

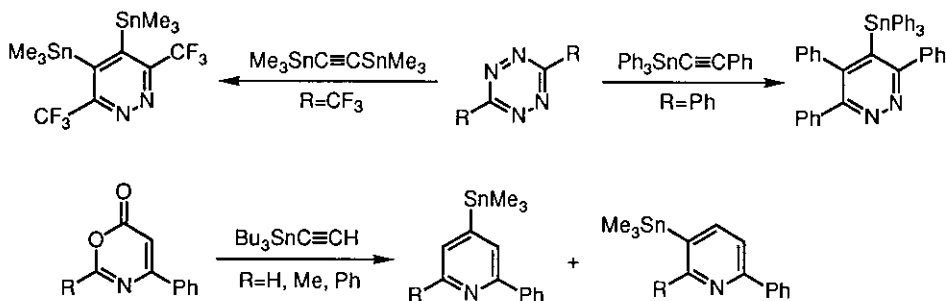
SYNTHESIS OF 4-(TRIBUTYLSTANNYL)PYRIDAZINES BY INVERSE ELECTRON-DEMAND DIELS-ALDER REACTION OF 1,2,4,5-TETRAZINES WITH TRIBUTYLSTANNYLACETYLENES

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Abstract—Inverse electron-demand Diels-Alder reaction of 3,6-disubstituted 1,2,4,5-tetrazines with tributylstannylacetylenes containing a substituent gave 4-(tributylstannyl)pyridazines. Particularly, dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate gave 4-(tributylstannyl)pyridazines in good yields. Substitution reaction of 3,6-diphenyl-4-(tributylstannyl)pyridazine was also described.

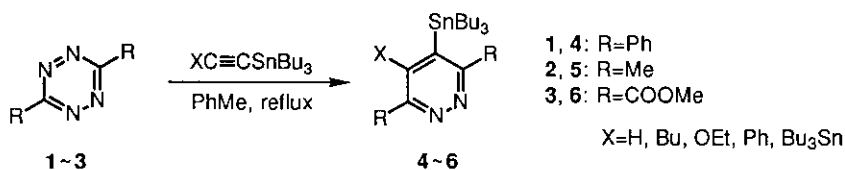
Inverse electron-demand Diels-Alder reaction of electron-deficient nitrogen heteroaromatics with electron-sufficient olefins or acetylenes has been becoming a useful method for the synthesis of various aromatics or heteroaromatics.¹ Meanwhile, it has been recognized that trialkylstannyl group is useful to introduce a functional group into heteroaromatics,² but there is a few papers for the synthesis of trialkylstannyl heteroaromatics by inverse electron-demand Diels-Alder reaction. For example, Neumann *et al.* reported that 3,6-diphenyl-1,2,4,5-tetrazine reacts with phenyltriphenylstannylacetylene at 130-150°C to give 3,5,6-triphenyl-4-(triphenylstannyl)pyridazine in 22% yield³ and Barlow *et al.* described that 3,6-bis(trifluoromethyl)-1,2,4,5-tetrazine readily reacts with 1,2-bis(trimethylstannyl)acetylene at 0°C to give 3,6-bis(trifluoromethyl)-4,5-bis(trimethylstannyl)pyridazine in 78% yield.⁴ Recently, Yamamoto *et al.* reported the synthesis of trialkylstannylpyridines from the reaction of 1,3-oxazin-6-ones with trialkylstannylacetylenes.⁵



Scheme 1

On the basis of these backgrounds, we describe, in this paper, the synthesis of 3,6-disubstituted 4-tributylstannylpyridazines by the Diels-Alder reaction of 3,6-disubstituted 1,2,4,5-tetrazines with various tributylstannylacetylenes and some reactions of 3,6-diphenyl-4-(tributylstannyl)pyridazine.

In order to examine the reactivity of the substituted tributylstannylacetylenes, the Diels-Alder reaction of 3,6-diphenyl-1,2,4,5-tetrazine (**1**) was carried out. When **1** was heated with tributylstannylacetylene in toluene under reflux for 60 h, 3,6-diphenyl-4-(tributylstannyl)pyridazine (**4 a**) was obtained in 85% yield, as a viscous liquid. But the reaction of **1** with butyltributylstannylacetylene, phenyltributylstannylacetylene, and bis(tributylstannyl)acetylene gave rise to the corresponding pyridazines (**4 b, c, e**) in 25-38% yields, and ethoxytributylstannylacetylene did not afford expected product (**4 c**).



