Synthesis of Unsymmetrical Aryl-Ethynylated Benzenes via Regiocontrolled Sonogashira Reaction of 1,3,5-Tribromobenzene

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Sonogashira coupling of trimethylsilylacetylene with 4-alkyloxy-1-iodobenzene derivatives gave 2-(4-(alkyloxy)phenyl)ethynyltrimethylsilanes which undergo deprotection via removal of TMS-group using tetrabutylammonium fluoride (TBAF) in THF at room temperature to afford the corresponding terminal 2-(4-(alkyloxy)phenyl)acetylenes. Regiocontrolled Sonogashira cross-coupling of 1,3,5-tribromobenzene with the terminal arylacetylenes in aqueous medium resulted in the formation of mono-, di- and tri-alkynylated benzene derivatives in moderate to good yields. Factors affecting the regioselective alkynylation were also examined.

Keywords: arylacetylenes, cross-coupling, catalysis, palladium, aqueous media

Introduction

Sonogashira cross-coupling, reaction of terminal alkynes with aryl halides in the presence of palladium(0)/copper(I) catalyst under basic conditions, has been established as one of the most convenient routes to symmetrical and unsymmetrical diarylethynes of potential biological and non-biological applications. Synthesis of terminal arylacetylenes can be achieved through palladium-catalyzed Sonogashira coupling of aryl halides with mono-protected acetylenes followed by removal of the protecting group. Furthermore, terminal arylacetylenes are involved in the construction of conjugated oligo- and polyarylethynes of wide range of industrial applications. Polyhalogenated arenes were employed in Sonogashira coupling reactions with terminal alkynes. In addition, aqueous organic solvents have been used for promotion of Sonogashira cross-coupling reactions in the presence of PdCl₂(PPh₃)₂. In continuation of our research work a regiocontrolled Sonogashira cross-coupling on 1,3,5-tribromobenzene as attractive strategy for synthesis of unsymmetrical ethynylated benzene derivatives. The effect of solvent/base ratios on the optimization of the regiocontrolled cross-coupling is evaluated.

Results and Discussion

At first, three different 4-alkyloxy-1-iodobenzene derivatives 1a-c were easily synthesized by reaction of 4-iodophenol with the appropriate alkyl bromides in dimethylsulfoxide (DMSO) in the presence of KOH at room temperature according to the reported Williamson method. Then, Sonogashira coupling of trimethylsilylacetylene with 4-alkyloxy-1-iodobenzene derivatives 1a-c using PdCl₂(PPh₃)₂ (1 mol%) and CuI (2 mol%) in water/toluene (2 mL, 1:1) in the presence of 2 equivalents of triethylamine (Et₃N) at room temperature for 24 h afforded 2-(4-(alkyloxy)phenyl)ethynyltrimethylsilane 2a-c in 74, 86 and 96% yields, respectively (Scheme 1).

Next, removal of the trimethylsilyl (TMS) group from 2-(4-(alkyloxy)phenyl)-ethynyltrimethylsilanes 2a-c is

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achieved under mild conditions using tetrabutylammonium fluoride (TBAF) in tetrahydrofuran (THF) following a related literature methodology. The deprotection process is completed within one hour at room temperature to afford the corresponding terminal arylacetylene products 3a-c in 74-85% yields. Further deprotection methods were reported using strong bases (such as NaH, NaOH, KOH, K$_2$CO$_3$ or t-BuOK) at high temperature.

Regio-controlled Sonogashira cross-coupling of 1,3,5-tribromobenzene 4 with 1-ethynyl-4-(alkyloxy) benzenes 3a-c

