Abstract

The world is slowly changing, and one of the biggest challenges humanity will have to face during the forthcoming years, decades is the storage of energy, the transport of energy, and even more, a certain efficiency concerning its use/production. The most suitable way is to apply science, especially chemistry, to provide better sustainable energy sources. In combination with organic chemistry, materials science has a huge role in these matters, and many organic compounds are being studied for organic semiconductors, battery electrodes, electrodes for storage, or even solar cells. One promising approach is the use of N-heterocycles, whose interest has risen during the past decades due to their favorable electronic and structural properties.

Quinoxalines and quinoxalinones are interconvertible and closely related classes of N,N heterocycle. In addition to applications in biology and drug development, quinoxaline-containing structures have been investigated and form an important part of current research in material science. The synthesis of defined quinoxaline oligomers has not been investigated yet, which explains the need to develop new processes. In this work, new synthetic routes toward quinoxaline-based oligomers are developed and investigated, where the quinoxaline backbone is modified, providing the widest range of applications possible. Different connections between quinoxaline units within the oligomer, especially direct C-C connections and C=C spacing bridges are prepared and tested regarding their optical properties (Figure 1).

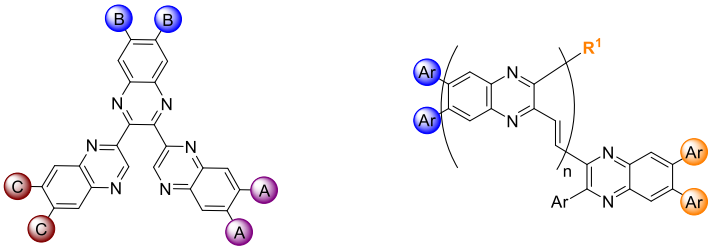


Figure 1. The shape of the different quinoxaline-based oligomers.

Concerning the C=C bridge oligomer, a two-step model was set up to build a fast, tunable and good yielding process alternating Wittig coupling and oxidation mechanism. Stille coupling is mainly used to generate such C-C connections, providing efficient and countless possibilities of oligomer building. Moreover, trimeric cyclization is evaluated to create asymmetric hexaazatrinaphthylene (HATN).

Kurzfassung

Die Welt verändert sich langsam, und eine der größten Herausforderungen, denen sich die Menschheit in den kommenden Jahren und Jahrzehnten stellen muss, ist die Energiespeicherung, der Energietransport und vor allem eine gewisse Effizienz bei der Nutzung/Produktion von Energie. Der geeignetste Weg ist die Anwendung der Wissenschaften, insbesondere der Chemie, um bessere und nachhaltige Energiequellen zu schaffen. Die Materialwissenschaft spielt in Verbindung mit der organischen Chemie eine wichtige Rolle, und viele organische Verbindungen werden für diese Zwecke untersucht, z. B. organische Halbleiter, Batterieelektroden, Elektroden für die Speicherung oder sogar Solarzellen. Ein vielversprechender Ansatz ist die Verwendung von N,N-Heterozyklen, deren Bedeutung in den letzten Jahrzehnten aufgrund ihrer günstigen elektronischen und strukturellen Eigenschaften zugenommen hat.

Quinoxaline und Quinoxalinone sind interkonvertible und eng verwandte Klassen von N,N-Heterozyklen. Neben Anwendungen in der Biologie und der Arzneimittelentwicklung bilden chinoxalinhaltige Strukturen einen wichtigen Teil der aktuellen Forschung in den Materialwissenschaften. Die Synthese definierter Chinoxalin-Oligomere wurde bisher noch nicht untersucht, was die Notwendigkeit der Entwicklung neuer Verfahren erklärt. In dieser Arbeit werden neue Synthesewege für Oligomere auf Chinoxalinbasis entwickelt und untersucht, bei denen das Chinoxalin-Grundgerüst so modifiziert wird, dass ein möglichst breiter Anwendungsbereich entsteht. Es werden verschiedene Verbindungen zwischen den Chinoxalin-Einheiten innerhalb des Oligomers hergestellt (direkte C-C-Verbindungen und C=C-Brücken) und hinsichtlich ihrer optischen Eigenschaften getestet (Abbildung 1).

