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# SYNTHESIS OF NOVEL AMPHIPHILIC DIACETYLENES WITH AMINO OR AMMONIUM FUNCTIONALITY

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***Abstract:*** An optimized procedure for the Cadiot-Chodkiewicz coupling of mono- and dipropargylamines with iodododecyne to yield the diynylamines bis(pentadeca-2,4-diyn-1-yl)amine (**1**) and pentadeca-2,4-diyn-1-ylamine (**3**) is given. The amines were converted in good yields into the corresponding amphiphilic quaternary ammonium salts dimethylbis(pentadeca-2,4-diyn-1-yl)ammonium iodide (**7**) and trimethylpentadeca-2,4-diyn-1-ylammonium iodide (**8**).

Since the possibility of topochemical polymerization of conjugated diacetylenes to polydiacetylenes has been recognized, this reaction has received considerable attention.[1,2] Polydiacetylenes are of large interest in view of their potential applications in devices for nonlinear optics,[3] microelectronics[4] and microlithography.[5] Moreover, the photo-polymerization of amphiphilic diacetylenes has been utilized to stabilize the bilayer structure of vesicles.[6] For topochemical polymerization, molecular order of the diacetylenic functions is required.[5] Besides polymerization in the crystalline phase by light, γ-radiation, temperature, and pressure, also alignment and polymerization of the diacetylenes can be achieved in supramolecular assemblies of amphiphilic molecules in monolayers, bilayers and multilayers. A number of diacetylenes with long alkyl chains as the nonpolar part and a carboxyl group as the polar head group have been synthesized and used for this purpose. Only recently, the synthesis of some amphiphilic diacetylenes with the carbamoyl and amino function have been reported.[7] Several methods are described in the literature for the preparation of tertiary diynylamines, *i.e.* the Cadiot-Chodkiewicz coupling of *N,N*-dimethyl-propargylamine with bromoacetylenes,[8] the ethanethiol elimination of 1,3-ene-yne derivatives,[9] the diethylaminomethylation of terminal acetylenes,[10] and oxidative coupling of *N,N*-dialkylamino-propargylamines.[11] However, for the preparation of primary and secondary diynylamines no satisfactory route has been reported yet. In this paper we report the synthesis of some novel amphiphilic diacetylenes with the primary and the secondary amino and quaternary ammonium functionalities.

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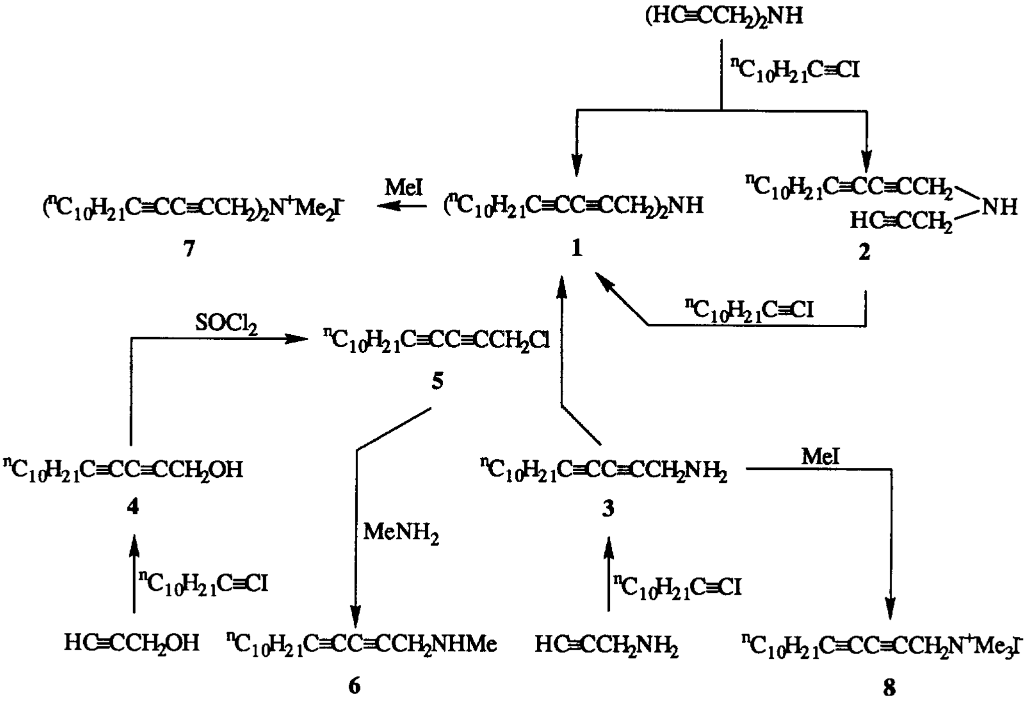
The synthetic routes are given in Scheme 1. Preparation of the diacetylenic function is performed by the Cadiot-Chodkiewicz coupling[12] and the procedures have been modified and optimized.



