Synthesis of Endoperoxides

Outline

1. Introduction
2. 1,2-dioxolanes, 1,2-dioxanes and 1,2-dioxenes
    a. triplet oxygen as O-O source
    b. singlet oxygen as O-O source
    c. hydroperoxide as O-O source
3. 1,2,4-trioxanes
4. 1,2,4,5-tetraoxanes

Not included:

- Small ring/Macrocyclic peroxides
- 1,2,4-trioxolanes (ozonolysis is the only method)
- Some harsh/specific methods

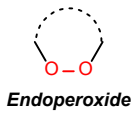
Key references:

Terent'ev, A. O.; Borisov, D. A.; Vil', V. A.; Dembitsky, V. M. *Beilstein J. Org. Chem.* **2014,** *10,* 34–114. doi:10.3762/bjoc.10.6

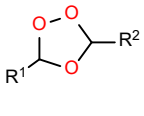
Ferrié, L. Advances in the synthesis of 1,2-dioxolanes and 1,2-dioxanes. **2021**, 57-146. https://doi.org/10.1016/bs.aihch.2021.03.001

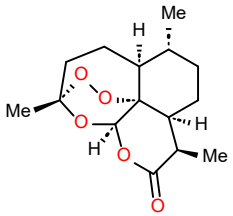
Korshin, E. E.; Bachi, M. D. Synthesis of Cyclic Peroxides. 2009. https://doi.org/10.1002/9780470682531.pat0351

1. introduction

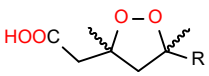


Endoperoxide

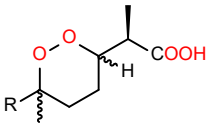




artemisinin



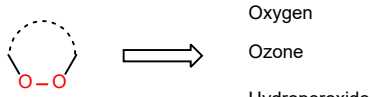
plakinic acids



norterpenes

General consideration:

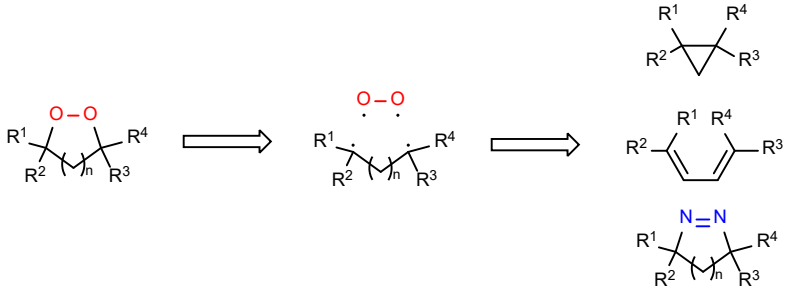
Since the direct formation of O-O bond is not really possible, reagents with O-O bond are usually required in endoperoxide synthesis.



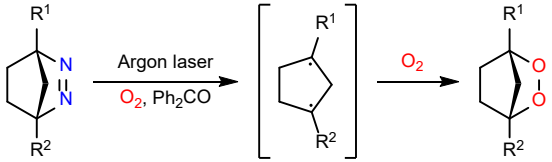
Synthesis of Endoperoxides

1,2-dioxolanes, 1,2-dioxanes and 1,2- dioxenes

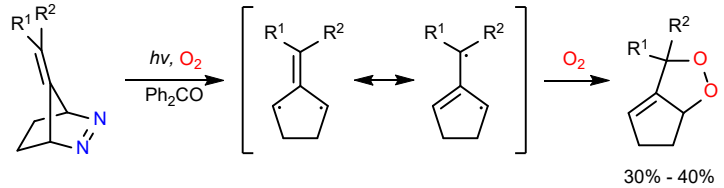
Radical peroxidation with triplet oxygen
Diradical peroxidation



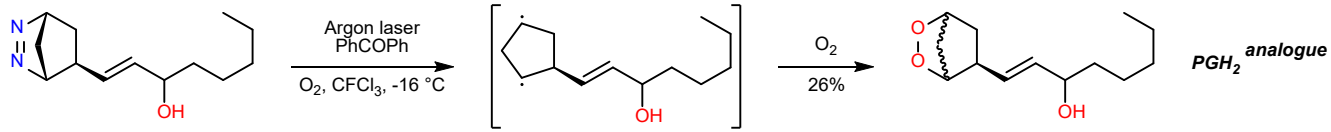
Diazo compounds as diradical precursor



Adam, W et al. J. Am. Chem.Soc., **1989**, 111, 751 doi.org/10.1021/ja00184a064

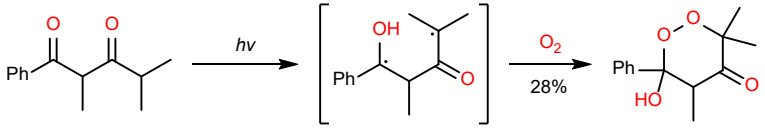


Wilson, R. M.; Geiser. F, *J. Am. Chem. Soc.,* 1978, 100, 2225. doi.org/10.1021/ja00475a039

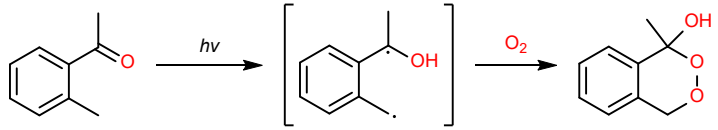


Wilson, R. M. Et al. *J. Org. Chem.* **1986**, 51, 4028. doi.org/10.1021/jo00371a021.

