borane derivatives,[13] where hydroboration is relatively facile. More recently, transition-metal catalyst precursors have been utilized[14,15] to activate alkenes and alkynes toward hydroboration of boranes for the production of small carboranes.

Detailed investigations are continuing in an effort to more fully define the scope of reaction reported herein with respect to other rhodacarboranes and alkenes.

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Supplementary Material Available: FT-NMR and IR data, *x*, *y*, *z*, and *B* values, atomic distances and angles, and X-ray data for II (32 pages). Ordering information is given on any current masthead page.

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Ortho-Alkylation of Acetanilides Using Alkyl Halides and Palladium Acetate

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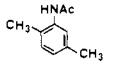
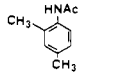
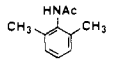
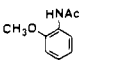
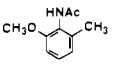
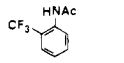
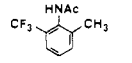
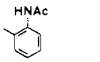
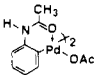
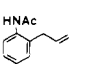
Palladium-mediated catalysis which is useful in carbon–carbon bond formation usually involves Pd^0 to Pd^{II} recycle.[1] The halogenation of azobenzene with palladium chloride represents an intriguing catalytic reaction that does not involve a palladium recycle.[2] A Pd^{II} to Pd^{IV} transformation has been postulated for this reaction. We wish to describe a new catalytic carbon–carbon bond-forming reaction that does not involve recycle of palladium and may involve a Pd^{IV} intermediate.

Our studies began with the observation of a direct one-pot synthesis of exclusively *o*-methylacetanilides using stoichiometric amounts of palladium acetate and methyl iodide (Table I). This reaction produced high yields of exclusively ortho-methylated products and can be used to synthesize a variety of highly functionalized acetanilides. By varying the solvent system, either mono- or di-ortho-substituted products were obtained. For example, the reaction of acetanilide with 2 equiv of palladium acetate and excess methyl iodide produced a quantitative yield of 2,6-dimethylacetanilide.[3] If the reaction of acetanilide with 1 equiv of palladium acetate was quenched with acetonitrile before methyl iodide was added to the reaction, then quantitative yields of *o*-methylacetanilide were produced. This *o*-alkylation reaction, which is summarized in Table I, represents a new direct method of ortho-alkylating highly functionalized acetanilides under mild conditions. Holton has previously demonstrated the synthesis of aryl ketones by acylation of preformed ortho-palladated benzylamines.[4]

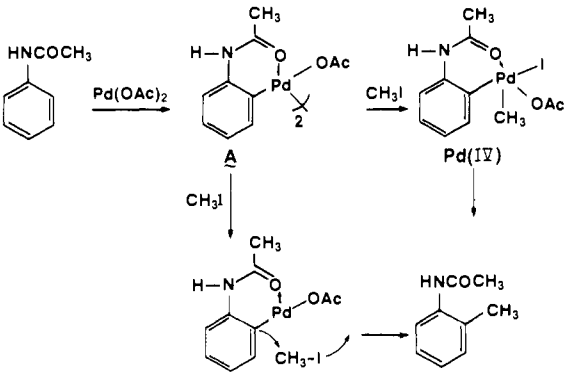
Other electrophiles such as ethyl iodide and allyl iodide reacted with acetanilide and palladium acetate to produce ortho-alkylated products (Table I). At 25 °C the reaction of allyl iodide with ortho-palladated acetanilide[6] produced *o*-allylacetanilide in a 76% yield (Table I);[5b] addition of triethylamine to this reaction, at 100 °C for 8 h, converted *o*-allylacetanlide to *N*-acetyl-2-methylindole in a 23% yield (eq 1).[5]

Table I. Ortho-Alkylation of Acetanilides with $Pd(OAc)_2$ and Alkyl Iodides[a]

Substrate	Method	Product[f]	Isolated[g] yield, %	glpc. yield, %
	A[b]		81	100
	A		81.4	
	A		86.4	
	B[c]		81.1	100
	B		79.7	
	C[d]		71.7	93.7
	A		71.3	100
	D[e]		76.2	

