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Triphenylamine-based novel PET sensors in selective recognition of dicarboxylic acids

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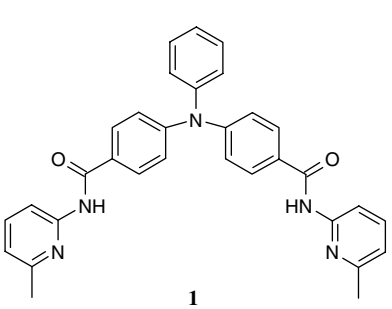
Abstract—The triphenylamine-based chemosensors **1** and **2** have been designed and synthesized, for the first time, for the selective recognition of dicarboxylic acids. Carboxylic acid binding takes place through charge neutral pyridyl amide receptor sites with concomitant quenching of fluorescence of the triphenylamine moiety. The bindings were examined using ^{1}H NMR, fluorescence and UV–vis spectroscopic methods. The receptor **1** was found to be selective for glutaric and adipic acids and the macrocycle **2** was specific for 2,2-dimethylmalonic acid.

Interest in the selective recognition and sensing of neutral species by synthetic receptors continues to attract the attention of the supramolecular chemistry community.[1] Given the important role of dicarboxylic acids in biology,[2] the need for their selective recognition by synthetic fluorescent sensors utilizing weak hydrogen bonding interactions is of great importance in molecular recognition research.[3] During the last decade, considerable progress has been made for the recognition of dicarboxylic acids by a number of synthetic receptors of various architectures.[4] Despite the development of dicarboxylic acid receptors with signalling information,[5,3a] there is continued interest in the search for new fluorescent based molecular sensors for selective recognition of dicarboxylic acids because of the many advantages including multiple modes of detection (such as quenching, enhancing, life time), extremely high sensitivity, relatively low cost and easy availability. We are interested in developing chromophores where the recognition takes place at charge neutral recognition sites with concomitant changes in the photophysical properties of a lumophore by modulation of the photoinduced electron transfer (PET) mechanism.[6,4d] In this context, we herein report the design and synthesis of triphenylamine-based PET chemosensors **1** and **2**, for the first time, for size selective recognition of aliphatic dicarboxylic acids. Although a number of receptors with a range of spacer groups for neutral dicarboxylic acids of different chain lengths are reported in the literature,[4,7] triphenylamine has not been used in this capacity until now.



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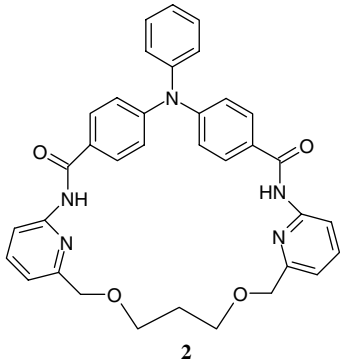

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Keywords: Triphenylamine; Selective recognition; Glutaric acid; 2,2-Dimethylmalonic acid; PET sensor.
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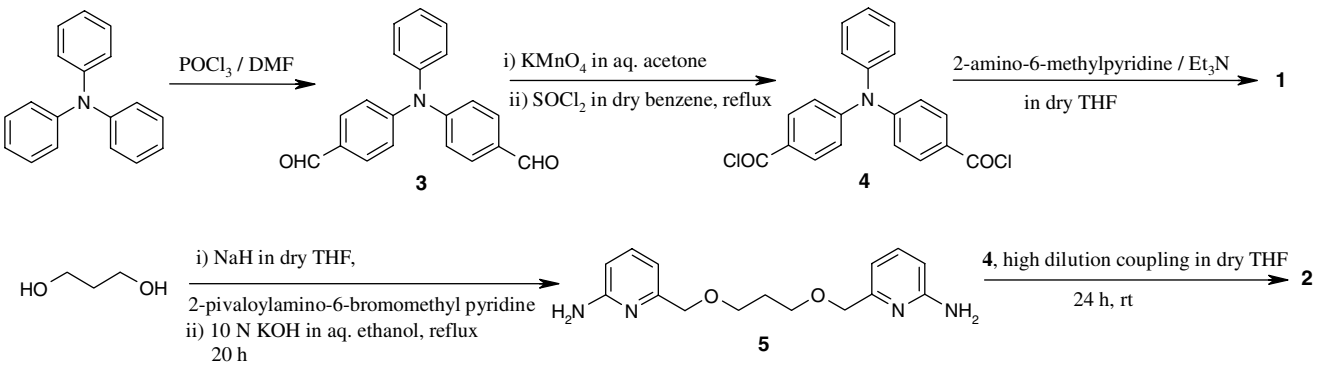
The triphenylamine moiety has been employed intensely because of its structural rigidity[8] and strong fluorescence property. The peripherally substituted binding sites are expected to modulate the electron density. The hydrogen bonding perturbation of the binding sites alters the excited state properties of the receptor. Considering these points, we placed the pyridine amide, a known carboxylic acid binding moiety,[9] onto the periphery of the rigid triphenylamine (**1** and **2**) unit, which provides a conformationally well-defined V-shape geometry for size selective complexation of dicarboxylic acids.