Norrish type II diradical precursor



Yoshioka, M. et al. *J. Chem. Soc., Chem. Commun.*, **1986,** 639. doi.org/10.1039/C39860000639

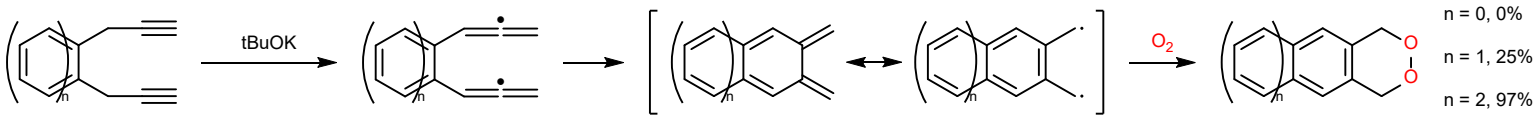


Yates, P et al, *Tetrahedron Lett.*,**1968**, 5389 doi.org/10.1016/S0040-4039(00)89786-5

1,2-dioxolanes, 1,2-dioxanes and 1,2- dioxenes

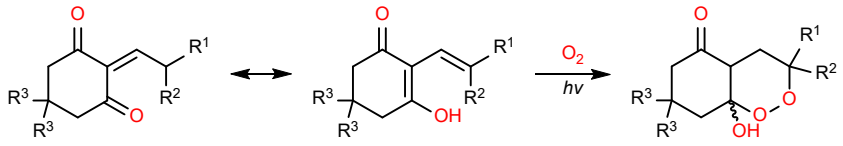
Radical peroxidation with triplet oxygen
Diradical peroxidation

Latent diradicals



Bowes, C. M. et al. *Tetrahedron Lett.*,**1973,** 3181 doi.org/10.1016/S0040-4039(00)79805-4

Formal [4 + 2]



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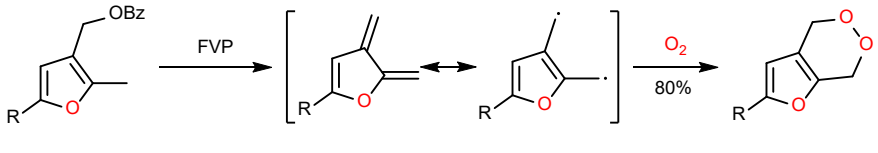
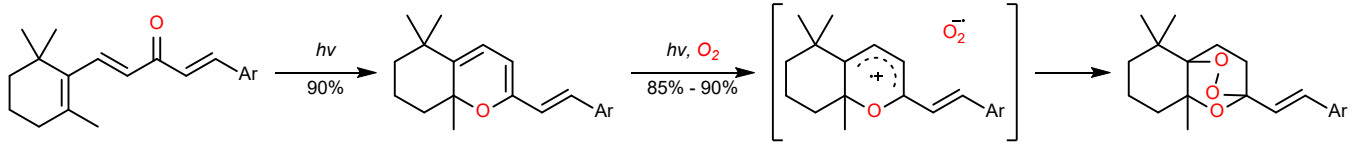
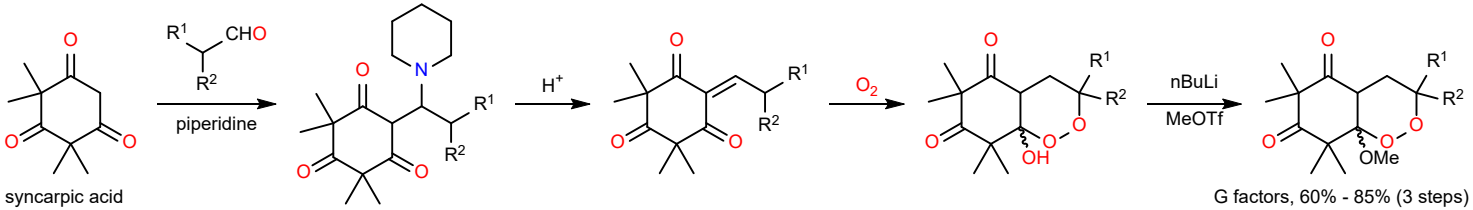


Chou, C.-H.; Trahanovsky, W. S. *J. Org. Chem.* **1995**, 60, 5449. doi.org/10.1021/jo00122a024



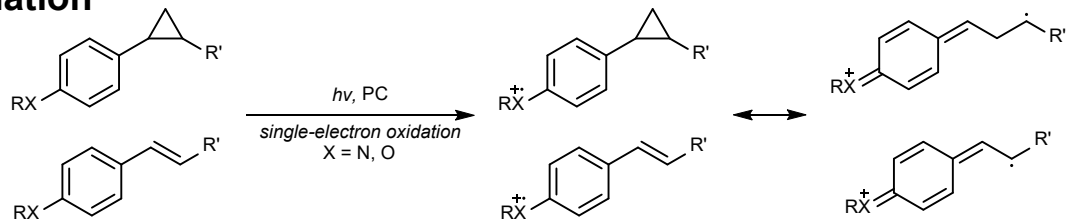
M. L. Bolte, W. D. Crow and S. Yoshida, *Austr. J. Chem.*, **1982, 35**, 1421 https://doi.org/10.1016/B978-0-08-029223-6.50018-5

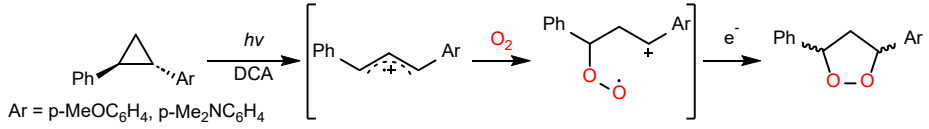


K. Fuchs and L. A. Paquette, *J. Org. Chem.*, **1994, 59,**, 528 doi.org/10.1021/jo00082a007

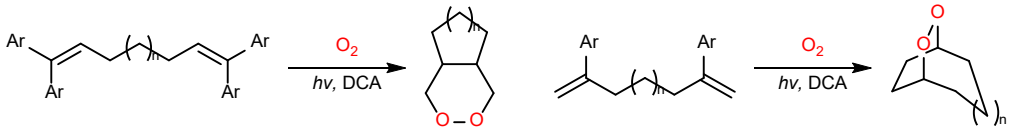
1,2-dioxolanes, 1,2-dioxanes and 1,2- dioxenes

