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SYNTHESIS OF SOME NEW MOLECULAR TWEEZER MOLECULES BEARING DIBENZOBARALLENE PINCERS USING A BRØNSTED-ACID IONIC LIQUID AS CATALYST

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Abstract: In the present study, we have synthesized some novel molecular tweezer molecules comprising a characteristic 9,10-dihydro-anthracene-9,10-α,β-succinimide structural unit as pincers. These derivatives were synthesized by the reaction of dibenzobarallene and aromatic diamines using 1-(4-sulfonylbutyl) pyridiniumhydrogensulfate[Py-$(CH_2)_4SO_3H$][HSO_4], a Brønsted acidic ionic liquid, as a green and reusable catalyst. The products were characterized on the basis of FT-IR, ^{1}H-NMR, ^{13}C-NMR spectra and elemental analyses.

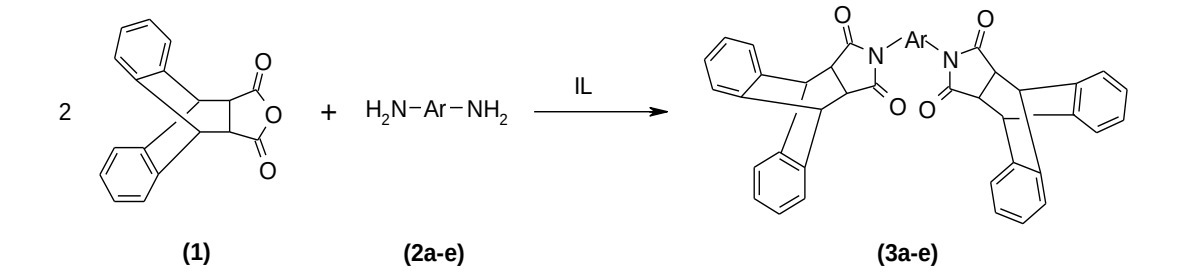
Keywords: Dibenzobarallene; Molecular tweezer; One-pot synthesis, Brønsted-acid ionic liquid.

Introduction

Dibenzobarallene (**1**) is readily synthesized by the Diels-Alder reaction, which involves the cycloaddition reaction of anthracene and maleic anhydride.[1]This compound is a key starting material for the synthesis of bioactive and novel heterocycle systems. Phthalazine-1,4-dione,[2] substituted isoindole-1,3-diones,[3] and 1,2,4-triazole derivatives[4] were obtained from the reaction of (**1**) with hydrazine, amine and thiosemicarbazide, respectively. Among a large variety of heterocyclic compounds derived from (**1**), isoindole-1,3-dione derivatives are of interest because they show some pharmacological and biological activities such as antibacterial,[5,6] antiinflamatory,[7] antimalarial,[8] anti-neoplastic and antiviral.[9]

It has also been reported that 9,10-dihydro-anthracene-9,10-α,β-succinimideframework is a favorable structural element for crystalline hosts, and promotes clathrate or crystalline inclusion formation.[10] One class of hosts is the molecular tweezers, defined by Whitlock as receptors in which two, generally aromatic pincers are linked by a rigid spacer to provide an approximately two-dimensional cleft into which a guest can bind.[11] Thus, the molecular tweezer, can be used for molecular recognition, and inhibition of amyloid-beta assembly which caused amyloid-related diseases including Alzheimer's disease,Parkinson's disease, Creutzfeldt-Jakob disease and Gerstmann-Sträussler-Scheinker disease.[12] Hence, we wish to report an efficient approach to the synthesis of some new molecular tweezer molecules (**3a-e**) by the reaction of dibenzobarallene and variousaromatic diamines using 1-(4-sulfonylbutyl)

pyridiniumhydrogensulfate[Py-$(CH_2)_4SO_3H$][HSO_4], a Brønsted acidic IL, as a green and reusable catalyst **(Figures 2 and 3**).



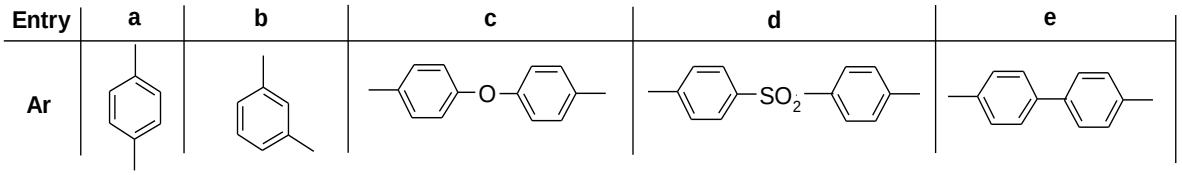


Figure 1: Synthesis of molecular tweezer molecules.

