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Facile two-pot syntheses of novel alternating benzene/imidazole systems

Kuangsen Sung,* Shu-Hwa Wu and Phon-I Chen

Department of Chemistry, National Cheng Kung University, Tainan 70101, Taiwan, ROC

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Abstract—The novel alternating benzene/imidazole systems with more than three consecutive aromatic rings were prepared by multi-component reaction of *c*-hexylisocyanide, substituted benzoic acid, *n*-butylamine, and phenylglyoxal hydrate, followed by condensation with ammonia. The two-pot syntheses were carried out easily with good yields.

1. Introduction

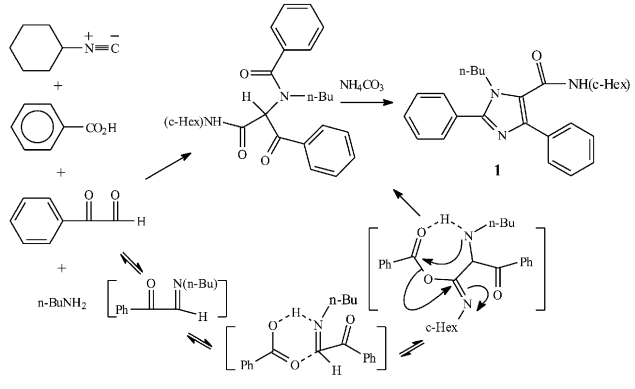
Oligoaryl compounds are known to exhibit a variety of fascinating optoelectronic properties.[1] The optoelectronic properties of the oligoaryls can be tuned by incorporation of five-membered heteroaryl moieties.[1] Therefore, synthesis of alternating aryl/heteroaryl systems has become an interesting topic. Most syntheses of oligoaryls containing heteroaryl moieties involve cross-coupling reactions catalyzed by transition metals.[2] Condensation and cyclization of 1,4-dicarbonylbenzenes with heteroatom-containing reagents provide an alternative way to construct oligoaryls containing heteroaryls.[3]

To our knowledge, alternating benzene/imidazole systems with more than three consecutive aromatic rings are still unknown. In this article, we demonstrate facile two-pot syntheses of the novel systems **1**–**3** by multi-component reactions (MCR)[4] followed by condensation with ammonia generated in situ.

2. Results and discussion

The multi-component reaction[4] was carried out by mixing *c*-hexylisocyanide, benzoic acid, *n*-butylamine, and phenylglyoxal hydrate in one pot with methanol as a solvent. (Scheme 1) The reaction mechanism[4] may involve reversible formation of imine by reaction of the amine with phenylglyoxal hydrate. The imine may be activated by protonation and then the isocyanide attacks the resulting iminium salt, followed by nucleophilic attack of the benzoate to form the labile 4-component adduct which undergoes irreversible intramolecular rearrangement to form a more stable α-amido-β-ketoamide in a good yield. Sterically crowded substituents make it a little bit high K_E value of 0.7 in chloroform solution.[5] In other words, its NMR spectra are quite complicated. After further condensation and cyclization with NH_3 generated in situ, the α-amido-β-ketoamide produces the alternating benzene/imidazole system **1** with three consecutive aromatic rings in an excellent yield.

When benzoic acid is replaced by isophthalic acid or terephthalic acid in the multi-component reaction, similar α-amido-β-ketoamides were formed. (Schemes 2 and 3) Since they consist of several keto–enol tautomers in solution, their NMR spectra are too complicated to be analyzed. The MCR reaction involving terephthalic acid is faster and has better yield than the one involving isophthalic acid, because the latter suffers from more steric hindrance than the former. After being treated with ammonium carbonate, the α-amido-β-ketoamides produce the alternating benzene/imidazole systems **2** or **3** with five consecutive aromatic rings in excellent yields. Attempts to make an alternating benzene/imidazole system with five consecutive aromatic rings and an *ortho*-disubstituted benzene ring in the middle



Scheme 1.

Keywords: imidazole; oligoaryl; optoelectronic.

