Tetrahedron Letters, Vol. 33, No. 46, pp. 7049-7052, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

Preparation and Reactions of 3- and 4-Tributylstannyl-2-(5H)-Furanones: Preparation of Aryl Furanones

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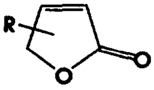
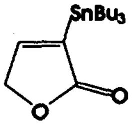
Keywords: Furanones, Stille coupling, vinylstannanes.

Abstract: *3- and 4-trialkylstannylfuranones (2) and (3) have been prepared by an interesting desulphurative stannylation reaction; 3- and 4-substituted 2-(5H)-Furanones (12) and (13) may be prepared* via *palladium-catalysed cross coupling of (2) and (3) with aryl iodides*

α,β-Unsaturated γ-lactones (2-(5H)-furanones, (1)) frequently occur as subunits of biologically active natural products.[1] In particular, there is great interest in the preparation of such lactones bearing aromatic substituents, since this class of compounds has great potential as pharmacologically powerful tools.[2] There is also interest in our group in the direct coupling of steroidal subunits to a furanone. Given these interests we sought a new route which would allow rapid and general synthesis of such furanones; we here report the preliminary results of our studies.


(1)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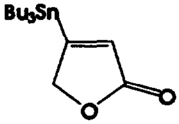
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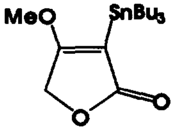
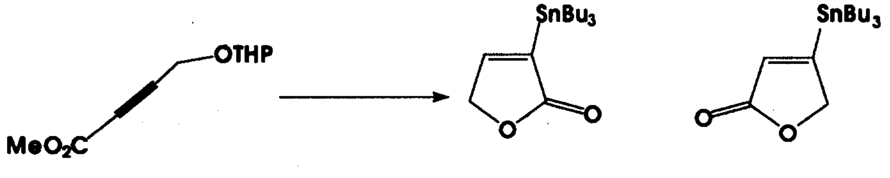

(4)

One intuitive route to prepare 4-substituted furanones, *viz.* addition-elimination reaction of suitable nucleophiles with 4-halofuranones, is hampered by the difficulty of preparation of suitable electrophiles;[3] the reaction of 4-chloro-2-(5H)-furanone with organometallic reagents has (briefly) been reported but has not been developed into a general synthetic method,[4] while Negishi has reported the coupling of homoallylzinc reagents with 4-bromo-2-(5H)-furanone.[5] In the case of the 3-substituted furanone there is no similar pathway which would allow direct introduction of alkyl or aryl groups. We reasoned that the use of the novel stannylfuranones (2) and (3) might neatly circumvent these problems. Firstly, we thought that Stille coupling[6] of (2) and (3) with aromatic iodides would give the desired aryl lactones directly; Ley *et al* have demonstrated that the 3-stannyl-4-methoxyfuranones (4) can serve as useful reagents in acylation reactions.[7] Secondly, we anticipated that (3) would serve as an efficient radical transfer reagent in reaction with suitable alkyl radical precursors. Thirdly, we hoped that halogenation of (2) would allow preparation of the elusive 4-halo-2-(5H)-furanones which would then allow further nucleophilic displacements to be attained.

This communication reports the preparation of (2) and (3) and their reactions with aryl iodides under palladium catalysis.



(2) (3)

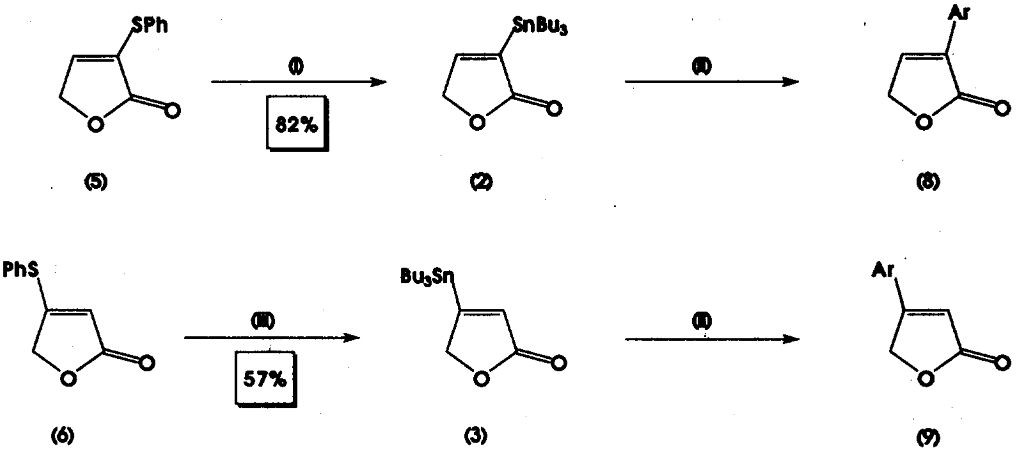
Conditions:
(i) See ref. 5
(ii) Bu_3SnH,
$Cl_2Pd(PPh_3)_2$ (cat.),
benzene,
room temperature

