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Synthesis and Intramolecular Hydrogen Bonding Networks of 2,4,6-Tri (*o*-hydroxyaryl)-1,3,5-Triazines

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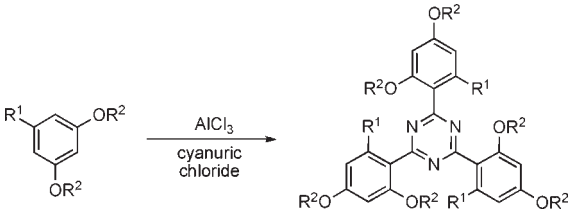
ABSTRACT



Functionalized, triaryl substituted triazines were synthesized via the Friedel–Crafts arylation reaction. These conjugated triazines possess unique, intramolecular hydrogen bonding motifs, which provide tunable planarity.

The value of highly conjugated carbon-rich molecules such as polycyclic aromatic hydrocarbons (PAHs) and other nanographenes toward the formation of advanced materials is well established.[1] Recent work has shown that a variety of carbon-rich, atomically precise graphene derivatives can be synthesized, where size and edge structure are programmable.[2] Their unique structural and electronic properties are enhanced by their ability to self-assemble, often resulting in the formation of liquid crystalline phases and supramolecular architectures.[3]

Extended graphene-based nanomaterials containing heteroatoms, however, are more rare than the primarily carbon based systems mentioned above, even though including atoms other than carbon presents an opportunity to vary the electronic and physical properties of the resulting graphitic structures.[4]

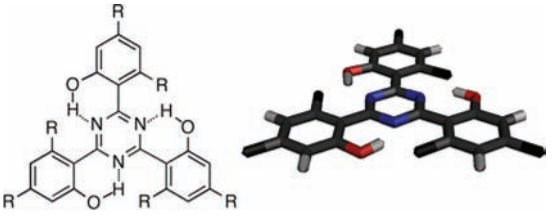


Figure 1. Hydrogen bonding motif of planar, triaryl triazines.

Maintaining conjugation in heteroatom-containing nanographenes is possible by connecting aryl subunits through both covalent and hydrogen bonds, a strategy that allows for design flexibility while maintaining or enhancing electronic properties.[5] *s*-Triazines are a convenient subunit for this purpose; they possess interesting electronic properties and are able to form multiple hydrogen bonds.[6,7]

For example, as shown in Figure 1, placement of *ortho*-hydroxy substituted aryl groups in the 2,4,6 positions of

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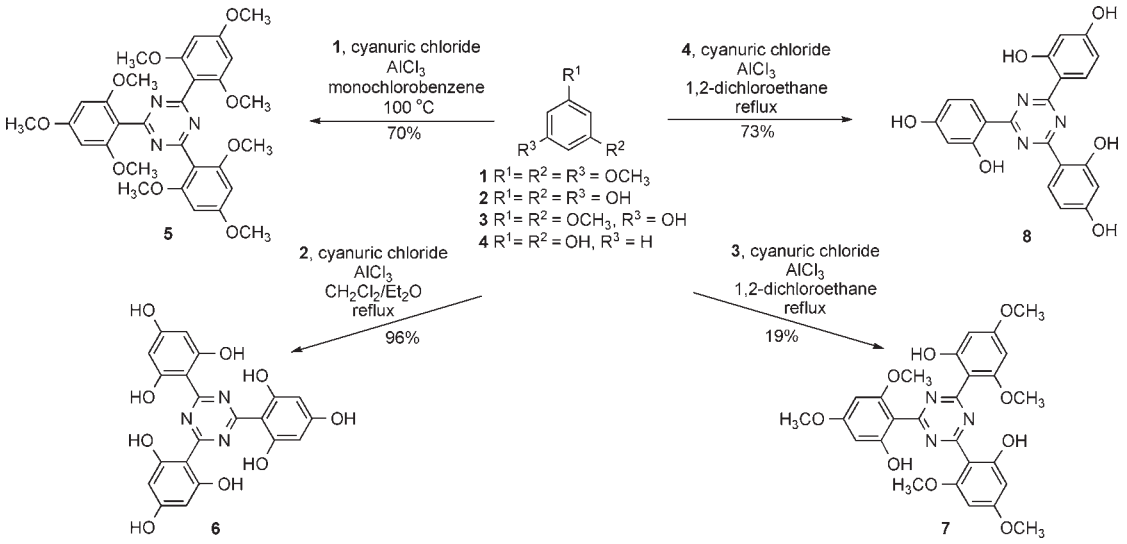
Scheme 1



