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Catalytic Oxidative Aromatic Cyclizations with Palladium.

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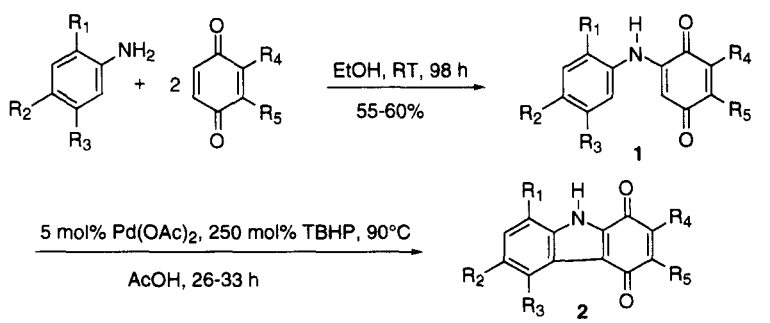
Abstract: Using *tert*-butyl hydroperoxide as oxidant, facile palladium-catalyzed cyclizations of arylaminoquiones have been performed.

The carbazole structure is found in a number of biologically active alkaloids.[1] Also, the related indolequinone ring system, common to the mitomycin antibiotics, shows interesting biological activity.[2] Some years ago we showed that palladium-promoted, stoichiometric cyclization of diphenylamine derivatives is a versatile reaction for preparation of different carbazoles.[3,4] Using a slight modification of our procedure, the alkaloid ellipticine, which shows activity aganist some forms of cancer, has been prepared.[5] Also carbazoloquinones such as **2b**[6], **2d**[7], murrayaquinone-A, **2e**, and pyrayaquinone-A and -B,[8] have been synthesized by this procedure. Murrayaquinone-A, **2e**, has recently been found to exhibit cardiotonic activity.[9] Because the procedure required stoichiometric amounts of palladium, attempts have been made to develop catalytic cyclization reactions.[6,7] In one of these attempts some catalytic activty was observed when 34% yield of **2d** was obtained, using 12 mol% $Pd(OAc)_2$ and 110 mol% $Cu(OAc)_2$ as oxidant.[7] We recently discovered that *t*-butyl hydroperoxide (TBHP), together with benzoquinone as co-catalyst, is a useful oxidant in palladium-catalyzed allylic carboxylations and lactonizations.[10] Although this system did not effect cyclization reactions, we have now found that TBHP alone is an efficient oxidant in palladium catalyzed cyclization of 2-arylamino-1,4-quinones. The preparation of some arylaminoquinones[11,12] and their subsequent cyclization is illustrated in Scheme 1. The cyclization reaction is performed in acetic acid at 90°C, using palladium acetate as catalyst and an excess of *tert*-butyl hydroperoxide as oxidant, giving good yields of carbazoloquinones **2 a-f**[12,13] (Table 1).



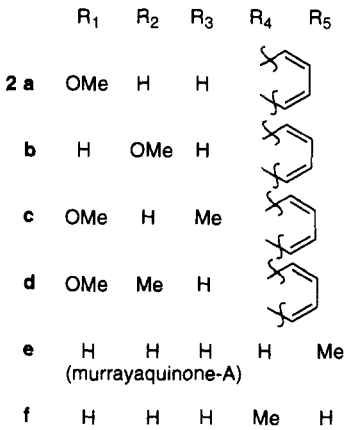
Scheme 1.

In order to probe the generality of the reaction, diphenylamine and diphenylether were reacted under similar conditions as the arylaminoquinones. With diphenylamine a moderate yield of carbazole was formed (ca. 30%, Table 1) but with diphenylether, no dibenzofuran could be detected. Both scope and optimum

Table 1. Oxidative Aromatic Ring Closure with $Pd(OAc)_2$ and TBHP.[a]

Product	Isolated Yield	Time
2 a	74%	27 h
2 b	66%	27 h
2 c	65%	26 h
2 d	59%	26 h
2 e	67%	33 h
2 f	60%	33 h
Carbazole	30%[b]	10 h

a) 5 mol% Pd(OAc), 250 mol% TBHP in acetic acid at 90°C. b) 110 mol% TBHP.



reaction conditions for the observed cyclization reaction are being studied further. With the exception of carbazole (70% yield with stoichiometric amount of $Pd(OAc)_2$)[3] and **2d** (84%)[7], the yields are approximately the same as found in the stoichiometric reactions, suggesting that the necessary reoxidation of palladium is the crucial step. The fact that the cyclization is strongly dependent on the quality of both palladium acetate and *tert*-butyl hydroperoxide indicates that the reaction conditions are crucial and gives hope that reaction conditions can be modified to broaden the scope of the reaction.

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References and notes.

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1. (a) Bergman, J.; Pelcman, B. in "Studies in Natural Products Chemistry", Atta-ur-Rahman; Le Quesne,P. W. (Eds) Springer-Verlag, Berlin, Heidelberg 1988. (b) Bhattacharyya, P.; Chakroborty, D. P. *Fortschritte der Chemie organisher Naturstoffe*, **1987**,*52*, 159. (c) Husson, H.-P. *The Alkaloids*, **1985**, *26*, 1.
2. Franck, R. W. in "Progress in the Chemistry of Organic Natural Products, Vol. 38, Springer-Verlag, New York, 1979, p. 1.
3. Åkermark, B.; Eberson, L.; Jonsson, E.; Petterson, E. *J. Org. Chem.* **1975**, *40*, 1365-1366.
4. For a general review of Palladium-assisted reactions see R. F. Heck, "Palladium Reagents in Organic Syntheses." Academic Press, Inc., London, 1985.
5. Miller, B. R.; Moock, T. *Tetrahedron Letters*, **1980**, *21*, 3319-3322.
6. Bittner, S.; Krief, P.; Massil, T. *Synthesis* , **1991**, 215-216.
7. Knölker, H.-J.; O'Sullivan, N. *Tetrahedron* , **1994**, *50*, 10893-10908.
8. Motoi, Y.; Ito, C.; Furukawa, H. *Chem. Pharm. Bull.*, **1991**, *39*, 328-334.
9. Takeya, K.; Itoigawa, M.; Furukawa, H. *Eur. J. Pharmacol.*, **1989**, *169*, 137.
10. Åkermark, B.; Larsson, M.; Oslob, J. *J. Org. Chem.* **1994**, *59*, 5729-5733.
11. ^1H NMR and elemental analyses were in full accordance with the proposed structures for **1a-d**.
12. ^1H NMR spectra for **1e-f** and **2e-f** were in full accordance with those reported in ref. 8.
13. ^1H NMR spectrum for **2b** was in full accordance with that reported in ref. 6, ^1H NMR spectrum for **2d** was in full accordance with that reported in ref. 7 and ^1H NMR spectra and elemental analyses were in accordance with the proposed structures for **2a, c**.

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