SCHEME 1

Our first attempt to prepare (2) and (3) was only partially successful: palladium-catalyzed hydrostannylation of methyl 4-hydroxybut-2-ynoate[8] delivered the compounds in a 1:1 ratio in 46% combined yield after column chromatography, but the isomers could not routinely be separated efficiently (Scheme 1) . Compound (2) proved much less stable than its isomeric twin: if crude reaction mixtures were left for longer than two or three hours even at low temperature (< 0°C), only (3) could be isolated after chromatography.

A more satisfying entry to (2) and (3) was provided by desulphurative stannylation[9] of phenylthiofuranones (5)[10] and (6).[11] The reaction of these vinylsulphides with two equivalents of tributylstannane provided (2) and (3) in 82% and 57 % yields, respectively (scheme 2). This is an interesting process because the expected product of the reaction of a vinyl sulphide with stannane is the corresponding alkene; in particular, the preparation of (2) is surprising because there is no addition elimination-type mechanism one could devise to account for its formation. We are currently exploring the generality of this transformation and the results of these investigations will be published elsewhere.

Armed with our desired stannylfuranones, we were gratified to observe that reaction of (2) and (3) with a variety of aryl iodides (7) in the presence of catalytic amounts of $PdCl_2(Ph_3)_2$ in refluxing toluene (scheme 2) led to efficient coupling reaction to give 3- and 4-substituted furanones (8 and 9, respectively) as shown in the table. Purification by flash chromatography[12] gave analytically pure furanones in the yields described.



Conditions:

(I) Bu_3SnH (2eq.), AIBN
benzene, reflux

(II) ArI (7), $Cl_2Pd(PPh_3)_2$ (1-2 mol%)
toluene, reflux

(III) Bu_3SnH (2eq.), AIBN
toluene, reflux

SCHEME 2

IODIDE	7a	7b	7c	7d	7e	7f
Ar	Ph	2-CO_2Me-C_6H_4	3-CF_3-C_6H_4	2-Me-C_6H_4	2-thienyl	4-NO_2-C_6H_4
FURANONE	8a	8b	8c	8d	8e	8f
YIELD/%	65	72	61	76	58	0
FURANONE	9a	9b	9c	9d	9e	9f
YIELD/%	45	65	23	36	-	-

It is noteworthy that 3-stannylated furanone (2) reacted much less efficiently than the corresponding 4-stannylfuranone in the coupling reaction, except in its reaction with 2-(carboxymethyl)iodobenzene. It is similarly interesting to note that in the stannylation reaction to prepare (2) and (3), (2) is formed more rapidly, in greater yield and more cleanly than its regioisomeric twin, despite the lack of an addition-elimination mechanism (which may be invoked to describe the formation of (3)) to account for its formation. The underlying mechanistic nuances of these reactions are under study in our laboratory.

We believe that the ease of preparation of stannanes (2) and (3) and the simplicity of their reaction with aryl iodides represents an important method for the preparation of a wide range of structurally diverse furanones.

We thank Mr. S.F. Ighter for useful comments, Mr. Ian Derrick for experimental assistance and acknowledge the financial support of the Nuffield foundation and the Science and Engineering Research Council.

General procedure for coupling of stannanes (2) and (3) with aryl iodides:
To a flame-dried nitrogen-flushed10 mL round-bottomed flask fitted with a reflux condenser and stirrer bar was added stannane (100 mg, 0.268 mmol), iodide (0.402 mmol, 1.5 eq.) and toluene (distilled, 5 mL). Dichlorobis(triphenylphosphine)palladium^{II} was then quickly added, stirring was commenced and the mixture was heated to reflux. Reflux was continued until all the stannane starting material had been consumed (as evinced by thin layer chromatography). The mixture was then poured into a separating funnel and washed with an aqueous solution of potassium fluoride (8M, 2 x 5 mL); the organic layer was dried ($MgSO_4$) and concentrated *in vacuo* to yield crude furanone. Flash chromatography furnished 3- and 4-substituted 2-(5H)-furanones in analytically pure form.

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(Received in UK 10 August 1992)