Dicarbamates: Synthesis and substituent effects on the barrier to rotation around the N-CO bond

Hamida Maouati, Inès Chniti, Mohamed Abderrahmène K. Sanhoury, Denis Merlet and Ikram Chehidi

Laboratory of Structural Organic Chemistry, Department of Chemistry, Faculty of Sciences of Tunis, University of Tunis El Manar, 2092 Tunis, Tunisia
Equipe de RMN en Milieu Orienté, ICMMO – UMR 8182, Université Paris-Sud 11, Bâtiment 420, 91405 ORSAY Cedex, France

(Received: 04 September 2016, accepted: 04 October 2016)

Abstract: A series of dicarbamates have been synthesized by addition of diols to isocyanates. These products were characterized by NMR, IR, and HRMS analyses. Substituent effects on the barrier to rotation around N-CO bond were investigated using variable temperature $^1$H NMR spectroscopy.

Keywords: Dicarbamates, diols, isocyanates, barrier to rotation, variable temperature $^1$H NMR.

INTRODUCTION

Carbamates (urethanes) are attracting considerable attention due to their potential scientific and technological applications [1-11]. For instance, they are widely used as raw materials in agrochemicals (pesticides, insecticides and herbicides) [1-4], dyestuffs [5] and pharmaceuticals [6, 7]. In addition, carbamates can be used to increase the abrasion resistance of polyurethane compositions [8], improving the hardness of urethane-based adhesives and sealants and adjusting viscosity values of oils and greases when used as additives [9]. Carbamates with alkyl side chains have potential applications as vehicles in reprography and ink jet printing technologies [10, 11].

Among the different routes of the synthesis of carbamates, the addition of alcohols to isocyanates is the most common method [12-16]. In a previous work in our laboratory, F-alkyl bis(N-aroxy or alkoxy sulfonyl)dicarbamates were prepared by the reaction of F-alkyldiols with alkoxy/aroxysulfonyl isocyanates [17]. In a recent work Soto et al. have reported on the reaction of fluorinated diols with aryl/alkyl isocyanates to give the corresponding dicarbamates [18].

On the other hand, the presence of C-N bond with a partially double character in carbamates can, in favorable cases, give rise to the two possible s-cis and s-trans stereoisomers following rotation around this bond [19-24]. In addition, it was generally shown that the pharmacological activity depends on molecular flexibility, which is governed by hindered rotation around chemical bonds as is the case of conjugated C–N linkages in amides, carbamates, thiocarbamates, and related systems [25-29].

In a previous work, we have described the synthesis of bis(thiocarbamates) from the reaction of dithiols with aryl/alkyl isocyanates as well as a conformational study using variable temperature (VT) NMR spectroscopy [30]. Herein, we extend this reaction to diols for the preparation of new dicarbamates. The rotational barriers around the C-N bond in these dicarbamates using VT NMR were measured and compared to those obtained in bis(thiocarbamates) analogues.
RESULTS AND DISCUSSION

1. Synthesis

The reaction of 1 equiv. of propane-1,3-diol or triethylene glycol with isocyanates in dry THF at room temperature gave the corresponding dicarbamates 2 and 3 in a 48-86% yield (Table I). They were obtained as white powders which are soluble in a mixture of dimethylsulfoxide (DMSO) and chloroform. It should be noted that compounds 2a, 3a and 3b were previously prepared by a different method [31-34]. The synthesized dicarbamates 2 and 3 were fully characterized by IR, (1H and 13C) NMR spectroscopy, and HRMS. The IR spectra show strong band absorptions at about 3300 and 1700-1620 cm⁻¹ assigned respectively to the N-H and C=O stretching vibrations. The (1H and 13C) NMR spectra of all dicarbamates show a doubling of signals at room temperature due to the rotation around N-CO bond which results in the presence of two conformational s-cis (anti) and s-trans (syn) rotamers with predominance of the s-cis (anti) form (Fig. 1). This assignment was based on the assumption that secondary carbamates and amides strongly prefer an s-cis (anti) conformation [35] and on our previous data for bis(thiocarbamates) [30].

The results of Table I show that lengthening the chain between the two carbamate moieties using a longer diol, triethylene glycol, led to a slight decrease in the reaction yield and a further increase in the proportion of the major isomer (s-cis vs. s-trans).

