Late-Stage Ortho-C-H Bond Arylation and Alkylation of 9(10H)-Acridone Utilizing 2-Pyridinyl as a Removable Directing Group

ABSTRACT

A synthetic methodology for the palladium-catalyzed ortho-C-H bond arylation and alkylation of 9(10H)-acridanone with potassium aryl/alkyltrifluoroborate was presented. In the study, 2-pyridinyl was employed as a directing group toward ortho-selective C-H bond activation. The key palladacycle was prepared by the stoichiometric reaction of 9(10H)-acridanone and palladium acetate in acetic acid in a good yield. Its absolute structure was confirmed by X-ray crystallography. *p*-Benzoquinone (BQ) and tert-butyl alcohol were the key promoter and best solvent, respectively for the reaction. A variety of ortho arylated and alkypated N-(2-pyridinyl)-9(10H)-acridones were synthesized in modest to excellent yields. Finally, the 2-pyridinyl group can be easily removed by the treatment of MeOTf and Hydrazine to afford ortho-arylated and alkylated 9(10H)-acridanone in good yields.

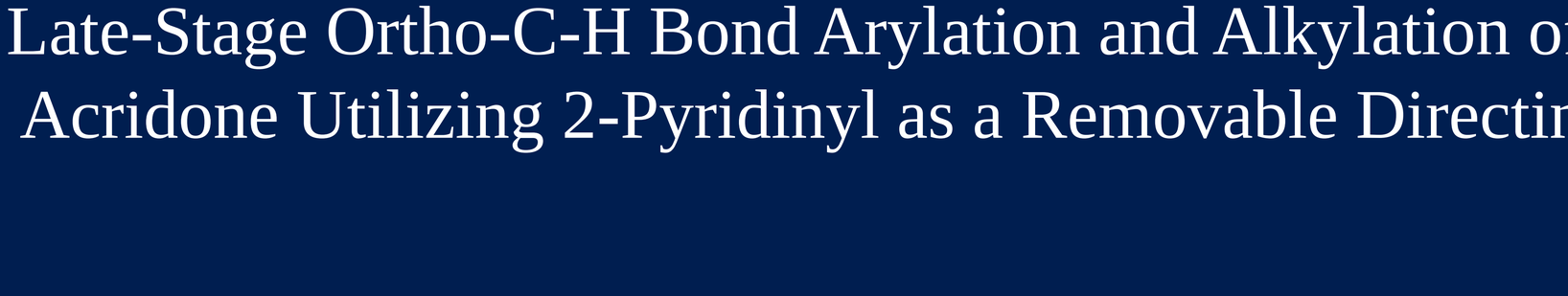
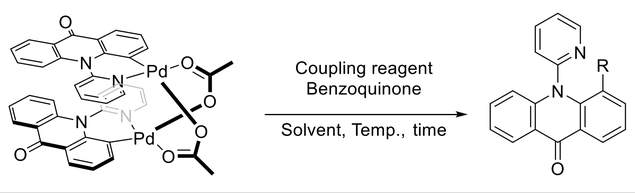


