CHEMOSELECTIVITY IN PERHYDROLYSIS OF KETONES, KETALS, AND EPOXIDES

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The potential of H_2O_2 as an inexpensive source of peroxy bonds in the synthesis of organic peroxides has been long recognized. However, because of its relatively low reactivity, incorporation of H_2O_2 into organic structures to date has not been as straightforward as one might expect. In fact, despite the continuing efforts over the decades since the late 1940s, mild, high-yielding and generally applicable protocols[1-5] (catalyzed by Re_2O_7, PMA (phosphomolybdic acid), $BF_3{\cdot}Et_2O$, and I_2, etc., using ketones, ketals, and epoxides as substrates) were not available until the late 1990s/early 2000s. As for differentiation between these reactive functional groups such as ketones, ketals, and epoxides in perhydrolysis, it remains impossible to date.

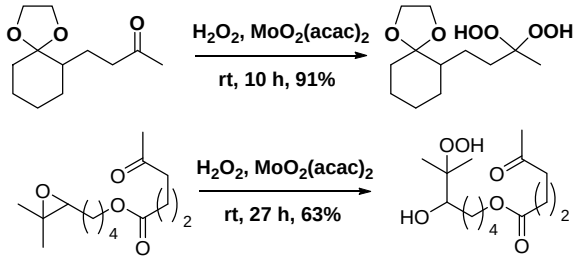

Figure 1. The first chemoselective perhydrolysis protocol.

Now we have developed the first chemoselective protocol for perhydrolysis of ketones, ketals, and epoxides, which uses $MoO_2(acac)_2$ as the catalyst and ethereal H_2O_2 as the source of hydroperoxyl groups. Under the newly established conditions, tri- or terasubstituted epoxides reacted preferentially while free ketone groups survived. For those bifunctional substrates containing both ketone and ethylene glycol ketal functionalities, perhydrolysis occurred predominantly at the ketone carbonyl groups without any intramolecular ketal exchange/cyclization (an unavoidable major interfering side reaction if using other known effective perhydrolysis catalysts such as BF_3-Et_2O, Re_2O_7 and PMA instead of $MoO_2(acac)_2$). The results with a range of representative substrates will be detailed.

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[2] Das, B.et al. *Tetrahedron Lett*. 2007, *48*, 6286-6289.

[3] Terent'ev, A. O. et al. *Synth. Commun.* 2007, *37*, 1281-1287.

[4] Ghorai, P. et al. *Org. Lett.* 2008, *10*, 4577-4579.

[5] Li, Y. et al. *Org. Lett*. 2009, *11*, 1615-1618.