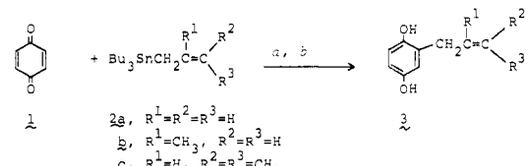
successfully accomplished. Typically the reaction was carried out by dropwise addition of an allyltributyltin (**2**) (2 mmol) to a dichloromethane solution (10 mL) of quinone (**1**) (1 mmol) and $BF_3{\cdot}OEt_2$ (1 mmol) under N_2 at −78 °C. After addition was completed, the temperature of the reaction mixture was

Scheme I



1 3

2a, $R^1=R^2=R^3=H$
b, $R^1=CH_3$, $R^2=R^3=H$
c, $R^1=H$, $R^2=R^3=CH_3$
d, $R^1=H$, $R^2=cis$-CH_3 a, $BF_3{\cdot}OEt_2$, CH_2Cl_2, −78°C
$R^3=trans$-$CH_2CH_2CH{=}CMe_2$ b, 2N-HCl

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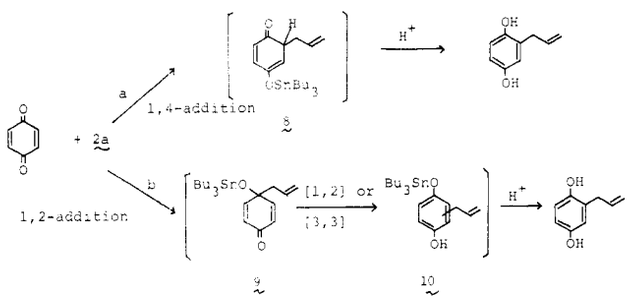
Table I. Allylation of Quinones with Allyltributyltin

quinone	allyltin	product[a]	% yield[b]
p-benzoquinone	**2a**	allylbenzoquinone[c]	66 (85)
p-benzoquinone	**2b**	(2-methyl-2-propenyl)benzoquinone[c]	45
p-benzoquinone	**2c**	(3-methyl-2-butenyl)benzoquinone[c]	55
p-benzoquinone	**2d**	geranylbenzoquinone[c,d]	58
2,3-dimethylbenzoquinone	**2a**	5-allyl-2,3-dimethylhydroquinone	72
2,3-dimethylbenzoquinone	**2c**	2,3-dimethyl-5-(3-methyl-2-butenyl)hydroquinone	61
2,5-dimethylbenzoquinone	**2a**	3-allyl-2,5-dimethylhydroquinone	90
2,5-dimethylbenzoquinone	**2c**	2,5-dimethyl-3-(3-methyl-2-butenyl)hydroquinone	69
2,6-dimethylbenzoquinone	**2a**	3-allyl-2,6-dimethylhydroquinone	82
2,6-dimethylbenzoquinone	**2c**	2,6-dimethyl-3-(3-methyl-2-butenyl)hydroquinone	70
trimethylbenzoquinone	**2a**	allyltrimethylhydroquinone	37
trimethylbenzoquinone	**2c**	trimethyl(3-methyl-2-butenyl)hydroquinone	35
2,5-di-*tert*-butylbenzoquinone	**2a**	2-allyl-6-*tert*-butylhydroquinone	36
2,3-dimethoxy-5-methylbenzoquinone	**2a**	2-allyl-5,6-dimethoxy-2-methylbenzoquinone[c]	61
2,3-dimethoxy-5-methylbenzoquinone	**2c**	coenzyme Q_1 (**4**)[c]	75
1,4-naphthoquinone	**2a**	2-allyl-1,4-naphthoquinone[c]	42
2-methoxy-1,4-naphthoquinone	**2a**	1-allyl-1-hydroxy-5-methoxy-4-naphthalenone (**6**)	90
2,6-dimethoxybenzoquinone	**2a**	4-allyl-4-hydroxy-3,5-dimethoxycyclohexan-2,5-dien-1-one (**7**)	52

[a] Characterized by infrared, NMR, and mass spectra, and elemental analysis. [b] Yield in parentheses determined by GLC; all others are of purified products after isolation based on quinone. [c] Products after oxidation with silver oxide or ferric chloride. [d] Stereochemistry at Δ^2, cis/trans 7:93.

