

## 2-(Hydroxyimino)aldehydes

2-(Hydroxyimino)aldehydes  $RC(=NOH)CHO$  are a class of organic compounds that has been sporadically investigated in the scientific literature, mainly in the context of organic synthesis. Convenient methods for the synthesis of 2-(hydroxyimino)carbonyl compounds are being continuously proposed: Sugamoto resorted to reduction nitrosation with *t*-butyl nitrite and triethylsilane in the presence of cobalt(II) porphyrin as a catalyst; 3-chloro-2-hydroxyiminopropanal was prepared by Gilchrist and Roberts by addition of nitrosyl chloride to acrylaldehyde at low temperature; Baidya and Yamamoto obtained several HIAs through oxidation of the corresponding aldehydes with aluminum nitrite. Finally, a convenient  $\alpha$ -oximation reaction of aldehydes has been developed in our laboratory, which affords good to excellent yields of HIAs via organo-SOMO catalysis. This reaction affords HIAs bearing substituents of different bulk and nature, so that a systematic investigation of their physico-chemical properties is now accessible. Oximes in general are highly versatile molecules and HIAs may exhibit yet more interesting properties, thanks to the presence of an oxime and aldehyde group in adjacent position. In the context of our research on stimuli-responsive polymers bearing the 2-(hydroxyimino)aldehyde (HIA) group, we explore the photochemical behavior and physico-chemical properties of a number of HIAs. Interpretation of experimental data is supported by quantum mechanical calculations.

### 1) Photochemistry and physico-chemical properties

*In collaboration with Dr. Francesca D'Acunzo (Istituto di Metodologie Chimiche – CNR), Dr. Fabrizio Vetica and Prof. Enrico Bodo (Dipartimento di Chimica, Università La Sapienza)*

Photocyclization of carbonyl compounds (known as the Norrish–Yang reaction) to yield cyclobutanols is, in general, accompanied by fragmentation reactions. The latter are predominant in the case of aldehydes so that secondary cyclobutanols are not considered accessible via the straightforward Norrish–Yang reaction. A noteworthy exception has been reported in our laboratory, where cyclobutanols bearing a secondary alcohol function were observed upon UV light irradiation of 2-(hydroxyimino)aldehydes (HIAs). This reaction is investigated in detail by combining synthesis, spectroscopic data, molecular dynamics, and DFT calculations. The synthetic methodology is generally applicable to a series of HIAs, affording the corresponding cyclobutanol oximes (CBOs) chemoselectively (i.e., without sizable fragmentation side-reactions), diastereoselectively (up to > 99:1), and in good to excellent yields (up to 95%). CBO oxime ether derivatives can be purified and diastereomers isolated by standard column chromatography.

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### 2) Synthesis of new sensitive multi-stimulus methacrylate copolymers

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Our goal is to obtain a new class of polymethacrylates exhibiting complex and tunable behavior. Specifically, we synthesized by RAFT copolymerization poly(HIABMA)-b-poly(OEGMA) and poly-(HIABMA)-b-poly(DEGMA-r-OEGMA) (where HIABMA is[(hydroxyimino)aldehyde]butyl methacrylate, OEGMA is oligo-(ethylene glycol)methyl ether methacrylate, and DEGMA is di(ethylene glycol)methyl ether methacrylate) and we investigate their physico-chemical properties. We induced nanoaggregation by pH-induced micellization (PIM) and by the standard solvent displacement (SD) method on a series of pH-, light-, and thermosensitive amphiphilic block copolymers. The weakly acidic HIA group ( $pK_a \approx 8$ ) imparts stability to micelles at neutral pH, unlike most of the pH-responsive copolymers investigated in the literature. With SD, only some of our copolymers yield polymeric micelles (34–59 nm), and their thermoresponsivity is either poor or altogether absent. In contrast, PIM affords thermoresponsive, smaller micelles (down to 24 nm), regardless of the polymer composition. In some cases, cloud points are remarkably well defined and exhibit limited hysteresis. By combining turbidimetric, dynamic light scattering, and small-angle X-ray scattering measurements, we show that SD yields loose micelles with POEGMA segments partly involved in the formation of the hydrophobic core, whereas PIM yields more compact core–shell micelles with a well-defined PHIABMA core.

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