CHEMOSELECTIVITY IN PERHYDROLYSIS OF KETONES, KETALS, AND EPOXIDES

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The potential of H₂O₂ 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 H₂O₂ 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 Re₂O₇, PMA (phosphomolybdic acid), BF₃·Et₂O, and I₂, 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 MoO₂(acac)₂ as the catalyst and ethereal H₂O₂ 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 BF₃-Et₂O, Re₂O₇ and PMA instead of MoO₂(acac)₂). The results with a range of representative substrates will be detailed.