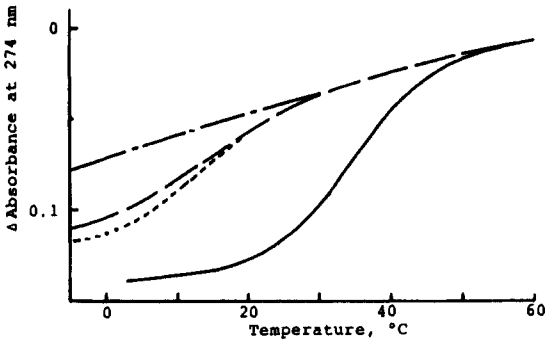

Figure 1. Melting profiles of platinated Duplexes 1-4 at 274 nm with 5.7 μM duplex concentration in 10 mM sodium phosphate buffer (pH 7) containing 0.5 M NaCl: Duplex 1 (—), Duplex 2 (---), Duplex 3 (--), Duplex 4 (---).

with the mismatch at the 5'-coordinated site with and without platination. (The T_m lowering of the platinated duplex by G-T mismatch was slightly larger than that of the nonplatinated one.)

5'-ACTCGGCTCA-3'
3'-TGAGXCGAGT-5'

X = C, T, A, G

Table I shows the T_m values of the modified and unmodified duplexes. Under a high salt condition, the decrease in the T_m of Duplex 1 by platination was 21.2 °C at pH 7,[21] which is consistent with earlier observations.[7,8] For the noncoordinated duplexes, the T_m was lowered by base substitution in the order C > T > A > G.[21] The reduction of the T_m of unplatinated Duplex 1 by the G-T mismatch was 14.1 °C and that by the G-G mismatch 23.3 °C. The destabilizing effect of the decanucleotide duplexes by platination was larger than that of the single base pair mismatches (except for the G-G mismatch), and thus the reduction of the T_m of the platinated duplexes was not due only to the alteration of the base pairing ability of the coordinated guanine residue. The extent of the T_m lowering of the platinated duplexes by base substitution was comparable with (slightly larger than) that of the unplatinated duplexes containing the corresponding base pair mismatch. The reduction of T_m by platination would not be attributable to alteration of the base pairing ability of the coordinated guanine.

Under basic conditions (pH 9), the T_m of Duplex 1 slightly decreased, regardless of platination of the duplex. The mismatched duplexes also showed the same behavior. Independent of pH, the order of stability of the platinated duplexes by the base substitution was C > T > A > G (Figure 1, Table I), the same as that of the unplatinated duplexes. Thus, effective G-T or G-G base pairing at the platination site does not occur even at pH above the pK of the platinated guanine. These G-X mismatches (X = T, A, G) showed weaker base pairing.[23] It thus appears quite likely that the base pairing selectivity of the guanine residue in the oligonucleotides is not altered by platination at the N(7) site. In addition, the results mentioned above were reproduced at more physiological conditions (Table I, 0.1 M NaCl).

It is still uncertain what decreases the stability of platinated duplexes. Table I shows the hypochromicity of each case in parentheses. At pH 7, the T_m of platinated Duplex 1 was slightly higher than that of unplatinated Duplex 4. However, the hypochromicity of the former case was even less than that of the latter case, independent of salt concentration. The base stacking disruption by platination is thus suggested and this may support the kinked cDDP-DNA structure models.[10]

In conclusion, our results suggest that cDDP coordination of N(7) of two adjascent guanines in the oligonucleotides hardly affects the base pairing ability or selectivity. The mutagenicity of cDDP may depend not on alteration of the above features of coordinated guanines but on a kinked structure or an unusual conformational feature[22] of cDDP-DNA complexes.

(21) The destabilization of the duplex structure may be attributed to stabilization of the single strand form by platination.[22] If it does so, this effect acts equally on Duplex 1-4, and therefore, the T_m of these duplexes should reflect the relative strength of the hydrogen bond of the coordinated guanines. At least the upper single strand decamer did not show the sigmoidal transition in UV vs temperature profiles, regardless of platination.