1,3,5-triazine allows for the formation of intramolecular hydrogen bonds between the nitrogen of the central triazine and the hydroxy group of the attached aryl groups.[8] These hydroxy groups allow for conjugation between the triazine ring and the pendant aryl groups, while also providing a handle for fine-tuning the degree of planarity in the system, a variable that is known to have a strong effect on the physical and electronic properties of molecules,[9] oligomers and polymers.[10] Although planar, aryl-substituted triazine systems are known and utilized frequently as structural units in coordination cages,[11] the highly functionalized, symmetrical structures as proposed in Figure 1 have yet to be synthesized. We present herein the synthesis and the physical and electronic properties of symmetrical, crowded, planar triazines bearing unique hydrogen bonded networks.

There are a number of established methods to form aryl-substituted 1,3,5-triazines. Suzuki cross-coupling and nitrile trimerization have both been used to form triaryl triazines.[11−13] The sterically hindered triazine derivatives of the type in Figure 1, where R ≠ H, are almost nonexistent in the literature, and these aforementioned methods were ineffective at forming the desired triazines.[14] A variety of organometallic reagents have also been used in the literature to produce symmetrical and unsymmetrical triazines,[15] although for our targets, the use of Grignard and organolithium reagents resulted only in the production of mono- and diaryl-substituted triazines.[16]

The Friedel−Crafts arylation reaction is the method of choice for appending bulky aryl substituents to the triazine core, Scheme 1.[14] Readily available starting materials can be used to obtain the desired products, column chromatography is not necessary for purification, and high yields are generally obtained.[17,18]

As shown in Scheme 1, *O*-methylated **5** was initially targeted to provide a derivative that is not capable of forming intramolecular hydrogen bonds with the triazine nitrogens. Molecule **5** can be formed in one step from compound **1** in 70% yield through reaction with $AlCl_3$ and

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cyanuric chloride in monochlorobenzene. Purification by recrystallization provided pure product. Encouraged by this result, nonaol **6**, which can form a petal-shaped network of hydrogen bonds around the triazine core consisting of six $-OH\cdots N$ interactions, was targeted. Phloroglucinol **2** was treated to very similar conditions as methylated **1**, although due to the low solubility of the starting material **2**, the reaction was carried out in a mixture of DCM and ether. Upon workup, triazine **6**, with a total of 9 hydroxy groups, was isolated in 96% yield in one step. Despite the low solubility of this very polar compound in most solvents, purification was easily performed via a centrifuge wash process.

Derivatives **7** and **8** were synthesized to determine the effect of altering the substitution at the *ortho* position on the hydrogen-bonding system around the triazine core. Selective methylation of phloroglucinol provided disubstituted phenol **3** in good yields.[19] Treatment with $AlCl_3$ and cyanuric chloride in 1,2-dichloroethane then provided the hexamethoxy derivative **7**, with only three $OH\cdots N$ interactions. As one would predict, molecule **7** was one of several products formed in this reaction as other less symmetrical triazine derivatives were also produced. However, triol derivative **7** could be obtained pure from the crude reaction mixture through a series of washes and extractions in 19% yield. Compound **8**, with a hydroxy and a hydrogen in the *ortho* positions, was synthesized according to literature procedure from resorcinol.[20]

The UV−visible spectra of compounds **5**, **6**, and **7** are presented to demonstrate the degree of planarity in these compounds, Figure 2. Nonplanar, fully methylated derivative **5** has a λ_{max} of 297 nm; the conjugation is limited by the bulky *ortho* substituents. The nonaol **6** displays a significantly red-shifted band, λ_{max} at 331 nm, indicating increased conjugation and therefore increased planarity between the phloroglucinol aryl groups and the triazine ring in comparison to methyl-protected derivative **5**. In addition, triazine **7**, with 3 methoxy groups in the *ortho* positions, also possesses a band at 335 nm. Presumably, the phenolic OH groups in **7** are forming a hydrogen-bonded network with the triazine nitrogens despite the added bulk of the methoxy groups. In fact, the increase in intensity of the absorption band of **7** over **6**, in addition to the slight red-shift of **7**, both indicate slightly more conjugation than in **6**.[21]

