SYNLETT
Spotlight

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

1,4-Naphthoquinone

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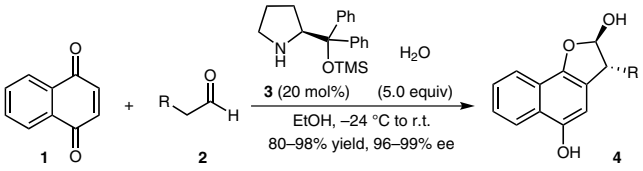
Introduction

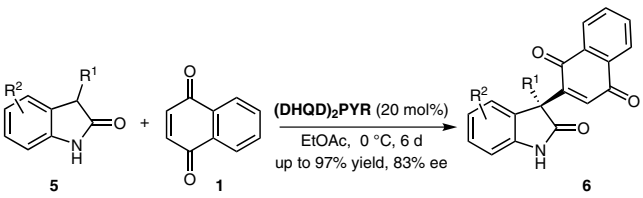
1,4-Naphthoquinone (**1**) is a yellow crystal, slightly soluble in water, soluble in benzene, diethyl ether, chloroform, glacial acetic acid, etc. Having two reactive functional groups, a C–C double bond and two ketone carbonyls, 1,4-naphthoquinone has been widely applied in organic reactions, such as Michael-type additions,[1] aldol-type reactions, Diels–Alder reactions,[2] cycloadditions,[3] Friedel–Crafts reactions,[4] and epoxidation.[5] Further, 1,4-naphthoquinones are widely used in antibacterial and antitumor drugs, and it is an important structural motif in many natural products, such as vitamin K. In addition, its derivatives are also used in industry on a ton scale as dye reagents. 1,4-Naphthoquinone is commercially available (CAS number: 130-15-4) and can be prepared industrially by the oxidation of naphthalene using vanadium pentoxide (V_2O_5) as catalyst.

Abstracts

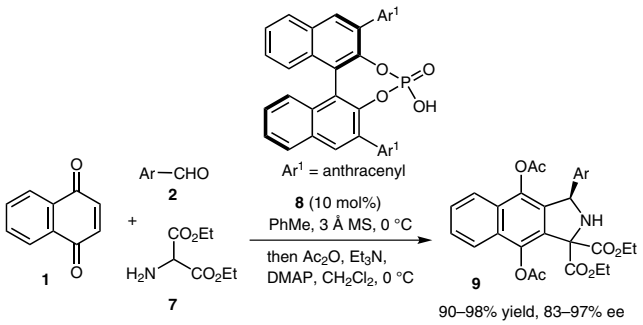
(A) Using 1,4-naphthoquinone (**1**) as arylation reagent, Jørgensen and co-workers realized the highly enantioselective α-arylation of aldehydes **2**, affording α-arylated products **4** with a dihydroquinone functionality.[6]



(B) Zhou[7] and Wang & Jiang[8] independently reported the organocatalytic asymmetric Michael addition of oxindole **5** to 1,4-naphthoquinone, which could furnish the 3,3-disubstituted oxindoles **6** that are widely presented in natural products and pharmaceutically active compounds.



(C) In the presence of phosphoric acid **8**, the asymmetric 1,3-dipolar cycloaddition of 1,4-naphthoquinone **1** with in situ generated azomethine ylides from aldehydes **2** and diethyl aminomalonate **7** was achieved by Gong and co-workers, which afforded the biologically active isoindolines **9** with excellent yield and ee.[9]



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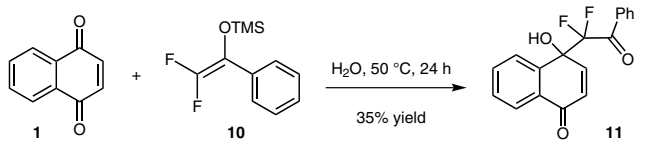
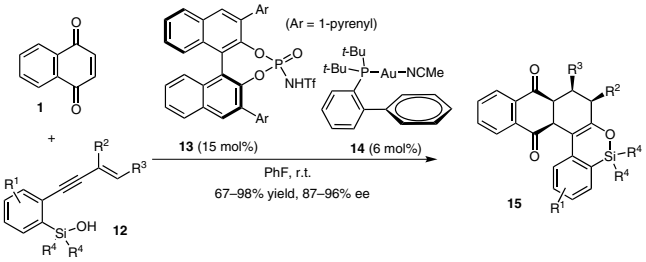
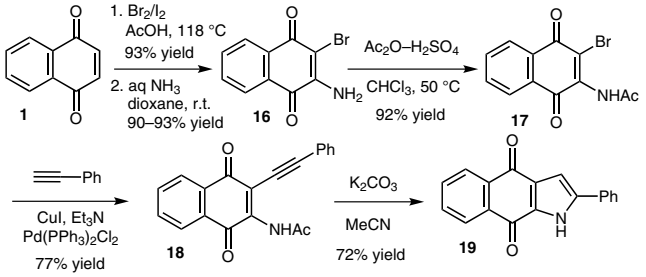
(D) An 'on water' catalyst-free Mukaiyama-aldol reaction of difluoroenoxysilane **10** with **1** was developed by Zhou and co-workers, which furnishes α,α-difluoro-β-hydroxy ketone **11**.[10]



