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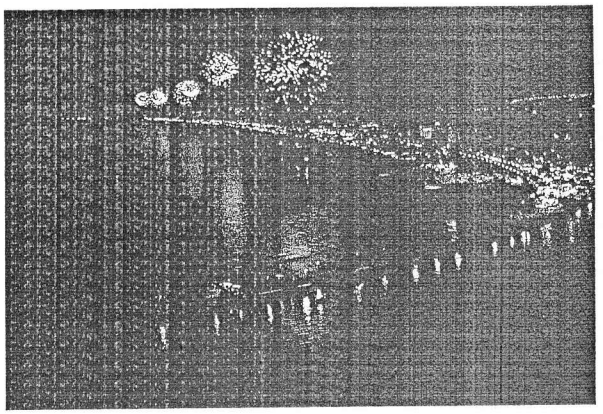

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CARBON MONOXIDE AS A REDUCTANT: SYNTHESIS OF INDOLES BY PALLADIUM CATALYZED REDUCTIVE CYCLIZATION OF β-NITROSTYRENES

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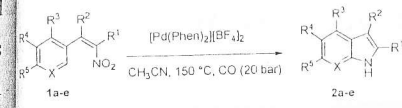
Several years ago, while investigating the possibility to use β-nitrostyrenes as aminating agents for olefins following our protocol originally devised for nitroarenes,[1] we found that a cyclization reaction to give indoles was observed instead. Better results were obtained employing palladium as catalyst in place of ruthenium. The reaction conditions were optimized using β-methyl-β-nitrostyrene (1a) as substrate and some results with different substrates are reported below.



	Yield
a. X = CH, R^1 = Me, R^2-R^5 = H	87.0
b. X = CH, R^1 = H, R^2 = Ph, R^3-R^5 = H	91.0
c. X = CH, R^1 = Me, R^2= Me, R^3-R^4 = H	66.2
d. X = CH, R^1 = Me, R^2 = OMe, R^3-R^4 = H	59.0
e. X = CH, R^1 = Me, R^3-R^4 = -CH=CH-CH=CH-, R^2, R^5 = H	68.5
e. X = N, R^1 =Me, R^2-R^5 = H	64.0

While our work was in progress, Hsieh and Dong reported a similar approach for the synthesis of 3-arylsubstituted indoles from α-aryl-β-nitrostyrenes (R1= H, R2 = Ar in the scheme above).[2] Experimental conditions reported in that paper are milder (100 °C, DMF, 2 bar CO absolute pressure) then ours. We reproduced those results and we confirm they work well for α-aryl-β-nitrostyrenes, but fail almost completely when R1 ≠ H, whereas our conditions are suitable also in this case. Unlike most reported cyclization reaction affording indoles, our strategy does not require the use of a doubly functionalized arene (e.g. an o-bromoaniline) and in most cases the starting materials can be easily prepared by a Henry reaction.

References

[1] a) Cenini, S.; Ragaini, F.; Tollari,S.; Paone,D., *J. Am. Chem. Soc.* **1996**, *118*, 11964. b) Ragaini,F.; Cenini,S.; Tollari, S.; Tummolillo, G.; Beltrami, R., *Organometallics* **1999**, *18*, 928. c) Ragaini, F.; Cenini, S.; Turra, F.; Caselli, A., *Tetrahedron* **2004**, *60*, 4989.

[2] T. H. H. Hsieh, V. M. Dong, *Tetrahedron* **2009**, *65*, 3062-3068.