The reaction of 2-chloro-1-methoxynaphthalene and 2-bromobiphenylene with 3-cyanophthalides under aryne-forming conditions: convenient synthesis of annular polycyclic aromatic compounds

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Abstract

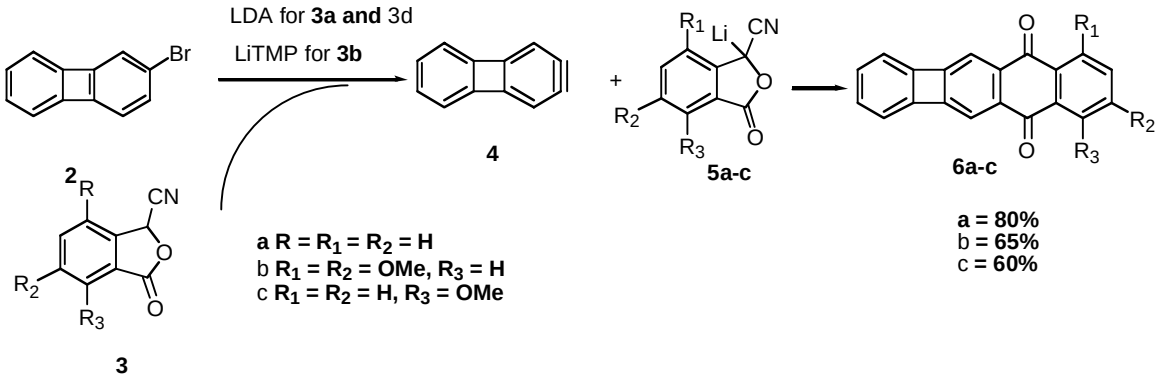
2-Bromobiphenylene and 2-chloronaphthalene react with 3-cyanophthalides in the presence of LDA or LiTMP to give functionalized benzo[3,4]cyclobuta[1,2-*b*]anthracene-6,11-dione and naphthacene-5,12-dione, respectively.

Keywords: Benzyne, aryne, cycloaddition, nucleophilic addition, polycyclic aromatic compounds

Introduction

Biphenylenes have recently been studied extensively because they can serve as units of new carbon allotropes and can function as spacers and building blocks for functionalized organic materials.[1] One of the more important syntheses of functionalized biphenyls involves the intramolecular coupling of benzo-annulated zinca-cyclopentadiene intermediates prepared from 2,2'-diaryls with $ZnCl_2$.[2] During the course of our studies on the synthetic use of aryne reaction, we have prepared a wide variety of functionalized polycyclic quinones from the reaction of haloarenes with 3-lithiophthalides in the presence of sterically hindered bases such as LDA and LiTMP.[3] It occurred to us that 2-bromobiphenylene might undergo similar reactions to give functionalized annulated biphenyls. Although 2-bromobiphenylene can, in principle give two benzynes, *i.e.*, 1,2-dehydro- and 2,3-dehydro-biphenylene, our calculations have shown the 2,3- intermediate to be 4.47 kcal/mol more stable than the 1,2- isomer. The relative stability of 1,2- and 2,3-dehydrobiphenyl were calculated with complete optimization of all geometric variables using the standard AM1 procedure[4] incorporated in version 3.1 of the Spartan Package.[5] Furthermore, the latter, being symmetric, would give a single aryne product.

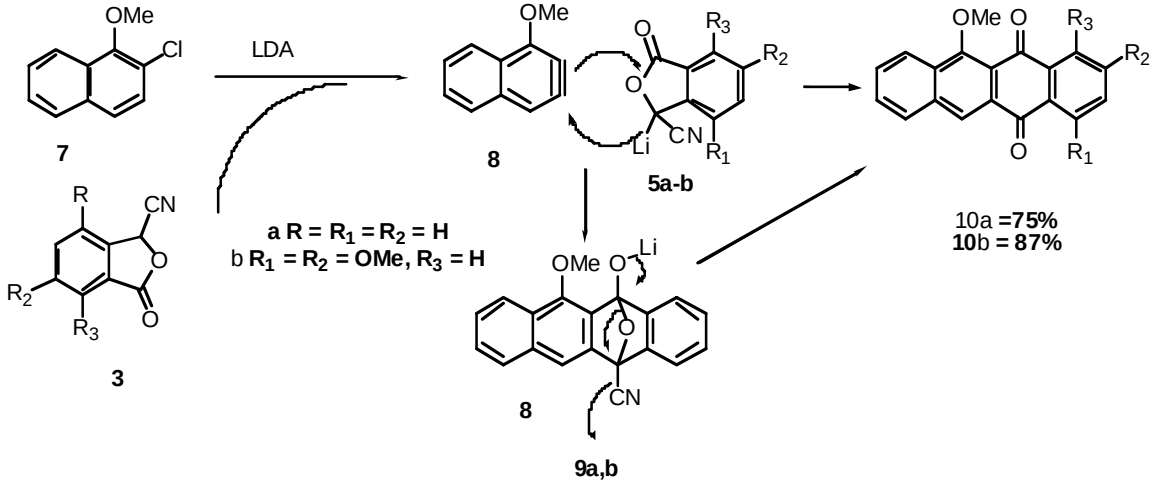
Along similar lines, we decided to investigate also the reaction of 2-chloro-1-methoxynaphthalene with certain 3-cyano-1(3*H*)isobenzofuranones (3-cyanophthalides). The well-proven *meta*-directing effect of the methoxy group[6] should also afford a single aryne product.



