Stereoselective Synthesis of Helical Dihydrodipyrrolophenanthroline and Hindrance Hexa *tert*-butyl carboxylatodipyrrolophenanthroline from Reaction Between 1,10-Phenanthroline and Dialkyl acetylenedicarboxylates

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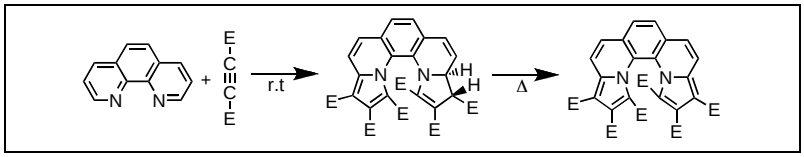

High hindrance Hexa *tert*-butoxy carbonyl dipyrrolophenanthroline and helical dihydropyrrolophenanthroline compounds were prepared from reactions between di *tert*-butyl acetylenedicarboxylate and 1,10-phenanthroline in polar solvents media.

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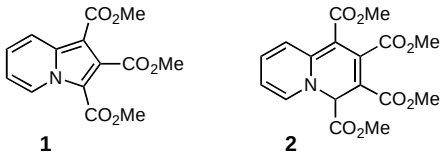
INTRODUCTION

During the course of our investigations, we were interested in the preparation of substituted pyrrolophenanthrolines. Bridgehead nitrogen heterocycles have been the subject of great consideration because they constitute an important class of natural and non-natural products, many of which exhibit useful biological activity [1-3]. Many diverse products can be prepared from the addition of acetylenic esters to nitrogen-containing heterocycles [4]. The interesting reaction between pyridine and acetylenic esters in methanol is typical, in which the indolizine-1,2,3-tricarboxylate **1** and in the other report 4*H*-quinolizine **2** are isolated (Scheme 1) [2,3,5,6].

Scheme 1



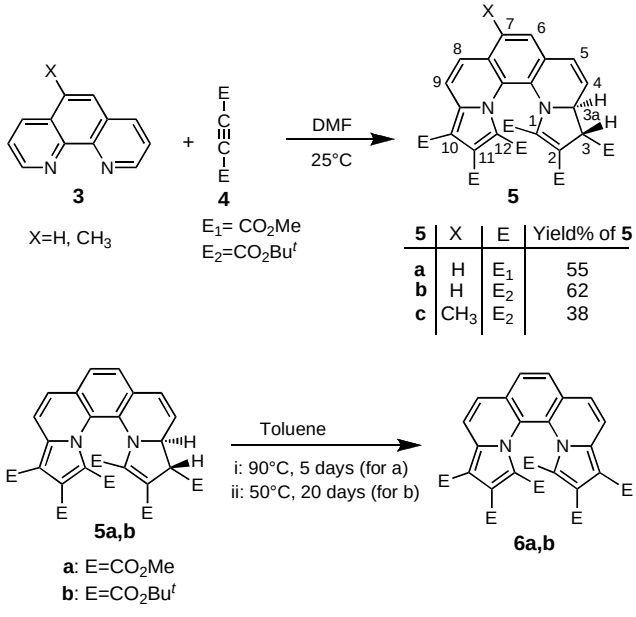
Recently other dicomponent condensation reactions between 1,10-Phenanthroline and dialkyl acetylenedicarboxylates have been reported for preparation of helical dipyrrolophenanthrolines [7,8]. In this report we could not prepare Hexa *tert*-butoxy carbonyl dipyrrolophenanthroline in the same as manner previously reported. Herein we wish to describe the synthesis of new compound **5** and also highly hindered macromolecule **6b** derived from the reaction between di *tert*-butyl acetylenedicarboxylates **4b** and 1,10-phenanthroline derivatives **3** with respect to the different employed method.

RESULTS AND DISCUSSION

1,10-Phenanthroline **3** undergoes a smooth reaction with dialkyl acetylenedicarboxylates **4** to give hitherto unknown 3a,3-dihydrodipyrrolo[1,2-*a*:2',1'-*k*][1,10]phenanthroline derivatives **5a-c** in moderate yields (see Scheme 2). The reaction proceeds with nucleophilic attack of nitrogen to DMAD then concomitant zwitterions attack another DMAD and produce intermediate **7** (see Scheme 3).