In the next part, the scope and limitations of the palladium-catalyzed regio-controlled Sonogashira cross-coupling reactions of 1,3,5-tribromobenzene 4 were investigated. Optimization of the reaction conditions for the regio-selective synthesis of mono-ethynylated dibromobenzene 5c from 1,3,5-tribromobenzene 4 was performed and the results are outlined in Table 1. Thus, firstly the cross-coupling reaction of 1,3,5-tribromobenzene 4 with 1-ethynyl-4-(octyloxy)benzene 3c in 1:1 molar ratio using PdCl$_2$(PPh$_3$)$_2$ (1 mol%) in the presence of CuI in toluene/water mixed solvent (1:1, v/v) led to the formation of one equivalent of Et$_2$N gave the products 5c and 6c in 70 and 5% isolated yields, respectively (Table 1, entry 4). Similarly, performing the coupling reaction in degassed neat water under argon in the presence of 2 equiv. of Et$_2$N gave the products 5c and 6c in 78 and 18%, respectively (Table 1, entry 5). Furthermore, the use of one equivalent of Et$_2$N in water/toluene (1:1, v/v) resulted in the formation 5c and 6c in 78 and 18%, respectively (Table 1, entry 6). Under the latter condition, coupling of 4 with 3c in toluene only afforded 5c and 6c in 45 and 9%, respectively (Table 1, entry 7). These results of entries 1-3 and 6, Table 1, are consistent with the reported ones declaring that aqueous organic solvents enhance Sonogashira cross-coupling reactions in the presence of PdCl$_2$(PPh$_3$)$_2$. According to the selectivity towards mono-ethynylated dibromobenzene 5c reached its maximum when 2 equiv. of Et$_2$N at 60 °C for 24 h till full conversion of 4 as examined by thin layer chromatography (TLC). After column chromatography, two products were isolated. The major product was obtained in 74% yield (Table 1, entry 1) and its structure was established as 1,3-dibromo-5-(2-(4-(octyloxy)phenyl)-ethynyl)-benzene 5c on the basis of its spectral analyses. The mass spectrum of 5c exhibited a peak at $m/z$ 464 corresponding to its molecular ion and its $^{13}$C nuclear magnetic resonance (NMR) spectra were in accordance with the assigned structure. The minor product was isolated in 20% and was confirmed as 1-bromo-3,5-di-(2-(4-(octyloxy)phenyl)-ethynyl)benzene 6c on the basis of its spectral analyses. Repeating the same reaction under similar conditions using three equiv. of Et$_2$N led to the formation of mono- and di-ethynylated bromobenzenes 5c and 6c in 80 and 12% isolated yields, respectively (Table 1, entry 2). Using two equiv. of Et$_2$N gave the desired products 5c and 6c in 90 and 8% isolated yields, respectively (Table 1, entry 3). The use of neat toluene as solvent under the optimized coupling conditions above employing 2 equiv. of Et$_2$N gave the products 5c and 6c in lower yields, 62 and 3% isolated yields, respectively (Table 1, entry 4). Similarly, performing the coupling reaction in degassed neat water under argon in the presence of 2 equiv. of Et$_2$N gave the products 5c and 6c in 70 and 5% isolated yields, respectively (Table 1, entry 5). Further deprotection of 5c and 6c was achieved as depicted in Table 2. Thus, cross-coupling of 1,3,5-tribromobenzene 4 with 1-ethynyl-4-(hexyloxy) benzene 3a and with 1-ethynyl-4-(heptyloxy)benzene 3b were carried out in 1:1 molar ratio using PdCl$_2$(PPh$_3$)$_2$ in the presence of CuI in toluene/water mixed solvent and triethylamine as a base under argon atmosphere at 60 °C for 24 h resulted, in both cases, in full conversion into two products (major and minor) as depicted in Table 2. The reaction molar ratios were typically: 1 mmol arylacetylenes 3a-b with 1,3,5-tribromobenzene 4 was achieved as depicted in Table 2. Thus, cross-coupling of 1,3,5-tribromobenzene 4 with 1-ethynyl-4-(hexyloxy) benzene 3a and with 1-ethynyl-4-(heptyloxy)benzene 3b were carried out in 1:1 molar ratio using PdCl$_2$(PPh$_3$)$_2$ in the presence of CuI in toluene/water mixed solvent and triethylamine as a base under argon atmosphere at 60 °C for 24 h resulted, in both cases, in full conversion into two products (major and minor) as depicted in Table 2. The reaction molar ratios were typically: 1 mmol arylacetylenes 3a-b, 1 mmol 1,3,5-tribromobenzene 4, 2 mmol Et$_2$N, 1 mol% PdCl$_2$(PPh$_3$)$_2$ and 2 mol% CuI in water/toluene (2 mL, 1:1 v/v). The major products were obtained in 94 and 93% yields, respectively (Table 2, entries 1 and 2) and their structures were established as 1-(3,5-dibromophenyl)-2-(4-hexyloxyphenyl)acetylene 5a and 1-(3,5-dibromophenyl)-2-(4-heptyloxyphenyl) acetylene 5b on the basis of their elemental and spectral analyses. The minor products were isolated in 2 and 4%, respectively (Table 2, entries 1 and 2), and were confirmed
Synthesis of Unsymmetrical Aryl-Ethynylated Benzenes via Regiocontrolled Sonogashira Reaction