Radical peroxidation with triplet oxygen
Radical cation peroxidation

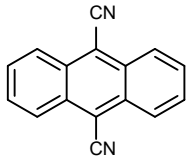




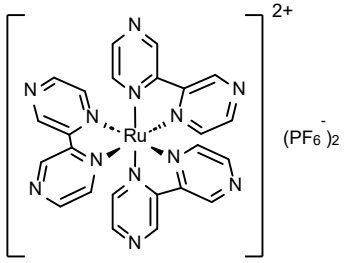
Maeda, H.; Nakagawa, H.; Mizuno, K. *Photochem. Photobiol. Sci.* 2003, 2 (11), 1056 doi.org/10.1039/B306186H.

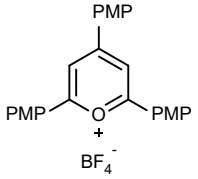


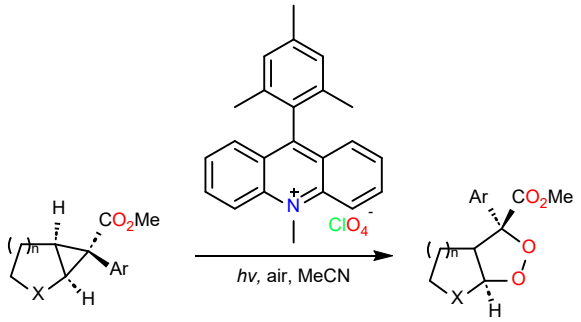
Lu, Z.; Parrish, J. D.; Yoon, T. P. Tetrahedron 2014, 70 (27–28), 4270 doi.org/10.1016/j.tet.2014.02.045



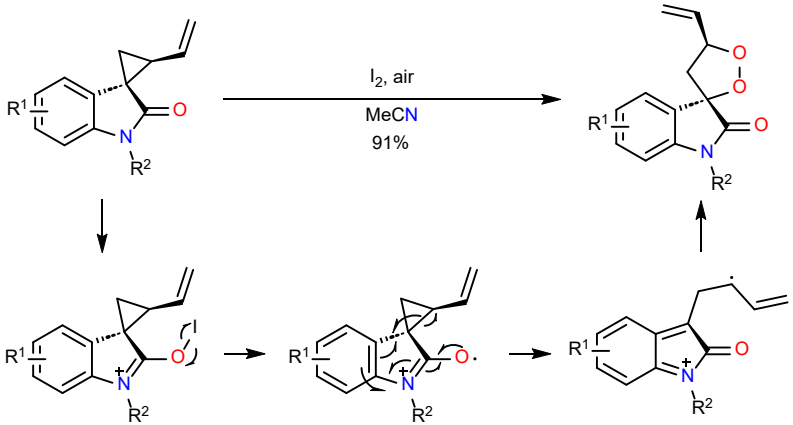
9,10-dicyanoanthracene (DCA)







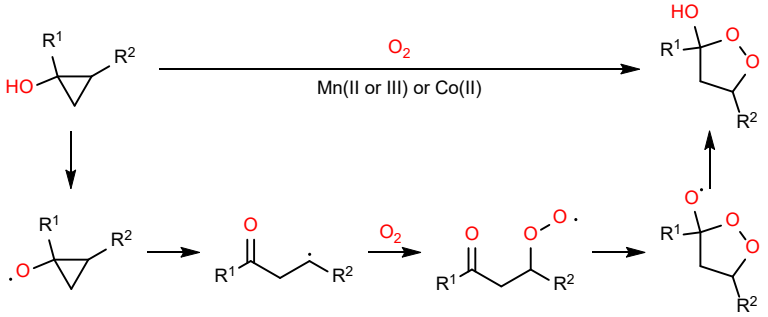
Budde, S. et al. Org. Chem. Front. 2020, 7 (14), 1789 doi.org/10.1039/D0QO00168F



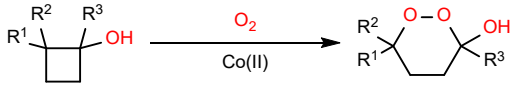
Xiong, C.; Cheng, K.; Wang, J.; Yang, F.; Lu, J.; Zhou, Q. J. Org. Chem. 2020, 85 (14), 9386–9395. https://doi.org/10.1021/acs.joc.0c00652.

1,2-dioxolanes, 1,2-dioxanes and 1,2- dioxenes

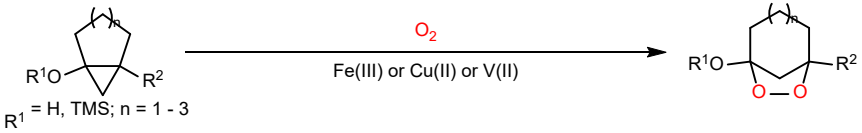
Radical peroxidation with triplet oxygen
Alkoxy radical peroxidation



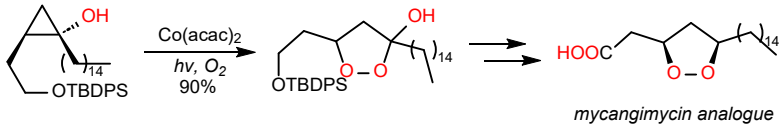
Gibson, D. H.; DePuy, C. H. Tetrahedron Lett. 1969, 10 (27), 2203 doi.org/10.1016/S0040-4039(01)88122-3



Elek, G. Z.; Borovkov, V.; Lopp, M.; Kananovich, D. G. Org. Lett. 2017, 19 (13),3544 doi.org/10.1021/acs.orglett.7b01519