Scheme 1

Results and Discussion

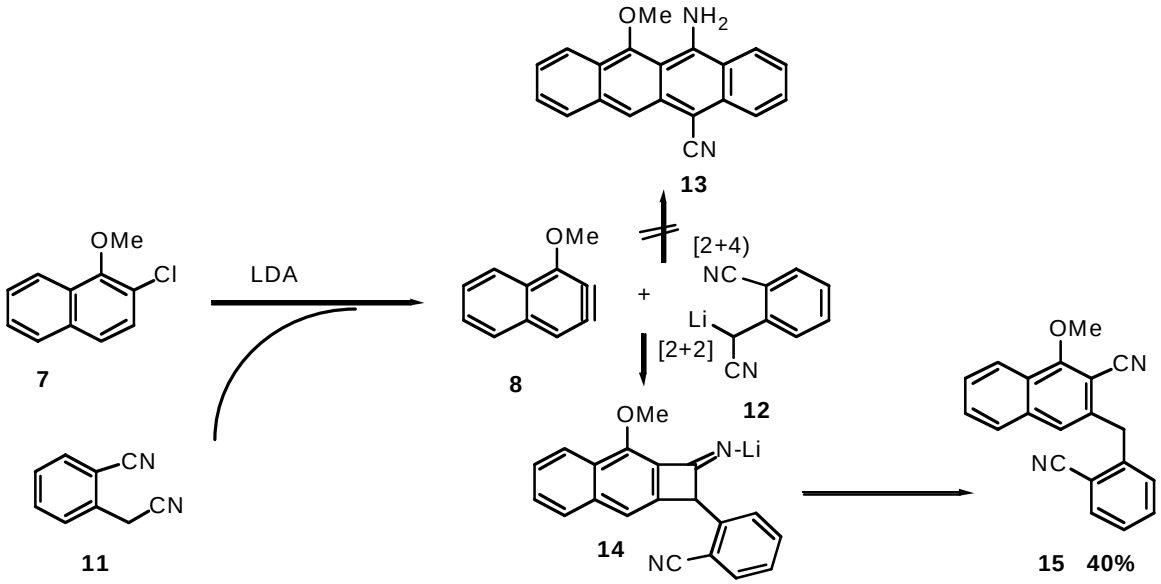
Our expectations were indeed realized, and are illustrated in Scheme 1 and Scheme 2. As shown in Scheme 1, 2-bromobiphenylene (**2**) reacted and the 3-cyanophthalides (**3a**–**c**) reacted with LDA or LiTMP, respectively, to produce 2,3-dehydrobiphenylene (**4**) and lithiated 3-cyanophthalides (**5a–c**). These intermediates then underwent cycloaddition to give the corresponding benzo[3,4]cyclobuta[1,2-b]anthracene-6,11-dione (**6a**–**c**) in 60–80% yields after the usual workup. The benzyne precursor, 2-bromobiphenylene (**2**) was prepared by the bromination of biphenylene (**1**) with DBU in the presence of $HgCl_2$ in 75% yield.[7] This method is superior to simple bromination which gives 2 in only 50% along with some polybromides.[8] The 3-cyanophthalides (**3a**–**c**) were on hand from previous studies and IR spectra were consistent with the proposed structures.