**Table 1.** Regio-controlled Sonogashira cross-coupling of 1,3,5-tribromobenzene 4 with 1-ethynyl-4-(octyloxy)benzene 3c

<table>
<thead>
<tr>
<th>entry</th>
<th>Solvent</th>
<th>Et,N / equiv.</th>
<th>Yield</th>
<th>5c</th>
<th>6c</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Toluene/water (1:1)</td>
<td>4</td>
<td>74</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Toluene/water (1:1)</td>
<td>3</td>
<td>80</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Toluene/water (1:1)</td>
<td>2</td>
<td>90</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Toluene</td>
<td>2</td>
<td>62</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Water</td>
<td>2</td>
<td>70</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Toluene/water (1:1)</td>
<td>1</td>
<td>78</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Toluene</td>
<td>1</td>
<td>45</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

*Reaction condition: bromide 4/alkyne 3c/PdCl₂(PPh₃)₂ (mol%)/CuI (mol%)/solvent (mL): 1:1:1:2:2, thermal heating under argon atmosphere at 60 °C.*

**Table 2.** Regio-controlled Sonogashira coupling of 1,3,5-tribromobenzene 4 with 1-ethynyl-4-(alkyloxy)benzenes 3a-c

<table>
<thead>
<tr>
<th>entry</th>
<th>R</th>
<th>Yield</th>
<th>5a-c</th>
<th>6a-c</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>n-C₆H₁₃</td>
<td>(5a) 94</td>
<td>(6a) 2</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>n-C₇H₁₅</td>
<td>(5b) 93</td>
<td>(6b) 4</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>n-C₈H₁₇</td>
<td>(5c) 90</td>
<td>(6c) 8</td>
<td></td>
</tr>
</tbody>
</table>

*Conditions: bromide 4/alkynes 3a-c/PdCl₂(PPh₃)₂ (mol%)/CuI (mol%)/Et₃N (equiv.)/water (mL)/toluene (mL): 1:1:1:2:2:1:1, thermal heating under argon atmosphere at 60 °C.*

as 1-bromo-3,5-di-(2-(4-hexyloxyphenyl)-ethynyl) benzene 6a and 1-bromo-3,5-di-(2-(4-heptyloxyphenyl) ethynyl)benzene 6b on the basis of their spectral analyses (¹H, ¹³C NMR and mass spectra) as mentioned in the experimental section.

Synthesis of unsymmetrical di- and tri-ethynylated benzenes

Next, cross-coupling of the mono-ethynylated dibromobenzene 5c with other terminal alkynes aiming to prepare unsymmetrical di- and tri-ethynylated benzenes
via two successive Sonogashira reactions is evaluated as shown in Scheme 2. Thus, Sonogashira cross-coupling reaction of 1,3-dibromo-5-(2-(4-(octyloxy)phenyl) ethynyl)-benzene 5c with 1-ethynyl-4-(heptyloxy)benzene 3b was performed applying the following reaction condition: 5c (1 mmol), 3b (1 mmol), PdCl\(_2\)(PPh\(_3\))\(_2\) (1 mol%), CuI (2 mol%) in toluene/water (2 mL, 1:1) using triethylamine (2 mmol) under argon atmosphere at 60 °C for 24 h to furnish two isolable products. After column chromatography, the obtained products were identified as 1-bromo-3-(2-(4-heptyloxyphenyl) ethynyl)-5-(2-(4-octyloxyphenyl)ethynyl)benzene (7) (40% yield) in addition to 1,3-di-(2-(4-heptyloxyphenyl) ethynyl)-5-(2-(4-octyloxyphenyl)ethyl)benzene (8) (4% yield), as shown in Scheme 2. Afterwards, the third regiocontrolled cross-coupling process for 1-bromo-3-(2-(4-heptyloxyphenyl) ethynyl)-5-(2-(4-octyloxyphenyl) ethynyl)benzene 7 was conducted via its reaction with 1-ethynylbenzene 9 in 1:1 molar ratio in the presence of PdCl\(_2\)(PPh\(_3\))\(_2\) (1 mol%), CuI (2 mol%) in toluene/water (2 mL, 1:1) using triethylamine (2 mmol) under argon at 60 °C for 24 h. This sequenced cross-coupling furnished the desired unsymmetrical tri-ethynylated benzene derivative; 1-(2-(4-heptloxy)phenyl)ethynyl)-3-(2-(4-octyloxy)phenyl)ethyl)-5-(2-phenyl-ethynyl)benzene (10) in 60% yield as outlined in Scheme 2. The tri-ethynylated benzene product 10 was confirmed on the basis of its nuclear magnetic resonance (\(^1\)H and \(^{13}\)C NMR) and mass spectra (MS) (see experimental section).