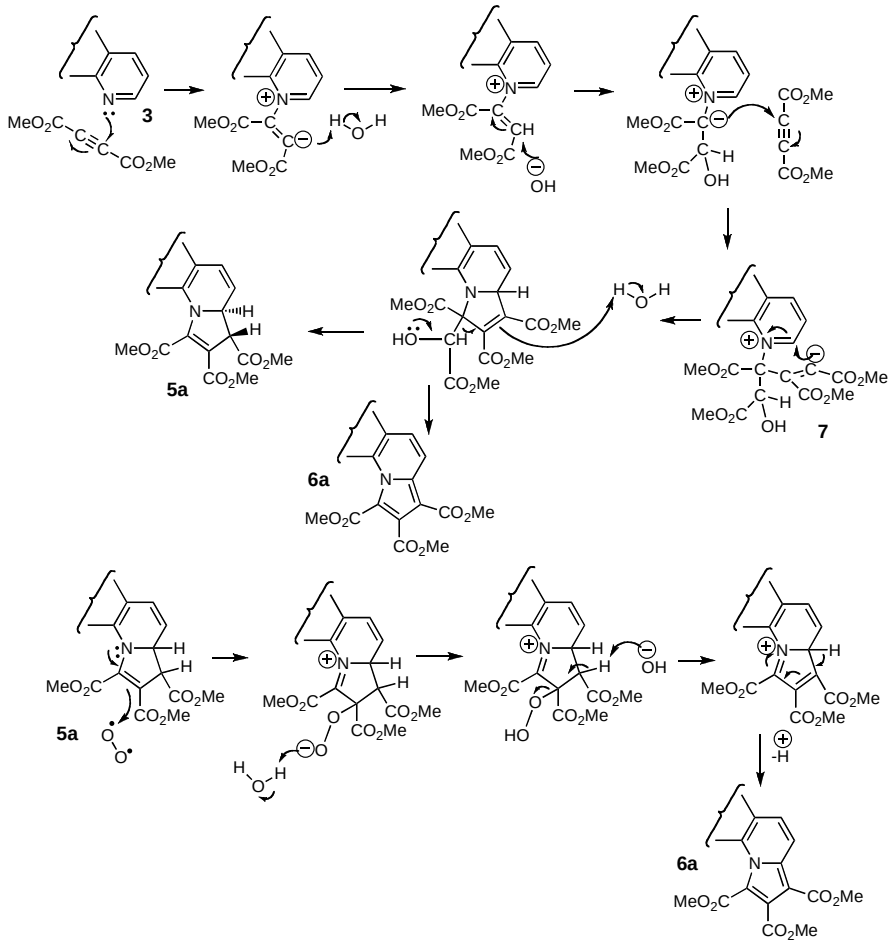
The products **6a**, **6b** produce from **5a** and **5b** for 5 and 20 days at 90 °C and 50 °C in toluene or *t*-butyl alcohol respectively. Compounds **6a** and **6b** could not be

Scheme 2



5	X	E	Yield% of 5
a	H	E_1	55
b	H	E_2	62
c	CH_3	E_2	38

Scheme 3



generated by the reflux process of **5a** and **5b** in toluene. Under experimental conditions, it was found from spectral data, preliminary cycloadditions, are stereoselective corresponding to geometric compounds [7].

The structures of compound **5a**-**c** and **6a,b** were deduced from their elemental analysis and their ^{1}H and ^{13}C NMR spectrum as well as from the IR spectra which exhibited strong signals due to carbonyl groups. The mass spectra of these compounds displayed molecular ion peaks at appropriate *m/z* values. Any initial fragmentations involve loss of the side chains.