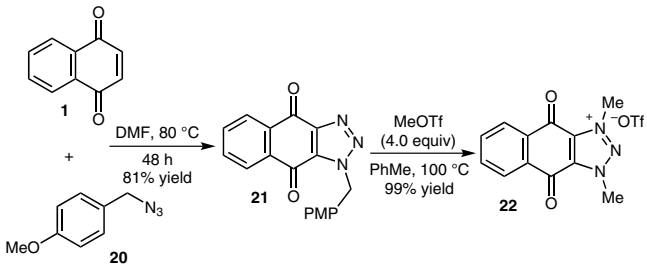
(E) Gong and colleagues discovered the asymmetric relay catalytic cascade intramolecular hydrosiloxylation–asymmetric D–A reaction of enynyl silanol **12** and 1,4-naphthoquinone by employing the hybrid Au(I)–Brønsted acid binary catalyst system, which provided the polycyclic compounds in high yield and ee.[11]



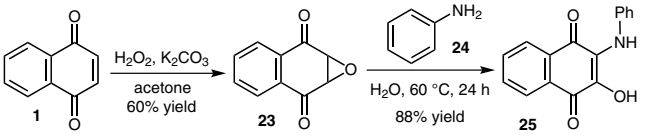
(F) Benz[*f*]indole-4,9-diones **19** can be synthesized from commercially 1,4-naphthoquinone through bromination of 1,4-naphthoquinone, followed by efficient cross-coupling of bromide **17** with phenylacetylene and intramolecular cyclization of acetylenic amide **18**.[12]



(G) The cycloaddition of azide **20** with 1,4-naphthoquinone **1** is contributing to a convenient and safe synthetic route to 4,9-dioxo-1,3-dimethylnaphtho[2,3-*d*][1,2,3]triazol-3-ium salt **22**, which showed significant anticancer activities against melanoma, non-small cell lung cancer, colon cancer and central nervous system cancer.[13]



(H) The synthesis of 2-hydroxy-3-anilino-1,4-naphthoquinone **25**, which shows in vivo antimalarial activity, had been achieved through the epoxidation of 1,4-naphthoquinone, and epoxide-opening reaction of epoxide **23** with aniline **24**.[14]



References

(1) (a) Alemán, J.; Jacobsen, C. B.; Frisch, K.; Overgaard, J.; Jørgensen, K. A. *Chem. Commun.* **2008**, 632. (b) Sun, J.-W.; Wang, X.-S.; Liu, Y. *J. Org. Chem.* **2013**, *78*, 10560.

(2) (a) Albrecht, Ł.; Gómez, C. V.; Jacobsen, C. B.; Jørgensen, K. A. *Org. Lett.* **2013**, *15*, 3010. (b) Lee, J.; Panek, J. S. *Org. Lett.* **2014**, *16*, 3320.

(3) He, Z.; Liu, T.; Tao, H.; Wang, C.-J. *Org. Lett.* **2012**, *14*, 6230.

(4) Murphy, B.; Goodrich, P.; Hardacre, C.; Oelgemöller, M. *Green Chem.* **2009**, *11*, 1867.

(5) Berkessel, A.; Guixà, M.; Schmidt, F.; Neudörfl, J. M.; Lex, J. *Chem. Eur. J.* **2007**, *13*, 4483.

(6) (a) Alemán, J.; Cabrera, S.; Maerten, E.; Overgaard, J.; Jørgensen, K. A. *Angew. Chem. Int. Ed.* **2007**, *46*, 5520. (b) Alemán, J.; Richter, B.; Jørgensen, K. A. *Angew. Chem. Int. Ed.* **2007**, *46*, 5515.

(7) Yu, J.-S.; Zhou, F.; Liu, Y.-L.; Zhou, J. *Beilstein J. Org. Chem.* **2012**, *8*, 1360.

(8) Siau, W.-Y.; Li, W.; Xue, F.; Ren, Q.; Wu, M.; Sun, S.; Guo, H.; Jiang, X.; Wang, J. *Chem. Eur. J.* **2012**, *18*, 9491.

(9) Wang, C.; Chen, X.-H.; Zhou, S.-M.; Gong, L.-Z. *Chem. Commun.* **2010**, *46*, 1275.

(10) Yu, J.-S.; Liu, Y.-L.; Tang, J.; Wang, X.; Zhou, J. *Angew. Chem. Int. Ed.* **2014**, *53*, 9512.

(11) Han, Z.-Y.; Chen, D.-F.; Wang, Y.-Y.; Guo, R.; Wang, P.-S.; Wang, C.; Gong, L.-Z. *J. Am. Chem. Soc.* **2012**, *134*, 6532.

(12) Shvartsberg, M. S.; Kolodina, E. A.; Lebedeva, N. I.; Fedenok, L. G. *Tetrahedron Lett.* **2009**, *50*, 6769.

(13) Shrestha, J. P.; Chang, C.-W. T. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 5909.

(14) Rezende, L. C. D.; Fumagalli, F.; Bortolin, M. S.; Oliveira, M. G.; Paula, M. H.; Andrade-Neto, V. F.; Emery, F. S. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 4583.