* Corresponding author. Tel.: +886-6-2757-575x65338; fax: +886-6-2740-552; e-mail: kssung@mail.ncku.edu.tw

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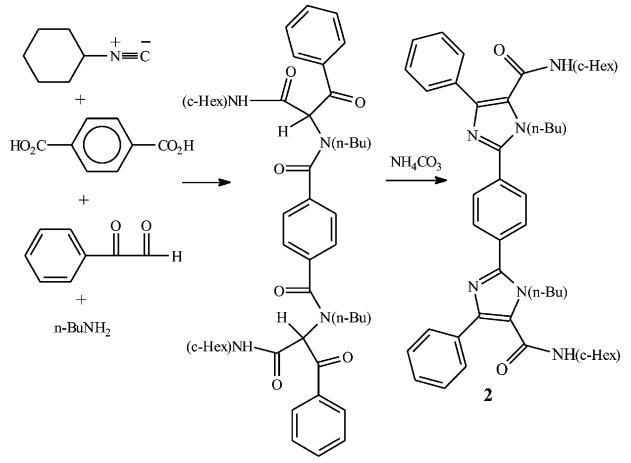
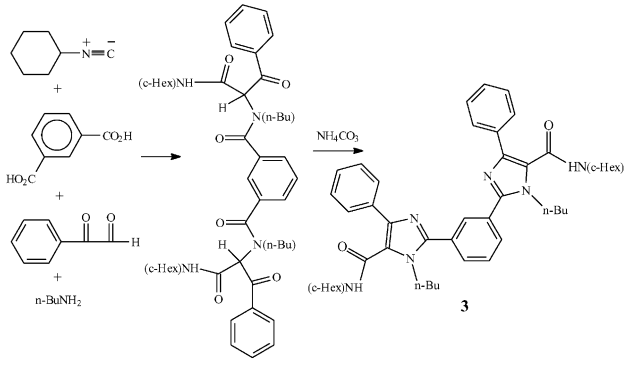


Scheme 2.



Scheme 3.

failed, presumably because the system suffers from too much steric hindrance.

Optimized structures of **1**–**3** are shown in Figs. 1–3. Dihedral angles between aromatic rings are 45.2 and 48.3° for **1**, 45.8, 45.6, 29.1, and 43.7° for **2**, and 44.0, 35.2, 34.1, and 42.6° for **3**. The system **2** has a shape of bowl with flat bottom, but bulky substituents force the system **3** to become twisted U-shaped.

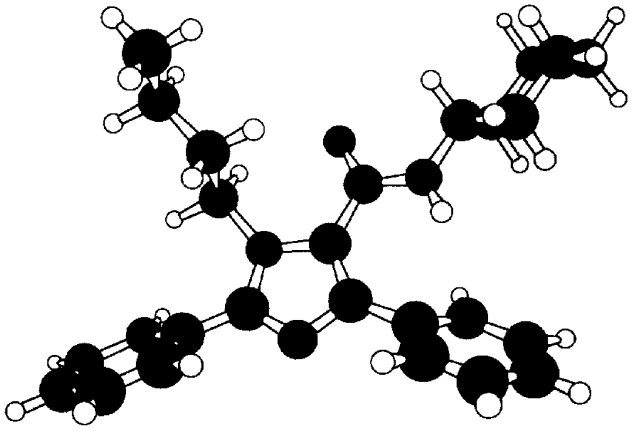


Figure 1. Optimized structure of **1** at level of HF/3-21G*.

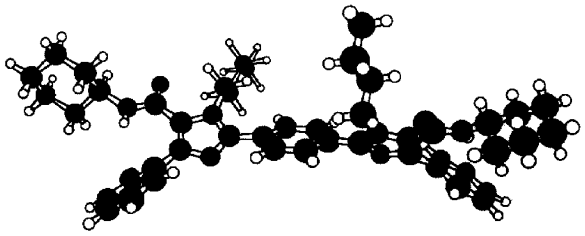


Figure 2. Optimized structure of **2** at level of HF/3-21G*.

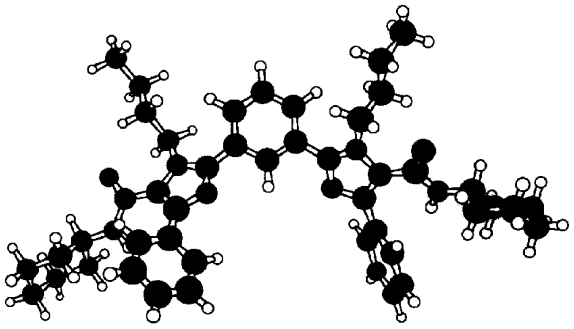


Figure 3. Optimized structure of **3** at level of HF/3-21G*.

Generally speaking, the method is quite good for the preparation of the alternating benzene/imidazole systems, because all the alternating benzene/imidazole systems **1**–**3** involve two-pot syntheses and they are easy to carry out with good yield even though some reactions are slow.