Zur Herstellung solcher C-C-Verbindungen wird hauptsächlich die Stille-Kopplung verwendet, die effiziente und unzählige Möglichkeiten zur Bildung von Oligomeren bietet. Darüber hinaus wird die trimere Zyklisierung zur Herstellung von asymmetrischem Hexaazatrinaphtylen (HATN) untersucht. Für C=C-Brückenoligomere wurde ein zweistufiges Modell erstellt, um einen schnellen, abstimmbaren und ertragreichen Prozess zu entwickeln, bei dem Wittig-Kupplung und Oxidationsmechanismus abwechselnd zum Einsatz kommen.

1. INTRODUCTION

1.1.Quinoxalines and Quinoxalinones

1.1.1. Introduction

Quinoxalines, also named benzopyrazines, are an important class of nitrogen-containing heterocyclic compounds that consist of a benzene ring fused to the 4a and 8a-positions of a pyrazine ring (Figure 2). They are isomers of other naphthyridines, including quinazoline**,** phthalazine, and cinnoline. The numbering for the ring system of quinoxaline proceeds clockwise from nitrogen (Figure 2).[1] Quinoxalines are weakly basic compounds; their lone electron pairs on the nitrogen atoms can form hydrogen bonds with the solvent, enhancing water solubility.[2-3] They are also considered electron-deficient heterocycles due to pyrazine moiety.

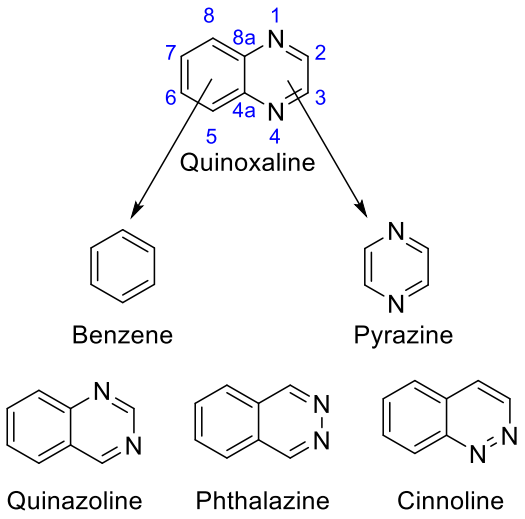


Figure 2. The chemical structure of quinoxaline is separated into its core aromatic structures and isomers.

Most quinoxaline derivatives are synthetic, and naturally occurring quinoxaline derivatives are rare. Only echinomycin and triostin-A exist as natural quinoxalines-based molecules (Figure 3).[4] However, the synthesis of quinoxaline is easy to perform and therefore enables the construction of numerous organic compounds.

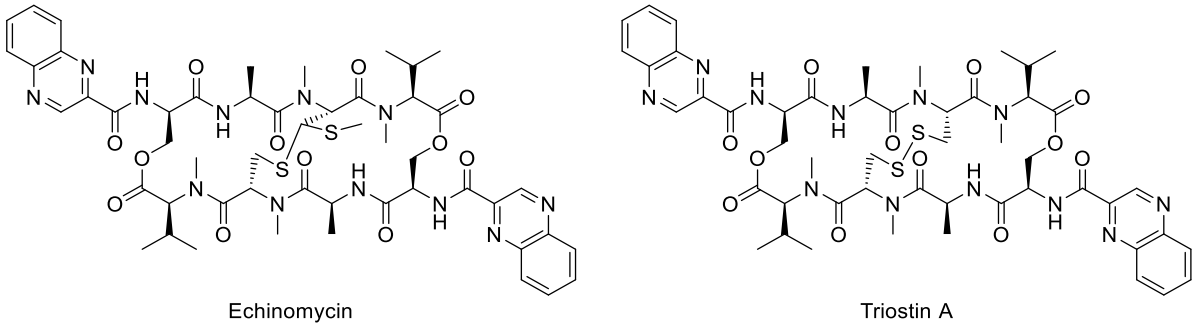
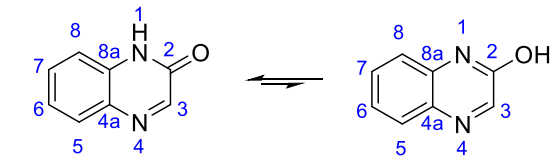