Scheme 2

As shown in Scheme 2, 1-methoxynaphthacene-5,12-dione (**10a**) and 1,3,11-trimethoxy-naphthacene-5,12-dione (**10b**), respectively, were obtained in 75 and 87% yields from the reaction of 2-chloronaphthalene (**7**) and the 3-cyanophthalides (**3a** and **3b**). The regioselective addition to 1-methoxy-2,3-dehydro-naphthalene (**8**) was clearly shown in the case of **5b** to give a single adduct (**9b**). Obviously, no regiochemistry is involved in the case of the unsubstituted lithiated nitrile **5a**. The IR, 1H NMR, ^{13}C- NMR, and mass spectra were consistent with the proposed structures.

We next treated **7** with α-cyano-*o*-tolunitrile **11** and LDA, expecting aryne **8** and α-lithio- α-cyano-*o*-tolunitrile (12) to undergo [2+4} cycloaddition[9] to give the aminonaphthacene **13**. However, as shown in Scheme 3, this reaction proceeded by a tandem addition–rearrangement pathway[10] in which **8** and **12** reacted via a [2+2]-cycloaddition pathway to the benzocyclobutenium adduct (**14**). Intermediate **14** then opened up to give the rearranged product, 3-(2'-cyanobenzyl)-1-methoxy-2-naphthalene-carbonitrile (**15**) in 40% yield, after quenching.



Scheme 3

In conclusion, we have shown that 2,3-dehydrobiphenylene and 1-methoxy-2,3-dehydronaphthalene can serve as valuable intermediates in the synthesis of functionalized benzo[3,4]cyclobuta[1,2-b]anthracene-6,11-dione and naphthacene-5,12-dione, respectively.

Experimental Section

General Procedures. Melting points were taken on a Mel-Temp apparatus and are not corrected. NMR spectra were recorded on a 400 MHz spectrometer: chemical shifts were related to TMS as internal standard.

Chemicals were purchased from commercial sources. LDA and BuLi were purchased as solutions in hexanes. The glassware heated at 125°C in an oven overnight prior to use. Benzyne reactions were done under an atmosphere of dry O_2-free N_2 contained in a balloon possessing a needle protruding through a rubber septum attached to one of the reaction flask necks.

Biphenylene (**1**),[2] 2-bromobiphenylene (**2**),[7] and 2-chloro-1-methoxynaphthalene (**7**)[11] were prepared by literature procedures. The 3-cyanophthalides (**4a**–**c**) were available from previous studies.

General procedure for the reaction of haloarenes (2 and 7) with 3-cyanophthalides (4a–c). In a flame-dried flask flushed with N_2, LDA (15 mmol) was prepared by adding 6 mL of *n*-BuLi (2.5 *M* in hexanes) to a solution containing diisopropylamine (15 mg, 15 mmol) in THF (30 mL) at -70°C. After stirring for 10 min, 5 mmol of the appropriate nitrile (**4a–c**) in 30 mL of THF was added and the temperature allowed to warm to -40 °C. At this point, 5 mmol of the haloarene (**2** or **7**) in 30 mL of THF was added over a period of 20 min while maintaining the temperature between -30 to -40 °C. After the addition of the haloarene, the resulting mixture was allowed to warm to r.t. where it was stirred for an additional 3 h. The resulting dark reddish solution was quenched with 30 mL of sat. NH_4Cl and the THF removed by rotary evaporator. The residue was extracted with CH_2Cl_2 (3 × 20 mL). The CH_2Cl_2 fractions were combined, washed with 25 ml of 5% HCl, then brine, then dried (Na_2SO_4) and concentrated (rotary evaporator) to provide a dark viscous liquid. The liquid was purified by flash chromatography (silica gel) using hexane/acetone (19:1) as eluent to give a solid product which was further purified by recrystallization from CH_2Cl_2–hexane. The physical properties of the products are given below.

Benzo[3,4]cyclobuta[1,2-*b*]anthracene-6,11-dione (8a). Yellow powder, mp 218–219 °C. IR (KBr) ν 1684 cm^{-1}. ^1H NMR ($CDCl_3$) δ 6.81 (d, J = Hz, 2 H), 6.92 (m, 2 H), 7.32 (d, J = 8.0 Hz, 1 H), 7.73 (m, 2 H), 7.79 (d, J = 8.1 Hz, 1 H), 8.23 (m, 1 H), 8.32 (m, 1 H). ^{13}C NMR ($CDCl_3$) δ 119.2, 120.1, 121.9, 123.6, 126.8, 127.7, 130.8, 130.9, 131.0, 131.8, 133.7, 133.8, 134.1, 149.3, 151.1, 153.5, 158.2, 181.8, 182.2. Anal. Calcd for $C_{20}H_{10}O_2$: C, 85.09; H, 3.57. Found: 85.15; H, 3.66%.

