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LEWIS ACID MEDIATED ALLYLATION OF 2-ALKANOYL-1,4-QUINONES WITH ALLYLSILANE AND ALLYLSTANNANE[1]

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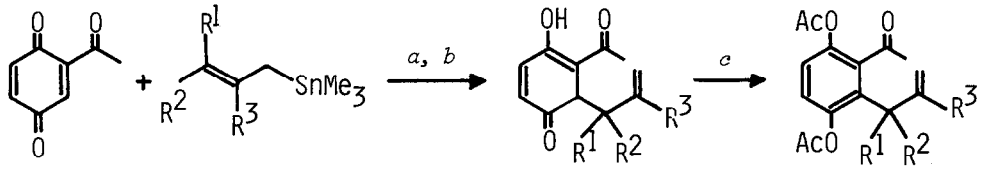
Summary: Allyltrimethylstannane reacts with 2-alkanoyl-1,4-quinones regioselectively to afford conjugate addition products which can be derived to 2-alkanoyl-3-allylhydroquinone diacetate, while allyltriphenylsilane reacts with the quinone to give naphthofuran.

Recently regioselective allylation of quinones with allylstannane was developed,[2] and successfully applied to the synthesis of naturally occurring isoprenylquinones (e.g. ubiquinones, plastoquinones, menaquinones, and phylloquinones).[3] As the result of the mechanistic study, it was established that the allylation of alkyl- and alkoxyquinones proceeds via 1,2 addition of allylstannane to quinone and followed by allylic migration to give allylhydroquinones. The applied Lewis acid plays both as the activator of carbonyl group and as the acid catalyst of allylic migration. Further investigation of the allylation of the other functionalized quinones is interesting in view of the mode of the addition reaction and in affording the starting materials for the synthesis of many naturally occurring quinones, which show versatile physiological activity.

In this paper, we descrive the allylation of 2-alkanoyl-1,4-quinones and related ones with allylstannanes and allylsilanes. There are two major aspects to the present reaction; (a) the mode of the nucleophilic addition (1,2 vs. 1,4 addition to quinone) of allylmetals, and (b) a simple derivation to the analogue of pyranonaphthoquinone antibiotics[4] (eleutherin, nanaomycins,[5] and frenolicin).

Although 3-position of alkanoylquinones posesses strong electrophilic character and could be easily attacked by some anionic species,[6] the reaction of the quinone with allyltrimethylstannane, which has moderate nucleophilic character, at room temperature was very slow and gave only complex mixture after four days. Addition of an appropriate Lewis acid (BF_3OEt_2) in the reaction mixture led to instantaneous formation of conjugate adduct even at -78°C. The typical reaction was performed as follows. To a dichloromethane solution (30 mL) of 2-acetyl-1,4-benzoquinone 1 (1.0 mmol), BF_3OEt_2 (1.0 mmol) was added at -78°C under nitrogen atmosphere followed by dropwise addition of *trans*-2-butenyltrimethylstannane 2b (1.2 mmol).[2] Stirred for



1 2a, $R^1=R^2=R^3=H$; 2b, $R^1=H$, $R^2=Me$, $R^3=H$; 2c, $R^1=R^2=H$, $R^3=Me$; 2d, $R^1=R^2=Me$, $R^3=H$ 3a-d 4a-d

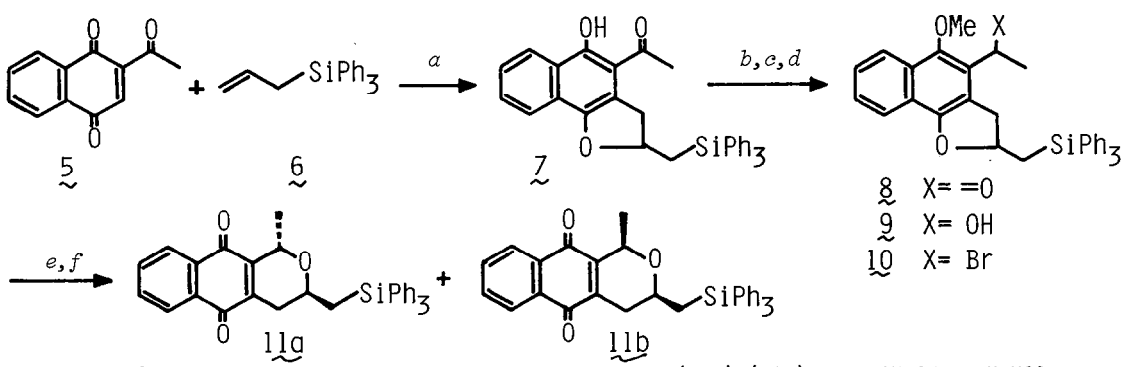
a, BF_3OEt_2, -78°C; *b*, H_2O; *c*, Ac_2O, Py