(22) Kline, T. P.; Marzilli, L. G.; Live, D.; Zon, G. *J. Am. Chem. Soc.* **1989**, *111*, 7057-7068.

(23) Ikuta, S.; Takagi, K.; Wallace, R. B.; Itakura, K. *Nucl. Acids Res.* **1987**, *15*, 797-811.

Stannylquinones. Synthesis and Utilization as Quinone Carbanion Synthetic Equivalents

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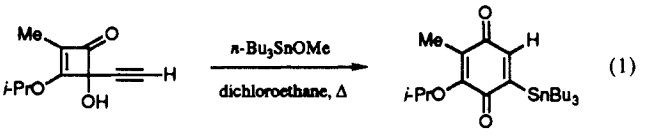
During the course of a search for effective catalysts for the metal-mediated ring expansion of 4-alkynyl-4-hydroxycyclobutenones,[2-5] an unexpected yellow-orange product was obtained in 44% yield (unoptimized) when 4-ethynyl-4-hydroxy-3-isopropoxy-2-methyl-2-cyclobuten-1-one (**1**) was treated with *n*-Bu_3SnOCH_3 in dichloroethane at reflux (eq 1). Spectroscopic analysis indicated that the alkynylcyclobutenol had been transformed into 2-isopropoxy-3-methyl-6-(tri-*n*-butylstannyl)-1,4-benzoquinone (**2**), a representative of a previously unknown class of compounds: stannylquinones.



(1)

1 **2**

The generality of this stannylquinone synthesis was established by preparation of the new compounds indicated in Table I. The precursor alkynylcyclobutenones and alkynylbenzocyclobutenones **4** were readily prepared according to established techniques[7] by addition of alkynyl anions to the substituted cyclobutenediones or benzocyclobutenediones **3**, available by previously described procedures.[8-13] Thermolysis of ≤0.1 M solutions of **4** in dichloroethane in the presence of 1.05 equiv of *n*-Bu_3SnOMe for 10-15 min led to good yields of most of the stannylquinones (2,3-dialkoxycyclobutenone and some of the benzocyclobutenone substrates took 2-4 h to react to completion); however, a few of the products were formed in low yield for reasons not yet determined. The stannylquinones, when pure, are fairly stable open

(1) Camille and Henry Dreyfus Foundation Teacher-Scholar, 1985-1990.
(2) Liebeskind, L. S.; Mitchell, D.; Foster, B. *J. Am. Chem. Soc.* **1987**, *109*, 7908.
(3) Liebeskind, L. S.; Chidambaram, R.; Mitchell, D.; Foster, B. *Pure Appl. Chem.* **1988**, *60*, 2734.
(4) Liebeskind, L. S. *Tetrahedron Symposium-in-Print* **1989**, *45*, 3053.
(5) Mitchell, D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1990**, *112*, 291.
(6) All new compounds were characterized spectroscopically by UV, IR, and ^1H NMR spectroscopy and gave satisfactory combustion analyses.
(7) Foland, L. D.; Karlsson, J. O.; Perri, S. T.; Schwabe, R.; Xu, S. L.; Patil, S.; Moore, H. W. *J. Am. Chem. Soc.* **1989**, *111*, 975.
(8) Liebeskind, L. S.; Baysdon, S. L. *Tetrahedron Lett.* **1984**, 1747.
(9) Liebeskind, L. S.; Fengl, R. W.; Wirtz, K. R.; Shawe, T. T. *J. Org. Chem.* **1988**, *53*, 2482.
(10) Reed, M. W.; Pollart, D. J.; Perri, S. T.; Foland, L. D.; Moore, H. W. *J. Org. Chem.* **1988**, *53*, 2477.
(11) Liebeskind, L. S.; Lescosky, L. J.; McSwain, C. M., Jr. *J. Org. Chem.* **1989**, *54*, 1435.
(12) Liebeskind, L. S.; Fengl, R. W. *J. Org. Chem.*, in press.
(13) Liebeskind, L. S.; Wang, J. *Tetrahedron Lett.*, in press.