Results and discussion

The ionic-liquid catalyst, was prepared according to the literature procedure.[13, 14] The new molecular tweezer molecules (**3a–e**) were synthesized by the one-pot reaction of dibenzobarallene and variousaromatic diamines using 1-(4-sulfonylbutyl) pyridiniumhydrogensulfate[Py-$(CH_2)_4SO_3H$][HSO_4] as a green catalyst.

In order, to optimize the reaction conditions, initially a model study was carried out on the synthesis of (**3a**) in different solvents and under solvent-free conditions both with and without catalyst (**Table 1**). It was found, that the use of 5% mol ratio of catalyst (mol percentage of IL to diamine) at 120 °C gave good yield. Therefore, all compounds were synthesized with 5% mol ratio of the catalyst at 120 °C.

Table 1: Synthesis of (**3a**) in different conditions

Solvent	HOAc	HOAc	DMF	DMF	Dioxane	Acetonitrile	Solvent-Free	Solvent-Free
Catalyst (mol %)	0	5	0	5	5	5	5	5
Time (h)	4	4	6	6	6	6	1	1
Temperature (℃)	120	120	152	152	100	80	120	100
Yield (%)	90	95	89.5[10]	90	78	73	95	83

In order, to evaluate the generality of the method, reaction of (**1**) with different aromatic diamines bearing either electron-donating (**2c**) or electron-withdrawing (**2d**) substituents were carried out in the optimized condition. The results shown that the electronic effects of the substituents on the aromatic ring did not show strongly obvious effects in terms of yields. In addition, to explore the steric effects on the reaction, different isomers of phenylenediamine (**2a**, **2b** and **2f**) were reacted with (**1**). The reaction of (**1)** with *m*-phenylenediamineor *p*-phenylenediamine gave bis-sucinimide derivatives (**3a** and **3b**), whereas amino-succinimide derivative (**3f**)was obtained when (**1**) reacted with *o*-phenylenediamine (**Figure 2**). These findings, show that steric hindrance as an important structural feature plays a key role on the reaction of (**1**) with diamines. It seems reasonable, because when one amine group of *o*-phenylenediamine reacted with (**1**), the bulky rigid

tetracyclic 9,10-dihydro-anthracene-9,10-α,β-succinimideis produced that prevents the reaction of second amine group with another molecule of (**1**).

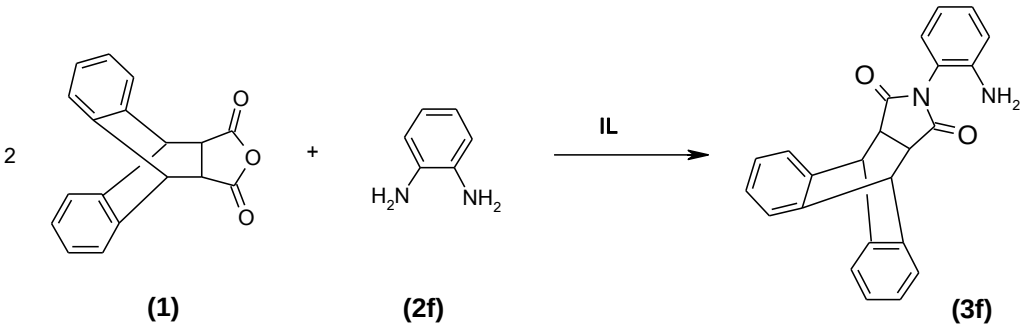


Figure 2: Reaction of dibenzobarallene with *o*-phenylenediamine

The structures of target compounds (**3a-f**) were confirmed by FT-IR, ^{1}H NMR, ^{13}C NMR spectroscopy and elemental analysis. The ^{1}H NMR spectra of (**3a-f**) showed the expected multiplicity and integration values. The ^{1}H NMR spectra of the compounds (**3a-f**) showed two characteristic singlet signals at δ ~ 4.9 ppm that was attributed to the two benzylic protons present in C(9) and C(12), and another at δ ~ 3.4 ppm, was assigned to the two protons present in C(10) and C(11). It is expected that both of them appear as doublet, but they showed two singlet signals due to the C(9)-H with C(10)-H and C(11)-H with C(12)-H are perpendicular[10] ($^{3}J_{90}$~ 0) (**Figure 3**). Moreover, the ^{13}C NMR spectra of (**3a-f**) showed three characteristic signals at δ ~ 45 ppm, δ ~ 47 ppm and δ ~ 175 ppm for carbons of [C(10), C(11)], [C(9), C(12)] and C=O in imide groups, respectively. Also, the ^{13}C NMR spectra showed signals at δ ~ 120-150 ppm characteristic for aromatic carbons. FT-IR spectra of (**3a-f**) showed bands at 1777 and 1710 cm^{-1} attributed to C=O in imide groups.Also, the elemental analysis data show very good agreement with the calculated values corresponding to the molecular formula.

