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SYNTHESIS AND REACTIONS OF 5-(TRIBUTYLSTANNYL)ISOXAZOLES

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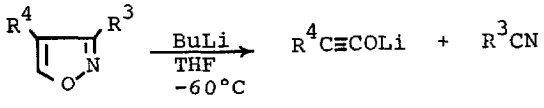
Abstract—— 3-Substituted 5-(tributylstannyl)isoxazoles were synthesized in good yields by the 1,3-dipolar cycloaddition reaction of ethynyltributylstannane with nitrile oxides generated in situ. 3-Methyl-5-(tributylstannyl)isoxazole was easily converted to the corresponding 5-benzoyl- and 5-arylisoxazoles by the palladium-catalyzed reaction.

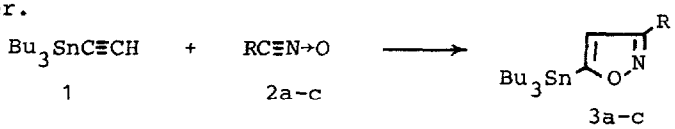
It is well known that isoxazole derivatives are versatile synthons in organic syntheses, because of their masked 1,3-dicarbonyl character. In spite of development of the methods for the synthesis of isoxazole derivatives, the preparation of 5-metalated isoxazoles has not yet been accomplished. For example, the lithiation of 3,4-disubstituted isoxazoles with butyllithium resulted in the ring cleavage[1].



Scheme 1

In the present communication, we report the synthesis of 3-substituted 5-(tributylstannyl)isoxazoles by the 1,3-dipolar cycloaddition of ethynyltributylstannane (**1**) with nitrile oxides. We also describe some reactions of the stannylisoxazoles thus obtained.

When ethynyltributylstannane (**1**) was treated in benzene with acetonitrile oxide (**2a**)[2] generated in situ, 3-methyl-5-(tributylstannyl)isoxazole (**3a**) was obtained in nearly quantitative yield. Similarly, 3-phenyl-5-(tributylstannyl)isoxazole (**3b**) was synthesized by the reaction of **1** with benzonitrile oxide (**2b**)[2]. Ethyl 5-(tributylstannyl)isoxazole-3-carboxylate (**3c**) was obtained in excellent yield by the reaction of **1** with ethoxycarbonylnitrile oxide (**2c**)[3] prepared in situ in ether.



1 2a-c 3a-c

a: R=Me b: R=Ph c: R=COOEt

Scheme 2

When **3a** was heated with benzoyl chloride in the presence of a catalytic amount of dichlorobis(triphenylphosphine)palladium under reflux in anhydrous dioxane for 3 h, 5-benzoyl-3-methylisoxazole (**4**), mp

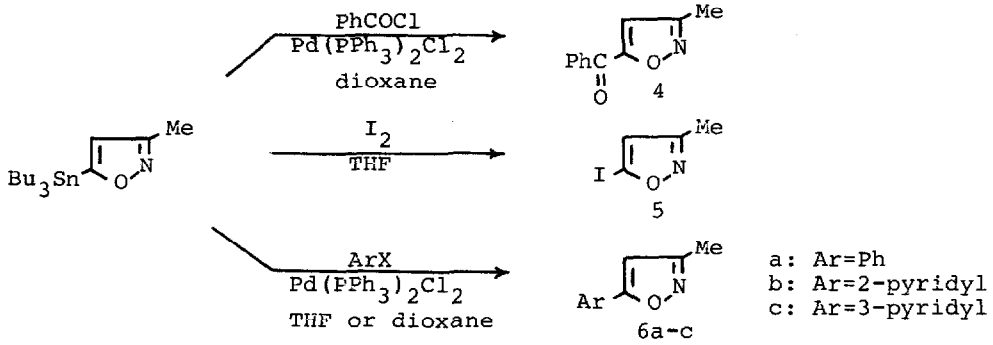
Table I. 3-Substituted 5-(Tributylstannyl)isoxazoles (**3a-c**)

Product	R	Yield(%)	^{1}H-NMR($CDCl_3$/TMS) δ
3a	Me	97	0.6-1.8(27H,m),2.33(3H,s),6.22(1H,s)
3b	Ph	100	0.6-1.8(27H,m),6.70(1H,s),7.2-7.6(3H,m) 7.8-8.0(2H,m)
3c	COOEt	85	0.7-1.9(30H,m),4.47(2H,q,J=7.0Hz),6.82(1H,s)

All products were obtained as viscous oil.

67-69°C, was obtained in 80 % yield. At room temperature, **3a** reacted with iodine in tetrahydrofuran to give 5-iodo-3-methylisoxazole (**5**), mp 78-79°C, in 57 % yield.

In order to inspect the possibility on the introduction of 5-isoxazolyl moiety as a masked 1,3-dicarbonyl side-chain into aromatic rings, the palladium-catalyzed cross-coupling of **3a** with bromobenzene, iodobenzene, 2-bromopyridine, and 3-bromopyridine was carried out, and the satisfactory results were obtained.



Scheme 3

Table II. Palladium-catalyzed Cross-coupling of Aryl Halides with **3a**

Product	Aryl halide	Solvent	Reaction time (h)	Yield (%)	mp(°C) or bp(°C)/mmHg
6a	Iodobenzene	THF	7	82	65-68
	Bromobenzene	THF	5.5	18	
		dioxane	6	59	
		dioxane	25	72	
6b	2-Bromopyridine	THF	14.5	17	55-57
		dioxane	6	64	
6c	3-Bromopyridine	THF	15	15	62-63
		dioxane	4	60	

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