Figure 3. Structures of naturally occurring quinoxaline-based molecules.[4]

A similar and related class of substance also used in this work is quinoxalinones. Quinoxalines and quinoxalinones are interconvertible molecules, accessible from one to the other by simple chemical reactions such as quinoxalinone chlorination or nucleophilic substitutions.[5-7] Each possesses specific properties allowing some synthetic easiness (precipitation of quinoxalinone ⇆ solubilization of quinoxaline, the introduction of protecting group ability, nucleophile or electrophile functional properties, etc.). Besides their very similar structures, quinoxalin-2(1*H*)-ones are in tautomeric equilibrium with quinoxalin-2-ols, but it has been demonstrated that they predominantly exist as cyclic amides rather than as hydroxyl compounds (Scheme 1).[8-10]



Scheme 1. Equilibrium between quinoxalin-2(1*H*)-ones and quinoxalin-2-ol.

1.1.2. Synthesis and applications of quinoxalines and quinoxalinones

O. Hinsberg reported the first recorded synthesis of quinoxaline and quinoxalinone in 1884.[11] Although his attempts to synthesize bases similar to quinolone by reducing quinoxalines failed, he synthesized such heterocycles by condensing aromatic *o*-phenylenediamines with glyoxal pyruvic acid, or diketones (Figure 4, a). From then, numerous methods were performed to produce new synthetic routes toward quinoxalines and quinoxalinones using other kinds of condensations or oxidations (Figure 4, c).[12-16] In recent years, many reports have been presented regarding the synthesis of different quinoxaline derivatives involving green methodologies, including

recyclable catalysts, microwave-assisted synthesis, and reactions in an aqueous medium.[17]

The electron density of quinoxalines has been calculated (Figure 4, b), enabling us to understand the reactivity of such N-heterocycles more efficiently.[18] Quinoxalines are deactivated toward electrophilic substitution; moreover, substitution is most likely to occur at the equivalent positions 5 and 8, where is the highest electron density. On the other hand, electron-donating substituents in the benzene ring promote electrophilic substitution, and when activating substituents are present on the aromatic core, the reaction site depends on the reaction conditions.[1]