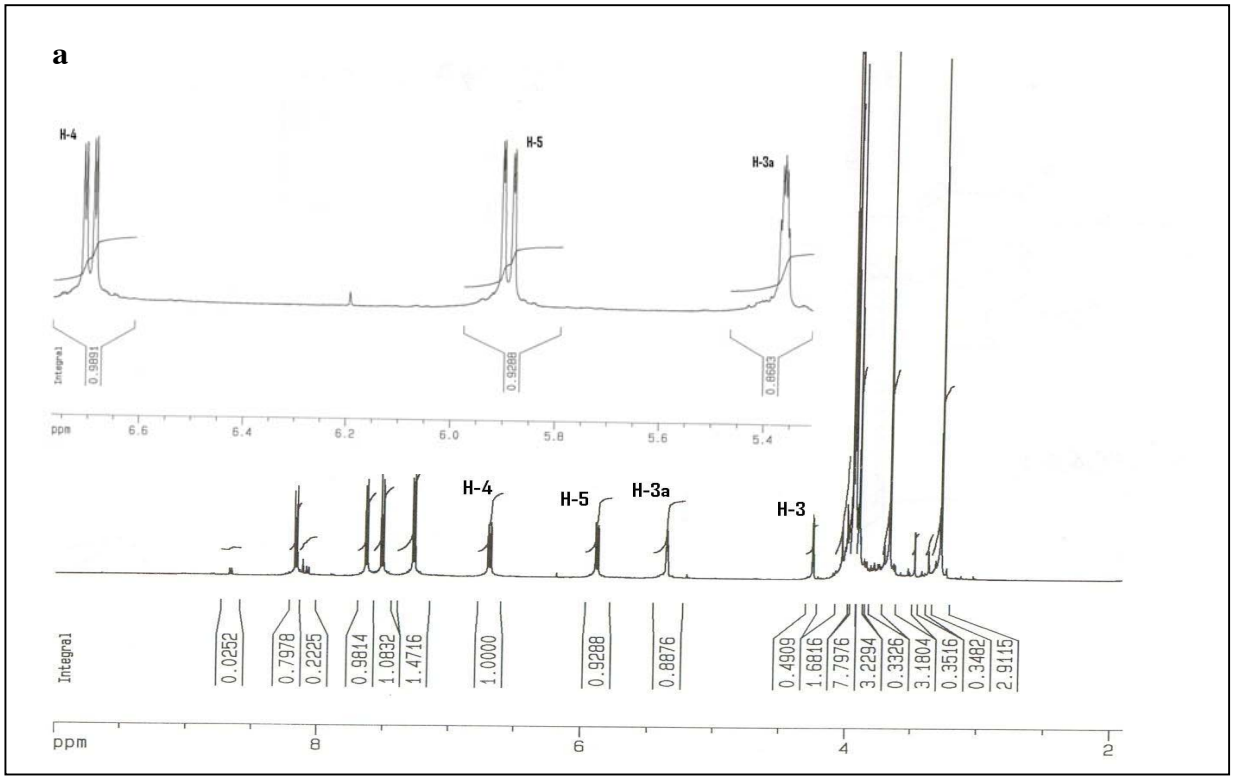
The ^{1}H NMR spectra of **5a** exhibited six single sharp lines at δ 3.31, 3.69, 3.93, 3.96, 3.97 and 3.98, readily recognizable as arising from methoxy protons. The protons of H_3, H_{3a}, H_4 and H_5 resonate at (δ 4.28, J=4.0 Hz), (δ 5.39, J_1=4.0, J_2=2.1, J_3=1.8, Hz), (δ 6.73, J_1=9.8, J_2=2.1 Hz) (δ 5.92, J_1= 9.8, J_2=1.8 Hz) respectively, (see Scheme 4). Other data are given in the experimental section.

