

PALLADIUM-CATALYZED CROSS-COUPLING REACTION: DIRECT ALLYLATION
OF ARYL BROMIDES WITH ALLYL ACETATE

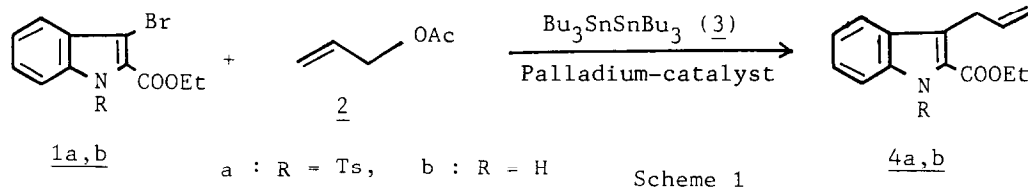
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Abstract: Various aryl bromides underwent a palladium-catalyzed cross-coupling reaction with allyl acetate in the presence of hexa-n-butyliditin to give the allylated products in very high yields.

The palladium-catalyzed cross-coupling reaction of an organotin reagent with an organic halide or its equivalent has been extensively studied^{1,2)} in recent years. Although it takes place under mild condition and tolerates a wide variety of functional groups, there are some limitations for synthesizing various organic frameworks, since the organometallic partner cannot conveniently be synthesized in some cases. On the other hand, there are only a few methods³⁾ for the direct cross-coupling reaction which does not involve an organometallic reagent as a coupling partner.

Previously we reported⁴⁾ the regioselective vinylation at the C₃-position of indole nucleus using palladium. In this communication, we describe that ethyl N-tosyl-3-bromoindole-2-carboxylate (1a) was directly coupled with allyl acetate (2) in the presence of hexa-n-butyliditin (3) and palladium catalyst to give C₃-allylated product (4a) in high yield (Scheme 1), and this one-step-allylation was applicable to various aryl bromides.



The typical experimental procedure is as follows. A mixture of bromide (1a, 1 mmol), allyl acetate (2, 1.5 mmol), ditin (3, 1.5 mmol), and palladium catalyst (9, 0.1 mmol) in DMF (1 ml) was heated at 120°C for 1.0 hr. The resulting black solution was worked up and purified by column chromatography on alumina to give the product (4a) in 88% yield as a colorless solid. The results are summarized in Table I. The use of palladium catalysts coordinated by bidentate ligands such as 9, 10, and 11 gave the product (4a) in very high yields (runs 1, 2, and 3),⁵⁾ but the use of monodentate phosphine palladium (12) was less effective (run 4). The N-unprotected indole (1b) and 5-bromo-

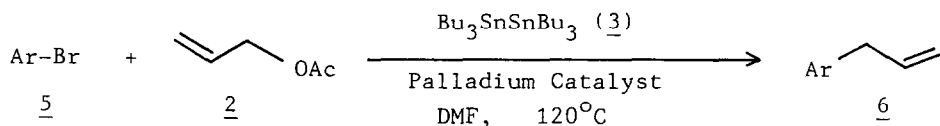
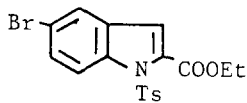
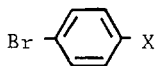


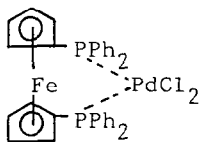
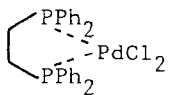
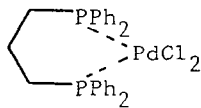
Table I

Run	Ar-Br	Palladium Catalyst	Reaction ^{a)} Time (hr)	Yield(%)	Product(<u>6</u>) ^{d)} mp(°C)
1	<u>1a</u>	<u>9</u>	1.0	88	68.5-71.5
2	<u>1a</u>	<u>10</u>	1.5	84	
3	<u>1a</u>	<u>11</u>	1.0	81	
4	<u>1a</u>	<u>12</u>	2.0	47	
5	<u>1b</u>	<u>9</u>	0.5 ^{b)}	49	85-87
6	<u>7</u>	<u>9</u>	4.5 ^{b)}	59	oil
7	<u>8a</u>	<u>9</u>	0.5 ^{b)}	86	137-139
8	<u>8b</u>	<u>9</u>	0.5 ^{c)}	86	oil
9	<u>8c</u>	<u>9</u>	0.5	69	89-92

