Synthesis of Stilbenes Using Various Catalysts and Investigation of their Optical Properties

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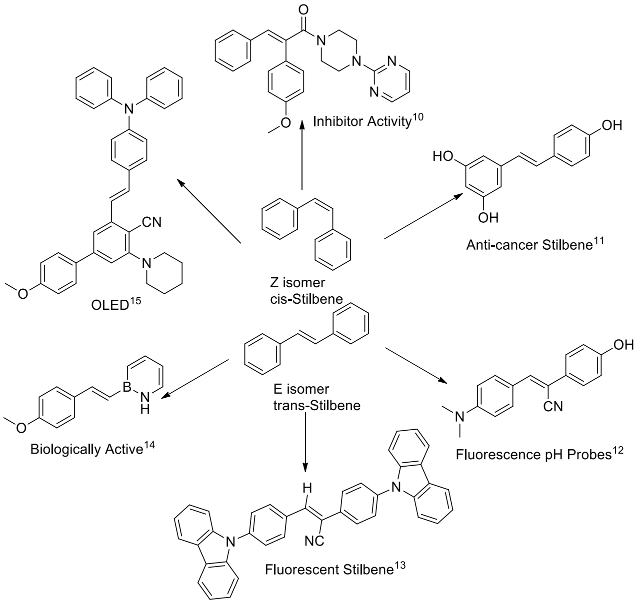
ABSTRACT: Stilbenes substituted with –CN, –OMe and –Br were synthesized using four different Lewis acid catalysts and their reaction efficiencies were compared. In addition to McMurry reagents known in literature, a more familiar and economical catalyst $ZnCl_2$ was used for the first time in our reaction procedures. Furthermore, bromine substituted stilbenes were subjected to Suzuki coupling reactions to append a triphenylamine (TPA) unit, which enhances fluorescence emissions. Solvatochromic properties of synthesized stilbenes were investigated and aggregation caused quenching (ACQ) properties of TPA containing molecules were systematically examined. Optical properties were also theoretically investigated.

Introduction

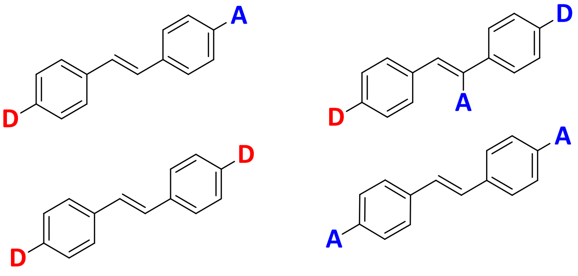
Stilbenes are characterized by two aromatic rings, linked by an ethylene bridge. Their π-conjugated structures and *E*/*Z* isomers exhibit excellent photophysical and photochemical properties.[1-5] Stilbene compounds are abundant in nature and act as defense compounds in some plants for pathogen attacks. Moreover, their antioxidant,[6] anti-inflammatory[7] and anticancer activities,[7,8] have been of great interest to scientists. Apart from biological features,[9] their interactions with radiation provide various applications in nonlinear optics, light emitting diodes, and optical brighteners (Scheme 1).[10-15]



Scheme 1. Structures of *E*/*Z* isomers of some stilbene compounds.[10-15]

The use of stilbenes for light emitting diodes and optical brighteners has led to tremendous innovation in display technology.[15] Stilbenes, with their luminophore characteristics, may experience two effects in aggregate state; aggregation caused quenching (ACQ) and aggregation induced emission (AIE). ACQ arises from intermolecular π-π stacking interactions between aromatic rings and leads to non-radiative decays in solid state.[16-17] TPA known for its electron donating, efficient charge transport abilities[18] is used in some AIEgens, to enhance exciton combination, charge transport and emission.[19-20] Furthermore, due to its charge transport ability, TPA is commonly used as donor in donor–acceptor (D–A) systems, to create a low energy charge-transfer (CT) transition.[21-22]

π-conjugated compounds with D–A type structures have been of great importance due to their efficient use in fluorescent sensors, biological imaging, photovoltaic cells and other optoelectronic applications. Substituted stilbenes are utilized to improve charge transfer characteristics in D-π-A systems (Scheme 2); moreover, TPA units incorporated to stilbenes cause bathochromic shifts. Furthermore, presence of strong acceptor units results in marked conjugation, thus, solvatochromic properties.[23] Solvatochromic properties of organic molecules is well-known, whereby, their emission and absorption bands are largely influenced by solvents with different polarities.[24-29]

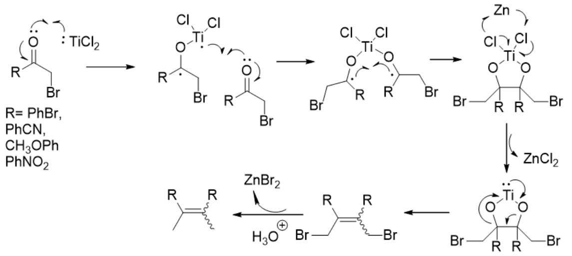


Scheme 2. Possible D-A structures of stilbene compounds.