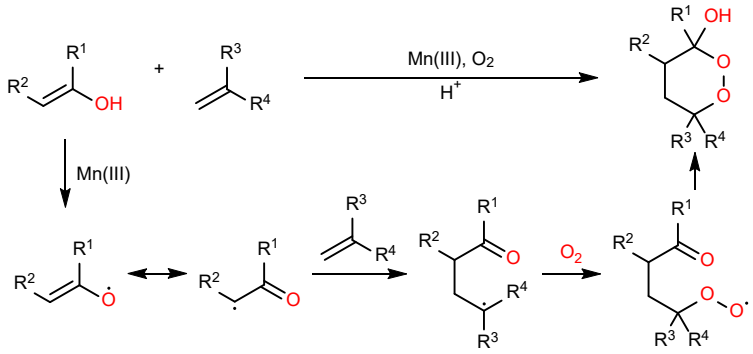
Han, W.-B.; Li, S.-G.; Lu, X.-W.; Wu, Y. Eur. J. Org. Chem. 2014, 2014 (18), 3841 doi.org/10.1002/ejoc.201402175

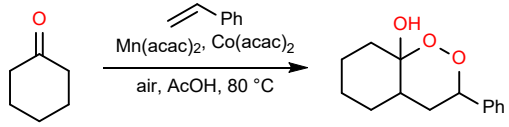


Nguyen, T. L.; Ferrie, L.; Figade`re, B. Tetrahedron Lett. 2016, 57 (47), 5286 doi.org/10.1016/j.tetlet.2016.10.051

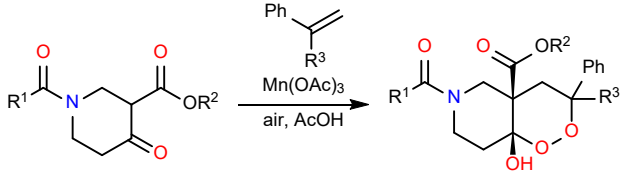
1,2-dioxolanes, 1,2-dioxanes and 1,2- dioxenes

Radical peroxidation with triplet oxygen
Formal [2 +2 +2] cycloadditions

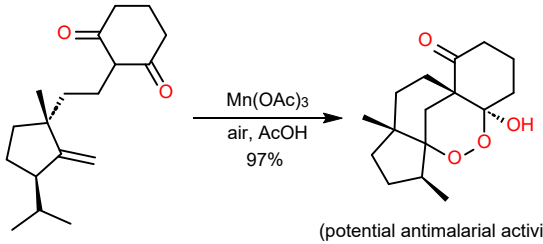




Iwahama, T.; Sakaguchi, S.; Ishii, Y. Chem. Commun. 2000, 23, 2317 doi.org/10.1039/B007182J



Kumabe, R. et al. Tetrahedron Lett. 2001, 42 (1), 69. doi.org/10.1016/S0040-4039(00)01884-0.

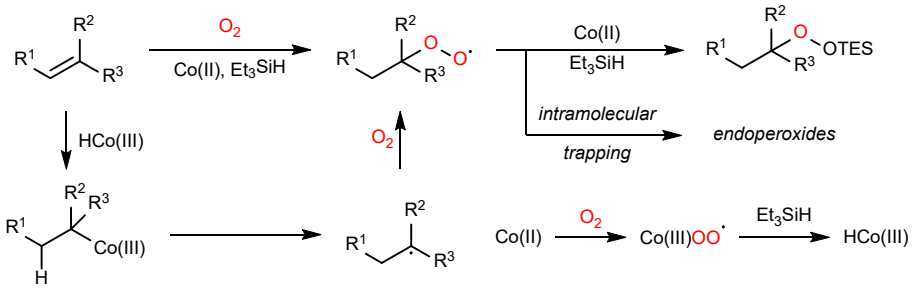


(potential antimalarial activity)

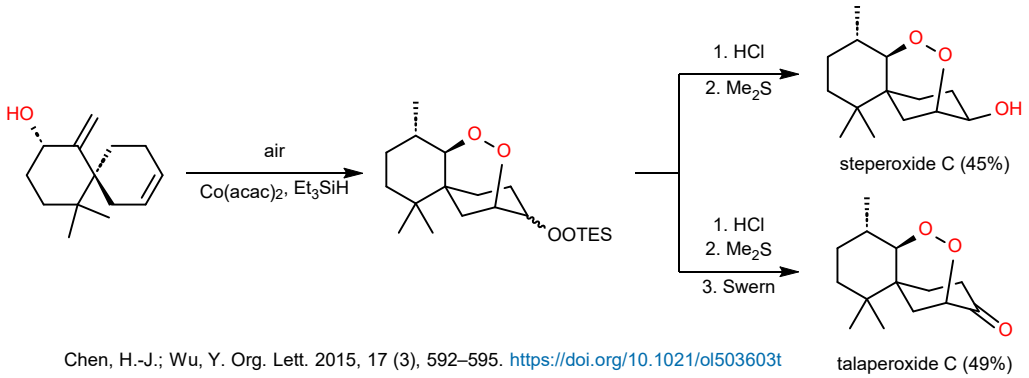
Daeppen, C.; Kaiser, M.; Neuburger, M.; Gademann, K. Org. Lett. 2015, 17 (21), 5420. doi.org/10.1021/acs.orglett.5b02773

1,2-dioxolanes, 1,2-dioxanes and 1,2- dioxenes

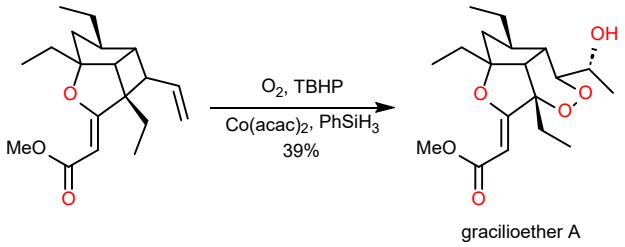
Radical peroxidation with triplet oxygen
Isayama-Mukaiyama hydroperoxylation