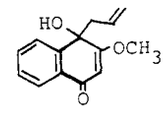
Scheme II



gradually elevated to room temperature within 1 h. The reaction was quenched by the addition of 2 N hydrochloric acid and crude products were extracted with ether. The ethereal extract was usually worked up and precipitated allylhydroquinone was purified by recrystallization from ether–hexane. In the cases of air-sensitive allylhydroquinones, the ethereal extract was immediately treated with an amount of ferric chloride solution to give allylated quinones, which were purified by preparative thin-layer chromatography on silica gel (developing solvent: 4:1 hexane–ether mixture). The products and their yields are summarized in the Table I.

The yield of the present allylations is high and the generality is obvious. The characteristics of our reaction are: (i) allylation occurs at the nonsubstituted site of the quinone ring with the exception of 2,5-di-*tert*-butylbenzoquinone; (ii) the prenyl group is introduced into the quinone ring without allylic isomerization; and (iii) the fair yields (61–90%) are not affected by the presence of two methyl groups on the quinone ring, but the allylations of trimethylbenzoquinone using **2a** and **2c** give rather unsatisfactory yields (35–37%). When our procedure was applied to the synthesis of coenzyme Q_1 and plastquinone-1, the attained yields reached to 75 and 61%,[6] respectively. Hitherto coenzyme Q_1 was prepared from 2,3-dimethoxy-5-methylbenzoquinone with the use of π-allylnickel complex, but in an unsatisfactory yield (26%) with lack of regioselectivity.[4c,7] Coupling reactions between the π-allylnickel complex and the protected quinone have also been reported to yield coenzyme Q_1 in an overall yield of ~20% via eight steps.[3b] In contrast, our procedure gives a single product in a fairly high yield accompanied by no regioisomers, and excludes several disadvantages observed in other allylations of quinones.[8]

Though the mechanism of the present allylation remains to be clarified, the present results are reasonably explained by either of two possible routes (paths a and b, see Scheme II). However, path a seems to be less probable, for in the allylation of 1,3-diphenyl-2-propen-1-one 3-methyl-2-butenyltributyltin (**2c**) adds to it to give 4,4-dimethyl-1,4-diphenyl-5-hexen-1-one.[9] In addition, the allylation of 2-methoxynaphthoquinone and 2,6-dimethoxybenzoquinone gives stable quinols, **6** and **7**, which also supports the path a.



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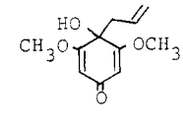

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Together with its easy accessibility,[5] allyltin reagents are a promising allylating reagent of the quinone ring.[10,11] The scope and the detailed mechanism of the reaction are under investigation.

References and Notes

(1) Synthesis of Naturally Occurring Quinones. Part 3. Part 2: K. Maruyama and Y. Naruta, *Chem. Lett.*, 431 (1978).
(2) For an excellent review of quinones and their chemistry see: (a) R. A. Morton, Ed., "Biochemistry of Quinones", Academic Press, New York, N.Y., 1965; (b) R. H. Thomson, "Naturally Occurring Quinones", 2nd ed, Academic Press, New York, N.Y., 1971; (c) S. Patai, Ed., "The Chemistry of the Quinonoid Compounds", Parts 1 and 2, Wiley, New York, N.Y., 1974.
(3) (a) K. Sato, S. Inoue, and K. Saito, *J. Chem. Soc., Chem. Commun.*, 953 (1972); (b) K. Sato, S. Inoue, and R. Yamaguchi, *J. Org. Chem.*, **37**, 1889 (1972); (c) K. Sato, S. Inoue, and K. Saito, *J. Chem. Soc., Perkin Trans. 1*, 2289 (1973); (d) S. Inoue, R. Yamagami, and K. Sato, *Bull. Chem. Soc. Jpn.*, **47**, 3098 (1974); (e) C. D. Snyder and H. Rapoport, *J. Am. Chem. Soc.*, **96**, 8046 (1974); (f) D. A. Evans and J. M. Hoffman, *ibid.*, **98**, 1983 (1976); (g) R. W. Raynolds, M. J. Manning, and J. W. Swenton, *J. Chem. Soc., Chem. Commun.* 499 (1977).
(4) (a) L. F. Fieser, *J. Am. Chem. Soc.*, **61**, 2559, 3467 (1939); (b) L. S. Hegedus, E. L. Waterman, and J. Catlin, *ibid.*, **94**, 7155 (1972); (c) L. S. Hegedus, B. R. Evans, D. E. Korte, E. L. Waterman, and K. Schöberg, *ibid.*, **98**, 3901 (1976); (d) A. Hosomi and H. Sakurai, *Tetrahedron Lett.*, 4041 (1977); (e) I. Tabushi, K. Fujita, and H. Kawakubo, *J. Am. Chem. Soc.*, **99**, 6456 (1977).
(5) Allyltributyltin (**2a**) and 2-methyl-2-propenyltributyltin (**2b**) were prepared according to the literature (ref 10d). 3-Methyl-2-butenyltributyltin (**2c**) and geranyltributyltin (**2d**) were prepared by the coupling of tributyltinlithium in THF with prenyl chloride and geranyl chloride, respectively, at −50 °C to room temperature: cf. E. Matarasso-Tchiroukhine and P. Cadiot, *J. Organomet. Chem.*, **121**, 155 (1976).
(6) Using the general oxidant, Ag_2O or $FeCl_3$, plasthydroquinone-1 was quantitatively converted to plastquinone-1.
(7) In their first communication, Hegedus et al. reported the 30% yield of