Experimental Synthesis

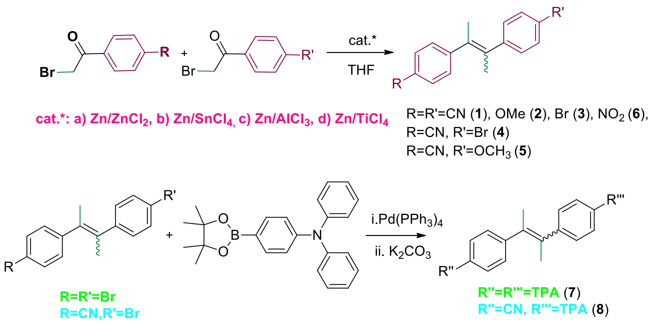
Stilbene derivatives can be synthesized *via* eight different reaction types: Aldol-type condensation, Siegrist method, Wittig–Horner reaction, Heck reaction, Negishi–Stille reaction, Barton–Kellogg–Staudinger reaction, McMurry reaction and Perkin reaction.[30] In the McMurry reaction, two aldehydes or ketones are coupled to form an alkene by using a reducing agent, Zn and titanium (IV) chloride. The low valent Ti-induced ($TiCl_2$) reductive deoxygenation of carbonyls to olefins takes place in two steps: 1) reductive dimerization of the starting ketones to form a carbon–carbon bond and, 2) deoxygenation of the 1,2-diolate intermediate to give an alkene (Scheme 3).[31-33] The stereoselectivity of olefin formation depends strongly on the steric bulk of the alkyl groups on the ketone. While McMurry reactions with bulky -R groups mainly lead to *E* isomers, surprisingly it was found that the *Z* isomer is the major product of McMurry coupling of acetophenones.[34-37] In this study, we chose to use

McMurry coupling to produce our target stilbenes (Scheme 4).



Scheme 3. Mechanism of McMurry coupling reaction.[31]

Although $TiCl_4$ is the first proposed catalyst in McMurry olefination procedures,[31] other catalysts such as $AlCl_3$, $SnCl_4$ and $InCl_3$ are also used to develop new synthesis procedures for McMurry coupling mechanism of carbonyl compounds to olefins.[38] In this study, in addition to $AlCl_3$, $SnCl_4$ and $TiCl_4$, we proposed a new McMurry reagent, $ZnCl_2$. Thus, we performed olefination mechanism with four different reagents and observed varying performances with each catalyst (see SI for further information). While $SnCl_4$ and $TiCl_4$ are with high reaction yields, $ZnCl_2$ is the next promising candidate, owing to its ease of handling and may be preferable over the very hazardous $SnCl_4$ and $TiCl_4$ reagents. In this study, it has been observed that the catalysts except $ZnCl_2$ do not work in reactions with α-bromo ketones. Therefore, for the purpose of observing the performance of $ZnCl_2$, α-bromo ketones are used as starting materials. On the other hand, $AlCl_3$ is the only catalyst which do not work in the synthesis of stilbenes from α-bromo ketones. After the successful synthesis of seven stilbene molecules (Table 1), solvatochromic effects on optical properties of **1**-**5**, **7** and **8** were studied. Stilbenes **3** and **4** were synthesized as precursors to **7** and **8**. Molecule **6** could not be isolated.



Scheme 4. Synthesis of stilbene derivatives **1–8**.

Optical Properties

The solvatochromic properties of compounds **1-5, 7** and **8** were investigated in eight different solvents with differing polarities. Table S2 shows the wavelengths of maximum absorptions obtained from UV-Vis spectra. Although no large differences are observed between the λ_{max} values, each compound showed different trends in solvents with different polarities. On the other hand, all stilbenes showed absorptions in the range of 200 to 450 nm. Generally, all compounds showed multiple peaks and expected bathochromic shifts are clearly observed in D-*π*- type structures.