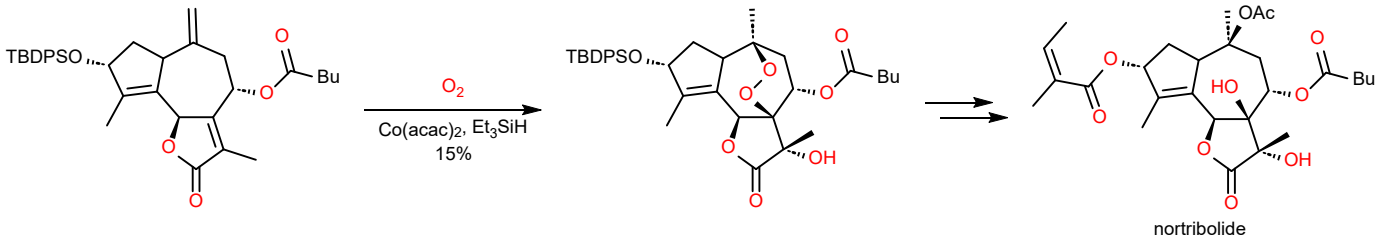
Isayama, S.; Mukaiyama, T. *Chem. Lett.* **1989,** 573. doi:10.1246/cl.1989.573



Chen, H.-J.; Wu, Y. Org. Lett. 2015, 17 (3), 592–595. https://doi.org/10.1021/ol503603t



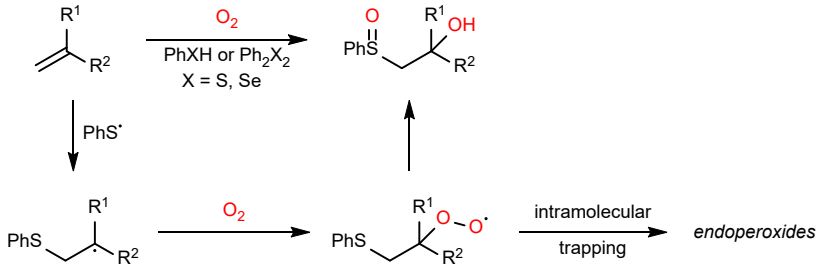
Hu, X et al. J. Am. Chem. Soc. 2019, 141 (37), 14904 doi.org/10.1021/jacs.9b08001

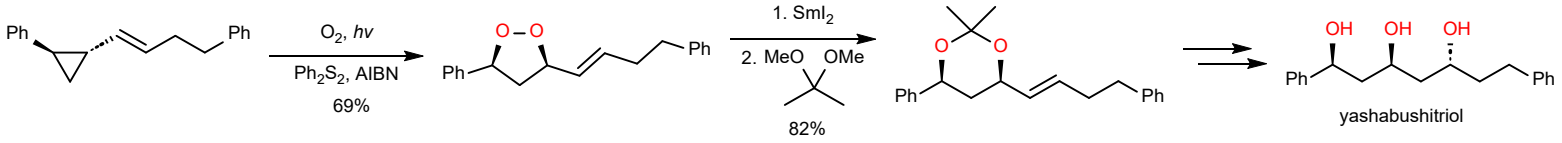


Li, Q.; Zhao, K.; Peuronen, A.; Rissanen, K.; Enders, D.; Tang, Y. J. Am. Chem. Soc. 2018, 140 (5), 1937. doi.org/10.1021/jacs.7b12903

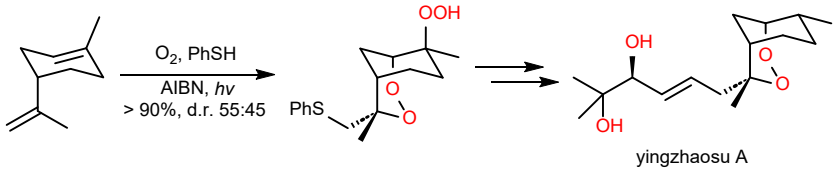
1,2-dioxolanes, 1,2-dioxanes and 1,2- dioxenes

Radical peroxidation with triplet oxygen
Thiol/Selenyl radical domino reactions

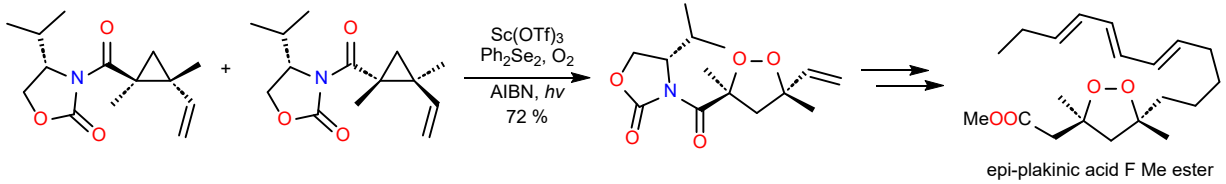




Feldman, K. S.; Simpson, R. E. Tetrahedron Lett. 1989, 30 (50), 6985. doi.org/10.1016/S0040-4039(01)93404-5



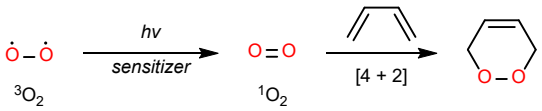
Korshin, E. et al. Tetrahedron 2002, 58 (12), 2449. doi.org/10.1016/S0040-4020(02)00126-6

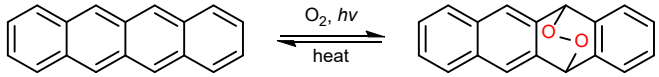


Tian, X.-Y.; Han, J.-W.; Zhao, Q.; Wong, H. N. C. Org. Biomol. Chem. 2014, 12 (22), 3686 doi.org/10.1039/C4OB00448E

