

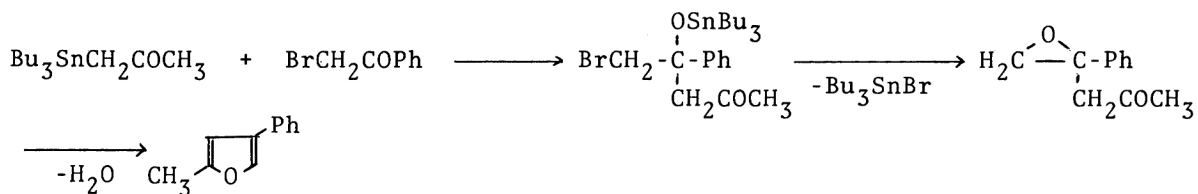
PALLADIUM OR RUTHENIUM CATALYZED REACTION OF  $\alpha$ -HALO KETONES WITH  
TRIBUTYLTIN ENOLATES: PREPARATION OF UNSYMMETRICAL 1,4-DIKETONES

Masanori KOSUGI, Izumi TAKANO, Motoi SAKURAI, Hiroshi SANO, and  
Toshihiko MIGITA\*  
Department of Chemistry, Faculty of Technology, Gunma University,  
Kiryu, Gunma 376

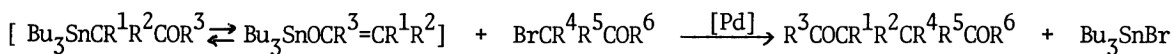
Palladium or ruthenium catalyzed cross-coupling of  $\alpha$ -halo  
ketones with tributyltin enolates gave unsymmetrical 1,4-diketones.  
The method was applied to the dihydrojasnone synthesis.

1,4-Diketones are useful intermediates for further transformation into  
furans,<sup>1)</sup> pyroles,<sup>2)</sup> thiophenes,<sup>3)</sup> or cyclopentenones.<sup>4)</sup> Although a number of  
efforts have been devoted to the preparation of 1,4-diketones,<sup>5)</sup> there is still a  
room for development of more convenient methods.

In our earlier communication, we reported that the reaction of  $\alpha$ -bromoaceto-  
phenone with acetonyltributyltin gave the furan derivatives.<sup>6)</sup> The reaction was  
explained in terms of an initial addition of tin enolates to the carbonyl group  
of the  $\alpha$ -bromo ketones, followed by elimination of tributyltin bromide to pro-  
duce the  $\beta,\gamma$ -epoxy ketone, which then underwent cyclodehydration.




During further works on the reaction of  $\alpha$ -halo ketone with tributyltin enol-  
ate, we found the reaction can be lead to give the cross-coupling product, 1,4-  
diketone by the presence of palladium catalysts.



Efficiency for producing 1,4-diketone of various catalysts was surveyed using  $\alpha$ -bromopinacolone as a substrate to which the addition of tin enolates was prevented by the bulky *t*-butyl group. The presence of  $\text{PdCl}_2(\text{PhCN})_2$  or  $\text{RuCl}_2(\text{PPh}_3)_3$  was found to enhance the yield of 1,4-diketone, although the reaction took place at some extent without a catalyst. Other catalysts used here lowered the yield of the product.

The reaction was carried out as follows: the mixture of tributyltin enolate (18 mmol),  $\alpha$ -bromo ketone (10 mmol),  $\text{PdCl}_2(\text{PhCN})_2$  (0.1 mmol), and benzene (5 ml) as a solvent was heated with stirring at 80 °C for 20 h under argon. After evaporation of the solvent, column chromatography of the residue (silica gel: cyclohexane followed by ether as eluants) and distillation gave the 1,4-diketone. The results are summarized in Table 1.