As shown in Figure 1, going from compound **1**, which is an A-*π*-A type structure to compounds **5** and **8**, which are D-*π*-A type structures, λ_{max} values increased and optical band gaps decreased. This expected trend is a consequence of increased charge transfer in D-*π*-A systems. Effect of donor strength in these systems was also studied by incorporating TPA unit in place of the –OMe unit. When two D-*π*-A systems, compounds **5** and **8** are compared, a clear red shift is observed in the absorption spectra of **8**, which is attributed to the excellent electron donating ability of the TPA unit in D-*π*-A or D-A systems (for more detail, see Figures S31, S32 and S33 in supporting info). Consequently, the weaker electron donating ability of the –OMe unit resulted in a blue shift, thus a higher optical band gap.

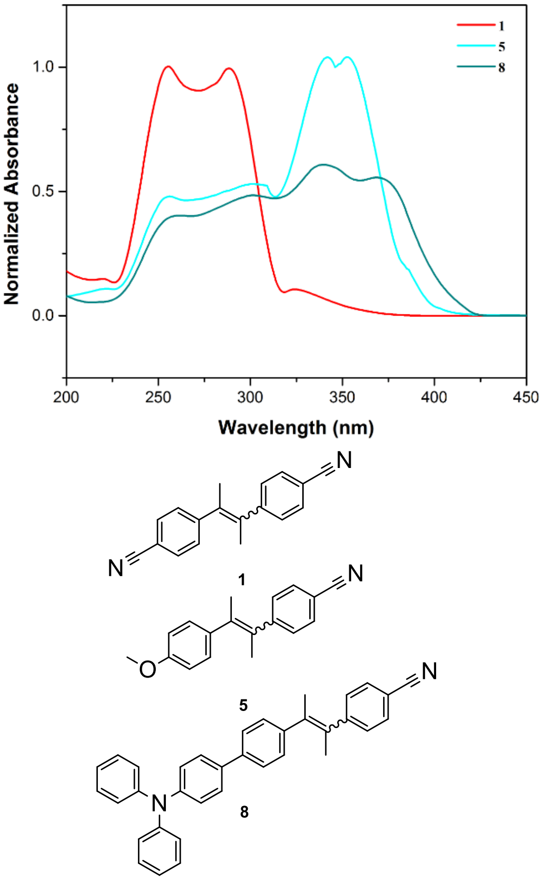
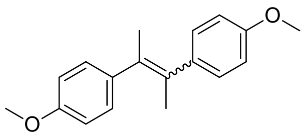
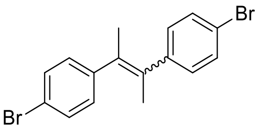
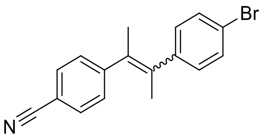
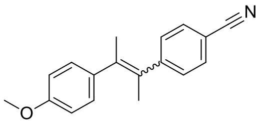
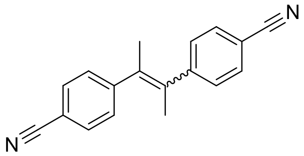
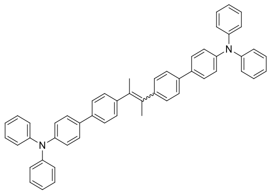
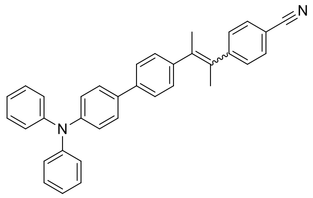


Figure 1. UV-Vis absorption spectrum of compounds **1**, **5** and **8** in dioxane**.**

Bathochromic shifts were observed in most solvents, with some exceptions. Going from **1** to **5**, a red shift is observed clearly in toluene, THF, dioxane, acetonitrile,

Table 1. Chemical formulas of compounds **1-5** and **7-8**.

Non-Fluorescent Stilbenes			
D- π-D  **2** (MeO-St-MeO)	 **3** (Br-St-Br)	 **4** (CN-St-Br)	D- π-A  **5** (CN-St-MeO)
Fluorescent Stilbenes			
A- π-A  **1** (CN-St-CN)	D- π-D  **7** (TPA-St-TPA)	D- π-A  **8** (CN-St-TPA)	

and DMF. From compound **1** to **8**, a red shift is observed in all solvents. On the other hand, effect of donor strength is visible in all solvents, except acetonitrile and DMF. Effect of incorporating two TPA units is also studied with compound **7**. Compounds **7** and **8** display similar behaviors in most solvents, and we have observed that stilbene **7** with two strongly electron donating TPA units, is as effective as compound **8** in terms of decreasing optical band gap, (for more details of absorption spectra of synthesized compounds, see S29 in supporting info).