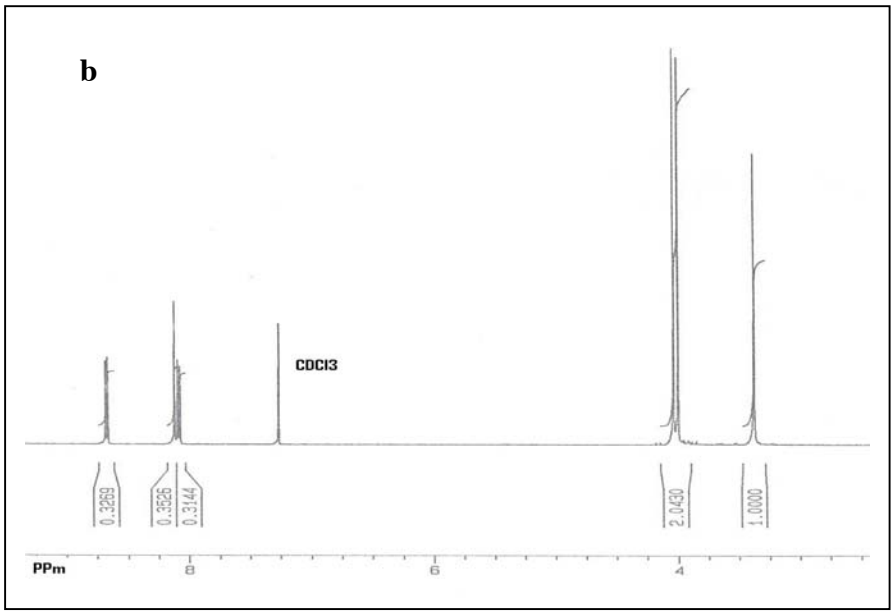
The stability of the dihydro derivatives **5** allowed us to draw the spontaneous generation of *trans* dihydro compound **5**, *trans* vicinal geometry of two protons (H_3, H_{3a}) in compound **5** are confirmed with respect to the coupling constant of dihydropyrrolo ring protons (J=4.0 Hz) [9].

The double resonance ^{1}H NMR spectroscopy has been shown the relation of these protons (H_3, H_{3a}, H_4 and H_5) and confirms the structure of dihydro ring region compound (**5a**-**c**). The ^{13}C NMR spectrum of **5a** displayed six signals for the carbomethoxy groups (δ 51.70, 52.15, 52.31, 52.65, 52.68 and 52.87). The C_{sp3} of carbons (C_3 and C_{3a}) and C_2 resonate at (δ 64.54, 73.95 and 104. 57) respectively, they are agreement with the helical structure of **5a**. The helical structure has been confirmed by diethyl acetylenic ester derivative [8]. The proton off resonance ^{13}C NMR spectra of compound **5a** confirms the C_{3a} and C_3 carbons and supports the exhibited structure of **5a**. On the other hand IR spectra of **5a** shows strong absorption for C=O of carbonyl groups (1723 and 1693) and the also for (C-O), (1231 and 1166) corresponding to the assignment structure.

In conclousion, we described a simple and efficient synthesis of macrocyclic functionalized 3a,3-dihydrodipyrrolophenanthrolines (**5a**-**c**) and highly hindered hexa *tert*-butoxycarbonyl dipyrrolophenanthroline derivatives (**6b**).

Scheme 4





a) ^{1}HNMR spectra of compound **5a**, Chemical shifts and multiplicity of H_3, H_{3a}, H_4 and H_5

b) ^{1}HNMR spectra of compound **6a**

EXPERIMENTAL

Melting points and IR spectra were measured on an Electrothermal 9100 apparatus and on a shimadzu IR-460 spectrometer respectively. Elemental analysis for C, H and N were performed using a Heraeus CHN-O-Rapid analyzer. The ^{1}H and ^{13}C NMR spectrum were also measured on a BRUKER DRX-500 AVANCE instrument with $CDCl_3$ as a solvent at 500.1 and 125.7 MHz respectively. In addition, the Mass Spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. 1,10-Phenanthroline and dialkyl acetylenedicarboxylates were obtained from Fluka and used without further purification.

General procedure (Exemplified by 5a, b and 6a, b). To a stirred solution of (0.198 g, 1 mmol) 1,10-phenanthroline in 12 mL DMF solvent was added, dropwise to a mixture of dimethyl acetylenedicarboxylate (0.639 g, 4.5 mmol) in DMF (3 mL) at room temperature over 5 minutes. The reaction mixture was then allowed to stay at room temperature for 20 hours. The solid phase was collected by filtration and washed with 3×5 mL methanol to give **5a** as light brown crystals (same procedure was employed to generate **5b)**. In order to generate **6a** or **6b**, these crystals (**5a**, **b**) were dried and added to the 10 mL of toluene solvent and then the reaction mixture heated for 5 and 20 days at 90 ˚C and 50 ˚C respectively. After this time new crystals were collected by filtration and washed with 3×5 mL methanol to give **6a** or **6b** as a yellow crystalline product.