2. NMR study

The duplication of signals observed in the NMR spectra of some dicarbamates (2 and 3), at room temperature, is mainly due to the dynamic exchange that occurs between the two conformers s-cis and s-trans resulting from the rotation around the N-CO bond. This rotational dynamic equilibrium was studied by the method of coalescence using variable temperature 1H NMR in DMSO + CDCl₃.

In these dicarbamates (2 and 3), the rate constants kc were calculated at the coalescence temperature (Tc) using the equation (kc = (kT/h) exp (ΔG¹/RT)) (1). The peak separation (Δυ) was obtained from spectra acquired at temperatures well below coalescence. As the system involves an exchange between two unequally populated sites [36], the rate constant k_c calculated by the above equation is therefore the average of the forward (k₁) and reverse (k₋₁) rate constants. In this case, we used the following approximation formulas most accurate when the molar fractions are between 0.2 and 0.8: k₁ = (1 + Δp)kc and k₋₁ = (1 - Δp)kc with Δp = p_b - p_A, the difference in mole of the two species A and B (assuming B is the predominant species) [36]. Considering the transmission coefficient to be unity, the free energies of activation (ΔG₁ and ΔG₋₁) were calculated according to Eyring Eq. (1) together with Eqs. (2) and (3) [37].

\[ k_c = (kT/h) \exp \left(\frac{\Delta G^\circ}{RT}\right) \]  
\[ \Delta G_1^\circ = 19.14 T_c \left(10.32 + \log \frac{T_c}{k_1}\right) \times 10^{-3} \]  
\[ \Delta G_1^\circ = 19.14 T_c \left(10.32 + \log \frac{T_c}{k_{-1}}\right) \times 10^{-3} \]

The results of the dynamic 1H NMR study of the dicarbamates 2a-f thus obtained are shown in Table II which indicates a clear difference in the rotational barrier between the dicarbamates 2a-b and 2c-f. In fact, aromatic derivatives 2a and 2b, showing a doubling of signals at room temperature, could not be brought to coalescence upon heating even at 358K (Fig. 2) where (ΔG₁ and ΔG₋₁) values are estimated. However, in dicarbamates 2c-f, the coalescence temperature was reached and in order to slow down the chemical exchange, these samples were cooled below 300 K (Fig. 2). This indicates that, electron-withdrawing N-substituents of phenyl and benzyl (2a and 2b) lead to higher barriers to rotation (ΔG₁ and ΔG₋₁) whilst electron-releasing N-substituents of c-C₆H₄, n-Pr, n-Bu and Cl-CH₂-CH₃ (2c-f) decrease the barrier to rotation, in agreement with behavior previously observed for their sulfur analogs, bis(thio-carbamates) [30]. The results shown in Tables II and III indicate that the difference in the barrier to rotation between dicarbamate 2a and 2e is more important than in dicarbamates 3a and 3e which could be explained
Table 1: Synthesis of dicarbamates 2a-f and 3a-f.

![Chemical Structures](image)