**Conclusions**

Three different 1-ethynyl-4-(alkyloxy)benzene candidates were prepared in three steps from 4-iodophenol. Then, these terminal acetylene candidates were employed in an efficient regiocontrolled Sonogashira cross-coupling with 1,3,5-tribromobenzene 4 for the preparation of unsymmetrical mono-, di- and tri-alkynylated benzene derivatives in moderate to good yields. Water/toluene mixed solvent was found to greatly enhance the cross-coupling reaction of 4-alkyloxyphenylacetylene with 1,3,5-tribromobenzene. These results encouraged us to

![Scheme 2. Regiocontrolled Sonogashira cross-coupling of compound 5c.](image)
conduct sequential Sonogashira followed by Suzuki cross-coupling reactions on analogous candidates and the results are under progress.

Experimental

Melting points were determined in open glass capillaries with a Gallenkamp apparatus. The infrared (IR) spectra were recorded in potassium bromide disks on a Pye Unicam SP 3-300 and Shimadzu FTIR 8101 PC infrared spectrophotometer. NMR spectra were recorded with a Varian Mercury VXR-300 NMR spectrometer at 300 MHz (1H NMR) and at 75 MHz (13C NMR) using CDCl3 as solvent and internal standard (δ 7.27 and 77.36 ppm, for 1H NMR and 13C NMR, respectively). Chemical shifts (δ) and J values are reported in ppm and Hz, respectively. Multiplicities are shown as the abbreviations: s (singlet), d (doublet), t (triplet), m (multiplet). Electrospray ionization mass spectrometry (EI-MS) analyses were obtained at 70 eV with a Shimadzu GCMQP 1000 EX spectrometer. Analytical thin-layer chromatography (TLC) was performed using pre-coated silica gel 60741 (70-230 mesh) was used for flash column chromatography. For the exclusion of atmospheric oxygen from the reaction medium, the aqueous solvent was firstly deoxygenated with a stream of argon for 30 min before use. 1-Hexyloxy-4-iodobenzene (1a), 1-heptyloxy-4-iodobenzene (1b), and 1-octyloxy-4-iodobenzene (1c) were prepared following literature procedures.

Synthesis of 4-(alkyloxy)phenylethynyltrimethylsilanes 2a-c

To a mixture of PdCl2(PPh3)2 (14 mg, 0.02 mmol), Cul (7.6 mg, 0.04 mmol), and 1-alkyloxy-4-iodobenzenes 1a-c (2 mmol) in toluene (2 mL) was added trimethylsilylacetylene (0.34 mL, 2.4 mmol) at room temperature under an argon atmosphere. Triethylamine (0.28 mL, 4 mmol) in water (2 mL) was then added drop-wise and stirring was continued for 24 h at room temperature. The resulting two-phase mixture was separated and the aqueous layer was extracted with diethyl ether (3 × 30 mL). The combined organic layer was concentrated under reduced pressure to leave a crude solid, which was purified by chromatography on silica gel (hexane-ethyl acetate) to furnish the corresponding cross-coupled products 2a-c.

4-(Hexyloxy)phenylethynyltrimethylsilane (2a): This compound was purified by ethyl acetate-hexane (1:30) to yield 0.406 g of 2a (74%); 1H NMR (300 MHz, CDCl3) δ 0.24 (s, 9H) 0.91 (t, 3H, J 6.6 Hz), 1.26-1.45 (m, 6H), 1.74-1.80 (m, 2H), 3.95 (t, 2H, J 6.6 Hz), 6.81 (d, 2H, J 9.0 Hz), 7.39 (d, 2H, J 9.0 Hz).