1h at -78°C, the reaction mixture was quenched by the quick addition of water. After extraction with dichloromethane, drying, and evaporation of the solvent the residue consisted of almost pure 2-(1-methyl-2-propenyl)-3-acetylcyclohexa-3,5-dien-1-one-4-ol 3b[7] in a quantitative yield; mp 73°C (decomp.). This conjugate adduct was rather unstable and easily enolated to the corresponding acetylhydroquinone during chromatographic separation on silica gel. In every run the primary product was esterified to the corresponding diacetate by Ac_2O-Py and isolated as pure form. The result is summarized in Table I.

Since direct allylation of these alkanoyl quinones is difficult so far, this method opens efficient synthesis of 2-alkanoyl-3-allyl-1,4-quinones. Moreover, quinones substitued by methoxycarbonyl or formyl groups instead of alkanoyl one were also effectively allylated by this method. In the latter case, it is interesting that conjugate addition took place in precedence over 1,2 addition to the reactive formyl group.

Isolation of the conjugate adduct in every reaction and selective formation of the γ-adduct with crotyl- and prenylstannanes support the occurrence of 1,4 addition.[9] If 1,2-addition followed by allylic migration is the predominant pathway, selective formation of the α-adduct would be expected on the basis of steric interaction between alkanoyl group and allylic moiety.[2a] This is the first example of 1,4 addition of allylstannane to substituted quinones.

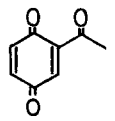
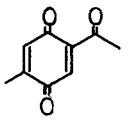
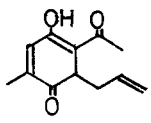
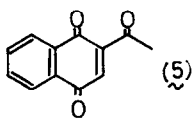
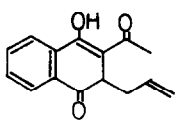
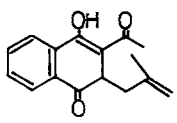
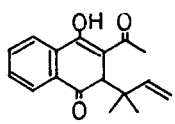
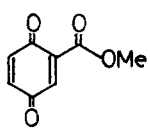
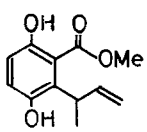
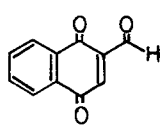
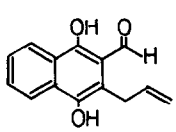
The reaction of acetylbenzoquinone 1 with allyltrimethylsilane gave the corresponding



5 6 7 8 X= =O; 9 X= OH; 10 X= Br 11a 11b

a, $AlCl_3$, 0°C; *b*, MeI, K_2CO_3; *c*, $NaBH_4$, MeOH; *d*, PBr_3; *e*, $Ce(NH_4)_2(NO_3)_6$, aq CH_3CN; *f*, $NaHCO_3$

Table 1. Allylation of alkanoylquinones and related quinones[a]

Entry	Alkanoylquinone	Allyl-stannane	Product (Yield, %)[b]		Diacetate Isolated yield, %[c]
1	 (1)	2a	3a	(64)[d]	80
2	1	2b	3b	(100)	91
3	1	2c	3c	(100)	93
4		2a		(100)	64
5	 (5)	2a		(100)	95
6	5	2c		(100)	84
7	5	2d		(100)[e]	80[f]
8		2b		(94)	84
9		2a		(39)[g]	34