[a] All reactions were run in HOAc except for method C. [b] Method A: 1.5 equiv of $Pd(OAc)_2$, 3 h; 10–15 equiv of MeI, 27 equiv of CH_3CN, 8 h, 60 °C. [c] Method B: 1.5 equiv of $Pd(OAc)_2$ per ortho-positioned hydrogen, 15 equiv of CH_3I, 100 °C. [d] 3 equiv of $Pd(OCOCF_3)_2$ in CF_3CO_2H, 80 °C, 3 h; 10 equiv of CH_3I, 2 h, 70 °C. [e] 10 equiv of allyl iodide, 0 °C, 4 h. [f] Products identical in all respects with material prepared by alternate procedures. [g] Isolated yields were purified by recrystallization.

Scheme I



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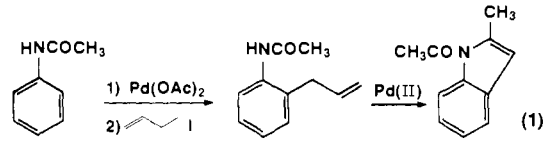

(1)

Two possible mechanisms of the ortho-methylation reaction are considered in Scheme I. The first step of this reaction involves the well-precedented ortho-metalation of acetanilides.[6] We found that the metalation reaction occurred readily with a variety of acetanilides including ortho-substituted compounds, even though it was reported that ortho-substituted acetanilides could not be metalated with $Pd(OAc)_2$.[6] Under our reaction conditions, the metalated products, such as A, could be isolated by omitting the alkylating agents. It was also found that the metalation reaction was inhibited by donor solvents such as DMF, DMA, and acetonitrile; this inhibiting effect allowed the synthesis of exclusively monomethylacetanilides (see Table I).

The alkylation step may involve either an electrophilic attack of MeI on the Pd–carbon bond[7] or a Pd^{IV} intermediate[8] as depicted by Scheme I. These mechanistic pathways are supported by the following observations: (1) EtI reacted 5.5 times slower than MeI at 50 °C in a competition experiment with complex A yielding, respectively, *o*-ethyl- and *o*-methylacetanilide. (2) Complex A was alkylated with methyl triflate and dimethyl sulfate. These reactivity patterns are consistent with an S_N2 mechanism and not a radical pathway.[9,10]

The following observations suggest that the slow step of the ortho-methylation reaction is the ortho-metalation step: (1) The rate of methylation of complex A was much faster than the overall rate of methylation of acetanilide with CH_3I and palladium acetate. (2) The overall rate of the reaction was increased by a factor of 12 when the more electrophillic palladium trifluoroacetate was used instead of palladium acetate.

One of the most interesting features of the ortho-methylation reaction is the observation that the oxidation state of palladium is conserved in the +2 state.[11] We considered the possibility of producing a catalytic cycle. When 4 equiv of acetanilide were reacted with 1 equiv of $Pd(OAc)_2$ and 10 equiv of MeI at 100 °C in HOAc, 1.5 turnovers/Pd^{2+} were obtained in 2.5 h. The only observed products of this reaction were *o*-methylacetanilide and palladium diiodide. When the above reaction was performed with palladium trifluoroacetate in trifluoroacetic acid, 1.8 turnovers/Pd^{2+} were achieved in 5.0 min. Further support for catalysis was demonstrated in the reaction of excess acetanilide, $Pd(OAc)_2$, and MeI in trifluoroacetic at 100 °C in the presence of excess AgOAc. Under these conditions 10 turnovers/Pd^{2+} were achieved in 10 min. Since PdI_2 (formed after the methylation step) does not metalate acetanilide under our reaction conditions, AgOAc was used to regenerate the more electrophillic $Pd(OAc)_2$ catalyst.

The results described in this manuscript demonstrate the feasibility of practical carbon–carbon bond formation that utilizes an ortho-metalation reaction in conjuction with electrophilic alkylating agents and avoids the need for Pd^0 to Pd^{II} recycle. We are presently studying the scope and mechanism of this reaction.