All the three compounds **1**–**3** are white solid. Under irradiation of UV light (λ=254 nm), chloroform solution of **1** is colorless, but chloroform solutions of **3** and **2** show pale blue and blue color of fluorescence light, respectively. The λ_{em} values measured in chloroform and the fluorescence quantum yields (Φ_f) for **1**–**3** are shown in Table 1. As expected, emission maximum of **2** shifts bathochromically. The potential optoelectronic applications are under investigation.

Table 1. Fluorescence properties of **1**–**3** in chloroform at 25°C

Compound	λ_{em} (nm)	$\%\Phi_f$
1	366	73
2	415	3
3	368	1

3. Conclusion

We have successfully demonstrated two-pot syntheses of novel alternating benzene/imidazole systems with good yield.

4. Computational details

All the calculations reported here were performed with Gaussian98 program.[6] Geometry optimizations of **1**–**3** were carried out at level of HF/3-21G* without any

symmetry restriction. Their optimized structures are shown in Figs. 1–3. After all the geometry optimizations were performed, analytically vibration frequencies were calculated at the same level to determine the nature of the located stationary points. Thus all the stationary points found were properly characterized by evaluation of the harmonic frequencies.

5. Experimental

5.1. General

Reagents were obtained from commercial suppliers and used as received. NMR spectra were obtained using Bruker-200 and Bruker 400 NMR spectrometers. High-resolution mass spectra were taken on a VG-70250S mass spectrometer. Cyclohexyl isocyanide was prepared according to the literature methods.[7] Fluorescence spectra were measured on Hitachi F-2000 fluorometry, and quantum yields of fluorescence in chloroform were measured against quinine bisulfate as standard. UV/Vis absorption spectra were measured on Perkin–Elmer Lambda 40.

5.2. General method for the preparation of alternating benzene/imidazole systems 1–3

To a solution of phenylglyoxal hydrate (1 mmol) in methanol (5 mL) was added *n*-butylamine (1 mmol), *c*-hexylisocyanide (1 mmol), and carboxylic acid [benzoic acid (1 mmol), isophthalic acid (0.5 mmol), or terephthalic acid (0.5 mmol)]. The solution was stirred for several hours at room temperature and then white solid started to precipitate. The solution was stirred until no more solid precipitated. After filtration, the white solid was collected and the product is α-amido-β-ketoamide. To a solution of the white solid product in acetic acid (4 mL) was added ammonium carbonate (50 mmol). The solution was stirred under reflux and nitrogen atmosphere for 2 h. After the solution was cooled down, 10 mL of ice was added into the solution and a white solid precipitated. After filtration, the white solid was purified by re-crystallization from methanol.

5.2.1. Alternating benzene/imidazole system 1. White solid; isolated yield of the two steps: 55%; mp 260–263°C; ν_{max} (thin film) 3412, 3149, 3140, 2980, 2916, 1659, 1618, 1577, 1539, 1510, 1486, 1411, 1356, 1310, 1219, 1183, 1148, 1063, 805, 777 cm^{-1}; $\lambda_{abs,max}$ (chloroform) 270 nm (ε=2.8×10^4); δ_H (400 MHz, $CDCl_3$) 0.79 (3H, t, J=7.3 Hz, CH_3), 0.92–2.10 (14H, m, CH_2), 3.90 (1H, m, CH), 4.31 (2H, t, J=7.4 Hz, CH_2), 6.04 (1H, d, J=8.2 Hz, NH), 7.27–7.70 (10H, m, PhH) ppm; δ_C (400 MHz, $CDCl_3$) 13.50, 19.67, 24.55, 25.32, 32.39, 33.35, 45.82, 48.27, 123.22, 126.40, 127.04, 128.33, 128.52, 128.60, 128.97, 129.49, 133.00, 141.38, 149.33, 160.28 ppm; *m/z* (EI) 401 (20, M^+), 303 (10), 126 (30), 98 (20), 83 (100); HRMS (EI): M^+, found 401.2464, $C_{26}H_{31}N_3O$ requires 401.2467.