coenzyme Q_1 without comments on the formation of regioisomers, using 4 equiv of π-allylnickel complex to 1 equiv of the quinone (see ref 4b).

(8) In other allylations of quinones polyalkylation, chromanol formation, side-chain cyclization, and other numerous difficulties concerned with product isolations are often observed: D. E. Wolf, C. H. Hoffman, N. R. Trenner, B. H. Arison, C. H. Shunk, B. O. Lin, J. F. McPherson, and K. Folkers, *J. Am. Chem. Soc.*, **80**, 4752 (1958); U. Gloor, O. Isler, R. A. Morton, R. Rüegg, and O. Wiss, *Helv. Chim. Acta*, **41**, 2357 (1958).

(9) Under the similar conditions to that of quinones, the α,β-unsaturated ketone gave the usual 1,4-conjugate addition product with allyltin.

(10) In addition, using BF_3·OEt_2 as activator of carbonyl, our reaction proceeds under mild conditions in contrast to the usual insertion reaction of the carbonyl group (ketone or aldehyde) into the allyltin Sn–C bond. Without BF_3·OEt_2 the usual reaction is limited to polarized carbonyls attached to electron-withdrawing groups or needed higher reaction temperature: (a) K. König and W. P. Neumann, *Tetrahedron Lett.*, 495 (1967); (b) C. Servans and M. Pereyre, *J. Organomet. Chem.*, **26**, C4 (1971); (c) *Ibid.*, **35**, C20 (1972); (d) E. A. Abel and R. J. Rowley, *Ibid.*, **84**, 199 (1975).

(11) Allylations using other allylating reagents such as allylsilane[4d] and π-allylnickel complex[4b,c] have been reported [see also Hegedus et al., *J. Am. Chem. Soc.*, **100**, 3461 (1978)]. However, coenzyme Q_1 was first prepared in a satisfactory yield by our procedure.

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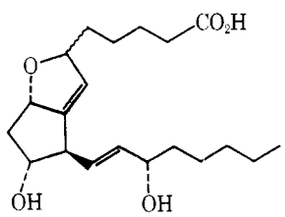
Synthesis of (6*R*)- and (6*S*)-6(9)-Oxy-11,15-dihydroxyprosta-7,13-dienoic Acids [(6*R*)- and (6*S*)-Δ⁷-PGI_1]: Nonidentity with the Proposed Arachidonic Acid Metabolite

Summary: This report describes the chemical synthesis of (6*R*)- and (6S)-Δ⁷-PGI_1; the spectral properties of the synthetic material were entirely different from those reported by Pace-Asciak and Wolfe for their proposed biosynthetic arachidonic acid metabolite.

Sir: In 1971, Pace-Asciak and Wolfe[1] reported the formation of two novel prostanoic acid derivatives during the incubation of arachidonic acid with rat stomach homogenates. The structure of the major component was assigned as 6(9)-oxy-11,15-dihydroxyprosta-7,13-dienoic acid (**1**) and the minor component as 6(9)-oxy-11,15-dihydroxyprosta-5,13-dienoic acid (**2**). The structural assignments of **1** and **2**[2] were based



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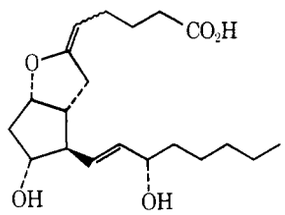