Scheme 1

Dipropargylamine was treated with two equivalents of 1-iodo-1-dodecyne, easily generated from 1-dodecyne,[13] in the presence of ethylamine and a catalytic amount of cuprous chloride in aqueous tetrahydrofuran at 20-25°C to give a mixture of bis(pentadeca-2,4-diyn-1-yl)amine (**1**) as the major product and *N*-(2-propynyl)-pentadeca-2,4-diyn-1-ylamine (**2**) as the minor product. Compound **2** was easily converted into **1** under similar conditions.

An alternative route for the preparation of **1** was investigated by the substitution of 1-chloropentadeca-2,4-diyne (**5**) with pentadeca-2,4-diyn-1-ylamine (**3**). Compound **5** was easily prepared from the reaction of pentadeca-2,4-diyn-1-ol (**4**) with thionyl chloride. Compounds **3** and **4** were obtained in satisfactory yield by the Cadiot-Chodkiewicz coupling of 1-iodo-1-dodecyne to propargylamine and propargyl alcohol , respectively. Reaction of **5** with methylamine gave *N*-methylpentadeca-2,4-diyn-1-ylamine (**6**) in good yield. However, the alkylation reaction of **3** with **5** gave **1** only in low yield. Therefore, the direct coupling of 1-iodo-1-dodecyne to dipropargylamine turned out to be the best method for the preparation of bisdiynylamine (**1**).

Amino compounds **1**, **3**, and **6** shows a good solubility in diethyl ether, tetrahydrofuran and chloroform, but are only poorly soluble in the more polar solvents methanol, dimethylformamide and dimethylsulfoxide.

Since **1**, **3** and **6** possess precursors the nucleophilic amino group, these compounds can be useful applied as precursors in the synthesis of amphiphiles with desired functionalities. For example, reaction of **1** and **3** with iodomethane under basic conditions[14] gave the corresponding quaternary ammonium salts, dimethylbis(pentadeca-2,4-diyn-1-yl)ammonium iodide (**7**) and trimethylpentadeca-2,4-diyn-1-ylammonium iodide (**8**) in good yields.

## EXPERIMENTAL

Melting points (mp) were determined on a Kofler hot-stage microscope and are uncorrected. Proton nuclear magnetic resonance ($^1$H-NMR) spectra and carbon nuclear magnetic resonance ($^{13}$C-NMR) spectra were determined at 200 MHz and 50 MHz, respectively, on Bruker AC 200-E, and chemical shifts are reported as $\delta$ values in parts per million (ppm) relative to internal tetramethylsilane ($\delta$ 0.00) in chloroform-d as the solvent. Infra red spectra (IR) were recorded on Philips PU 2706 infrared spectrophotometer. Electron impact mass spectra (EIMS) were recorded on AEI MS 902 spectrometer equipped with a VG ZAB console. Elemental analysis were determined on Carlo Erba elemental analyzer 1106. Tetrahydrofuran for the Cadiot-Chodkiwicz coupling was distilled from sodium borohydride. Chromatographic solvents (chloroform and petroleum ether) were distilled prior to use. Column chromatography was carried out on E. Merck silica gel 60 (230-400 mesh), and thin layer chromatography on E. Merck silica gel 60 $F_{254}$ pre-coated sheet.