We aimed to see the effect of D-π-A structures on absorption spectra and our results supported the expected behaviors of these kind of systems. Surprisingly, different polarities of solvent molecules caused no changes in some absorption spectra and all stilbene compounds were shown to have very broad, similar peaks in DCM and acetone. Moreover, we also investigated emission characteristics of stilbene compounds. Stilbenes **1**, **7** and **8** are fluorescent compounds, their fluorescence spectra details are given in Table S2. Figure 2A shows emission spectra and colors of the brightest stilbenes, **7** and **8**.

Compounds **7** and **8** display fluorescence as shown in Figure 2A, and it is clearly observed that in DMF, DCM and MeCN, these compounds have maximum intensity at the same wavelengths. For compound **7,** increased polarity caused a red shift in the fluorescence spectra, except in THF and dioxane. For compound **8**, from *n*-Hexane to DMF, a red shift is observed with exceptions in THF and dioxane. Surprisingly, compound **8** has almost the same fluorescence spectra with compound **7.**

Previous studies on substituted stilbenes showed enhanced or quenched emission characteristics in aggregate state. In this study, aggregate formation was induced by decreasing solubility of stilbenes in THF/water mixtures.

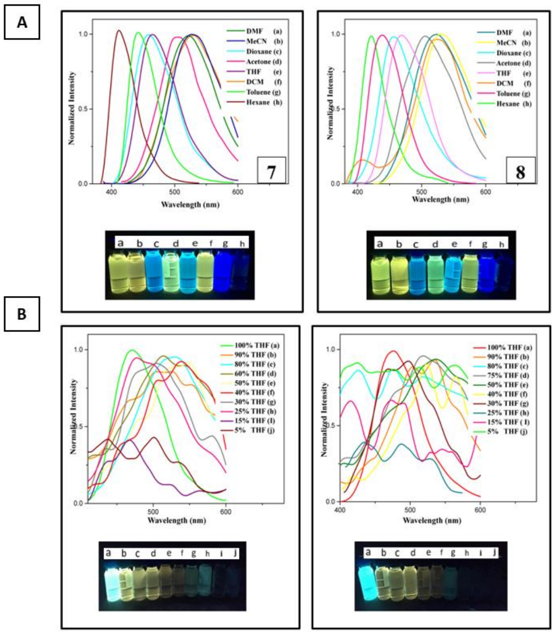
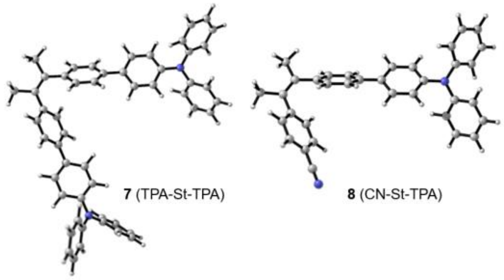


Figure 2. Fluorescence spectra of **7** and **8 (A)** and ACQ spectra of compounds 7 and 8 (**B**).

As mentioned in the introduction, we used the TPA unit to enhance charge transfer in our target stilbenes. In addition to its charge transfer characteristic, TPA is a well-known ACQ-active compound. Unlike AIEgens, ACQ-active compounds decay radiatively and shine brighter when they are separated. This trend is observed due to compact packing and strong π-π stacking interactions in ACQ luminophores, leading to undesirable quenching effects in emission.[17]

To observe whether compounds **7** and **8** show such characteristics, we probed the emission behavior of stilbenes in THF/H_2O mixtures. For this, stock solutions with varying THF/water ratios were prepared and their fluorescence measurements were performed. Figure 2B shows emission intensity changes in THF/H_2O mixtures and it is obvious that increasing water concentration results in quenching of the emission, as expected from the TPA unit. For compound **7**, with the increase of water percentage from 0% to 50%, a red shift was observed from 470.76 nm to 548.45 nm. When the water fraction further increased from 50% to 95%, the fluorescence emission was blue shifted from 548.45 nm to 500.87 nm. For compound **8**, red shifted emission from 475.64 nm to 564.976 nm was observed, until the water fraction reaches 60%, subsequently, as water ratio further increased from 60% to 85%, the spectra was blue shifted from 564.976 nm to 489.89 nm. While red shifted emission spectra is a consequence of enhanced intermolecular charge transfer effects between solutes and polar solvents, blue shifted spectra may originate from the suppression of further charge transfer.[39]



7 (TPA-St-TPA)

8 (CN-St-TPA)

Figure 3. Z isomers of ACQ-active stilbene compounds.