^1H NMR spectroscopy gives some insight into the hydrogen bonding pattern at the core of these molecules and their spectra in d_6-DMSO are compared in Figure 3. Hexaol **8** has two downfield OH peaks; the peak at 10.45 ppm is assigned to the *para*-hydroxy and the downfield

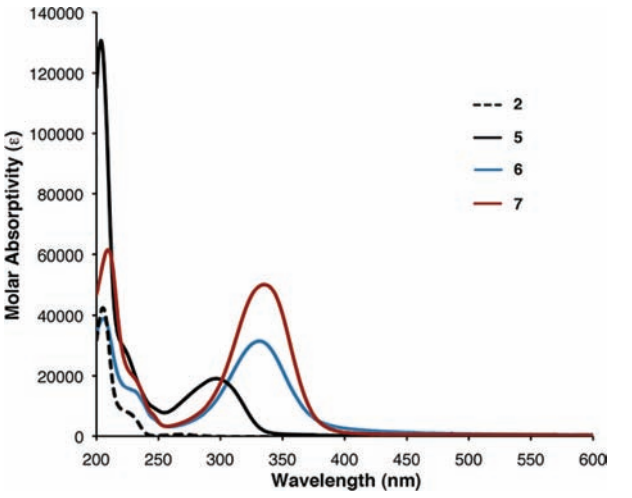

Figure 2. Absorption properties of compounds **2**, **5**, **6**, and **7** in acetonitrile.

peak at 12.84 ppm is assigned as the *ortho*-hydroxy that is forming a hydrogen bond with the triazine. Similar peaks are observed for nonaol **6** at 12.28 ppm for the *ortho*-hydroxy groups, and at 10.12 ppm for the *para*-hydroxy group.[22] The downfield position of the *ortho* peak in comparison to the *para*-hydroxy group in **6** indicates that intramolecular hydrogen bonds are formed between the *ortho*-hydroxy moieties and the triazine ring, despite the steric bulk present at the *ortho* positions. However, the broadness of the *ortho*-hydroxy peak of **6** and the fact that it is upfield in comparison to the equivalent peak in **8** indicate that while still providing conjugation, the three-centered hydrogen bonding network is weaker in the more symmetrical nonaol **6** than in **8**.[23]

Replacing one of the *ortho*-hydroxy groups of **6** with a methoxy group as in compound **7** resulted, surprisingly, in the formation of what appears to be a much stronger hydrogen bonded network. The intramolecular $OH\cdots N$ hydrogen-bond of **7** appears at 14.97 ppm, 2.69 ppm downfield from **6** and 2.13 ppm downfield from **8** (in fact, 1.13 ppm downfield of any comparable molecule in the literature).[24] The methoxy groups supply minimal bulkiness as they can flip away from the nitrogen without disturbing the conjugation between the triazine and the pendant rings. The strong hydrogen bond network observed in **7** is likely due in part to the lone pair on the methoxy oxygen, allowing the formation of a three−center, bifurcated hydrogen bond.

The effect of concentration on compounds **6** and **7** was explored to determine if the intramolecularly hydrogen bonded network around the triazine core was available for

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(21) Two bands appear in the UV−visible spectrum of compound **8** corresponding to $\pi\pi^*$ and CT bands, an electronic feature observed in **8** due to the possession of fewer OR groups than **5**, **6**, and **7**. As such, a useful comparison cannot be made with **8** in this study. See ref 8c.

(22) Integrations support this assignment.

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(24) As measured in $CDCl_3$ for comparison with literature values. See: Sosnovskikh, V.; Usachev, B. I.; Sizov, A. Y.; Vorontsov, I. I.; Shklyaev, Y. V. *Org. Lett.* **2003**, *5*, 3123–3126.

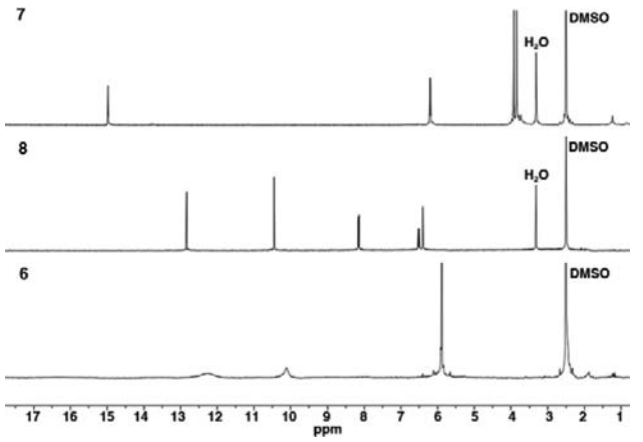

Figure 3. ^{1}H NMR spectra in d_6-DMSO at 298 K of nonaol **6**, hexaol **8**, and triol **7**.