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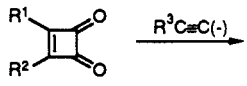
Table I. Synthesis of Stannylquinones



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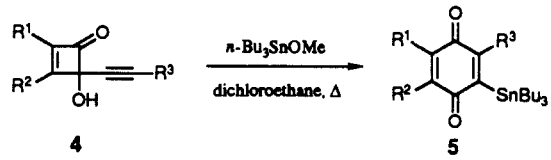
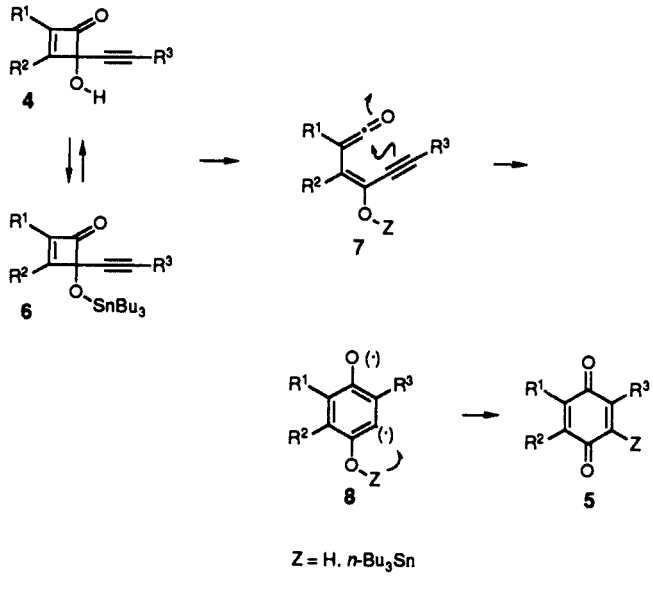


4 5

entry	R^1	R^2	R^3	compd, % yield	compd, % yield
1	Me	Me	H	**4a**, 32 (64)[a]	**5a**, 78
2	Me	Me	$SiMe_3$	**4b**, 71	**5b**, 67
3	Me	Me	Me	**4c**, 96	**5c**, 78
4	Me	Me	Bu	**4d**, 81	**5d**, 90
5	Me	MeO	H	**4e**, 33 (43)[a]	**5e**, 20
6	Me	MeO	Bu	**4f**, 80	**5f**, 45
7	Me	*i*-PrO	Bu	**4g**, 94	**5g**, 64
8	Me	*i*-PrO	H	**4h**, 49	**5h**, 61
9	*i*-PrO	*i*-PrO	Bu	**4i**, 85	**5i**, 46
10	MeO	MeO	Bu	**4j**, 66	**5j**, 32
11	benzo		Bu	**4k**, 59	**5k**, 59
12	benzo		Me	**4l**, 62	**5l**, 79
13	benzo		$SiMe_3$	**4m**, 83	**5m**, 76

[a] Overall yield, prepared from R^3 = TMS by desilylation at room temperature with 1.5 equiv of KF in MeOH. The yield for the desilylation step is given in parentheses.

Scheme I



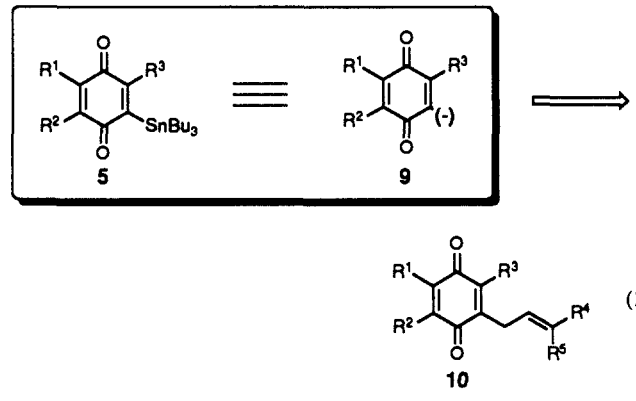
Z = H, *n*-Bu_3Sn

to the air and can be stored for prolonged periods in the refrigerator under N_2 with little decomposition. All stannylquinones were yellow-orange to red in color and showed CO stretching absorptions between 1657 and 1622 cm^{-1} in the infrared. No unusual spectroscopic characteristics were noted.