Hexamethyl-3a,3-dihydrodipyrrolo[1,2-*a*:2',1'-*k*][1,10]-phenanthroline-1,2,3,10,11,12-hexacarboxylate (5a). This compound was obtained as yellow crystals in 55% yield (0.33 g); mp. 239- 241 ˚C; IR (KBr) ν_{max}= 1723, 1693 (C= O) and 1231, 1166 (C–O) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ_H 3.31, 3.69, 3.93, 3.96, 3.97 and 3.98 (18H, 6s, 6CO_2*Me*), 4.28 (1H, d, *J*=4.0 Hz, H_3), 5.39 (1H, dt, J_1=4.0, J_2=2.1, J_3=1.8 Hz, H_{3a}), 5.92 (1H, dd, J_1=9.8, J_2=1.8 Hz, H_5), 6.73 (1H, dd, J_1=9.8, J_2=2.1 Hz, H_4), 7.31 (1H, d, *J*=8.0 Hz, H_6), 7.55 (1H, d, *J*=9.3 Hz, H_8), 7.66 (1H, d, *J*=8.0 Hz, H_7) and 8.20 (1H, d, *J*=9.3 Hz, H_9); ^{13}C NMR ($CDCl_3$): δ_C 51.70, 52.15, 52.31, 52.65, 52.68 and 52.87 (6 CO_2*Me*), 64.54 (C_3), 73.95 (C_{3a}), 104.57 (C_2), 117.54, 122.39, 123.91, 125.11, 125.17, 126.57, 126.95, 127.02, 127.38, 128.94, 129.93, 131.25, 134.71, 137.59 and 141.14 (15 C_{rings}), 159.88, 161.75, 163.63, 166.13 and 167.29 (6 C=O of ester); MS (EI, 70 EV) m/z (%): 606 (M^+, 9), 515 (45), 453 (51), 277 (22), 108 (80), 57 (100). *Anal*. Calc for $C_{30}H_{26}N_2O_{12}$ (605.9): C, 59.40; H, 4.29; N, 4.62%; Found: C, 59.51; H, 4.23; N, 4.57%.

Hexa-*tert*-butyl-3a,3-dihydrodipyrrolo[1,2-*a*:2',1'-*k*][1,10]-phenanthroline-1,2,3,10,11,12-hexacarboxylate (5b). This compound was obtained as yellow crystals in 62% yeild (0.53 g); mp. 214- 216 ˚C; IR (KBr) ν_{max}= 1723, 1690 (C= O) and 1245, 1154 (C–O) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ_H 1.14, 1.44, 1.55, 1.57, 1.62 and 1.64 (54H, 6s, 6CO_2C*Me*$_3$), 4.10 (1H, d, *J*=3.8 Hz, H_7), 5.54 (1H, dt, J_1=3.8, J_2=2.2, J_3=1.7, Hz, H_{3a}), 5.84 (1H, dd, J_1=1.7, J_2=9.8 Hz, H_5), 6.65 (1H, dd, J_1=2.2, J_2=9.8 Hz, H_4), 7.18 (1H, d, *J*=7.7 Hz, H_6), 7.39 (1H, d, *J*=9.3 Hz, H_8), 7.50 (1H, d, *J*=7.7 Hz, H_7) and 7.97 (1H, d, *J*=9.3 Hz, H_9); ^{13}C NMR ($CDCl_3$): δ_C 27.62, 28.04, 28.17, 28.53, 28.57 and 28.82 (6 CO_2C*Me*$_3$), 65.45 (C_3), 77.35 (C_{3a}), 80.59, 81.89, 82.09, 82.37, 82.51 and 82.56 (6 O*C*Me$_3$), 108.34 (C_2), 117.51, 123.52, 124.46, 124.62, 125.15, 125.37, 125.90, 126.65, 129.09, 129.20, 130.36, 134.79, 136.56, 138.27 and 139.03 (15 C_{rings}), 159.44, 161.40, 161.92, 162.37, 164.08 and 166.36 (6 C=O of ester); MS (EI, 70 EV) m/z (%): 858 (M^+, 7), 785 (6), 617 (14), 561 (22), 533 (83), 459 (100), 415 (80), 56 (30). *Anal*. Calc for $C_{48}H_{62}N_2O_{12}$ (858.5): C, 67.13; H, 7.22; N, 3.26%; Found: C, 66.83; H, 7.62; N, 3.08%.