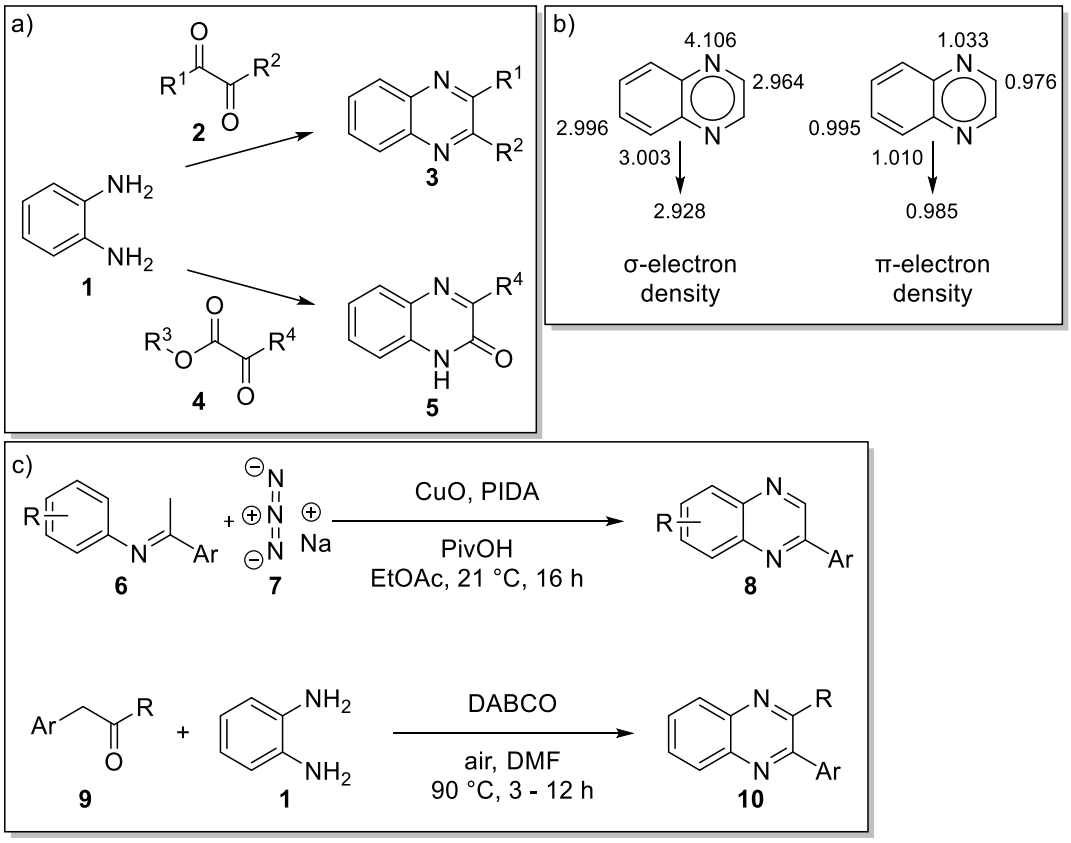


Figure 4. a) General synthetic routes toward quinoxalines and quinoxalinones *via* a condensation reaction, b) Calculated electronic densities of quinoxaline,[18] c) Examples of alternative synthesis routes of quinoxaline.[15-16]

Quinoxaline structures are very important scaffolds in biological research since many of their derivatives possess biological activities such as anti-inflammatory,[19] antibacterial,[20] anti-angiogenic, anti-depressive,[21] and anti-viral[22] activity. Moreover, quinoxalines have been the focal point of many cancer treatment studies during the last

decade[23-26] since their analogs have already been identified as inhibitors of heparin-induced tau fibril formation, cyclophilin A, kinases (p110δ of PI3 kinase, JSP-1), phosphatases (cdc25B, MAPK phosphatase-1) and isomerases (peptidyl-prolyl-*cis-trans* isomerase).[27-33] The quinoxaline scaffold can also be found in commercially available drugs such as Varenicline, Brimonidine, and Quinacilin (Figure 5).[34]

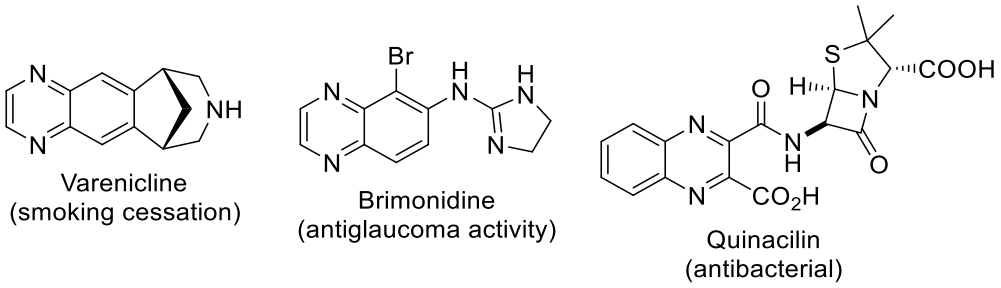


Figure 5. Drugs with quinoxaline core structure.[34]

The applications of quinoxalines are also widely known in materials science. Quinoxalines being an electron-poor heterocycle, especially π-deficient, can be easily used as an electron acceptor (A) moiety combined with another electron donor (D) moiety to create a dipolar moment, enhancing chemical and physical properties, especially toward emission.[35] Therefore, quinoxalines have been used in push-pull structures inducing luminescent properties (Figure 6, a).[35] Using again quinoxaline electron-deficient property, quinoxaline-based dyes were synthesized and applied as sensitizers for dye-sensitized solar cells (Figure 6, b).[36-37] Moreover, nitrogen atoms with lone electron pairs enable the quinoxaline ring to be an efficient and stable complexing agent.[35,38-39] Complexes consisting of copper, zinc, iron, and cobalt were created using quinoxaline as ligands leading to the study of quinoxaline-based transition metal complexes (Figure 6, c).