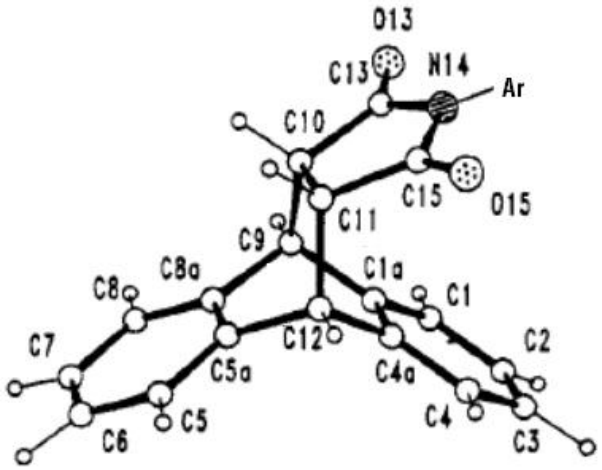


Figure 3: Perspective view for 9,10-dihydro-anthracene-9,10-α,β-succinimidewith atom numbering[10].

Experimental

All the chemicals were purchased from Merck Company. Dibenzobarallenewas prepared according to the literature procedure.[1] Melting points were obtained in open capillary tubes and were measured on an Electrothermal 9100 apparatus. FT-IR spectra were recorded using a Bruker Tensor 27 spectrometer on KBr pellets. ^{1}H and ^{13}C NMR spectra were determined

on a Bruker 300 DRX Avance instrument using DMSO-d_6 or $CDCl_3$ as solvent and tetramethylsilane as an internal standard. Elemental analysis was performed on a ThermoFinnigan Flash EA microanalyzer.

Typical procedure for the synthesis of molecular tweezer molecules:

A mixture of an aromatic diamine (5 mmol), dibenzobarallene (10 mmol, 2.76 gr) and [Py-$(CH_2)_4SO_3H$][HSO_4](5 mol%, 0.16 gr) was heated on an oil bath at 120 °C. The progress of the reaction was monitored by TLC. After completion of the reaction (1 h), the reaction mixture was cooled to room temperature, cold ethanol was added to the mixture and the precipitate was filtered off, washed with ethanol, and dried.

Reusability of the catalyst:

The Brønsted-acid ionic liquid catalyst, [Py-$(CH_2)_4SO_3H$][HSO_4], was soluble in ethanol, therefore it is retrievable from reaction mixture. Then the catalyst was washed with dichloromethane, dried in vacuum oven at 70 °C for 2 h, and reused in another reaction. The recycled catalyst was used for three further reactions without observation of sizeablelost in its catalytic activities.

Spectral data of new molecular tweezer molecules:

*1,3-bis[1,3-dioxo-3a,4,9,9a-tetrahydro-4,9-benzeno-benz[f]isoindol-2-yl]benzene***(3b):**whitepowder;m.p.> 300 °C; yield: 95%; FT-IR (KBr) (υ_{max}/cm^{-1}): 3044, 2962, 1777, 1711, 1602, 1491, 1464, 1373, 1262, 1190, 764; ^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 3.36 (s, 4H, C(10)-H, C(11)-H), 4.89 (s, 4H, C(9)-H, C(12)-H), 6.35 (s, 1 H), 6.39 (d, 2H, *J*=7.8 Hz), 7.18 (t, 1 H, *J*=7.8 Hz), 7.29 (d, 4H, *J*=5.4 Hz), 7.32 (d, 4H, *J*=5.4 Hz), 7.34 (dd, 4H, *J*=4.8 Hz, *J′*=3.3 Hz), 7.44 (dd, 4H, *J*=4.8 Hz, *J′*=3.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ(ppm):45.8 [C(10), C(11)], 46.9 [C(9), C(12)], 123.9, 124.4, 125.1, 126.1, 126.9, 127.3, 131.6, 138.5, 141.2, 175.5 (C=O); Anal. Calcd. for $C_{42}H_{28}N_2O_4$:C, 80.75; H, 4.52; N, 4.48, Found: C, 80.56; H,4.61; N, 4.35%.

