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Review

Squaraine dyes: The hierarchical synthesis and its application in optical detection

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ABSTRACT

Squaraine dyes, a four-membered ring system with structural rigidity, possess unique photoelectrical properties and are marked by their exceptionally sharp and intense absorption associated with a strong fluorescent emission in solution. These favorable characteristics have prompted their exploitation in a number of state of the art applications including photoconductivity, data storage, light-emitting field-effect transistors, solar cells and fluorescent histological probes. In this review, we first summarize the recently proposed novel methods in the synthesis of these versatile derivatives. Subsequently, their extensive applications in the prevalent optical detection of the surrounding medium such as ions, pH, thiol-based compounds, biomolecules and cell over the past decades are covered and discussed. In addition, different categories for the synthesis and sensing mechanisms for various squaric acid-based chemo-/bio- sensors are illustrated. Finally, the challenges and opportunities in the synthesis and application of these derivatives are also briefly discussed.

Contents

Abbreviations: PDT, Photodynamic therapy; $SOCl_2$, Thionyl chloride; $AlCl_3$, Aluminium trichloride; TFA, Trifluoroacetic acid; C_6H_6, Benzene; NEt_3, Triethylamine; Bu^nOH, Butanol; $Zn(OTf)_2$, Zinc triflate; THF, Tetrahydrofuran; DMF, Dimethyl formamide; DMSO, Dimethylsulfoxide; EtOH, Ethyl alcohol; DIPEA, *N,N*-Diisopropylethylamine; MeCN, Acetonitrile; DBU, 1,8-Diazabicyclo[5.4.0]undec-7-ene; Bu^tOk, Potassium *tert*-butoxide; EtONa, Sodium ethoxide; NaOH, Sodium hydroxide; KOH, Potassium hydroxide; Cs_2CO_3, Cesium carbonate; Pr^iOH, Isopropanol; AcOH, Acetic acid; H_2O, Water; HCl, Hydrochloric acid; $AcONH_4$, Ammonium acetate; DMAP, 4-dimethylaminopyridine; HOMO, Highest Occupied Molecular Orbital; LUMO, Lowest Unoccupied Molecular Orbital; DSSC, Dye-sensitised solar cell; BHJ, Bulk heterojunction; NIR, Near infrared reflection; UV, Ultraviolet; $CHCl_3$, Trichloromethane; CH_2Cl_2, Dichloromethane; HEPES, 4-(2-hydroxyethyl)-1-Piperazineethanesulfonic acid; PBQ, *p*-benzoquinone; NMP, Nmethylpyrrolidinone; β-CD, β-cyclodextrin; NPs, nanoparticles; PEG, Polyethylene glycol; TNT, Trinitrotoluene; DNT, Dinitrotoluene; TBACl, Tetrabutylammonium chloride; EDTA, Ethylene diamine tetraacetic acid; DNA, Deoxyribonucleic acid.

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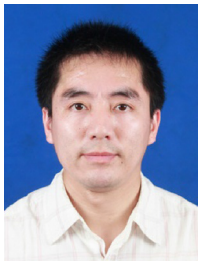

Hongming Wang received his PhD degree from Dalian Institute of Chemical Physics, CAS, in 2006. He carried out postdoctoral research in Leuven University, Belgium and worked as a research fellow in Nanyang Technological University, Singapore. Currently, he is a Ganjiang professor in the Institute for Advanced Study at Nanchang University. His research mainly focuses on synthetic chemistry, photochemistry, fluorescence probes and computational chemistry.

1. Introduction

Squaric acid (diketocyclobutenediol), which was firstly reported in 1959 by Cohen et al. [1], has been extensively investigated in various optical applications due to its structural rigidity [2,3], special aromaticity [4–6], as well as high chemical reactivity [7]. In general, electrophilic squaric acid and its alkoxyl-, halogenated-, amino-derivatives [8] can easily undergo condensation process with electron-rich precursors to form various squaric acid derivatives [9], which possesses favorable photoelectricity that could be applied to a number of technologically relevant fields including photoconductivity [10], data storage [11], light-emitting field-effect transistors [12], solar cells [13–19], nonlinear optical materials, [20–22] and current PDT [23,24], optical bioimaging [25–28], NIR-fluorescence probes, and labels [29–32].

Optical detecting techniques are powerful detective and analysis tools for visually monitoring analytes because of their technical simplicity, high sensitivity, operability for *in situ* and real-time detection, and manipuility for potentially quantitative and kinetic measurement of molecular interaction [33,34]. Generally, a typical optical chemosensor requires a recognition site linked to a chromo/fluorophore, which signals the recognition event via colorimetric changes and/or fluorescence changes [35–39]. As far as we know, Squaric acids have been widely studied as scaffoldings for novel chemosensors designing [40–42] in recent years due to: 1) the sharp and intense low energy absorption associated with a strong fluorescence in solution [43], 2) vast flexibility of synthetic precursors like amines [44], arenes, pyrroles, and anhydrobases [45–47] for architectural design, 3) functional modification of amino acid residue [48], carboxylic acid [49], phosphate [50] or boric acid [51] for detecting targeted analytes located in extreme and complicated biological and environmental systems, and 4) the inherited electron-deficient centre for nucleophilic analytes sensing [52].