### General Procedure for the Cadiot-Chodkiewicz Coupling

To a stirred solution of a terminal acetylene (2.0 mmol), 70% ethylamine solution (1.0 ml), water (2.0 ml) and tetrahydrofuran (7.0 ml), hydroxylamine hydrochloride (0.1 g) and cuprous chloride (0.05 g) was added under nitrogen and the mixture was stirred for 5 minutes. Then, 1-iodo-1-dodecyne (0.58 g, 2.0 mmol) was added during 20 minutes. The temperature of the reaction mixture was maintained between 20-25°C, and the nitrogen flow was continued during the addition. Stirring was continued for an appropriate time under same conditions. The mixture was poured into a solution of potassium cyanide (1.0 g) in water (50 ml). The whole was extracted with ether (3x50 ml). The combined ethereal solution was washed with water (3x50 ml), dried over potassium carbonate and evaporated. The residue was subjected to column chromatography on silica gel with chloroform-petroleum ether (bp 40-60°C) (1:9) to remove less polar substances, then with an appropriate solvent system to give the desired product.[15]

### Bis(pentadeca-2,4-diyn-1-yl)amine (1) and *N*-(2-propynyl)-pentadeca-2,4-diyn-1-ylamine (2)

In this reaction, dipropargylamine[16] (0.19 g, 2.0 mmol) and 2 equivalents of 1-iodo-1-dodecyne (1.17 g, 4.0 mmol) were used. Elution with chloroform-petroleum ether (bp 40-60°C) (1:4) gave **1** (0.64 g, 76%) as pale yellow oil; $^1$H-NMR: 3.52 (s, 4H), 2.20 (t, *J*=6.8 Hz, 4H), 1.47 (t, *J*=6.8 Hz, 4H), 1.21 (m, 28H), 0.83 (t, *J*=6.2Hz, 6H). $^{13}$C-NMR: 79.62, 76.20, 68.78, 64.44, 37.33, 31.64, 29.31, 29.24, 29.06, 28.84, 28.58, 27.96, 22.43, 18.95, 13.85. IR (film) $\nu_{max}$: 3340, 2920, 2850, 2260, 1460, 1420, 1380, 1350, 1320, 1210, 1100 cm$^{-1}$. EIMS m/z : 421 (M$^+$). *Rf*=0.45 (silica gel with chloroform). Then fraction eluted with chloroform-petroleum ether (bp 40-60°C) (1:1) gave **2** (0.04 g, 7%) as pale yellow oil; $^1$H-NMR: 3.54 (s, 2H), 3.48 (d, *J*=2.5 Hz, 2H), 2.22 (t, *J*=6.7 Hz, 2H), 2.20 (d, *J*=2.5 Hz, 1H), 1.48 (t, *J*=6.8 Hz, 2H), 1.22 (m, 14H), 0.84 (t, *J*=6.3 Hz, 3H). $^{13}$C-NMR: 80.79, 79.68, 73.14, 71.65, 68.64, 64.41, 37.31, 36.68, 31.63, 29.29, 29.06, 28.83, 28.57, 27.94, 22.43, 18.96, 13.87. IR (film) $\nu_{max}$: 3400, 2920, 2850, 2260, 1460, 1425, 1375, 1350, 1320, 1210, 1100 cm$^{-1}$. EIMS m/z: 256 (M$^+$-1). *Rf*=0.15 (silica gel with chloroform).

**Bis(pentadeca-2,4-diyn-1-yl)amine (1)**

The general procedure was followed using **2** (0.51 g) as the terminal acetylene. The reaction time was 3 hours. Elution with chloroform-petroleum ether (bp 40-60°C) (1:4) gave **1** (0.76 g, 90%).

**Pentadeca-2,4-diyn-1-ylamine (3)**

The general procedure was followed using propargylamine (0.11 g) as the terminal acetylene. The reaction time was 2 hours. Elution from chloroform-petroleum ether (bp 40-60°C) (1:1) gave **3** as colorless prisms (0.30 g, 68%), mp 33-34°C. $^1$H-NMR: 3.39 (s, 2H), 2.19 (t, *J*=6.7 Hz, 2H), 1.48 (s, 2H), 1.45 (t, *J*=7.1 Hz, 2H), 1.19 (m, 14H), 0.81 (t, *J*=6.1 Hz, 3H). $^{13}$C-NMR: 79.83, 77.05, 76.51, 67.24, 64.41, 31.75, 31.62, 29.21, 29.04, 28.81, 28.55, 27.96, 22.41, 18.94, 13.83. IR (KBr) $\nu_{max}$: 2920, 2840, 2250, 1460, 1425, 1380, 1325, 1220 cm$^{-1}$. EIMS m/z: 219 (M$^+$). *Rf*=0.10 (silica gel with chloroform).