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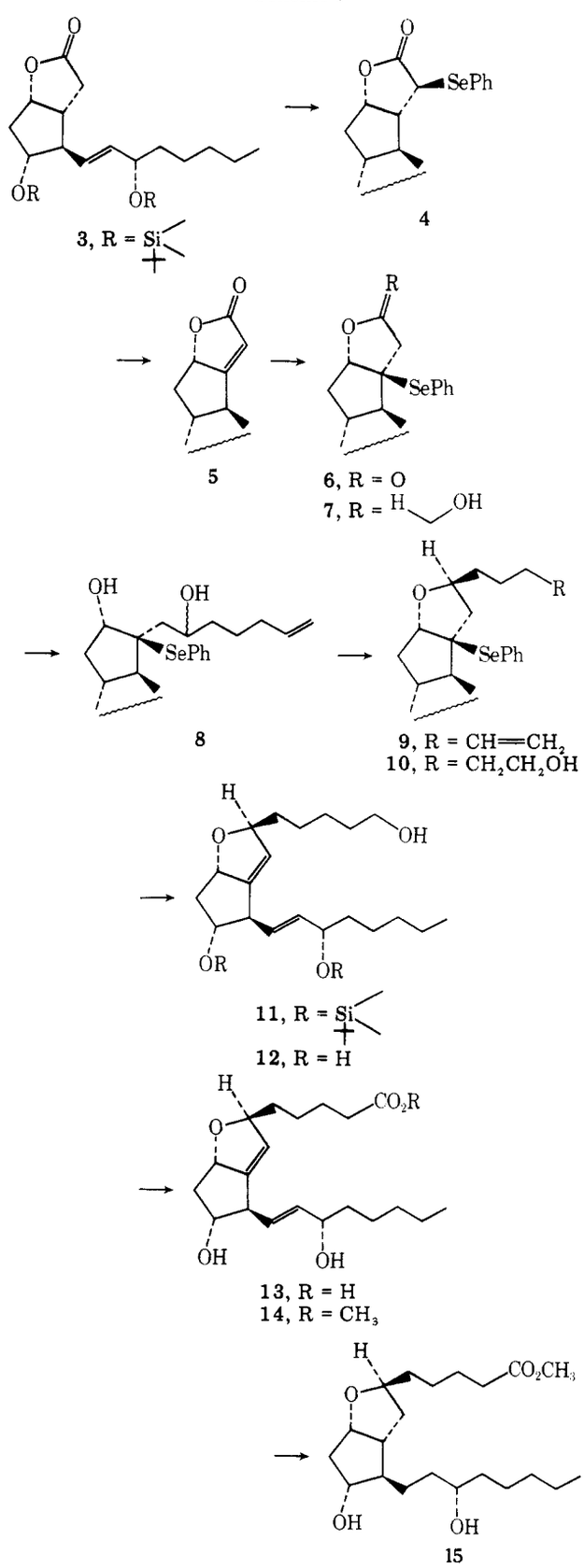
on mass spectrometric evidence and products derived from oxidative ozonolysis. The recent discovery[3] of prostacyclin (PGI_2), the 5*Z* isomer of **2**,[4-6] has revived interest in this area of prostaglandin research.[7-9] In view of the finding that PGI_2 is rapidly hydrolyzed to 6-oxoprostaglandin $F_1\alpha$ at pH's as high as 7.6,[4] the isolation of **2** under the acidic conditions employed[1] must be regarded as unlikely. However, the existence of a structurally related 6(9)-oxy-11,15-dihydroxyprosta-7,13-dienoic acid (**1**, Δ⁷-PGI_1) cannot be excluded on this basis. In this communication we describe a chemical synthesis of (6*R*)- and (6*S*)-Δ⁷-PGI_1 and compare the nuclear magnetic resonance and mass spectrometric properties of our synthetic material to those reported by Pace-Asciak and Wolfe for their alleged biosynthetic metabolite.

Reaction of the 11,15-bis(dimethyl-*tert*-butylsilyl) lactone **3** in tetrahydrofuran (THF) with 1.1 equiv of lithium diisopropylamide (−78 °C, 15 min) and treatment of the resulting enolate with 1.3 equiv of PhSeCl for 20 min at −78 °C afforded the 7-phenylselenenyl lactone **4** in 90% yield (Scheme I).[10] Exposure of lactone **4** in CH_2Cl_2 to 10% aqueous H_2O_2 (10 equiv, room temperature for 1 h) gave via phenyl selenoxide elimination the α,β-unsaturated lactone **5** [mp 36.5–38 °C; UV

Scheme I



3, R = Si(+)
4
5
6, R = O
7, R = H, OH
8
9, R = CH=CH₂
10, R = CH₂CH₂OH
11, R = Si(+)
12, R = H
13, R = H
14, R = CH₃
15

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