<table>
<thead>
<tr>
<th>Isocyanate</th>
<th>Diol</th>
<th>Bis(carbamate)</th>
<th>Yield (%)</th>
<th>Isomer ratio (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="N=C=O" /></td>
<td>HO(\text{-}\text{OH})</td>
<td>2a</td>
<td>86</td>
<td>95:05</td>
</tr>
<tr>
<td><img src="image" alt="N=C=O" /></td>
<td>HO(\text{-}\text{O}^\text{-}\text{OH})</td>
<td>3a</td>
<td>84</td>
<td>98:02</td>
</tr>
<tr>
<td><img src="image" alt="N=C=O" /></td>
<td>HO(\text{-}\text{OH})</td>
<td>2b</td>
<td>79</td>
<td>90:10</td>
</tr>
<tr>
<td><img src="image" alt="N=C=O" /></td>
<td>HO(\text{-}\text{O}^\text{-}\text{OH})</td>
<td>3b</td>
<td>71</td>
<td>92:08</td>
</tr>
<tr>
<td><img src="image" alt="N=C=O" /></td>
<td>HO(\text{-}\text{OH})</td>
<td>2c</td>
<td>73</td>
<td>51:49</td>
</tr>
<tr>
<td><img src="image" alt="N=C=O" /></td>
<td>HO(\text{-}\text{O}^\text{-}\text{OH})</td>
<td>3c</td>
<td>68</td>
<td>55:45</td>
</tr>
<tr>
<td><img src="image" alt="N=C=O" /></td>
<td>HO(\text{-}\text{OH})</td>
<td>2d</td>
<td>84</td>
<td>85:15</td>
</tr>
<tr>
<td><img src="image" alt="N=C=O" /></td>
<td>HO(\text{-}\text{O}^\text{-}\text{OH})</td>
<td>3d</td>
<td>75</td>
<td>91:09</td>
</tr>
<tr>
<td><img src="image" alt="Cl-N=C=O" /></td>
<td>HO(\text{-}\text{OH})</td>
<td>2e</td>
<td>76</td>
<td>79:21</td>
</tr>
<tr>
<td><img src="image" alt="Cl-N=C=O" /></td>
<td>HO(\text{-}\text{O}^\text{-}\text{OH})</td>
<td>3e</td>
<td>69</td>
<td>93:07</td>
</tr>
<tr>
<td><img src="image" alt="Cl-N=C=O" /></td>
<td>HO(\text{-}\text{OH})</td>
<td>2f</td>
<td>52</td>
<td>90:10</td>
</tr>
<tr>
<td><img src="image" alt="Cl-N=C=O" /></td>
<td>HO(\text{-}\text{O}^\text{-}\text{OH})</td>
<td>3f</td>
<td>48</td>
<td>91:09</td>
</tr>
</tbody>
</table>

<sup>a</sup> Approximate s-cis/s-trans ratio measured at room temperature from integration of NH NMR signals in CDCl\(_3\)/DMSO-d\(_6\) (80:20)
Figure 2: NH region of 1H NMR spectra of dicarbamates 2a (a) and 2d (b) in CDCl$_3$ + DMSO-$d_6$ at variable temperature.

Table II: Activation parameters measured for dicarbamates (2c-f).

<table>
<thead>
<tr>
<th>Product</th>
<th>$T_c$(K)</th>
<th>$\Delta \nu_c$ (Hz)</th>
<th>$\Delta p$</th>
<th>$k_s$ (s$^{-1}$)</th>
<th>$k_i$ (s$^{-1}$)</th>
<th>$k_{-i}$ (s$^{-1}$)</th>
<th>$\Delta G^#_1$ (kJmol$^{-1}$)</th>
<th>$\Delta G^{-1}_1$ (kJmol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>&gt;358</td>
<td>297.31</td>
<td>0.90</td>
<td>660.12</td>
<td>1254.23</td>
<td>66.01</td>
<td>&gt;66.96</td>
<td>&gt;75.11</td>
</tr>
<tr>
<td>2b</td>
<td>&gt;340</td>
<td>441.36</td>
<td>0.95</td>
<td>979.95</td>
<td>1910.92</td>
<td>48.99</td>
<td>&gt;62.28</td>
<td>&gt;72.56</td>
</tr>
<tr>
<td>2c</td>
<td>300</td>
<td>62.55</td>
<td>0.93</td>
<td>138.88</td>
<td>247.20</td>
<td>30.55</td>
<td>59.73</td>
<td>67.79</td>
</tr>
<tr>
<td>2d</td>
<td>315</td>
<td>100.94</td>
<td>0.83</td>
<td>224.25</td>
<td>426.08</td>
<td>22.42</td>
<td>62.57</td>
<td>68.84</td>
</tr>
<tr>
<td>2e</td>
<td>310</td>
<td>63.75</td>
<td>0.65</td>
<td>141.54</td>
<td>233.54</td>
<td>49.54</td>
<td>61.57</td>
<td>67.21</td>
</tr>
<tr>
<td>2f</td>
<td>320</td>
<td>101.41</td>
<td>0.9</td>
<td>255.16</td>
<td>427.80</td>
<td>25.51</td>
<td>62.40</td>
<td>69.93</td>
</tr>
</tbody>
</table>

$\Delta p = p_{cis} - p_{trans}.$

Table III: Activation parameters measured for dicarbamates (3c-f).