[a] All reactions were performed in 1.0 mmol scale by the same procedure described in the text. [b] ^{1}H-NMR data were in accord with the assigned structures. Yield was determined by ^{1}H-NMR using an internal standard. [c] Fully characterized by spectroscopic methods and elemental analyses. [d] 2-Acetyl-3-allylhydroquinone (18%) was accompanied. [e] A mixture of two regioisomers (γ/α=70/30). [f] A mixture of two regioisomers (γ/α=88/12) after purification by column chromatography. [g] Reaction conditions were not optimized.

allylhydroquinone in a low yield (~40%) accompanied by several other products. When allyltriphenylsilane 6 was added to the dichloromethane solution of 2-acetyl-1,4-naphthoquinone 5 and $AlCl_3$ (2.0 equiv. to the quinone) at 0°C and the resulting solution was stirred for 0.5 h, cyclized product 7[7,8] was isolated in 61.4% yield; mp 164-165°C. Product 7 is a promising material for the synthesis of pyranonaphthoquinones. Following derivation to pyranonaphthoquinone 11 illustrates the utility of 7. Methylation of 7 (MeI, K_2CO_3) followed by reduction with $NaBH_4$ in methanol gave the corresponding alcohol 9 as a 1:1 mixture of two diastereomeric isomers in 99% yield. Bromination of 9 (PBr_3, Et_2O) gave 10 (84%). Demethylative oxidation of 10 with ceric(IV) ammonium nitrate (aq. CH_3CN) was followed by treatment of alkaline solution (aq. $NaHCO_3$) to give the mixture of pyranonaphthoquinone isomers (11a and 11b, ca. 1:1; 61% yield).[7,8]

This methodology is useful for the synthesis of other pyranonaphthoquinone antibiotics, of which total synthesis is in the way.

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References and footnotes

1. Synthesis of Naturally Occurring Quinones Part 9; Part 8 see ref. 3.
2. (a) Y.Naruta, J. Am. Chem. Soc., 102, 3774 (1980). (b) Y.Naruta, H.Uno, and K.Maruyama, Nippon Kagaku Kaishi, 1981, 831. (c) K.Maruyama, A.Takuwa, Y.Naruta, K.Satao, and O.Soga, Chem. Lett., 1981, 47.
3. Y.Naruta, J. Org. Chem., 45, 4097 (1980).
4. For a review of pyranonaphthoquinones, R.H.Thomson, "Naturally Occurring Quinones", 2nd ed., Academic Press, New York, N.Y., 1971, pp. 282-312.
5. S.Omura, H.Tanaka, Y.Okuya, and H.Marumo, J. Chem. Soc., Chem. Commun., 320 (1976) and references cited therein.
6. (a) F.Farina and J.Valdename, Synthesis, 1971, 315. (b) G.A.Kraus and B.Roth, J. Org. Chem., 43, 4973 (1978).
7. All new compounds gave satisfactory elemental analyses and their spectroscopic data were in accord with the assigned structure.
8. ^{1}H-NMR data of typical compounds (δ; in $CDCl_3$);
3b; 1.20(d, 3H, J=7Hz), 2.80(s, 3H), 2.58(m, 1H), 3.42(d, 1H, J=4Hz), 4.75-5.04(m, 2H), 5.50(ddd, 1H, J=8, 11, 15Hz), 6.30(d, 1H, J=11Hz), 6.85(d, 1H, J=11Hz), 15.54(s, 1H).
7; 1.92(dd, 1H, J=8, 14.5Hz), 2.17(s, 3H), 2.28(dd, 1H, J=6, 14.5Hz), 2.88(dd, 1H, J=8, 15.5Hz), 3.22(dd, 1H, J=9, 15.5Hz), 5.16(m, 1H), 7.2-7.8(m, 18H), 8.35(m, 1H), 13.94(s, 1H).
11a and 11b; 1.94(m, 5H), 2.94(m, 2H), 4.18(m, 1H), 5.03 and 5.24(each q, intensity ca. 1:1, total 1H, J=7Hz), 7.2-7.8(m, 17H), 8.00(m, 2H).
9. Conjugate addition of allyltrimethylsilane and allyltrimethylstannane to simple α,β-unsaturated ketones, see A.Hosomi, H.Iguchi, and H.Sakurai, Chem. Lett., 1979, 977 and references cited therein.

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