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SYNTHESIS AND CHARACTERIZATION OF NEW MOLECULAR TWEEZER MOLECULES CONTAINING 4-(4-(PHENANTHRIMIDAZOLE-2-YL)PHENYL)PYRIDINE AS HINGE REGION

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Abstract: In the present study we have synthesized new moleculartweezer molecules containing 1*H*-phenanthro[9, 10-d]imidazole and pyridine rings. These derivatives were synthesized by the reaction of phenanthrene-9,10-dione, terephthalaldehyde and ammonium acetate in acetic acid and then mixing by acetyl aromatic compounds. The newly synthesized compounds were characterized on the basis of IR, ^{13}C NMR, ^{1}H NMR spectra, and elemental analyses. These new compounds were subsequently studied for their fluorescence properties.

Keywords: Phenanthrimidazole, Pyridine, Molecular Tweezer, Fluorescence.

Introduction

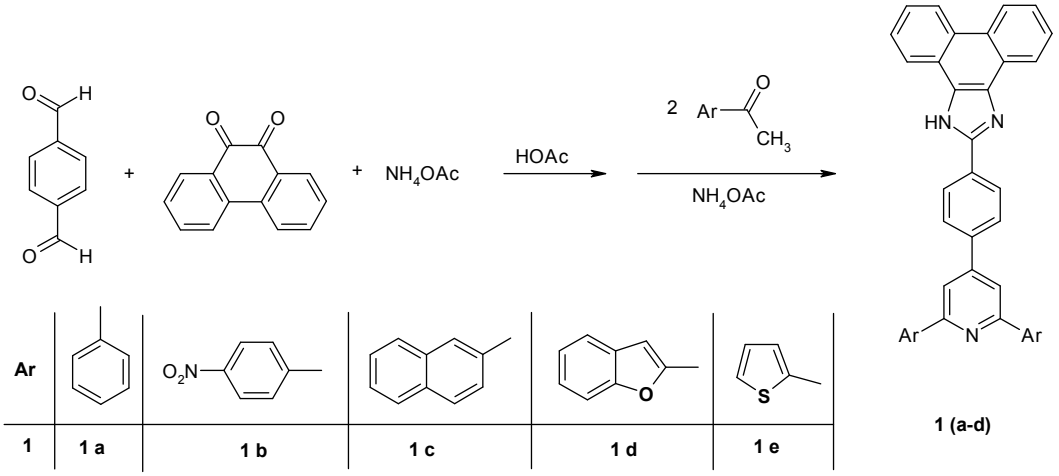
Recently, multicomponent reactions have received great attention, due to their environmental friendliness, atom economy, and their ability to generate a wide range of diverse, highly functionalized molecules, in a single reaction vessel without need to isolate any intermediate, which reduces time, saves initial reactants, and increases yield.[i]

One class of hosts is the molecular tweezers, defined by Whitlock as receptors in which two, flat, generally aromatic "pincers" or chromophores are linked by a rigid spacer (hinge region) to provide an approximately two-dimensional cleft into which a guest can bind.[ii] These open-structure molecules have a certain degree of flexibility, provided that the cavity is large enough and the geometry is optimal to accommodate the desired guest molecule. Thus, the molecular tweezer, can be used for molecular recognition. The phenomenon of molecular recognition has been studied through a number of synthetic hosts of various shapes and sizes.[iii-v]Hosts being chosen to exhibit complementarity to various guests on the bases of size, shape, and specific, directional, molecular interaction. Binding in molecular tweezers may be mediated by a number of interactions, including dispersion forces, stacking, hydrogen bonding, and salt bridging, among others.[vi]

Recently, a molecular tweezer with electron-rich pincers [i.e. phenathrimidazole pincers] and diphenylpyridine as hinge region, has been successfully used for explosive detection.[vii, viii] Also, the molecular tweezers and derivatives inhibit the assembly and toxicity of amyloid-beta in a non-neurotoxic manner,[ix]so the molecular tweezer represents a potential drug for

the treatment of Alzheimer's disease.[x]They can be developed for other amyloid-related diseases including Parkinson's disease, Creutzfeldt-Jakob disease and Gerstmann-Sträussler-Scheinkerdisease.[xi]

Herein, we describe the synthesis of a new molecular tweezer in which the 4-(2-phenylphenanthrimidazole)pyridine was used as spacer and two aryl or heteroaryl molecules as pincers (**Scheme 1**).The ready availability of these tweezers with different pincers allows us to demonstrate that they bind a variety of electron acceptors as guests via electron donor-acceptor, anintramolecular π-π interaction or charge-transfer interactions.



