EX SITU GENERATION OF $^{18}O_2$ AND $^{17}O_2$ FROM ENDOPEROXIDES FOR *O-LABELLING AND MECHANISTIC STUDIES OF OXIDATIONS BY DIOXYGEN

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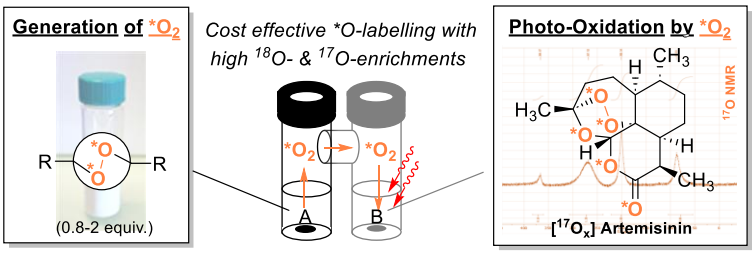
Among the various elements, oxygen plays a key role in many functional groups, and its isotopic labelling often proves determinant for mechanistic insights. Indeed, [^{18}O] can be easily differentiated by mass analysis from the predominant [^{16}O] and recent advances in NMR instrumentation allows efficient detection of the chemical shift of [^{17}O] (-30 to +1000 ppm). It is however necessary to use isotopically enriched compounds because of the low natural abundance of [^{18}O] and [^{17}O] (0.204% and 0.037%, respectively). Synthetic methodologies for the incorporation of labelled oxygen (*O) have been extensively studied.[1] They generally rely on the use of one of the cheapest isotope precursors: [*O]H_2O, but often require harsh conditions limiting their use to simple synthons, and/or involve reversible isotopic exchange yielding lessened isotopic enrichments. Some examples using gaseous *O-labelled dioxygen were reported, whose *O-atom molar cost is comparable to [*O]H_2O. However, the need to employ large excesses of this gas and the difficulty to manipulate it precisely greatly increase the overall cost of these procedures, which made them under-used. To solve these major drawbacks, we developed solid and stable precursors that can release quasi-stoichiometric amounts of [$^{18}O_2$] and [$^{17}O_2$]. After activation in a two-chamber glassware,[2] these compounds generated quasi-stoichiometric amounts of [$^*O_2$]dioxygen that can be photosensitized to oxidise various substrates. This method provided in a single step ^{18}O- and ^{17}O-labelled endoperoxides, quinones and phenols, in moderate to good yields and very high isotopic enrichments (up to 83%). As exemplified by the syntheses of [$^{18}O_x$]artemisinin and [$^{17}O_x$]artemisinin, this strategy is particularly suitable for affordable investigation of the chemical mechanisms involved in dioxygen oxidations using mass spectrometry and ^{17}O NMR.[3]



References

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