1-Methoxybenzo[3,4]cyclobuta[1,2-*b*]anthracene-6,11-dione (8b). Yellow powder, mp 238–240 °C. IR (KBr) ν 1667 cm^{-1}. ^1H NMR ($CDCl_3$) δ 4.01 (s, 3 H), 6.91 (m, 4 H), 7.3 1(d, J = 8.1, 1 H), 7.41(s, 1 H), 7.52 (s, 1 H), 7.7 (t, J = 8.1 Hz, 1 H), 7.94 (d, J = 8.1 Hz, 1 H), 8.2 (m, 1 H), 8.3 (m, 1 H). ^{13}C NMR ($CDCl_3$) δ 56.6, 113.0, 113.9, 117.8, 119.6, 119.7, 119.8, 1303, 130.4, 134.8, 135.2, 137.0, 137.9, 149.6, 156.2, 157.3, 160.1, 171.2, 182.1, 182.9. Anal. Calcd for $C_{21}H_{12}O_3$: C, 80.76; H, 3.87. Found: 80.87; H, 3.90%.

1,3-Dimethoxybenzo[3,4]cyclobuta[1,2-*b*]anthracene-6,11-dione (8c). Yellow powder, mp 208–210 °C. IR (KBr) ν 1682 cm^{-1}. ^1H NMR ($CDCl_3$) δ 4.0 (s, 6 H), 6.8 (d, *J* = 8.0 Hz, 2H), 6.9 (m, 2 H), 7.3 (d, *J* = 8 Hz, 1 H), 7.7 (m, 2 H), 7.8 (d, J = 8 Hz, 1 H), 8.2 (m, 1 H), 8.3 (m, 1 H). ^{13}C NMR ($CDCl_3$) δ 130.9, 131.0, 131.8, 133.7, 133.8, 134.1, 149.3, 151.1, 153.5, 158.2, 181.8, 182.2. Anal. Calcd for $C_{20}H_{10}O_2$: C, 85.09; H, 3.57. Found: 85.15; H, 3.66%.

1-Methoxynaphthacene (10a). colorless prisms, mp 283–284 °C. IR (KBr) ν1677 cm^{-1}. ^1H NMR δ 4.21 (s, 3 H), 7.82 (m, 4 H), 8.10 (m, 1 H), 8.33 (m, 2 H), 8.44 (m, 1 H), 8.70 (s, 1 H). ^{13}C NMR δ 63.0, 120.0, 124.7, 125.8, 127.0, 127.5, 129.5, 130.0, 130.3, 130.9, 132.0, 133.5, 133.6, 134.3, 135.9, 126.0, 160.0, 182.2, 183.2. Anal. Calcd for $C_{19}H_{12}O$: C, 79.16; H, 4.20. Found: C, 79.31; H, 4.26%.

1,3,11-Trimethoxynaphthacene (10b). light yellow powder, mp 216–217 ^{o}C. IR (KBr) 1667cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 3.91 (s, 3 H), 4.01 (s, 3 H), 4.12 (s, 3 H), 6.72 (d, J = 4.2 Hz, 1 H), 7.50 (d, J = 4.1 Hz, 1 H), 7.72 (m, 2 H), 8.13 (m, 1 H), 8.41 (m, 1 H), 8.58 (m, 1 H). ^{13}C NMR ($CDCl_3$) δ 56.0, 56.6, 63.1, 103.1, 104.4, 116.7, 120.0, 124.5, 125.2, 128.9, 130.1, 131.1, 132.5, 136.3, 140.0, 159.2, 162.3, 164.9, 181.2, 182.4. Anal. Calcd for $C_{21}H_{16}O_3$: C, 72.41; H, 4.63. Found: C, 72.45; H, 4.70%.

3-(2'-Cyanobenzyl)-1-methoxy-2-naphthalenecarbonitrile (15). Colorless crystals, mp 142–143 ^{o}C. IR (KBr) ν 2223 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 4.21 (s, 3 H), 4.51 (s, 2 H), 7.30–7.80 (m, 8 H), 8.21 (8.21 (d, J = 8.1 Hz, 1 H). ^{13}C NMR ($CDCl_3$) δ 38.5, 63.0, 101.3, 113.1, 122.8, 124.2, 126.1, 127.0, 127.4, 127.8, 130.0, 130.2, 133.1, 133.2, 136.0, 136.4, 142.5, 162.5. Anal. Calcd for $C_{20}H_{14}N_2O$: C, 80.52, H, 4.73, N, 9.39. Found: C, 80.55; H, 4.74; N, 9.44%.

Acknowledgements

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