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Structure-reactivity relationships of *N*-hydroxysaccharin analogues as organocatalysts for aerobic oxidation

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ABSTRACT

The structure-reactivity relationships of new *N*-hydroxysaccharin analogous organocatalysts for aerobic oxidation have been theoretically explored based on the replacements of carbonyl groups in the succinimide ring of *N*-hydroxyphthalimide and *N*,*N*-dihydroxypyromellitimide by sulfinyl or sulfonyl groups. Both sulfinyl and sulfonyl groups largely change catalytic reactivity by altering the planar resonance/conjugation structures of precursors. Sulfinyl group largely decreases the reactivity, and the reactivity of catalyst with single sulfonyl group in the succinimide ring is higher than that with double sulfonyl groups. The reactivity of multi-nitroxyl catalysts is higher than that of the corresponding mono-cases, which is even comparable to that of *N*,*N*-dihydroxypyromellitimide.

1. Introduction

Selective organocatalytic oxidation strategies with molecular oxygen under mild conditions have been receiving substantial interest in preparing valuable fine chemicals and pharmaceuticals from the long-term environmental considerations [1–3]. Of these developed strategies, the strategies utilizing hydroxyimide organocatalysts (typically *N*-hydroxyphthalimide (NHPI, Fig. 1)) is particularly attractive owing to their established idiosyncratic performance in various catalytic oxidation transformations [4–10]. The critical mechanistic steps in their catalysis are demonstrated to be the hydrogen-abstraction process from the generic C—H bonds by their *in situ* generated reactive nitroxy radicals (typically phthalimide-*N*-oxyl radical (PINO**.**)) induced by metallic or metal-free radical initiators [8,9,11], and their rapid thermal auto-decomposition as the main limitations [6,12]. Their recent center of both experimental [4–10] and theoretical attentions [11,13–20] are improving their recovery and recycling [18], solubility in hydrocarbons [21], product selectivity [4–10], reactivity toward targeted substrates [16–18], thermal stability [20,22,23], and reducing usage of sacrificial radical initiators [20,23,24] and polar cosolvents [25], and also improving catalytic systems owning light-induced [26], metal-free [20,23], solvent-free [25] or initiator-free [23,24] features for practical applications.

Based on the literature survey, most of these available design strategies are established based on the structural modifications on the phenyl ring of NHPI either by changing the substituents on it [17–19,21,22,24,26] or replacing it by heterocyclic rings [19]. The effect of the structural modifications on the succinimide ring of NHPI on their reactivity remains largely unknown. In 2004, *N*-hydroxysaccharin (NHS, CT-3, Fig. 1) was used in the oxidation of cycloalkanes, alcohols and ethylbenzene [27]. The performace of NHS toward cycloalkanes is higher than that of NHPI, but lower toward other subtrates, which was mainly explained by the rate-limiting steps tuned from the H-abstraction reaction by nitroxy radicals to the equilibrium reaction between catalyst and peroxyl radical to generate nitroxy radicals [4]. This hypothesis was questioned theoretically [14], which revealed that the catalytic efficiency of nitroxyl radicals was not affected by the C—H nature of substrates, but the catalyst deactivation or generated radical concentration. Besides, two analogues of CT-3[28], namely *N*-hydroxy-*O*-benzenedisulfonimide (CT-5, Fig. 1) and *peri*-substituted bissulfonylhydroxylamine have been synthesized, and their main structural difference is that their aromatic rings are benzene ring and naphthalene ring, respectively. It was found that their nitroxy radicals can be completely recovered to themselves

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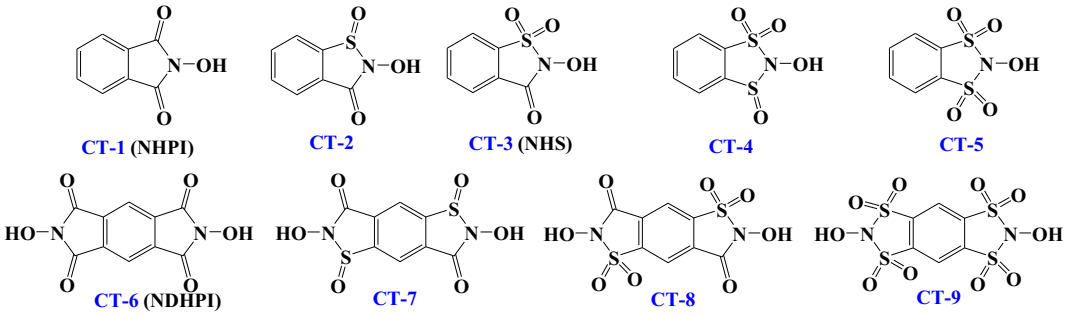

Fig. 1. NHPI, NDHPI and a series of *N*-hydroxysaccharin (NHS) analogues.

via H-abstraction. Most recently, a series of nonplanar hydroxyimide catalysts have been synthesized by replacing one carbonyl group of NHPI by trifluoromethyl group and its derivatives, which afforded good yields in the benzylic oxidation [29]. At present, the examples of relevant catalysts used in oxidation are very limited.