Computational Methodology and Results

To further elucidate the optical and solvatochromic effects observed for stilbene compounds under study, a DFT investigation was performed, with the main focus to investigate the differences in optical properties between *E* and *Z* conformers of compounds **1**-**5**, **7** and **8** and to verify that experimental results are in the range of expected *E* and *Z* spectra. For this purpose, meta-hybrid M06-2X functional[40] and 6-31G(d,p) basis set were used for ground-state optimizations using the Gaussian09 software package.[41] Single point energy refinements were performed using B2PLYP,[42] PBE1PBE[43] and ωB97XD[44] levels of theory to obtain relative energies of *E* and *Z* isomers. Solvent effects were taken into account employing a polarizable continuum (IEF-PCM) model.[45,46] Absorption spectra were produced using Time-Dependent Density Functional Theory (TD-DFT).[47,48] To include dynamic effects, 35 conformations for both *E* and *Z* isomers were generated via Wigner distribution[49] as implemented in the Newton-X software package[50] (performed at the M062X/6-31G(d,p) level). Vertical transitions were convoluted using Gaussian functions of full-width at half length (FWHL) of 0.15 eV to ensure comparison with experimental data. Since the experimental spectra did not exhibit strong shifts among different solvents, only three solvents (hexane, dioxane and *N,N*-dimethyl formamide) with largely differing polarities were studied computationally.

In Figure 4, it is clearly observed that for DMF, shapes of the *Z* isomers' spectra are in close agreement with the experimental spectra. This trend is also shown in hexane and dioxane. (For more details, see Fig S31 – S34 in supporting info). As shown in Figure 4, when the spectra of *Z*-conformers of **1** and **5** are compared, bathochromic shifts, due to the D-A structure, is observed in compound **5.** However, for compound **8**, the effect of the D-A structure and increased donor character of the TPA unit on absorption wavelengths are not clear in theoretical spectra of *Z*-conformers.

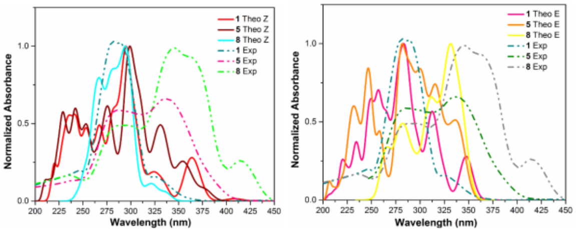


Figure 4. Experimental and computational UV-Vis absorption spectra of **1**, **5** and **8** in DMF.

In addition to calculations of spectral data, energy refinements for *E* and *Z* isomers were performed, and although *E* isomers are shown to be energetically more stable compared to their *Z* counterparts, experimental spectra are very similar to those calculated for *Z* conformers, as expected from the McMurry coupling reaction of carbonyl compounds with aromatic moieties. (For more details, see Table S3-S4, Fig S31 – S34 in supporting info).

Conclusion

Seven different stilbene compounds were synthesized *via* the McMurry coupling reaction, using different catalysts, and their solvatochromic properties were examined in solvents with varying polarities. The most effective synthesis procedure is suggested to be with $SnCl_4$ and $ZnCl_2$. While $SnCl_4$ works well in the synthesis of all stilbenes, $ZnCl_2$ is the new promising candidate, owing to its ease of handling. Results reveal that TPA containing stilbenes (**7** and **8**) exhibit excellent fluorescence properties, a trend which can be attributed to the strong electron donating ability of the TPA unit and the effective charge transfer within these molecules. Although the compounds without TPA unit have no emission properties, they exhibit different behaviors in solvents with different polarities. Aggregation caused quenching properties of TPA consisting molecules (**7** and **8**) were also studied and increasing water concentrations led to decreased emissions in both compounds. To sum up, a new synthesis procedure for *Z*-stilbenes was developed and it was shown that suitable modifications may lead to light emitting stilbene compounds for various applications. Moreover, *Z*-isomers of stilbenes **2** and **5** are especially suitable candidates for cancer treatments due to higher anti-metastatic activity than their *E*-isomers.[11]

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Supporting Information

Experimental procedures, spectroscopic data, level of theory study, calculated absorption spectra and Cartesian coordinates of optimized structures.

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