**Pentadeca-2,4-diyn-1-ol (4)**

The general procedure was followed using propargyl alcohol (0.11 g) as the terminal acetylene. The reaction time was 2 hours. Elution with chloroform-petroleum ether (bp 40-60°C) (1:4) gave **4** as colorless needles (0.37 g, 77%), mp 49-50°C. $^1$H-NMR: 4.26 (s, 2H), 2.61 (s, 1H), 2.23 (t,*J*=6.7 Hz, 2H), 1.48 (t, *J*=6.8 Hz, 2H), 1.22 (m, 14H), 0.83 (t, *J*=6.0 Hz, 3H). $^{13}$C-NMR: 81.47, 73.32, 70.46, 64.14, 51.05, 31.64, 29.31, 29.24, 29.07, 28.83, 28.60, 27.90, 22.43, 18.99, 13.85. IR (KBr) $\nu_{max}$: 3315, 3190, 2960, 2860, 2250, 1470, 1350, 1230, 1025, 925 cm$^{-1}$. EIMS m/z: 191 (M$^+$-29). Anal Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.97. Found: C, 81.89; H, 11.12. *Rf*=0.45 (silica gel with chloroform).

**1-Chloropentadeca-2,4-diyne (5)**

To a stirred solution of **4** (0.33 g, 1.5 mmol) and pyridine (0.13 g, 1.7 mmol) in ether (10 ml), thionyl chloride (0.15 ml, 1.6 mmol) was added under cooling in an ice bath. The mixture was stirred at room temperature for 15 hours. The resulting pyridinium chloride was filtered off and washed with ether (2x5 ml). The combined ethereal solution was evaporated, and the residue was subjected to column chromatography on silica gel with chloroform-petroleum ether (bp 40-60°C) (1:4) to give **5** (0.27 g, 77%) as faintly yellow oil. $^1$H-NMR: 4.17 (s, 2H), 2.26 (t, *J*=6.7 Hz, 2H), 1.51 (t, *J*=6.8 Hz, 2H), 1.24 (m, 14H), 0.86 (t, *J*=6.2 Hz, 3H). $^{13}$C-NMR: 82.75, 71.33, 69.31, 63.96, 31.65, 30.69, 29.29, 29.22, 29.06, 28.81, 28.57, 27.79, 22.44, 19.04, 13.88. IR (film) $\nu_{max}$: 2930, 2860, 2250, 1460, 1420, 1370, 1265, 1240 cm$^{-1}$. *Rf*=0.90 (silica gel with chloroform).

**Bis(pentadeca-2,4-diyn-1-yl)amine (1)**

A mixture of **3** (0.22 g, 1.0 mmol) and **5** (0.24 g, 1.0 mmol), and sodium bicarbonate (0.10 g, 1.0 mmol) in tetrahydrofuran (5.0 ml) was stirred at room temperature for 18 hours. After removal of the solvent by rotary evaporation, chloroform (5.0 ml) and water (5.0 ml) were added to the residue. The chloroform layer was separated, dried over potassium carbonate and evaporated. The residue was subjected to column chromatography on silica gel with chloroform-petroleum ether (bp 40-60°C) (1:4) to give **1** (0.17 g, 41%).