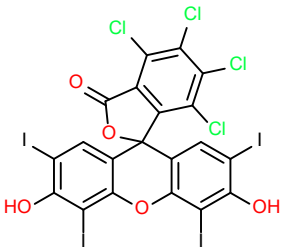
1,2-dioxolanes, 1,2-dioxanes and 1,2- dioxenes

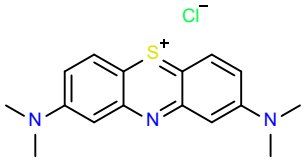
Peroxidation with singlet oxygen

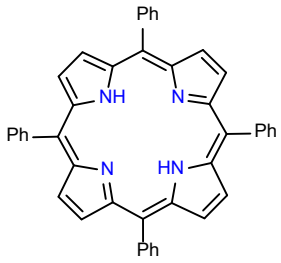




J. Fritzsche, *Compt. Rend.*, **64**, 1035 (1867).

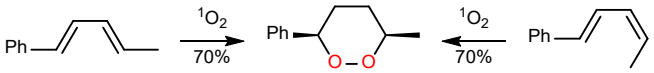

rose bengal


methylene blue

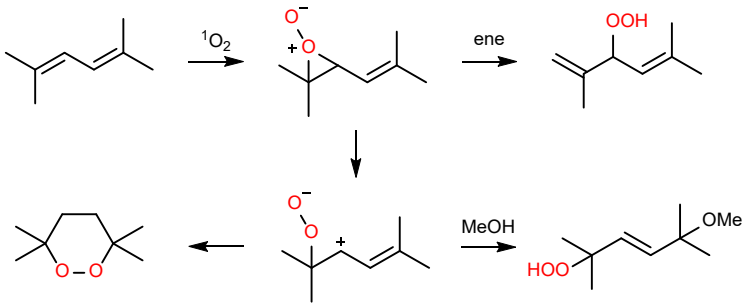

tetraphenylporphyrin (TPP)

- Reaction discovered in 1867
- Reactive species identified in 1930
- Product identified in 1976

An alternative mechanism



Motoyoshiya, J. et al. *J. Org. Chem.*, **1999**, 64, 493 doi.org/10.1021/jo981506r



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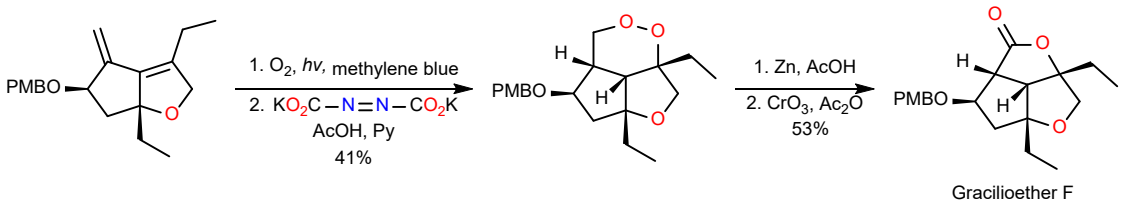
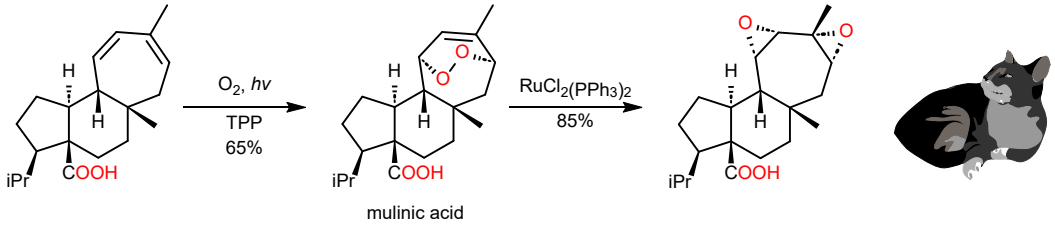
1,2-dioxolanes, 1,2-dioxanes and 1,2- dioxenes

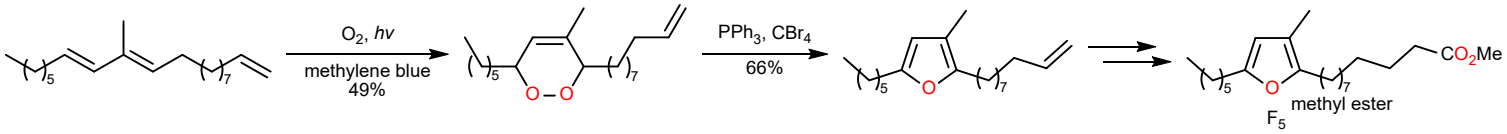
Peroxidation with singlet oxygen



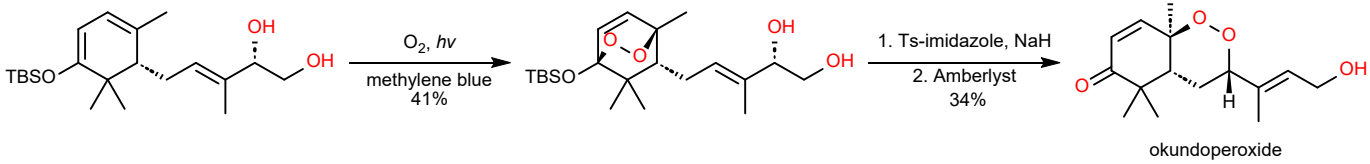
Shen, X.-Y.; Peng, X.-S.; Wong, H. N. C. Org. Lett. 2016, 18 (5), 1032–1035. https://doi.org/10.1021/acs.orglett.6b00161



Liu, Y.-T.; Li, L.-P.; Xie, J.-H.; Zhou, Q.-L. Angew. Chem. Int. Ed. 2017, 56 (41),12708–12711. https://doi.org/10.1002/anie.201706994