3-Methyl hexa-*tert*-butyl-3a,3-dihydrodipyrrolo[1,2-*a*:2',1'-*k*]-[1,10]phenanthroline-1,2,3,10,11,12-hexacarboxylate (5c). This compound was obtained as yellow crystals in yield 38% (0.33 g); mp. 246- 248 ˚C; IR (KBr) ν_{max}= 1735, 1690 (C= O) and 1230, 1160 (C–O) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ_H 1.14, 1.47, 1.58, 1.60, 1.64 and 1.66 (54H, 6s, 6CO_2CMe_3), 2.47 (3H, s, C*Me*), 4.11 (1H, d, *J*=4.0 Hz, H_3), 5.52 (1H, dt, J_1=4.0, J_2=2.4, J_3=2.0, Hz, H_{3a}), 5.88 (1H, dd, J_1=2.0, J_2=10.0 Hz, H_5), 6.85 (1H, dd, J_1=2.4, J_2=10.0 Hz, H_4), 7.32 (1H, d, *J*=9.0 Hz, H_8), 7.35 (1H, s, H_6) and 7.96 (1H, d, *J*=9.0 Hz, H_9); ^{13}C NMR ($CDCl_3$): δ_C 18.62 (CMe), 27.59, 28.05, 28.17, 28.54, 28.60 and 28.86 (6 CO2CMe_3), 64.74 (C_3), 77.35 (C3a), 80.50, 81.90, 82.13, 82.33 and 82.49 (6 OCMe_3), 108.27 (C_2), 117.54, 121.70, 123.20, 124.42, 125.67, 126.00, 126.52, 127.61, 128.12, 130.22, 131.62, 134.62, 136.41, 138.24 and 139.17 (15 C_{rings}), 159.59, 161.45, 161.95, 162.40, 164.22 and 166.42 (6 C=O of ester); MS (EI, 70 EV) m/z (%): 872 (M^+, 3), 857 (6), 815 (1), 787 (9), 703 (11), 558 (11), 434 (83), 40 (100). *Anal*. Calc for $C_{49}H_{64}N_2O_{12}$ (872): C, 67.43; H, 7.34; N, 3.20%; Found: C, 67.06; H, 7.52; N, 3.09%.

Hexamethyl dipyrrolo[1,2-*a*:2',1'-*k*][1,10]phenanthroline-1,2,3,10,11,12-hexacarboxylate (6a). ^{1}H NMR ($CDCl_3$): δ_H 3.38, 4.00 and 4.04 (6s, 18H, 6CO_2*Me*), 8.09 (d, 2H, *J*=9.0 Hz, $H_{8,5}$), 8.12 (s, 2H, $H_{7,6}$), 8.67 (d, 2H, *J*=9.0, $H_{9,4}$). Other data is available in reference [8].

Hexa-*tert*-butyl dipyrrolo[1,2-*a*:2',1'-*k*][1,10]phenanthroline-7,8,9,12,13,14-hexacarboxylate (6b). This compound was obtained as Yellow crystals in yield 45% (0.39 g); mp. 331- 333 ˚C; IR (KBr) ν_{max}= 1735, 1690 (C= O) and 1230, 1145 (C–O) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ_H 1.21, 1.70 and 1.74 (54H, 6s, 6$COMe_3$), 7.89 (2H, d, *J*=9.0 Hz, $H_{8,5}$), 7.96 (2H, s, $H_{7,6}$), 8.37 (2H, d, *J*=9.0, $H_{9,1}$); ^{13}C NMR ($CDCl_3$): δ_C 27.94, 28.52, and 28.76 (6 CO2CMe_3), 81.01, 82.22 and 82.61 (6 OCMe_3), 135.77, 131.19, 128.59, 126.34, 125.90, 124.93, 121.27, 118.00 and 109.74 (18 C_{rings}), 157.29, 162.23 and 163.83 (6 C=O of ester); MS (EI, 70 EV) m/z (%): 856 (M^+, 5), 841 (5), 799 (1), 755 (2), 434 (58), 149 (58), 40 (100). *Anal*. Calc for $C_{48}H_{60}N_2O_{12}$ (856): C, 67.29; H, 7.00; N, 3.27%; Found: C, 66.92; H, 7.28; N, 3.52%.

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