*4,4′-bis[1,3-dioxo-3a,4,9,9a-tetrahydro-4,9-benzeno-benz[f]isoindol-2-yl]diphenyl ether***(3c):**Light brownpowder; m.p. 238-240 °C; yield: 97%; FT-IR (KBr) (υ_{max}/cm^{-1}):3071, 2959, 1777, 1712, 1596, 1501, 1465, 1390, 1247, 1194, 1161, 762;^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 3.42 (s, 4H, C(10)-H, C(11)-H), 4.88 (s, 4H, C(9)-H, C(12)-H), 6.46 (d, 4H, *J*=8.7 Hz), 6.97 (d, 4H, *J*=8.7 Hz), 7.20 (d, 4H, *J*=3.3 Hz), 7.23 (d, 4H, *J*=5.2 Hz), 7.32 (dd, 4H, *J*=5.2 Hz, *J′*=3.3 Hz), 7.52 (dd, 4H, *J*=5.2 Hz, *J′*=3.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ(ppm): 45.3 [C(10), C(11)], 47.1 [C(9), C(12)], 119.5, 124.8, 125.2, 126.8, 127.2, 128.8, 139.7, 142.1, 156.5, 176.5 (C=O); Anal. Calcd. for $C_{48}H_{32}N_2O_5$: C, 80.43; H, 4.50; N, 3.91, Found: C, 80.60; H, 4.39; N, 3.69%.

4,4′-bis[1,3-dioxo-3a,4,9,9a-tetrahydro-4,9-benzeno-benz[f]isoindol-2-yl]diphenyl sulfone **(3d):** Light brownpowder; m.p. 285-287 °C; yield: 90%; FT-IR (KBr) (υ_{max}/cm^{-1}): 3069, 3024, 2961, 1781, 1711, 1593, 1497, 1464, 1378, 1325, 1296, 1158, 1104, 762, 752;^{1}H NMR (300 MHz, DMSO-d_6) δ(ppm): 3.47 (s, 4H, C(10)-H, C(11)-H), 4.90 (s, 4H, C(9)-H, C(12)-H), 6.69 (d, 4H, *J*=8.7 Hz), 6.97 (d, 4H, *J*=8.4 Hz), 7.20 (d, 4H, *J*=3.3 Hz), 7.21 (d, 4H, *J*=4.8 Hz), 7.33 (dd, 4H, *J*=4.8 Hz, *J′*=3.3 Hz), 7.59 (dd, 4H, *J*=4.8 Hz, *J′*=3.3 Hz), 7.99 (d, 4H, *J*=8.4 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ(ppm): 45.4 [C(10), C(11)], 47.3 [C(9), C(12)], 124.9, 125.2, 126.9, 127.2, 128.0, 128.9, 136.8, 139.6, 140.7, 141.9, 175.9 (C=O); Anal. Calcd. for $C_{48}H_{32}N_2O_6S$:C, 75.39; H, 4.19; N, 3.66, Found: C, 75.62; H, 4.03; N, 3.53%.

*2-[2-amino-phenyl]-3a,4,9,9a-tetrahydro-4,9-benzeno-benz[f]isoindole-1,3-dione***(3f):**whitepowder; m.p. 276-278 °C; yield: 93%; FT-IR (KBr) (υ_{max}/cm^{-1}): 3542, 3469, 3042, 2963, 1777, 1710, 1512, 1464, 1390, 1291, 1194, 763; ^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 3.40 (s, 2H, C(10)-H, C(11)-H), 3.88 (s, 2H, -NH_2), 4.91 (s, 2H, C(9)-H, C(12)-H), 6.43 (d, 2H,*J*=8.1 Hz), 7.07 (d, 2H, *J*=8.1 Hz), 7.23-7.26 (m, 4 H), 7.37 (dd, 2H, *J*=5.4 Hz,

J′=3.3 Hz), 7.44 (dd, 2H, *J*=5.4 Hz, *J′*=3.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ(ppm): 45.9 [C(10), C(11)], 47.1 [C(9), C(12)], 124.4, 125.1, 126.5, 126.9, 127.2, 129.7, 138.7, 141.0, 141.3, 176.2 (C=O); Anal. Calcd. for $C_{26}H_{21}NO_2$:C, 82.30; H, 5.58; N, 3.69, Found: C, 82.43; H, 5.55; N, 3.61%.

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