Scheme 2

Table I. Diels-Alder Reaction Products of 3,6-Diphenyl-1,2,4,5-tetrazines with Tributylstannylacetylenes

Compd. No.	R	X	Reaction time (h)	Yield (%)	¹ H-Nmr (δ: CDCl ₃ /TMS)
4 a	Ph	H	60	85	0.4-1.6 (27H, m), 7.24 (1H, s), 7.4-7.7 (8H, m), 8.0-8.2 (2H, m)
4 b	Ph	Bu	48	38	0.4-1.8 (34H, m), 1.5-2.9 (2H, m), 7.2-7.7 (10H, m)
4 c	Ph	EtO	48	0	
4 d	Ph	Ph	36	25	0.5-1.7 (27H, m), 7.2-7.7 (15H, m)
4 e	Ph	Bu ₃ Sn	32 ^{a)}	30	0.5-1.7 (54H, m), 7.3-7.7 (10H, m)
5 a	Me	H	15	81	0.5-1.8 (27H, m), 2.53 (3H, s), 2.60 (3H, s), 7.17 (1H, s)
5 b	Me	Bu	72	5	0.7-1.7 (34H, m), 2.3-2.7 (2H, m), 2.63 (3H, s), 2.70 (3H, s)
6 a	COOMe	H	54	70	0.7-1.8 (27H, m), 4.13 (6H, s), 8.50 (1H, s)
6 b	COOMe	Bu	14	78	0.7-1.8 (27H, m), 2.6-3.2 (2H, m), 4.03 (6H, s)
6 c	COOMe	EtO	2	75	0.7-1.7 (30H, m), 4.08 (6H, s), 4.17 (2H, q, J=7 Hz)
6 d	COOMe	Ph	1	77	0.6-1.5 (27H, m), 3.70 (3H, s), 4.10 (3H, s), 7.1-7.6 (5H, m)
6 e	COOMe	Bu ₃ Sn	6	64	0.6-1.7 (54H, m), 4.09 (6H, m)

a) Reflux in mesitylene.

From the results shown in Table I, it is found that the reactivity of the substituted tributylstannylacetylenes as dienophile decreases in the following order: tributylstannylacetylene > butyltributylstannylacetylene ≈ phenyltributylstannyl-

Na_2SO_3 , and 0.5M KF aqueous solution, and dried over MgSO_4 . The residue obtained from the ethereal solution was purified by silica gel column chromatography using benzene- CHCl_3 (1:4). The crude product was recrystallized from hexane-AcOEt to give colorless scales, mp 167-168°C. Yield 0.28 g (77%). $^1\text{H-Nmr}$ (CDCl_3/TMS) δ (ppm): 7.3-7.8 (8H, m), 8.0-8.2 (2H, m), 8.39 (1H, s). *Anal.* Calcd for $\text{C}_{16}\text{H}_{11}\text{N}_2$: C, 53.66; H, 3.10; N, 7.82. Found: C, 53.46; H, 3.13; N, 7.74.

3,6-Diphenyl-4-pyridazinyI Phenyl Ketone (8)

A mixture of **4a** (0.78 g, 1.5 mmol), benzoyl chloride (0.25 g, 1.5 mmol), $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (53 mg, 0.075 mmol), and Et_4NCl (0.25 g, 1.5 mmol) in dry benzene (10 ml) was refluxed for 41 h. After removal of the solvent, the residue was dissolved in CHCl_3 and washed with satd. NaHCO_3 aqueous solution. The residue obtained from the CHCl_3 extract was purified by silica gel column chromatography using AcOEt-hexane (1:3). The crude product was recrystallized from EtOH to give colorless needles, mp 183-184°C. Yield 0.19 g (38%). Ir (KBr) cm^{-1} : 1670. $^1\text{H-Nmr}$ (CDCl_3/TMS) δ (ppm): 7.1-7.7 (13H, m), 7.75 (1H, s), 8.0-8.2 (2H, m). *Anal.* Calcd for $\text{C}_{23}\text{H}_{16}\text{N}_2\text{O}$: C, 82.12; H, 4.79; N, 8.33. Found: C, 82.30; H, 5.06; N, 8.40.

3,4,6-Triphenylpyridazine (9)

A mixture of **4a** (1.04 g, 2 mmol), iodobenzene (0.49 g, 2.4 mmol), $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (70 mg, 0.1 mmol), and Et_4NCl (0.33 g, 2.4 mmol) in dry DMF (10 ml) was heated at 80°C for 30 h. After removal of the solvent, the residue was purified by silica gel column chromatography using AcOEt-hexane (1:3). The crude product was recrystallized from EtOH to give colorless needles, mp 171-173°C (lit.⁶ mp 170-172°C). $^1\text{H-Nmr}$ (CCl_4/TMS) δ (ppm): 7.1-7.6 (13H, m), 7.75 (1H, s), 8.0-8.3 (2H, m).

According to the above procedure, **9** was obtained in 26% from bromobenzene.

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