Mori, N.; Sakoda, D.; Watanabe, H. Tetrahedron Lett. 2017, 58 (40), 3884–3886.https://doi.org/10.1016/j.tetlet.2017.08.064

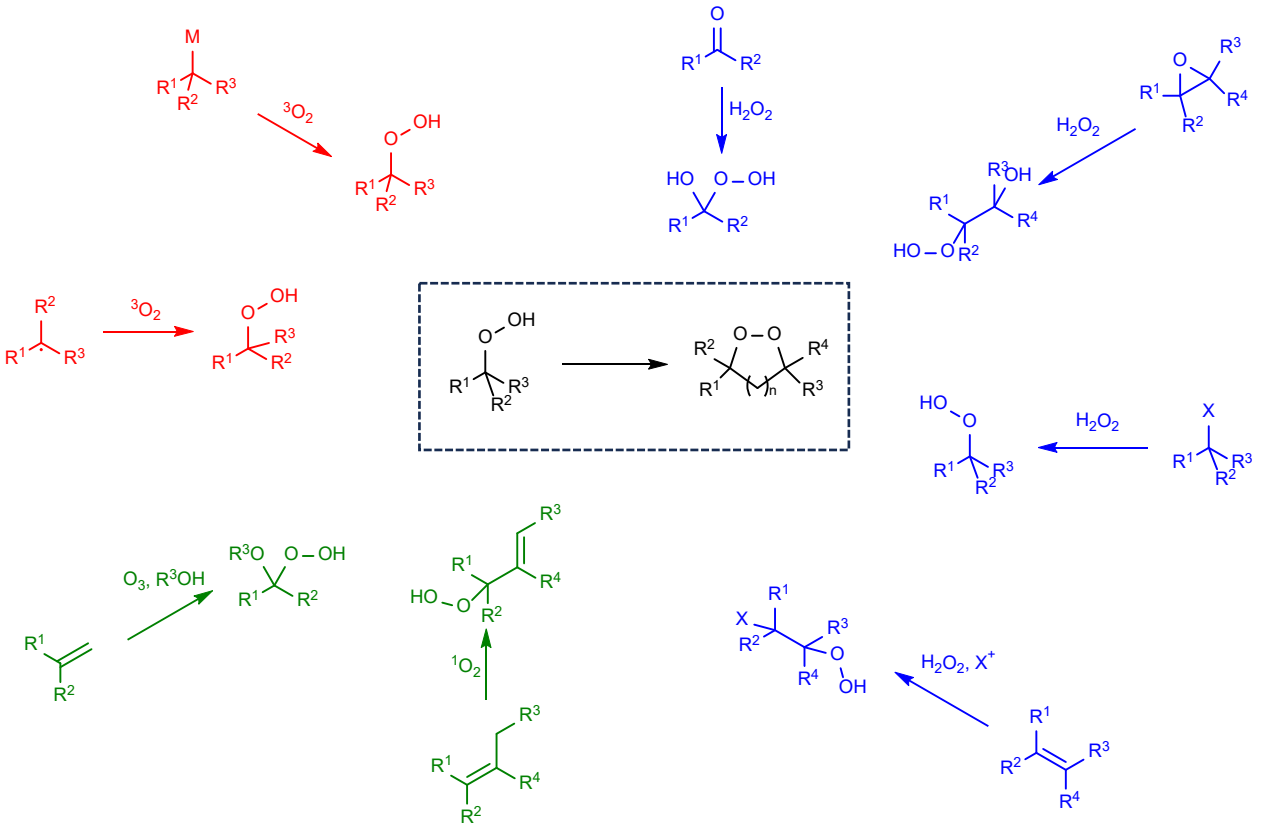


Liu, Y.-T.; Li, L.-P.; Xie, J.-H.; Zhou, Q.-L. Angew. Chem. Int. Ed. 2017, 56 (41),12708–12711. https://doi.org/10.1002/anie.201706994.

1,2-dioxolanes, 1,2-dioxanes and 1,2- dioxenes

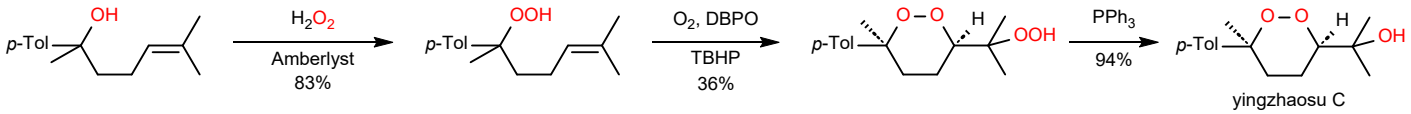
Ring-closing reactions of hydroperoxides

Synthesis of hydroperoxides

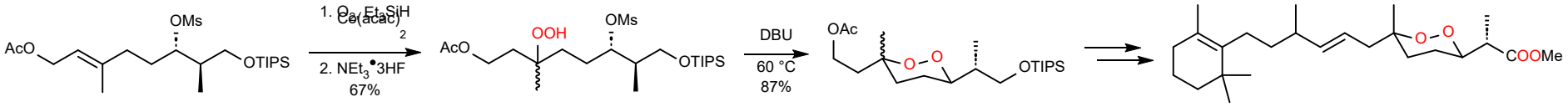


1,2-dioxolanes, 1,2-dioxanes and 1,2- dioxenes

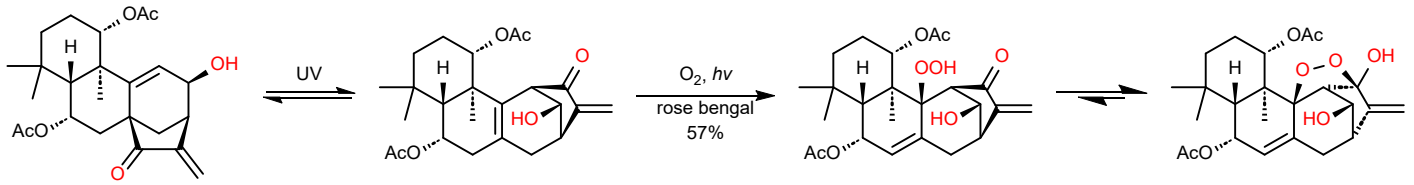
Ring-closing reactions of hydroperoxides
Cyclization of hydroperoxides