<table>
<thead>
<tr>
<th>Product</th>
<th>$T_c$(K)</th>
<th>$\Delta \nu_c$ (Hz)</th>
<th>$\Delta p$</th>
<th>$k_s$ (s$^{-1}$)</th>
<th>$k_i$ (s$^{-1}$)</th>
<th>$k_{-i}$ (s$^{-1}$)</th>
<th>$\Delta G^#_1$ (kJmol$^{-1}$)</th>
<th>$\Delta G^{-1}_1$ (kJmol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>&gt;340</td>
<td>458.78</td>
<td>0.96</td>
<td>1018.63</td>
<td>1996.52</td>
<td>40.74</td>
<td>&gt;62.15</td>
<td>&gt;73.15</td>
</tr>
<tr>
<td>3b</td>
<td>&gt;340</td>
<td>486.35</td>
<td>0.80</td>
<td>1079.85</td>
<td>1943.73</td>
<td>215.97</td>
<td>&gt;63.89</td>
<td>&gt;68.44</td>
</tr>
<tr>
<td>3c</td>
<td>318</td>
<td>6.0026</td>
<td>0.11</td>
<td>13.32</td>
<td>14.79</td>
<td>11.86</td>
<td>70.92</td>
<td>71.50</td>
</tr>
<tr>
<td>3d</td>
<td>350</td>
<td>128</td>
<td>0.32</td>
<td>284.20</td>
<td>375.14</td>
<td>193.25</td>
<td>68.93</td>
<td>70.86</td>
</tr>
<tr>
<td>3e</td>
<td>340</td>
<td>144.9</td>
<td>0.36</td>
<td>321.72</td>
<td>437.53</td>
<td>333.30</td>
<td>66.44</td>
<td>67.21</td>
</tr>
<tr>
<td>3f</td>
<td>330</td>
<td>138.1</td>
<td>0.34</td>
<td>306.62</td>
<td>410.87</td>
<td>202.37</td>
<td>64.58</td>
<td>66.52</td>
</tr>
</tbody>
</table>

$\Delta p = p_{cis} - p_{trans}.$
by the fact that the electronic effects of the R group on the barrier to rotation in dicarbamates 2a-f are more important than those due to steric hindrance in dicarbamates 3a-f (Table III). However, the latter effect could not be excluded.

In order to get more insights into the effect of substitution of oxygen by a sulfur atom on the rotation barrier around the N–CO bond in dicarbamates 2d-f, the free energies of activation and corresponding coalescence temperatures of dicarbamates 2d-f were compared with bis(thiocarbamates) 4d-f obtained from reaction of ethane-1,2-dithiol with propyl, butyl and 2-chloroethyl isocyanates, respectively [30]. The results are gathered in Table IV.

The results reveal that bis(thiocarbamates) have lower energies of activation than the corresponding dicarbamate counterparts. A straightforward difference can already be seen from their variable temperature 1H NMR spectra which show also for compound 2d two broad NH features at room temperature, whilst only one NH broad signal was observed for its bis(thiocarbamate) analog 4d at this temperature (Fig. 3). This is consistent with the less electron withdrawing nature of the S-alkyl group which would lead to a less partial double bond character of the N–CO bond giving lower barrier to rotation for the bis(thiocarbamates) compared to corresponding dicarbamates [38].

CONCLUSIONS
A series of dicarbamates 2 and 3 were synthesized from the reaction of propan-1,3- diol or triethylene glycol with aryl/alkyl isocyanates. These products were obtained in good to excellent yields and characterized by different spectroscopic techniques. The effects of the N-substituent on the s-cis/s-trans conformation was studied using VT NMR spectroscopy and showed that the rotation around N–CO bond is slower for electron withdrawing groups compared to donor substituents with a more remarkable effect for dicarbamates as compared to bis(thiocarbamates).

EXPERIMENTAL
All commercially available chemicals including starting isocyanates and diols were used without any purification. All solvents were dried, distilled, and stored over molecular sieves (4A°). Melting points were measured using an “Electrothermal 9100” apparatus and are uncorrected. 1H (300 MHz) and 13C (75.47 MHz) NMR spectra were recorded with a Bruker AC 300 spectrometer. The VT NMR spectra were recorded with a Bruker AC 400 apparatus. Probe temperatures (±0.5 K) were measured with a calibrated digital thermocouple. TMS was used as the internal standard for 1H and 13C NMR spectroscopy. Infrared spectra were obtained on a

![Figure 3: The NH region of 1H NMR spectra of bis(thiocarbamate) 4d (a) and its dicar-bamate analogues 2d (b) in CDCl3 + DMSO-d6 at room temperature.](image-url)
YL2000 FT-IR spectrometer. HRMS (ESI) data were recorded on a high-resolution Micromass microTOF-Q II 10027 spectrometer.