Confirmation of the stannylquinone structure was achieved by the facile destannylation of **5g** (Zn, 2:1 HOAc/TFA, then Ag_2O) giving 2-*n*-butyl-5-isopropoxy-6-methyl-1,4-benzoquinone, which was identical with a sample prepared by thermolysis of **4g** according to the procedure of Moore.[7]

Apparently, the stannylquinones are being formed by a novel variant of the Moore rearrangement,[7,14-16] the thermal isomerization of 4-alkoxy-4-alkynylcyclobutenones to quinones according to Scheme I. In the absence of *n*-Bu_3SnOMe, 4-(1-alkynyl)-4-hydroxy-2-cyclobuten-1-ones undergo thermal conversion to 1,4-benzoquinones via the reaction sequence **4** → **7** → **8** → **5** (Z = H). In the presence of *n*-Bu_3SnOMe, alkoxy exchange leads to an equilibrium between **4** and **6**, the quinone-forming reaction occurring exclusively via the stannylated intermediate **6**. This observation leads to the interesting suggestion that, relative to a 4-hydroxy substituent, the 4-stannyloxy intermediate is activated toward electrocyclic ring opening of the cyclobutenone. Qualitative confirmation of this point was achieved by comparison of the time to completion of reaction for quinone formation from **4g** in the absence (130 min) and presence (15 min) of *n*-Bu_3SnOMe (1 M in reactants in 1,2-dichloroethane at 84 °C).

Direct attachment of the tri-*n*-butylstannyl group to a quinone nucleus provides the option of synthesizing substituted quinones by a palladium-catalyzed cross coupling of the stannylquinone with various organic halides or their equivalents (the Stille reaction[17,18]), the stannylquinone functioning as a formal quinone carbanion equivalent, **9** (eq 2). This has been reduced to practice,



5 9

10 (2)

in a preliminary fashion, using allylic halides as reaction partners.[6] Good yields of allylated quinones are obtained in all cases except from stannylquinones **5**, R^3 = H, in which case R^3 = $SiMe_3$ can function as a surrogate for R^3 = H [R^1 = R^2 = R^3 = Me, R^4 = 2-propenyl (80%), R^4 = 3-methyl-2-butenyl (56%); R^1 = R^2 = Me, R^3 = *n*-Bu, R^4 = 2-propenyl (62%); R^1 = R^2 = Me, R^3 = $SiMe_3$, R^4 = 2-propenyl (84%), R^4 = 3-methyl-2-butenyl (90%); R^1,R^2 = benzo, R^3 = Me, R^4 = 3-methyl-2-butenyl (90%); R^1,R^2 = benzo, R^3 = $SiMe_3$, R^4 = 3-methyl-2-butenyl (92%)].[19]

The uniquely mild carbon–carbon bond forming conditions of the palladium-catalyzed cross coupling of organostannanes and various organic electrophiles should allow the preparation of highly functionalized quinones from stannylquinone precursors. These and other issues relating to the use of stannylquinones in synthesis are currently under investigation.

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Supplementary Material Available: Full synthetic details and spectroscopic and analytical characterization of all compounds (23 pages). Ordering information is given on any current masthead page.

(14) Moore, H. W.; Decker, O. H. W. *Chem. Rev.* **1986**, *86*, 821.
(15) Decker, O. H. W.; Moore, H. W. *J. Org. Chem.* **1987**, *52*, 1174.
(16) Decker, O. H. W.; Moore, H. W. *J. Org. Chem.* **1987**, *52*, 1174.
(17) Stille, J. K. *Pure Appl. Chem.* **1985**, *57*, 1771.
(18) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.
(19) Desilylation of silylquinones is readily achieved by reduction to the hydroquinone under acidic conditions followed by reoxidation to the quinone (Zn in CH_3COOH/CF_3COOH followed by Ag_2O). Additional details regarding the allylation of stannylquinones will be reported separately.