Benzocarbazolquinones and Benzonaphthofurandiones by Palladium Catalyzed Oxidative C-H Functionalization

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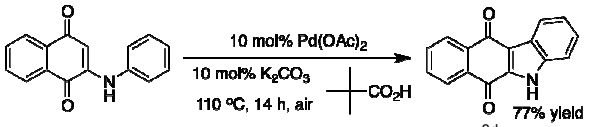
INTRODUCTION

Quinones are very interesting compounds not only because of their bright colours but also because of their diverse biological properties for example in the treatment of: tuberculosis, malaria, bacterial and parasitic infections and as antineoplastics.[1]

Within a program investigating C-H functionalization reactions we recently described improved methodology for the oxidative coupling of anilines with naphthoquinone.[2] Additionally, we have now studied the oxidative cyclization (formation of a C-C bond from two C-H bonds) of 2-anilino- and 2-phenyloxy- naphthoquinones.

RESULTS AND DISCUSSION

There are a number of precedents in the literature for the oxidative cyclization of 2-anilinonaphthoquinones to benzocarbazolquinones.[3] In the present study, we have developed upon the method reported by the group of Fagnou (scheme 1).[3d] We have investigated the use of other co-oxidants (such as $Cu(OAc)_2.H_2O$) and the effect of temperature upon the reaction (Table 1).



Scheme 1. Synthesis of benzocarbazolquinone.[3d]

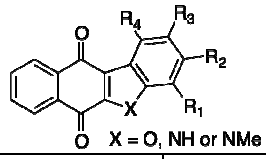
Table 1. Reaction conditions (Reaction time: 210 minutes)

Reac.	$Pd(OAc)_2$[a]	$Cu(OAc)_2$[a]	K_2CO_3[a]	Temp. (°C)	Yield (%)
1	10	---	10	110	71[b]
2	10	20	15	110	92[b]
3	10	20	20	120	63
4	10	20	20	160	78
5	10	20	25	180	75
6	10	---	25	160	52
7	---	20	20	160	0
8	10	20	---	160	15

[a] Quantities in mol %. [b] 19 hour reaction time.

Initially we reproduced the results of Fagnou and subsequently found that the inclusion of $Cu(OAc)_2.H_2O$ had a beneficial effect upon the reaction yield (Table 1, entries 1 and 2). At a shorter reaction time (210 min.) a lesser yield was obtained (entry 3). Increasing the reaction temperature made a substantial improvement to the yield whilst maintaining the shorter reaction time (entries 4 and 5). Control experiments revealed the importance of the individual components (entries 6, 7 and 8). The methodology was applied to other anilino-and phenyloxy- naphthoquinones (table 2). Regio-selective cyclization was observed (entries 3 and 4).

Table 2. Tetracyclic quinones prepared by oxidative C-H functionalization.



	Quinone	Reac. time (min)	Yield (%)
1	X = N; R_3 = CN	240	78
2	X = N; R_1 = OCH_3	340	71
3	X = N; R_4 = OCH_3	180	69
4	X = NMe; R_4 = OCH_3	120	68
5	X = N; R_1/R_4 = OCH_3	340	83
6	X = O; R_3 = OMe	180 (140°C)	61
7	X = O; All R = H	180 (140°C)	57

CONCLUSION

The present study has developed a new methodology for oxidative cyclization via functionalization of C-H bonds in anilino- and phenyloxy- naphthoquinones to give benzocarbazolquinones and benzonaphthofuran-diones in short reaction times and in good yields.

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