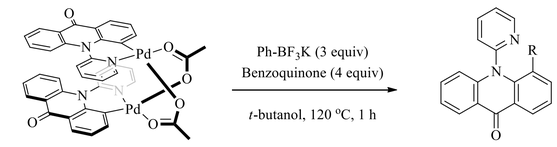
Table 1. Optimization Reaction

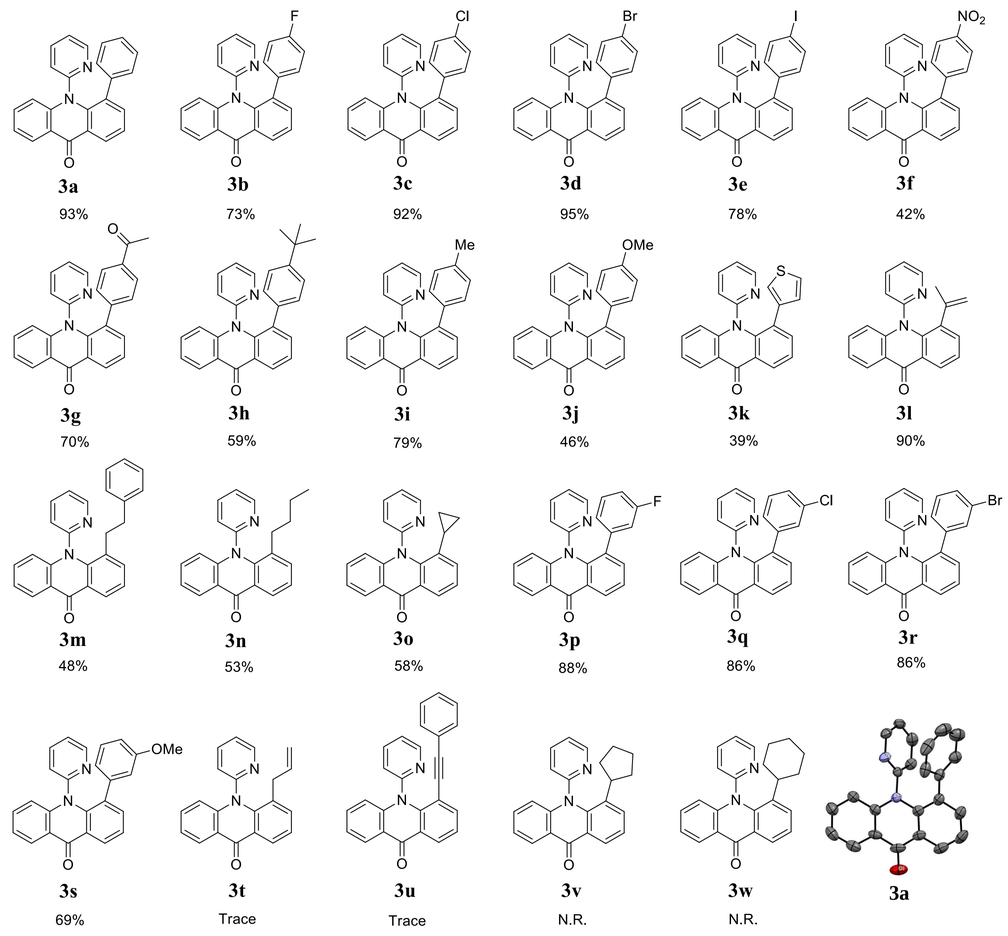


Entry	Solvent	Ph-BF_3K	BQ	Temp.(°C)	Yield(%)[a]
1	NMP	2 (equiv)	4 (equiv)	120	Trace
2	1,4-dioxane	2 (equiv)	4 (equiv)	120	Trace
3	*tert*-amylalcohol	2 (equiv)	4 (equiv)	120	33
4	*tert*-butylalcohol	2 (equiv)	4 (equiv)	120	51
6	*tert*-butylalcohol	3 (equiv)	4 (equiv)	120	93
7	*tert*-butylalcohol	4 (equiv)	4 (equiv)	120	94
8	*tert*-butylalcohol	5 (equiv)	4 (equiv)	120	71
9	*tert*-butylalcohol	3 (equiv)	0.5 (equiv)	120	38
10	*tert*-butylalcohol	3 (equiv)	1 (equiv)	120	51
11	*tert*-butylalcohol	3 (equiv)	2 (equiv)	120	53
12	*tert*-butylalcohol	3 (equiv)	3 (equiv)	120	54
13	*tert*-butylalcohol	3 (equiv)	4 (equiv)	120	79
14	*tert*-butylalcohol	3 (equiv)	4 (equiv)	80	79
15	*tert*-butylalcohol	3 (equiv)	4 (equiv)	90	83
16	*tert*-butylalcohol	3 (equiv)	4 (equiv)	100	85
17	*tert*-butylalcohol	3 (equiv)	4 (equiv)	110	82
18	***tert*-butylalcohol**	**3 (equiv)**	**4 (equiv)**	**120**	**93**

[a]Yields were determined by 1H NMR spectroscopy analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene as an internal standard.

Table 2. Substrate Scope





[a]Yields were determined by 1H NMR spectroscopy analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene as an internal standard.

Table 3. Proposed Mechanism

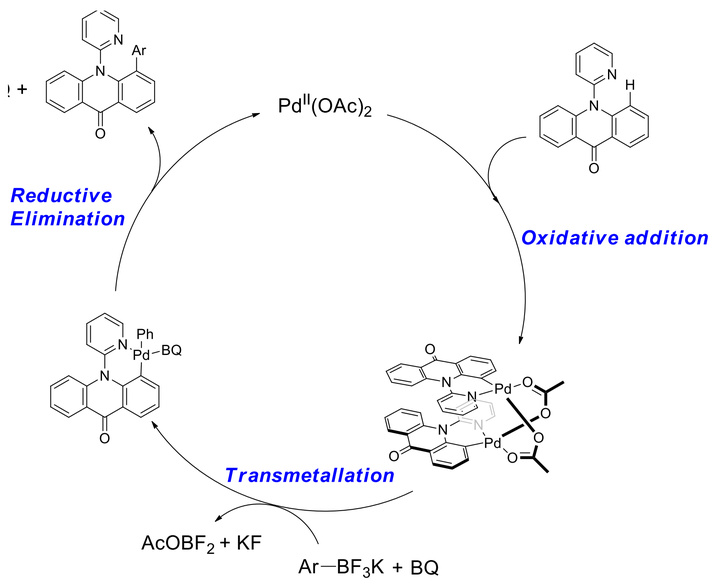
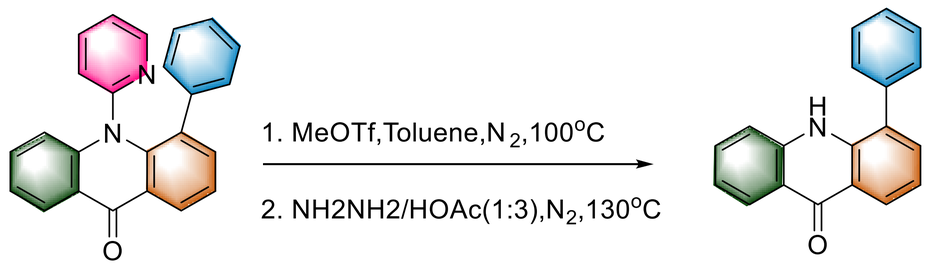


Table 4. Depyridination



Reference: [1] Chu, J.-H.; Chen, C.-C.; Wu, M.-J. *Organometallics* **2008**, *27*, 5173-5176.
[2] Chu, J.-H.; Wu, C.-C.; Chang, D.-H.; Lee, Y.-M.; Wu, M.-J. *Organometallics* **2013**, *32*, 272-282.