Scheme 1: Synthesis of new molecular tweezer molecules

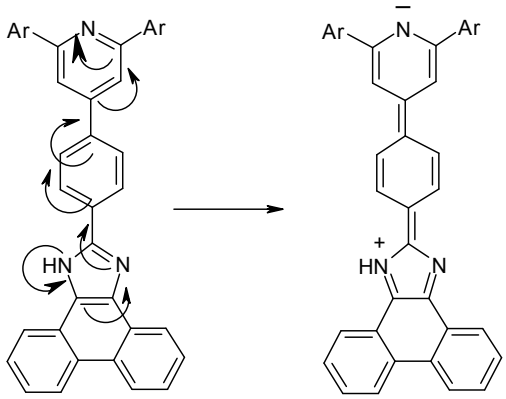
Results and Discussion

The new 2,6-bis(aryl)pyridine derivatives (**1a–e**) were synthesized via a one-pot reaction from 9,10-phenanthraquinone, terephthalaldehyde, ammonium acetate in acetic acid and then by mixing with aryl methylketones.

Mechanistically, it is reasonable that the first step involves a phenanthrimidazole ring formation from recation of 9,10-phenanthraquinone with one carbonyl group of terephthalaldehyde in presence of ammonium acetate. At the second step, an Aldol condensation of an arylmethylketone with other carbonyl group of terephthalaldehyde and after losing of water and Michael addition to the second mole of arylmethylketone, leading to 1,3,5-diaryl-1,5-diketone.[xii, xiii]Then through the ring closure with ammonium acetate and oxidation by air, the products (**1a–e**) can be obtained.

The structures of compounds (**1a–e**) were characterized by elemental, FT-IR, ^{1}H and ^{13}C NMR analyses. The FT-IR spectra of compounds (**1a-e**) exhibit absorption at 3311-3442 $cm^{-1}$for N-H stretching of phenanthrimidazole and 1645-1659 cm^{-1} for C=N bond. The ^{1}H NMR spectra of compounds (**1a-e**) in DMSO-$d_6$showed singlet (δ ≈ 8.1 ppm) for pyridine protons as well as a broad band (δ ≈ 13.5ppm) for NH proton and the characteristic doublet signals at δ ≈ 8.1 ppm and δ ≈ 8.4 ppm for para-substituted aromatic ring. All this evidence plus the ^{13}C NMR spectra, and microanalyticaldata strongly confirmed the structure of compounds (**1a-e**).

The introduction of a 2-phenyl-1Hphenanthro-[9,10-d]imidazole functional group in molecular core structure makes n–π conjugation system to be augmented dramatically resulting in a strong fluorescence.[xiv]In addition, a typical photoinduced charge transfer system consists of a donor (D) and acceptor (A) couple, which can be separate chromophores within a large molecule, leading to intramolecular charge transfer (**Scheme 2**).



Scheme 2: Resonance structures for compounds (1a-e).

Additionally, it has been reported that the 2-phenylphenanthro[9,10-d]imidazole moiety is essentially planar.[xv]The λ_{abs}, and λ_{flu} data of these compounds are presented in **Table**.

Table: Wavelengths of maximum absorbance (λ_{abs}) andFluorescence emission (λ_{flu}).

Compound	**1 a**	**1b**	**1c**	**1d**	**1e**
λ_{abs}	484	478	485	498	466
λ_{flu}	591	585	599	619	599

As seen from **Scheme 1**, the molecules are related, but their chemical structures are differentiated by introducing various aromatic rings, for instance phenyl, 4-nitrophenyl, 2-naphthyl, benzofuran-2-yl or 2-thienyl. Such a structural modification could be expected to result in some changes in the π-conjugated length and in the absorption and emission spectra. These compounds present a strong intramolecular charge transfer (ICT) absorption band within 420–540 nm, the maximum absorption peaks of ICT absorption band undergo a redshift from **1a** (484 nm) to **1e** (466 nm), and to **1d** (498 nm). Concerning compounds **1a** and **1d**, the benzofuran-2-yl moieties for **1d** caused a bathochromic effect of approximately 14 nm relative to the phenyl moieties for **1a**, suggesting that the conjugation of **1d** is larger than that of **1a**. As a result, the red-shift of absorption can possibly occur. It was also noted that replacement of 2-thienyl group with a phenyl donor on 2,6 positions of pyridine resulted in a hypsochromic shift (22 nm), which implied that **1a** seems to possess a larger conjugated system than **1e**.