5.2.2. Alternating benzene/imidazole system 2. White solid; isolated yield of the two steps: 43%; mp 265–268°C; ν_{max} (thin film) 3410, 3150, 3133, 2981, 2915, 1657, 1623, 1617, 1586, 1567, 1527, 1507, 1487, 1411, 1390, 1352, 1296, 1161, 1080, 892, 867, 780 cm^{-1}; $\lambda_{abs,max}$(chloroform) 298 nm (ε=1×10^4); δ_H (400 MHz, $CDCl_3$) 0.78 (6H, t, J=7.3 Hz, CH_3), 0.82–2.11 (28H, m, CH_2), 3.90 (2H, m, CH), 4.35 (4H, t, J=7.4 Hz, CH_2), 5.63 (2H, d, J=8.1 Hz, NH), 7.24–7.70 (10H, m, PhH), 7.74 (4H, s, PhH) ppm; δ_C (400 MHz, $CDCl_3$) 13.62, 19.76, 24.57, 25.37, 32.45, 33.56, 45.90, 48.25, 123.54, 128.30, 128.56, 129.03, 129.67, 131.41, 133.73, 142.52, 148.97, 160.44 ppm; *m/z* (FAB) 725 (40, MH^+), 670 (30), 446 (20), 316 (60), 288 (100), 133 (75); HRMS (FAB): MH^+, found 725.4547, $C_{46}H_{57}N_6O_2$ requires 725.4543.

5.2.3. Alternating benzene/imidazole system 3. White solid; isolated yield of the two steps: 40%; mp 256–258°C; ν_{max} (thin film) 3413, 3149, 3139, 3121, 2914, 1658, 1624, 1580, 1510, 1487, 1412, 1402, 1354, 1282, 1228, 1046, 960, 881, 810, 780 cm^{-1}; $\lambda_{abs,max}$ (chloroform) 280 nm (ε=1.1×10^4); δ_H (400 MHz, $CDCl_3$) 0.80 (6H, t, J=7.3 Hz, CH_3), 0.90–2.10 (28H, m, CH_2), 3.90 (2H, m, CH), 4.35 (4H, t, J=7.4 Hz, CH_2), 5.65 (2H, d, J=8.1 Hz, NH), 7.26–8.14 (14H, m, PhH) ppm; δ_C (400 MHz, $CDCl_3$) 13.58, 19.71, 24.55, 25.34, 32.41, 33.52, 45.91, 48.23, 123.46, 128.21, 128.50, 128.95, 129.31, 130.16, 130.36, 130.99, 133.71, 142.40, 148.90, 160.45 ppm; *m/z* (FAB) 725 (100, MH^+), 668 (10), 625 (10), 569 (10), 154 (25); HRMS (FAB): MH^+, found 725.4542, $C_{46}H_{57}N_6O_2$ requires 725.4543.

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References

1. Mullen, K.; Wegner, G. *Electronic Materials: The Oligomer Approach*; Wiley-VCH: Weinheim, 1998.
2. (a) Pelter, A.; Jenkins, I.; Jones, D. E. *Tetrahedron* **1997**, *53*, 10357. (b) Yassar, A.; Garnier, F.; Deloffre, F.; Horowitz, G.; Richard, L. *Adv. Mater.* **1994**, *6*, 660. (c) Pelter, A.; Rowlands, M.; Jenkins, I. H. *Tetrahedron Lett.* **1987**, *28*, 5213. (d) Pelter, A.; Rowlands, M.; Clements, G. *Synthesis* **1987**, 51. (e) Fanta, P. E. *Synthesis* **1974**, 9. (f) Crisp, G. T. *Synth. Commun.* **1989**, *19*, 307.
3. (a) Verheyde, B.; Dehaen, W. *J. Org. Chem.* **2001**, *66*, 4062. (b) Sonpatki, V. M.; Herbert, M. R.; Sandvoss, L. M.; Seed, A. J. *J. Org. Chem.* **2001**, *66*, 7283. (c) Lipshutz, B. H. *Chem. Rev.* **1986**, *86*, 795. (d) Schulz, B.; Knochenhauer, G.; Brehmer, L.; Janietz, S. *Synth. Metals* **1995**, *69*, 603. (e) Chen, Z.-K.; Meng, H.; Lai, Y.-H.; Huang, W. *Macromolecules* **1999**, *32*, 4351. (f) Shin, D.-C.; Ahn, J.-H.; Kim, Y.-H.; Kwon, S.-K. *J. Polym. Sci. A: Polym. Chem.* **2000**, *38*, 3086.
4. Domling, A.; Ugi, I. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 3168.
5. Sung, K., Chen, P.-I., unpublished results.
6. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.;

Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; AlLaham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzales, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian98* Revision A9, Gaussian, Inc.: Pittsburgh, PA, 1998.

7. Ugi, I.; Meyr, R.; Lipinski, M.; Bodesheim, F.; Rosendahl, F. *Organic Synthesis*, Collect. Vol. V; 1973; p 300.