In the early 1968, Sprenger and Ziegenbein [53] had already reviewed the synthetic methods of some specific squaric acids including mono-, di-, tri-, and even tetra-substituted derivatives based on limited reports. Since then, there have been tremendous exciting and significant findings about the synthesis and photoelectrical application of functionalized squaric acids. However, up to now, the related reviews are all about the physical properties, synthesis and applications of squaric acid derivatives on 1,3-squaraine dyes [13,18,19,23,40–42,45–47,54]. Hence, it is of vital importance to systematically review the recent synthesis and applications of mono-, di- and tri-substituted squaraine dyes.

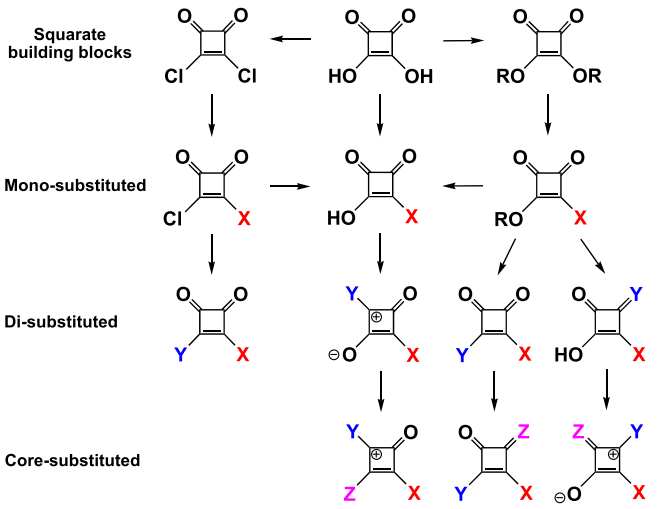

Fig. 1. Hierarchical synthesis of squaraic acid derivatives.

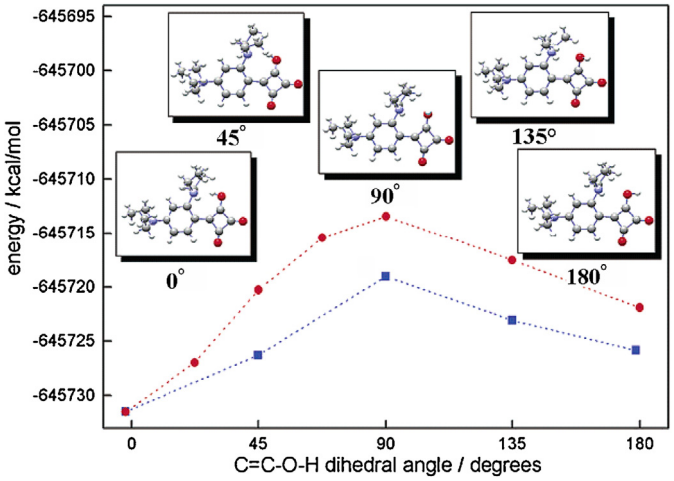

Fig. 2. Potential energy diagram as a function of the C═C—O—H dihedral angle derived from ab initio calculations on a preoptimized geometry of ortho-diethylamino-substituted semisquarates. Nonoptimized, single-point calculations (red circles) and fully optimized calculations for a given dihedral angle (blue squares) as well as selected respective fully optimized structures for 0°, 45°, 90°, 135°, and 180° are shown. Reproduced from Ref. [103] with permission. Copyright 2004 American Chemical Society.

In the present review, we classify squaric acid derivatives into mono-, di- (1,2- and 1,3-), and core-regioisomers according to the numbers and positions replaced by nucleophiles on the core four-membered ring, and further hierarchically outline their synthetic approaches in Fig. 1 based on the Hartmann's sketch [55]. Moreover, we primarily focus on the recently proposed novel methods of synthesizing these versatile derivatives and their rising applications as the prevalent optical chemsensors responding to the surrounding medium such as ions, pH, thiol-based compounds, and biomolecules. We believe this review will be helpful for comprehensive understanding and bring in horizons for exploiting this fascinating mine of molecular materials (Fig. 2).

2. Syntheses of squaric acid derivatives

2.1. Mono-substituted derivatives

Mono-substituted squaric acid derivatives, which can be shortly referred to as "semisquarates", serve as the key substrates for further condensed synthesis of superior analogues. As such, there is a