4-(Heptyloxy)phenylethynyltrimethylsilane (2b): This compound was purified by ethyl acetate-hexane (1:50) to yield 0.496 g of 2b (86%); 1H NMR (300 MHz, CDCl3) δ 0.24 (s, 9H), 0.91 (m, 3H), 1.28-1.46 (m, 8H), 1.76-1.81 (m, 2H), 3.95 (t, 2H, J 6.6 Hz), 6.81 (d, 2H, J 8.1 Hz, 2H), 7.39 (d, J 7.8 Hz, 2H).

4-(Octyloxy)phenylethynyltrimethylsilane (2c): This compound was purified by ethyl acetate-hexane (1:70) to yield 0.58 g of 2c (96%); 1H NMR (300 MHz, CDCl3) δ 0.25 (s, 9H) 0.90 (m, 3H), 1.27-1.44 (m, 10H), 1.75-1.80 (m, 2H), 3.94 (t, 2H, J 6.6 Hz), 6.80 (d, 2H, J 8.7 Hz), 7.39 (d, 2H, J 9.0 Hz).
Synthesis of mono- and dialkynylated benzene derivatives

To PdCl₂(PPh₃)₂ (7 mg, 0.01 mmol), CuI (3.8 mg, 0.02 mmol) in toluene (1 mL) and Et₃N (140 µL, 2 mmol) in water (1 mL) were added 1,3,5-tribromobenzene 4 (315 mg, 1 mmol) and 4-alkoxyphenylethyne 3a-c (1 mmol) under an argon atmosphere. Stirring was continued for 24 h at 60 °C. Two phases of the resulting mixture were separated and the aqueous layer was extracted three times with diethyl ether (3 × 30 mL). The combined organic layer was concentrated under reduced pressure to leave a crude solid, which was purified by flash column chromatography using hexane/ethyl acetate (20:1) to give the corresponding mono and dialkynylated products 5a-c and 6a-c.

1,3-Dibromo-5-(2-(4-(hexyloxy)phenyl)ethynyl)benzene (5a): yield: 409.5 mg (94%) as white powder; m.p. 54–55 °C; IR (KBr) ν max/cm⁻¹ 3065, 2926, 2210, 1550, 1464, 1243; ¹H NMR (300 MHz, CDCl₃) δ 0.92 (t, 3H, J 5.6 Hz), 1.28-1.85 (m, 8H), 3.99 (t, 2H, J 6.6 Hz), 6.89-7.03 (m, 2H), 7.43-7.49 (m, 2H), 7.58 (s, 2H), 7.61 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 14.1, 22.8, 26.1, 29.0, 31.8, 68.2, 85.3, 92.5, 114.1, 114.5, 122.7, 127.4, 132.9, 133.5, 133.8, 160.1; MS (EI, 70 eV) m/z 557 (M⁺, 37.6%), 532 (100%), 271 (3.4%), 192 (20.8%), 163 (32.7%), 87 (7.9%), 55 (15.5%); anal. calcd. for C₂₉H₂₂BrO: C, 55.7; H, 4.62%; found: C, 55.35; H, 4.79%.

1-Bromo-3,5-bis-(2-(4-(hexyloxy)phenyl)ethynyl)benzene (6a): yield: 11 mg (2%) as white crystals; m.p. 108 °C; IR (KBr) ν max/cm⁻¹ 3068, 2929, 2206, 1592, 1463, 1245; ¹H NMR (300 MHz, CDCl₃) δ 0.92 (t, 3H, J 5.6 Hz), 1.28-1.83 (m, 16H), 3.99 (t, 4H, J 6.4 Hz), 6.87-6.95 (m, 4H), 7.44 (d, 4H, J 7.7 Hz), 7.47-7.58 (m, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 14.0, 23.1, 26.5, 28.5, 31.8, 68.4, 83.6, 91.7, 114.3, 114.8, 122.1, 132.4, 133.1, 133.6, 133.7, 159.7; MS (EI, 70 eV) m/z 557 (M⁺, 35.0%), 258 (4.0%), 250 (27.6%), 235 (59.4%), 205 (53.7%), 189 (95.1%), 179 (55.6%), 124 (59.1%), 93 (31.0%), 75 (27.7%), 53 (100%); anal. calcd. for C₂₉H₂₂BrO: C, 56.92; H, 5.21%; found: C, 56.85; H, 5.09%.