Experimental

All chemicals were commercially available and used without further purification. Melting points were recorded on an electrothermal type 9100 melting point apparatus. The FT-IR spectrometer used was Bruker Tensor 27. The FT-IR spectra were taken using KBr pellets. The ^{1}HNMR and ^{13}CNMR (500 MHz) spectra were recorded on a Bruker DRX 500 spectrometer. Elemental analysis was performed on a ThermoFinnigan Flash EA microanalyzer. Absorption and fluorescence spectra were recorded on a Varian 50-bio UV–Vis spectrophotometer and a Varian Cary Eclipse spectrofluorophotometer, respectively. UV–Vis and fluorescence scans were recorded from 350 to 700 nm.

Synthesis of 4-(4-(phenanthrimidazole-2-yl)phenyl)-2,6-diarylpyridines:

To a solution of phenanthrene-9,10-dione (10 mmol, 2.1 g), terephthalaldehyde (10 mmol, 1.4 g) and ammonium acetate (40 mmol, 4.0 g), 20 ml acetic acid were added, then the resulting mixture was heated at 100 °C for 2 h. Then intermediate compound was reacted with reagentsseparately to give final products (1a-e). Reagents were ammonium acetate (4 g)

and acetophenone(20 mmol, 2.4 g), 2-acetyl naphthalene (20 mmol, 3.4 g), 4-nitro-acetophenone (20 mmol, 3.3 g), 2-acetyl benzofuran(10 mmol, 1.61 g), or 2-acetylthiophene (20 mmol, 2.52 g). After that all of solutions were heated under reflux for 4 h the remaining solutions were filtered and washed with ethanol and then the solid product purified by recrystallization from ethanol.

2-(4-(2,6-diphenylpyridin-4-yl)phenyl)-1H-phenanthro[9,10-d]imidazole(1a),

Light orange powder, yield, 80%,m.p. 280–285 °C, IR, ν_{max}/cm^{-1}: 3422, 1653, 1589, 1480, 1455, 1334, 1222, 1118, 1018, 757,^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm): 7.61–7.88 (m, 9 H), 8.07 (s, 1 H), 8.11 (s, 1 H), 8.146-8.167 (d, 2 H, J = 8.4 Hz), 8.219-8.237 (d, 2 H, J = 7.2 Hz), 8.415-8.436 (d, 2H, J = 8.4 Hz), 8.56-8.68 (m, 4 H), 8.85-8.92 (m, 3 H), 13.60-13.63 (b, 1 H, NH),^{13}C NMR (500 MHz, DMSO-d_6) δ (ppm): 120.23, 120.65, 122.83, 123.12, 123.22, 124.34, 125.21, 125.75, 126.45, 126.84, 127.39, 127.85, 128.16, 128.33, 129.22, 129.54, 129.65, 130.53, 131.94, 133.44, 137.65, 151.32, 157.22, Anal. Calcd for $C_{38}H_{25}N_3$: C, 87.16, H, 4.81, N, 8.02. Found, C, 87.80, H, 4.61, N, 7.95%.

2-(4-(2,6-(4-nitrophenyl)pyridin-4-yl)phenyl)-1H-phenanthro[9,10-dimidazol (1 b),

Orange powder, yield, 82%,m.p. 238–241 °C, IR, ν_{max}/cm^{-1}: 3385, 1659, 1585, 1517, 1480, 1323, 1212, 1030, 852, 822, 753,^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm): 7.57–7.78 (m, 5 H), 7.85-7.92 (m, 2 H), 8.02 (d, 2 H, J= 8 Hz), 8.25 (d, 4 H, J= 7 Hz), 8.26 (s, 2 H), 8.33 (d, 2 H, J= 8 Hz), 8.47-8.60 (m, 2 H), 8.73-8.80 (m, 2 H), 13.45-13.49 (b, 1 H, NH),^{13}C NMR (DMSO-d_6, 500 MHz), δ (ppm): 122.79, 124.58, 127.19, 127.72, 127.91, 18.02, 128.76, 130.40, 130.59, 130.62, 130.65, 133.15, 135.72, 137.47, 142.90, 143.05, 145.16, 145.54, 149.08, 150.55, 150.59. Anal. Calcd for $C_{38}H_{23}N_5O_4$: C, 74.38, H, 3.78, N, 11.41. Found, C, 74.65, H, 3.85, N, 11.35%.