The syntheses of **1** and **2** were accomplished according to Scheme 1. Triphenylamine was initially formylated using $POCl_3$/DMF to yield mono-, di- and tri-formylated products. The desired 4,4′-diformyltriphenylamine **3**, isolated in 57% yield, was next oxidized to the diacid, which on treatment with thionyl chloride gave diacid chloride **4** in an overall 80% yield. Coupling of 2-amino-6-methylpyridine with **4** in dry THF afforded the sensor **1** in 78% yield as yellowish solid,[10] which was soluble in common organic solvents such as CH_2Cl_2, $CHCl_3$ and CH_3CN. The macrocycle **2** was synthesized by high dilution coupling of diacid chloride **4** with diamine **5**, which was obtained by reaction of 2-pivaloylamino-6-bromomethyl pyridine (obtained via NBS reaction of 2-pivaloylamino-6-methylpyridine in dry carbon tetrachloride) with 1,3-propanediol followed by alkaline hydrolysis. This method gave **2** in 10–12% yield as brownish solid. All the compounds were fully characterized by conventional methods.[10]

In **1**, the hydrogen bonding groups are conveniently arranged in a concave face to bind dicarboxylic acids, and can have three conformations of comparable energy values (in–in, in–out and out–out) in the solution phase. MMX calculations[11] on the 'in–in' conformation of **1** ($E_{min} = 61.99$ kcal/mol) indicates a separation of 10.83 Å between the two-pyridine ring nitrogens and 7.92 Å between two amide NH's. The phenyl rings of the triphenylamine moiety are slightly twisted from the plane containing the central nitrogen atom. In **2** ($E_{min} =$ 84.06 kcal/mol), the pyridine ring nitrogens and amide NH's are 8.80 and 7.54 Å apart, respectively. Thus both open and macrocyclic cavities can accommodate dicarboxylic acids of various chain lengths, and selective binding occurs only when the cavity dimension matches the chain length of the dicarboxylic acids.

The sensitivity and selectivity of these ditopic receptors towards a series of aliphatic dicarboxylic acids of various chain lengths was evaluated by observing the change in the fluorescence emission spectra in $CHCl_3$ and the ^1H NMR upon dicarboxylic acid titration in $CDCl_3$. The fluorescence emission spectra of **1** and **2** consisted of bands at 417 and 430 nm, respectively, when excited at 360 nm. Upon addition of dicarboxylic acids of different chain lengths (prepared in $CHCl_3$ containing 0.02% DMSO) the emission was drastically quenched due to the formation of receptor–diacid complexes. During the course of titration there was no other spectral change in the emission spectra. Concurrently, the changes in the absorption spectra (peaks at 360, 328 and 290 nm in the case of **1** and at 360, 323 and 291 nm in the case of **2**) of both the sensors were only minor during titration with dicarboxylic acids thus indicating typical PET behaviour. This typical PET behaviour is attributed due to separation of the triphenylamine unit from the receptor sites by rigid amide spacers; the only interaction between the two moieties is through electron transfer. Once binding has occurred, fluorescence quenching is therefore caused by electron transfer between the pyridine amide-carboxylic acid complexes and the chromophore triphenylamine units in both **1** and **2**.

Upon addition of increasing concentrations of dicarboxylic acids of various chain lengths, the fluorescence of the open receptor **1** was essentially quenched to different extents. The greater quenching for glutaric acid (ca. 39%) as revealed in the Stern–Volmer plot (Fig. 3; inset) at 417 nm, is considerable due to its ability to form a tight and stable hydrogen bonded complex (Fig. 1) with the ditopic receptor **1** compared to its higher and lower homologues (quenching ca. 18–30%). The significant red shift ($\Delta\lambda = 21$ nm) along with the presence of an isobastic point during the titration with glutaric acid (Fig. 5) clearly indicates the formation of a 1:1 hydrogen bonded complex. This is attributed to the complementary size of the binding space of **1** with the chain length of glutaric acid. A slightly greater quenching for 2,2-dimethylmalonic acid than adipic acid as observed in Figure 3 (inset), is possibly due to its higher acidity. In the case



Scheme 1. The syntheses of receptors **1** and **2**.