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(11) A Pd^0 intermediate has been ruled out for the following reasons: (1) The well-precedented ortho-metalation step (first step) has been characterized as an electrophilic attack of Pd^{2+} on the aromatic ring. (2) The alkylation step of complex A (Pd^{II}) with CH_3I proceeds readily under mild conditions (25 °C in toluene) where reduction of Pd^{2+} to Pd^0 is unlikely to occur. (3) Rigorous exclusion of air or deliberate inclusion of air have no effect on the reaction.

Acknowledgment. We are grateful to Drs. Clark Landis, Patrick Lennon, and Don Morris for helpful discussions and Dr. Robert Kaley, Jim Scanlon, and Dr. Don Willis for technical assistance.

Registry No. PhNHAc, 103-84-4; *m*-MeC_6H_4NHAc, 537-92-8; *p*-MeC_6H_4NHAc, 103-89-9; *o*-$MeOC_6H_4NHAc$, 93-26-5; *o*-$CF_3C_6H_4NHAc$, 344-62-7; *o*-MeC_6H_4NHAc, 120-66-1; *o*-EtC_6H_4NHAc, 33098-65-6; $Pd(OAc)_2$, 3375-31-3; *o*-acetamidophenylpalladium acetate dimer, 72573-63-8; *N*-(2,5-dimethylphenyl)acetamide, 2050-44-4; *N*-(2,4-dimethylphenyl)acetamide, 2050-43-3; *N*-(2,6-dimethylphenyl)acetamide, 2198-53-0; *N*-(2-methoxy-6-methylphenyl)-acetamide, 50868-76-3; *N*-[2-(trifluoromethyl)-6-methylphenyl]acetamide, 91759-50-1; *N*-[2-(2-propenyl)phenyl]acetamide, 68267-69-6; 1-acetyl-2-methyl-1*H*-indole, 37842-85-6.

Aza Macrocycle That Selectively Binds Lithium Ion with Color Change

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As a part of program directed to a study of the aza macrocyclic compounds related to porphyrines and phthalocyanines, new deeply colored tetraaza macrocycles have been synthesized. We have recently reported a synthesis and tautomerism, shown by Scheme I, of a hexaaza macrocycle containing four pyridine rings connected by two nitrogen bridges.[1] In this paper we report the synthesis and a survey of the complexing properties of the related tetraaza macrocycles. Borror and Haeberer had shown that 2-chloroquinoline reacted with α-cyanoacetamide to give 2-quinolyl-2(1*H*)-quinolylideneacetonitrile.[2] We then applied this reaction to 6,6′-dibromo-2,2′-bipyridine to gain a macrocycle involving pyridine rings connected by carbon bridges.

α-Cyanoacetamide in DMF was treated with sodium hydride to give the sodium salt to which was added 0.25 mol equiv of 6,6′-dibromo-2,2′-bipyridine.[3] The deep-red suspension obtained was stirred for 6 h at 120 °C, water was added then filtered, and the precipitate was washed with acetone to furnish the red fine needles. The spectral data obtained with these crystals clearly indicate that it exists as the fully conjugated form composed of two 2-pyridyl-2(1*H*)-pyridylideneacetonitrile residues (**1**) (20% yield, mp >400 °C dec)[4,5] (Scheme II).

Dicyano macrocycle **1** can be hydrolyzed by 70% sulfuric acid at 120 °C to give dark-red tetraaza macrocycle **2**. ^1H NMR spectrum shows a singlet (2 H) of strongly hydrogen-bonded NH protons at δ 14.9. The tautomerism of a series of dipyridylmethanes has been studied by Daltrozzo, Scheibe, et al.[6] It is noteworthy that while *meso*-cyanodi-2-pyridylmethane is colorless and therefore the dipyridylmethane form predominates over the methine form,[7] deep-red fully conjugated methine forms are favored for our cyclic derivatives (**1** and **2**).

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(4) Satisfactory elemental analysis and mass spectral data were obtained for all new compounds.

(5) The IR spectrum shows conjugated nitrile absorption at 2180 cm^{-1}. The electronic spectrum points to a highly conjugated system, showing absorption maxima at 357 (ε 36600), 375 (37000), 508 (7000), 541 (5600), and 592 nm (3000) in 1-chloronaphthalene. No ^1H NMR data are available owing to the poor solubility of the product.

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