intermolecular interactions.[25] The *ortho* and *para* phenol peaks of **6** are clearly observable at 12.28 and 10.12 ppm, respectively, at low concentration. The resonance corresponding to the *ortho*-hydroxy resonance broadens significantly as the solution is concentrated, while the *para* peak remains at the same position. At the final concentration of 52 mM, the *ortho* peak disappears completely into the baseline, indicating that exchange of these protons is faster at higher concentration. It is likely that compound **6** loosely associates at high concentrations and the *ortho*-hydroxy groups undergo exchange with adjacent molecules. Presumably, the *para*-hydroxy is hydrogen bonded to the DMSO solvent at all concentrations, hence the lack of concentration dependence. A concentration experiment was also performed on triol **7**, with different results. No broadening or shifting of the *ortho*-hydroxy peak was observed at all, indicating that the strong intramolecular bonds formed in **7** successfully maintain planarity as concentration is increased.[26] This result supports the ^{1}H NMR and the UV−visible spectroscopic data presented above, indicating that the *ortho*-OH groups on **6** are available for exchange with adjacent molecules and are in fact capable of participating in both intra- and intermolecular interactions. In contrast, for molecule **7** no visible change with concentration is observed, indicating that the *ortho*-OH is strongly held in the intramolecular hydrogen bond and is not available for facile exchange. A series of NOESY and saturation transfer experiments were performed on samples of compounds **6**−**8** to probe this feature. 2-D NOESY experiments revealed that the *ortho*- and *para*-hydroxy groups of nonaol **6** undergo rapid exchange with each other and with water, while hexaol **8** did not appear to undergo exchange with H_2O. A more sensitive 1-D NOESY indicated that compound **8** does in fact undergo medium-slow exchange. However, triol **7** was not observed to undergo exchange with H_2O in either the NOESY or saturation transfer experments, indicating that the exchange rate was below the limit of detection in this tightly bound system on the NMR time scale.

Calculations have provided some insight into the structural differences between structures **6**, **7** and **8**, Figure 4.[27] The results indicate that while triol **7** and hexaol **8** possess very planar structures with average dihedral angles of 3° and 7°, respectively, and possess near perfect bond angles for the intramolecular hydrogen bond, nonaol **6** is at its lowest energy conformation when the pendant phloroglucinyl arms are twisted by approximately 20° from the central triazine ring. As can be seen in Figure 4a, the *ortho*-hydroxy groups are pointed in toward the triazine nitrogens to form weak hydrogen bonds with the lone pairs. Combined with the ^{1}H NMR data, the calculations indicate that this nonaol system of compound **6** is dynamic, with the phloroglucinyl arms rotating back and forth around the triazine core.

In conclusion, we have successfully synthesized new, crowded, triazine based aromatic compounds. These highly conjugated structures possess interesting hydrogen bonding patterns that allow for fine-tuning of planarity.

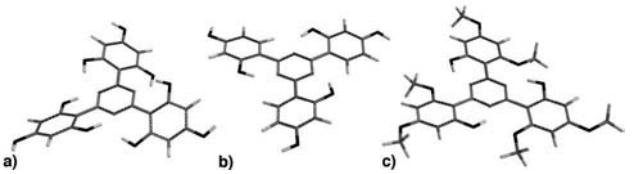

Figure 4. Minimized structures for triazines: (a) nonaol **6**, (b) hexaol **8**, and (c) triol **7**. Geometry optimization was undertaken at the B3LYP/6-31G* level.

This feature will be exploited in the future through the synthesis of extended, conjugated networks containing these monomer units.

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Supporting Information Available. Synthetic procedures, characterization data, and ^{1}H and ^{13}C NMR spectroscopic data (including NOESY experiments) for compounds **5**−**8**. This material is available free of charge via the Internet at http://pubs.acs.org.

(25) Concentration experiment for compound **6** is reproduced in the Supporting Information.

(26) Due to the low solubility of compound **7** in DMSO, the concentration dependence experiment of triol **7** could only be performed in the lower concentration range. This concentration experiment for **7** was therefore also repeated in $CDCl_3$ and is reproduced in the Supporting Information.

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