1,3-Dibromo-5-(2-(4-(octyloxy)phenyl)ethynyl)benzene (5b): yield: 417.5 mg (90%) as white powder; m.p. 58-59 °C; IR (KBr) ν max/cm⁻¹ 3040, 2922, 2213, 1577, 1463, 1250; ¹H NMR (300 MHz, CDCl₃) δ 0.93 (t, 3H, J 5.4 Hz), 1.28-1.85 (m, 12H), 3.98 (t, 2H, J 6.5 Hz), 6.85-6.91 (m, 2H), 7.42-7.47 (m, 2H), 7.58 (s, 2H), 7.61 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 14.1, 22.6, 26.0, 29.1, 29.2, 29.3, 31.8, 68.1, 85.2, 92.3, 113.9, 114.6, 122.6, 127.2, 132.7, 133.2, 133.4, 159.8; MS (EI, 70 eV) m/z 464 (M⁺, 29.4%), 352 (100%), 192 (23.3%), 163 (37.4%), 71 (13.9%), 57 (44.4%), 55 (28.9%); anal. calcd. for C₂₉H₂₂BrO: C, 56.92; H, 5.21%; found: C, 56.85; H, 5.09%.

1-Bromo-3,5-bis-(2-(4-(octyloxy)phenyl)ethynyl)benzene (6b): yield: 23.4 mg (4%) as white powder; m.p. 55-56 °C; IR (KBr) ν max/cm⁻¹ 3042, 2923, 2219, 1550, 1463, 1249; ¹H NMR (300 MHz, CDCl₃) δ 0.92 (t, 6H, J 6.8 Hz), 1.28-1.83 (m, 20H), 3.99 (t, 4H, J 6.9 Hz), 6.88-6.97 (m, 4H), 7.44 (d, 4H, J 7.7 Hz), 7.47-7.54 (m, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 14.2, 22.8, 26.2, 29.1, 29.6, 31.8, 68.1, 86.1, 91.2, 114.1, 114.4, 121.8, 132.4, 133.0, 133.3, 134.2, 159.4; MS (EI, 70 eV) m/z 585 (M⁺, 6.6%), 519 (6.9%), 457 (7.8%), 254 (9.0%), 80 (52.9%), 64 (73.7%), 57 (100%), 50 (18.8%); anal. calcd. for C₂₉H₁₈Br₂O: C, 57.83; H, 7.06%; found: C, 73.59; H, 7.15%.

1,3-Dibromo-5-(2-(4-(octyloxy)phenyl)ethynyl)benzene (5c): Yield: 418.5 mg (90%) as white powder; m.p. 58-59 °C; IR (KBr) ν max/cm⁻¹ 3048, 2921, 2205, 1577, 1465, 1250; ¹H NMR (300 MHz, CDCl₃) δ 0.92 (t, 3H, J 5.4 Hz), 1.28-1.85 (m, 12H), 3.98 (t, 2H, J 6.5 Hz), 6.85-6.91 (m, 2H), 7.42-7.47 (m, 2H), 7.58 (s, 2H), 7.61 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 14.1, 22.6, 26.0, 29.1, 29.2, 29.3, 31.8, 68.1, 85.2, 92.3, 113.9, 114.6, 122.6, 127.2, 132.7, 133.2, 133.4, 159.8; MS (EI, 70 eV) m/z 464 (M⁺, 29.4%), 352 (100%), 350 (54.7%), 192 (23.3%), 163 (37.4%), 71 (13.9%), 57 (44.4%), 55 (28.9%); anal. calcd. for C₂₉H₂₂BrO: C, 56.92; H, 5.21%; found: C, 56.85; H, 5.09%.

Synthesis of 1-(2-(3-bromo-5-(2-(4-(octyloxy)phenyl)ethynyl)phenyl)phenyl)ethynyl)-4-(hexyloxy)benzene (7)
under argon atmosphere. The reaction mixture was stirred for 24 h at 60 °C. Two phases of the resulting mixture were separated and the aqueous layer was extracted three times with diethyl ether (3 × 30 mL). The combined extracts were evaporated under reduced pressure to leave a crude solid, which was purified by flash column chromatography on silica gel using hexane/ethyl acetate (10:1) to furnish 7 (40% yield) and 8 (4% yield).