2-(4-(2,6-di(2-naphthyl)pyridin-4-yl)phenyl)-1H-phenanthro[9,10-d]imidazole (1 c),

Light orange powder, yield, 84%,m.p. 288–292 °C, IR, νmax/cm^{-1}: 3311, 1657, 1594, 1455, 1357, 1330, 1213, 1119, 889, 872, 756,^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm): 7.63–7.76 (m, 5 H), 7.85 (s, 1 H), 7.89 (s, 1 H), 7.93 (s, 1 H), 8.03-8.10 (m, 4 H), 8.16-8.28 (m, 4 H), 8.44 (d, 2 H, J= 8 Hz), 8.55 (s, 1 H), 8.60-8.63 (m, 3 H), 8.85-8.87 (m, 4 H), 8.99 (d, 2 H, J= 8 Hz), 13.51-13.65 (b, 1 H),^{13}C NMR (DMSO-d_6, 500 MHz), δ (ppm): 122.51, 122.99, 123.58, 124.83, 125.94, 126.88, 127.04, 127.47, 127.66, 128.21, 128.97, 129.20, 129.92, 130.06, 130.11, 130.97, 131.04, 132.47, 132.79, 132.81, 135.30, 135.38, 135.82, 137.26, 143.48, 143.65, 148.35, Anal. Calcd for $C_{46}H_{29}N_3$: C, 88.58, H, 4.69, N, 6.74. Found, C, 88.75, H, 4.74, N, 6.45%.

2-(4-(2,6-di(2-benzofuryl)pyridin-4-yl)phenyl)-1H-phenanthro[9,10-d]imidazole (1 d),

Orange powder, yield, 78%,m.p. 204–208 °C, IR, νmax/cm^{-1}: 3442, 1651, 1590, 1546, 1476, 1454, 1360, 1257, 1140, 1043, 830, 751,^{1}H NMR (500 MHz, DMSO- d_6) δ (ppm): 7.35–7.38 (m, 1 H), 7.52-7.62 (m, 1 H), 7.60-7.62 (m, 2 H), 7.69-7.96 (m, 8 H), 8.09 (d, 2 H, J= 8 Hz), 8.30 (s, 1 H), 8.385 (d, 2 H, J= 7.5 Hz), 8.50 (s, 1 H), 8.55-8.60 (m, 2 H), 8.80-8.83 (m, 2 H), 13.58-13.65 (b, 1 H, NH),^{13}C NMR (500 MHz, DMSO-d_6) δ (ppm): 118.39, 121.32, 121.61, 122.75, 123.22, 124.35, 125.18, 125.78, 126.44, 126.79, 127.15, 127.58, 128.13, 128.28, 129.38, 130.89, 131.65, 131.79, 134.33, 150.56, 157.12, 160.77, Anal. Calcd for $C_{42}H_{25}N_3O_2$: C, 83.56, H, 4.17, N, 6.96. Found, C, 83.71, H, 4.25, N, 7.15%.

2-(4-(2,6-di(2-thienyl)pyridin-4-yl)phenyl)-1H-phenanthro[9,10-d]imidazole (1 e),

Light brown powder, yield, 76%,m.p. 185–189 °C, IR, νmax/cm^{-1}: 3442, 1645, 1588, 1515, 1455, 1413, 1354, 1236, 1118, 757, 722,^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm): 7.29–7.33

(m, 1 H), 7.59-8.08 (m, 12 H), 8.33-8.37 (m, 2 H), 8.50-8.62 (m, 3 H, J= 7 Hz), 8.78-8.84 (m, 2 H), 13.51-13.55 (b, 1 H, NH),^{13}C NMR (DMSO-d_6, 500 MHz), δ (ppm): 122.85, 123.22, 127.25, 128.00, 129.81, 130.28, 130.44, 134.66, 136.38, 141.89, 143.25, 144.16, 147.55, 149.28, 150.58, 150.61, Anal. Calcd for $C_{34}H_{21}N_3S_2$: C, 76.23, H, 3.95, N, 7.84. Found, C, 76.14, H, 4.11, N, 7.36%.

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