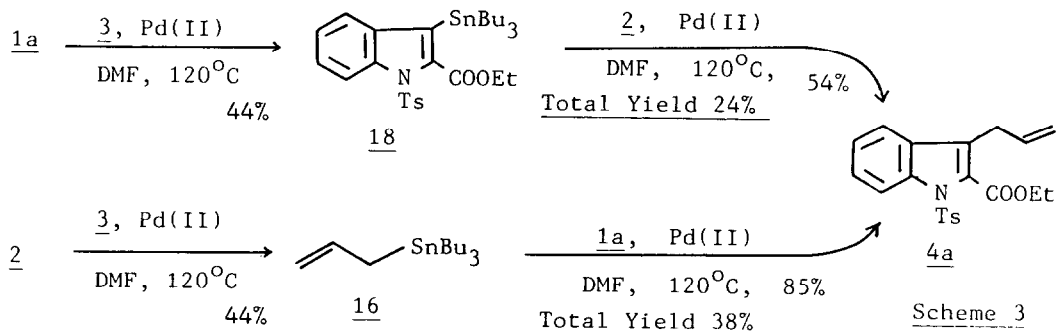
a) Ar-Br : Allyl acetate : Bu₃SnSnBu₃ : Catalyst = 1 : 1.5 : 1.5 : 0.1 b) Ar-Br : Allyl acetate : Bu₃SnSnBu₃ : Catalyst = 1 : 2 : 3 : 0.1 c) Toluene was used as a solvent at reflux temperature. d) All new compounds were satisfactorily identified by spectral data and elemental analyses.

78

a: X=CONH₂
b: X=COPh
c: X=NHCOCH₃

91011

(PPh₃)₂PdCl₂
12



Although palladium-catalyzed allylation using allyltin (16)^{2a)} or aryltin (14)^{2d)} has been already reported, there is no literature concerning the direct allylation like our present work. Consequently we believe that this reaction could be classified as a new type of cross-coupling reaction and provide a new methodology for carbon-carbon bond formation. Further investigation for the mechanistic detail and application of this direct cross-coupling are now in progress.

References and Notes

This paper forms Part XIII of "Synthetic Studies on Indoles and Related Compounds"

- 1) a) M. Kosugi, Y. Shimizu, and T. Migita, *Chem. Lett.*, 1423 (1977). b) D. Milstein and J. K. Stille, *J. Amer. Chem. Soc.*, 100, 3636 (1978). c) M. W. Logue and K. Teng, *J. Org. Chem.*, 47, 2549 (1982). d) K. Kikukawa, K. Kono, F. Wada, and T. Matsuda, *J. Org. Chem.*, 48, 1333 (1983). e) E. Keinan and M. Peretz, *J. Org. Chem.* 48, 5302 (1983). f) W. F. Goure, M. E. Wright, P. D. Davis, S. S. Labadie, and J. K. Stille, *J. Amer. Chem. Soc.*, 106, 6417 (1984).
- 2) a) M. Kosugi, K. Sasazawa, Y. Shimizu, and T. Migita, *Chem. Lett.*, 301 (1977). b) B. M. Trost and E. Keinan, *Tetrahedron Lett.*, 21, 2595 (1980). c) J. P. Godschalx and J. K. Stille, *Tetrahedron Lett.*, 21, 2599 (1980). d) F. K. Sheffy, J. P. Godschalx, and J. K. Stille, *J. Amer. Chem. Soc.*, 106, 4833 (1984).
- 3) For example, copper-promoted Ullmann reaction is known to be slow and often results in extensive homo-coupling. W. Carruthers, In "Comprehensive Organometallic Chemistry"; G. Wilkinson, et al., Ed.; Pergamon Press: New York, 1982; Vol. 7, p 661.
- 4) Y. Murakami, Y. Yokoyama, and T. Aoki, *Heterocycles*, 22, 1493(1984).
- 5) It has been reported that 9 is the most effective catalyst among these palladium complexes. T. Hayashi, M. Konishi, Y. Kobori, M. Kumada, T. Higuchi, and K. Hirotsu, *J. Amer. Chem. Soc.*, 106, 158 (1984).

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