1-Bromo-3-(2-(4-(heptyloxy)phenyl)ethylthynyl)-5-(2-(4-(octyloxy)phenyl)ethylthynyl)benzene (7): yield: 239.5 mg (40%) as white powder; m.p. 56-57 °C; IR (KBr) ν\text{max}/cm\text{-1} 3096, 2926, 2205, 1595, 1464, 1246; 1H NMR (300 MHz, CDCl\text{3}) δ 9.2 (s, 9H), 7.45-7.46 (m, 2H), 7.58 (s, 1H); 11C NMR (75 MHz, CDCl\text{3}) δ 141.1, 122.6, 22.7, 25.9, 29.0, 29.15, 29.2, 29.3, 29.7, 31.7, 68.1, 68.2, 81.9, 85.9, 87.9, 91.4, 114.5, 114.6, 121.8, 125.7, 125.8, 125.9, 132.7, 132.8, 133.9, 158.9, 159.7; MS (EI, 70 eV) m/z 718 (15.9%), 575 (19.5%), 486 (24.5%), 462 (36.7%), 410 (24.5%), 351 (23.6%), 220 (43.7%), 107 (74.5%), 82 (100%), 65 (34.7%), 50 (13.5%); anal. calcd. for C\text{39}H\text{34}BrO\text{2}: C, 74.11%; H, 7.23%; found: C, 73.85; H, 7.09%.

Synthesis of 1-(2-(4-(heptyloxy)phenyl)ethylthynyl)-3-(2-(4-octyloxy)phenyl)ethylthynyl)-5-(2-phenylethynyl)benzene (10)

To a mixture of 1-(2-(3-bromo-5-(2-(4-octyloxy)phenyl)-ethylthynyl)phenyl)ethylthynyl)-4-(heptyloxy)benzene (7) (599 mg, 1 mmol) and phenylethyne (9) (90 μL, 1 mmol), in toluene (1 mL) and water (1 mL), was added Et\text{3}N (140 μL, 2 mmol) followed by adding PdCl\text{2}(PPh\text{3})\text{2} (7 mg, 0.01 mmol) then Cul (3.8 mg, 0.02 mmol) under argon atmosphere. The reaction mixture was stirred for 24 h at 60 °C. Two phases of the resulting mixture were separated and the aqueous layer was extracted three times with diethyl ether (3 × 30 mL). The combined extracts were evaporated under reduced pressure to leave a crude solid, which was purified by flash column chromatography on silica gel using hexane/ethyl acetate (10:1) to give compound 10 in 372.5 mg (60% yield) as yellow oil. IR (KBr) ν\text{max}/cm\text{-1} 3046, 2922, 2205, 1573, 1464, 1246; 11H NMR (300 MHz, CDCl\text{3}) δ 0.91-0.94 (m, 6H), 1.30-1.84 (m, 22H), 3.99 (t, 4H, J 6.4 Hz), 6.90 (d, 4H, J 6.7 Hz), 7.37-7.39 (m, 3H), 7.49 (d, 4H, J 5.7 Hz), 7.56 (d, 2H, J 3.9 Hz), 7.63 (s, 3H); 11C NMR (75 MHz, CDCl\text{3}) δ 14.1, 22.6, 22.6, 25.9, 26.0, 29.0, 29.1, 29.2, 29.2, 29.7, 31.7, 31.8, 68.1, 86.6, 88.0, 90.3, 90.7, 114.5, 114.6, 122.9, 123.9, 124.4, 128.3, 128.5, 131.7, 132.8, 133.1, 133.5, 133.7, 159.5; MS (EI, 70 eV) m/z 881 (M+, 22.5%), 598 (0.4%), 430 (29.9%), 406 (36.3%), 234 (51.2%), 210 (100%), 181 (18.2%), 57 (70.3%), 55 (20.6%); anal. calcd. for C\text{46}H\text{36}O\text{2}: C, 87.05; H, 7.79%; found: C, 86.87; H, 7.68%.

Supplementary Information

Supplementary data are available free of charge at http://jbcs.sbq.org.br as PDF file.

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References


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