**N-Methylpentadeca-2,4-diyn-1-ylamine (6)**

A solution of **5** (0.24 g, 1.0 mmol) in ether (5.0 ml) was added to a solution of methylamine (3.10g, 10 mmol) in ether (10 ml), and the whole was stirred at room temperature for 15 hours. A solution of potassium hydroxide (0.1 g, 2.0 mmol) in water (5.0 ml) was added to the solution. The ethereal layer was separated and the aqueous layer was extracted with ether (2x5 ml). The combined ethereal solution was dried over potassium carbonate and evaporated to give **6** as pale yellow oil (0.21 g, 90%). $^1$H-NMR: 3.41 (s, 2H), 2.44 (s, 3H), 2.22 (t, *J*=7.0 Hz, 2H), 1.49 (t, *J*=6.9 Hz, 2H), 1.23 (m, 14H), 0.84 (t, *J*=6.8 Hz, 3H). $^{13}$C-NMR: 79.40, 74.22, 68.27, 64.48, 40.36, 35.03, 31.63, 29.29, 29.22, 29.05, 28.82, 28.58, 27.98, 22.42, 18.97, 13.85. IR (film) $\nu_{max}$: 3380, 2920, 2850, 1790, 2260, 1465, 1445, 1425, 1380, 1350, 1320, 1220, 1110 cm$^{-1}$. EIMS m/z: 233 (M$^+$). *Rf*=0.10 (silica gel with chloroform).

**Dimethylbis(pentadeca-2,4-diyn-1-yl)ammonium Iodide (7)**

A mixture of **1** (0.21 g, 0.5 mmol), iodomethane (0.21 g, 1.5 mmol), and sodium bicarbonate (0.17 g, 2.0 mmol) in tetrahydrofuran (10 ml) was stirred at room temperature for 2 days. After removal of the solvent by rotary evaporation, chloroform (10 ml) was added to the residue and the whole was stirred vigorously for 10 minutes and filtered. The filtrate was evaporated and the residue was dissolved in ether (5 ml). To this ethereal solution, petroleum ether (bp 40-60°C) was added to crystallize **7** (0.25 g, 87%) as colorless needles, mp 73-74°C. $^1$H-NMR ($CDCl_3$, 200 MHz): 4.92 (s), 3.52 (s), 2.28 (t, *J*=6.8 Hz), 1.53 (t, *J*=7.1 Hz), 1.24 (m), 0.85 (t, *J*=6.3 Hz); the integrated ratio is 2:3:2:2:14:3. $^{13}$C-NMR ($CDCl_3$, 50 MHz): 85.21, 77.99, 63.11, 61.09, 55.31, 50.09, 31.64, 29.32, 29.21, 29.06, 28.80, 28.63, 27.56, 22.44, 19.05, 13.88. IR (KBr) $\nu_{max}$: 2960, 2910, 2900, 2840, 2260, 1465, 1405, 1355, 1030, 1000, 960, 855 cm$^{-1}$. EIMS m/z: 563 (M$^+$-15). Anal. Calcd for $C_{32}H_{52}NI$: C, 66.53; H, 9.07; N, 2.42. Found: C, 66.24; H, 9.11; N, 2.74.

**Trimethylpentadeca-2,4-diyn-1-ylammonium Iodide (8)**

A mixture of **3** (0.11 g, 0.5 mmol), iodomethane (0.28 g, 2.0 mmol), and sodium bicarbonate (0.21 g, 2.5 mmol) in tetrahydrofuran (10 ml) was stirred at room temperature for 2 days. After removal of the solvent by rotary evaporation, chloroform (10 ml) was added to the residue, and the whole was stirred vigorously for 10 minutes and filtered. The filtrate was evaporated and the residue was digested with ether to remove impurities. Colorless crystals were obtained (0.18 g, 93%), mp 120-121°C. $^1$H-NMR: 4.81 (s, 2H), 3.45 (s, 9H), 2.20 (t, *J*=6.5 Hz, 2H), 1.44 (t, *J*=6.0 Hz, 2H), 1.15 (m, 14H), 0.76 (t, *J*=6.1 Hz, 3H). $^{13}$C-NMR: 84.70, 77.28, 63.18, 61.80, 57.50, 53.14, 31.56, 29.25, 29.15, 28.98, 28.74, 28.58, 27.55, 22.36, 19.00, 13.84. IR (KBr) $\nu_{max}$:2960, 2840, 2250, 1570, 1480, 1460, 1420, 1400, 1365, 1295, 1265, 1240, 1230, 1200, 1090 cm$^{-1}$. EIMS m/z: 247 (M$^+$-142; iodomethane). Anal. Calcd for $C_{18}H_{32}NI$: C, 55.52; H, 8.28; N, 3.59. Found: C, 55.27; H, 8.22; N, 3.58.

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