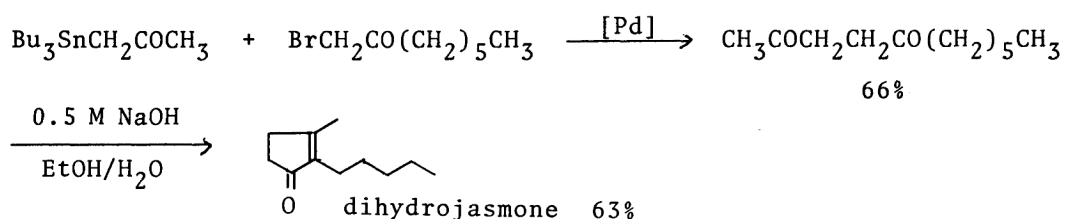
Table 1. Preparation of 1,4-Diketones

Entry	Tin enolate $\text{Bu}_3\text{SnCR}^1\text{R}^2\text{COR}^3$	$\alpha$ -Halo ketone $\text{BrCR}^4\text{R}^5\text{COR}^6$	Catalyst	Yield/% <sup>a)</sup> $\text{R}^3\text{COCR}^1\text{R}^2\text{CR}^4\text{R}^5\text{COR}^6$
1	$\text{Bu}_3\text{SnCH}_2\text{COCH}_3$	$\text{BrCH}_2\text{COBu}^t$	-	(56)
2			$\text{Pd}(\text{PPh}_3)_4$	(21)
3			$\text{PdCl}_2[\text{P}(\text{o-tolyl})_3]_2$	(26)
4			$\text{PdCl}_2(\text{PhCN})_2$	(88), 83
5			$\text{RhCl}(\text{PPh}_3)_3$	(21)
6			$\text{RuCl}_2(\text{PPh}_3)_3$	(81)
7		$\text{BrCHMeCOBu}^t$	$\text{PdCl}_2(\text{PhCN})_2$	73
8		$\text{BrCHMeCOEt}$		70
9		$\text{BrCHMeCOMe}$		41 <sup>b)</sup>
10		$\text{BrCMe}_2\text{COMe}$		0
11		$\text{BrCH}_2\text{CO}(\text{CH}_2)_5\text{Me}$		66 <sup>b)</sup>
12	$\text{Bu}_3\text{SnCH}_2\text{COBu}^t$	$\text{BrCH}_2\text{COBu}^t$		97
13	$\text{Bu}_3\text{SnOCMe}=\text{CMe}_2$			35
14	$\text{Bu}_3\text{Sn-O}$ 			95
15		$\text{BrCHMeCOEt}$		21

a) Isolated yield based on the bromide (GLC yield in parentheses).

b) 5 Mol% of the catalyst was used.


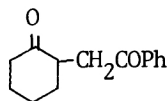
The reaction seems sensitive to the steric hindrance at the reaction sites of both reagents and substrates. The presence of methyl group at the reaction site makes the yield of 1,4-diketone lower (entries 10, 13, and 15 in Table 1). Entries 9 and 11 show that effective cross-coupling of less hindered  $\alpha$ -bromo ketone with tin enolate needed 5 mol% of the catalyst, whereas the mixture of products (1,4-diketone and  $\beta,\gamma$ -epoxy ketone) was obtained when 1 mol% of the catalyst was used. The product of entry 11 (2,5-undecanedione) is the well-known precursor of dihydrojasmone. Thus, treating the product with alkaline ethanol gave dihydrojasmone in 63% isolated yields.<sup>5)</sup> The reaction cannot be applied to



$\alpha$ -bromoacetone or  $\alpha$ -bromo aldehyde because the addition of tin enolate to the carbonyl group of these substrates cannot be excluded.

To lead the reaction of  $\alpha$ -bromo aromatic ketones with tin enolates into the formation of 1,4-diketones, somewhat different reaction conditions were required. Thus,  $\text{RuCl}_2(\text{PPh}_3)_3$  was the best catalyst and hexamethylphosphoric triamide (HMPA) which is an unfavorable solvent for the formation of furan or  $\beta,\gamma$ -epoxy ketone, was the effective solvent. These results are shown in Table 2.

Table 2. 1,4-Diketone from  $\alpha$ -Bromo Phenyl Ketone

Tin enolate (15 mmol)	$\alpha$ -Halo ketone (10 mmol)	Catalyst (1 mmol)	Product	Isolated yield %
$\text{Bu}_3\text{SnCH}_2\text{COCH}_3$	$\text{BrCH}_2\text{COPh}$	$\text{RuCl}_2(\text{PPh}_3)_3$	$\text{CH}_3\text{COCH}_2\text{CH}_2\text{COPh}$	34
	$\text{BrCHMeCOPh}$		$\text{CH}_3\text{COCH}_2\text{CHMeCOPh}$	38
$\text{Bu}_3\text{Sn-O}$ 	$\text{BrCH}_2\text{COPh}$			53

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