In this paper, we intend to theoretically explore the structure-reactivity relationships of a series of new hydroxyimide catalysts (Fig. 1) that are designed *via* the replacement of the carbonyl groups in the succinimide ring of NHPI and *N*,*N*-dihydroxypyromellitimide (NDHPI) [30] with electron-withdrawing sulfinyl or sulfonyl groups, and try to gain a mature understanding of the advantages and limitations of this particular catalysis for rational design guidance. The following questions will be addressed: What is the order of carbonyl, sulfinyl and sulfonyl groups in altering reactivity? To what extent does the solvent effect affecting the reactivity order? How does the carbonyl, sulfinyl and sulfonyl groups change the structural and electronic properties that are responsible for their different reactivity?

2. Computational details

Unless stated otherwise, hybrid functional B3LYP method combined with 6-311 + G* basis set within the Gaussian03 suite of programs [31] was employed for the whole geometry optimizations and frequency calculations, which has been widely used in the theoretical studies on the catalytic mechanisms and rational design of hydroxyimide catalysts for aerobic oxidation [11,13–20]. The vibrational frequency calculations were performed to ensure that a transition state have a single imaginary frequency and all other structures have none imaginary frequencies. The minimum energetic pathways from transition states to both products and reactants were confirmed by intrinsic reaction coordinates [32]. The B3LYP/6-311++G**// B3LYP/6-311 + G* method was utilized to calculate the H-abstraction barriers from toluene by nitroxyl radicals, which has been demonstrated earlier to give satisfied H-abstraction results for this kind of catalysts [13–19]. According to the suggestions of functionals for the barrier calculations by Peverati and Truhlar[33], the other functionals like B3PW91, HCTH, M06-2X and wB97X-D within the Gaussian09 suite of programs [34] were also employed in the cases of CT-n (n = 1,2,3,5) to confirm the main trend of the above results. The isodesmic work reaction with phenol samely described in Refs. [17–19] was employed to estimate the >NO—H bond dissociation energies (BDEs) of catalysts. To get close to the real catalytic environment, these H-abstraction barriers were also corrected by the liquid-phase single-point energy calculations in the commonly used solvent of acetonitrile by using polarizable continuum model (PCM) [35] with a dielectric constant of 35.688 at the B3LYP/6-311++G** level. The B3LYP/6-31G** method was used as well for the relaxed potential energetic profiles of the C—N—O—H dihedral angles of representative catalysts [CT-n (n = 2,3,5)] in both gas phase and liquid phase with a step size of 5° and maximum 74 steps.

3. Results and discussion

3.1. Molecular geometries and electronic properties

The conformational properties of representative catalysts were firstly considered (Figs. 2 and 3 *and S1) based on the relaxed energetic scan of their C—N—O—H dihedral angles. Previous studies have showed that the distribution of the gauche and planar conformers of hydroxyimide catalysts would affect their catalytic capacity [11], where the large coexistence of planar conformers does not favor their catalysis due to the strong intramolecular hydrogen bond. We find that, though the scan profile of NHPI [11] and CT-n (n = 2,3,5) vary differently, their gauche conformers are almost dominant either in gas phase or liquid phase, which indicates that their performances may be independent of their conformations. The optimized geometries of CT-n (n = 1–9) and their key parameters are shown in Fig. 4 and Table 1, respectively.

Obviously, the replacement of carbonyl groups by sulfinyl or sulfonyl groups significantly changes the planar resonance/conjugation geometries of NHPI and NDHPI. Both sulfinyl and sulfonyl groups lean on the phenyl ring of catalysts and induce a great enlargement of original succinimide ring of NHPI and NDHPI, where the mono-effect of sulfinyl group is stronger than that of sulfonyl group. The N—S bond length is *ca.* 0.40 Å larger than N—C bond length (Table 1). Besides, the minimum intramolecular H-bonding separations between the H atoms of OH groups and O atoms of adjacent carbonyl, sulfinyl or sulfonyl groups are among 3.2–3.8 Å except for the cases of CT-5/9 (*ca.* 2.4 Å), which is favorable for their interactions with H-bonding solvents. The difference of O—H bond lengths (*ca.* 0.01 Å) is very small. The N—O—H angles range from 104.1° to 105.9° except for CT-5/9 (109°). Moreover, the structural parameter of CT-5 is very close to its crystal data [28].

Additionally, the N—O bond lengths are *ca.* 1.37–1.40 Å for catalysts and *ca.* 1.22–1.26 Å for their nitroxy radicals (Fig. S2). Compared with that of NHPI and NDHPI, the N—O bond lengths of CT-n (n = 2–5,7–9) are much longer, which are much shorter in their nitroxy radicals. It indicates that removing H atom from these catalysts would cause greater alteration on their structural properties. All the N—O bonds of nitroxy radicals are shortened by 0.14–0.17 Å as compared with that of their precursors, which is larger than that of NHPI and NDHPI (*ca.* 0.12 Å).

The H removal from active >N—OH sections of catalysts leads to the different spin density distributions in their nitroxy radicals (Table 2), which is caused by the partial electronic delocalization from N atoms to their bonded O atoms. The SD_N and SD_O values of CT-n (n = 2–5,7–9) range from 0.228 to 0.337 and from 0.545 to 0.600, respectively. These SD_N values are larger than that of