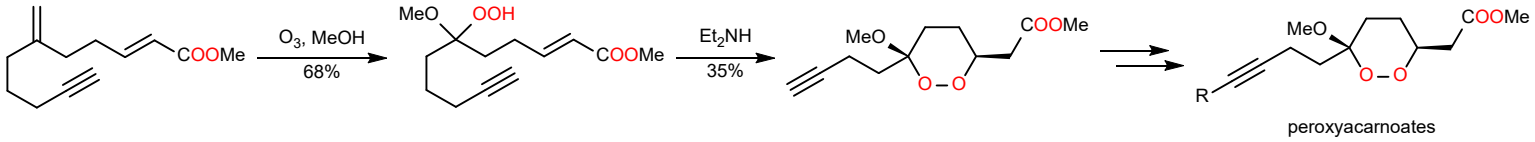
Boukouvalas, J.; Pouliot, R.; Frechette, Y. Tetrahedron Lett. 1995, 36 (24), 4167. doi.org/10.1016/0040-4039(95)00714-N



Schneider, M.-A.; Seifert, K. Eur. J. Org. Chem. 2017, 2017 (45), 6739. doi.org/10.1002/ejoc.201700922



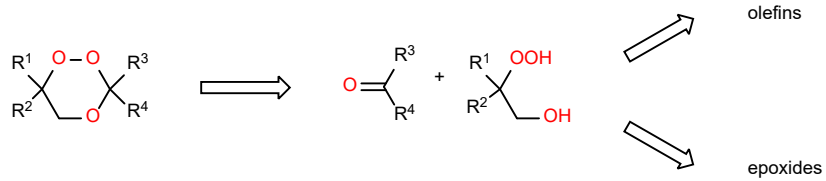
Wu, J.; Kadonaga, Y.; Hong, B.; Wang, J.; Lei, X. Angew Chem. Int.Ed. 2019, 58 (32), 10879. doi.org/10.1002/anie.201903682



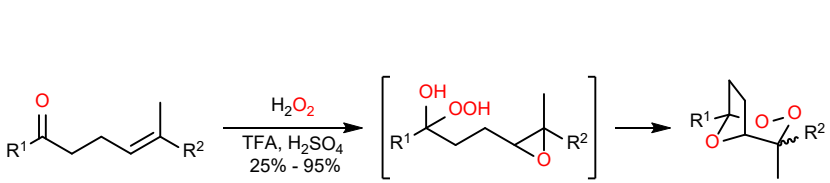
Xu, C.; Raible, J. M.; Dussault, P. H. Org. Lett. 2005, 7 (12), 2509. doi.org/10.1021/ol050291m

Synthesis of Endoperoxides

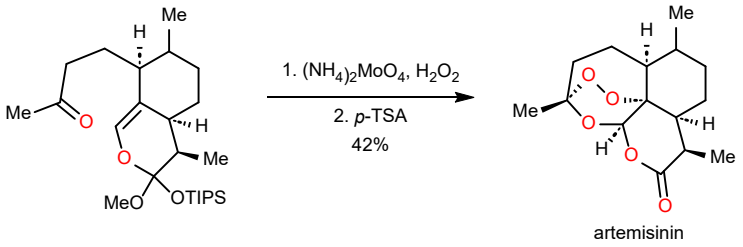
1,2,4-trioxanes



Same methods as discussed before could be used to synthesize this β-hydroxy hydroperoxide. (e.g. Isayama-Mukaiyama, ene reaction with $^1O_2$)

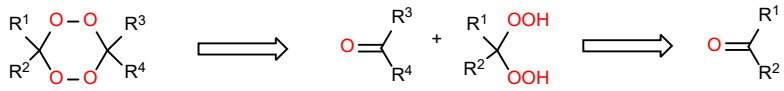


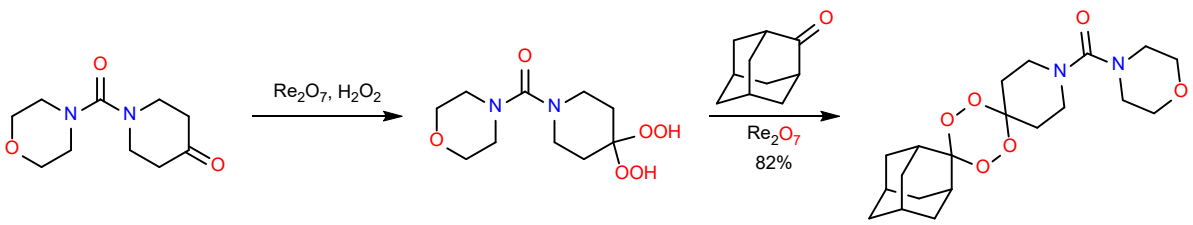
Ramirez, A. P.; Thomas, A. M.; Woerpel, K. A. *Org. Lett.* **2009,** *11,* 507. doi:10.1021/ol8022853



Zhu, C.; Cook, S. P. *J. Am. Chem. Soc.* **2012**, *134* (33), 13577 doi.org/10.1021/ja3061479

1,2,4,5-tetraoxanes





Other catalysts include: $MeReO_3$, protic acids, TMSOOTMS and I_2. These reactions are usually highly substrate dependent.

Ghorai, P.; Dussault, P. H. *Org. Lett.* **2009,** *11,* 213. doi:10.1021/ol8023874