1. General procedure for the preparation of dicarbamates (2a-f and 3a-f):

To a solution of isocyante (20 mmol) in 10 mL of dry THF, was added the diol (10 mmol) under nitrogen atmosphere and at room temperature. The reaction mixture was stirred for 48 h to obtain a cloudy solution. Then, 30 mL of petroleum ether was added and the mixture was stirred for few hours to have a white precipitate, which was filtered to give white solids. These products were purified by recrystallization in (CCl3) to give white powders. Compounds 2a, 3a and 3b were prepared as previously described [31-34].

**Propylene-1,3-bis(N-benzylcarbamate) (2b).**

White solid; mp 127.1°C; IR (CHCl3) (υN-H) 3332, (υC=O)1684, (υC,N) 1265 cm⁻¹; ¹H NMR (DMSO+CDCl3, 400 MHz) δ 1.88(m, 2H), 4.08(t, 3JH,H= 6Hz, 4H), 4.215(d, 3JH,H = 6Hz, 4H), 6.65 (broad signal (NH, s-trans)), 6.89(broad signal (NH, s-cis)), 7.15-7.25(m, H arom); ¹³C NMR (DMSO+CDCl3, 75 MHz) δ 28.44, 44.04, 60.91, 126.54, 126.85, 127.93, 139.07, 156.34; HRMS (M+Na⁺) calecd for C19H18N3NaO4, 365.1469, found 365.1458.

**Propylene-1,3-bis(N-cyclohexylcarbamate) (2c).**

White solid; mp 116.8°C; IR (CHCl3) (υN-H) 3324, (υC=O)1684, (υC,N) 1229 cm⁻¹; ¹H NMR (DMSO+CDCl3, 300 MHz) δ 1.12-1.77(m, 20H), 1.83(m, 2H), 3.23(m, 2H), 3.99(t, 3JH,H= 8Hz, 4H), 6.84(broad signal (NH)); ¹³C NMR (DMSO+CDCl3, 75 MHz) δ 24.60, 25.13, 28.65, 32.64, 49.37, 60.35, 155.25; HRMS (M+Na⁺) calecd for C17H22N2NaO4, 349.2093, found 349.2099.

**Propylene-1,3-bis(N-propylcarbamate) (2d).**

White solid; mp 73.7°C; IR (CHCl3) (υN-H) 3285, (υC=O)1682, (υC,N) 1250 cm⁻¹; ¹H NMR (DMSO+CDCl3, 400 MHz) δ 0.82(t, 3JH,H= 6Hz, 8H), 1.42(m, 4H), 1.44(m, 2H), 2.99(m, 4H), 4.03 (m, 4H), 5.6(broad signal (NH, s-trans)), 5.84 (broad signal (NH, s-cis)); ¹³C NMR (DMSO+CDCl3, 75 MHz) δ 11.23, 11.37, 22.9, 23.44, 28.8, 41.36, 42.32, 60.78, 76.50, 158.74; HRMS (M+Na⁺) calecd for C11H22N2NaO4 269.1474, found 269.1474.

**Propylene-1,3-bis(N-butylcarbamate) (2e).**

White solid; mp 97.9°C; IR (CHCl3) (υN-H) 3290, (υC=O) 1682, (υC,N) 1261 cm⁻¹; ¹H NMR (DMSO+CDCl3, 300 MHz) δ 0.88(t, 3JH,H= 6Hz, 6H), 1.22-1.44(m, 8H), 1.84(m, 2H), 2.98(q, 3JH,H= 6Hz, 4H), 4.01(t, 3JH,H=6Hz, 4H), 6.6(broad signal, (NH, s-trans)), 6.87(broad signal, (NH, s-cis)); ¹³C NMR (DMSO+CDCl3, 75 MHz) δ 13.48, 19.36, 28.65, 31.5, 40.45, 60.39, 156.09; HRMS (M+Na⁺) calecd for C13H26N2NaO4 297.1781, found 297.1785.

**Propylene-1,3-bis(N-2-chloroethyl carbamate) (2f).**

White solid; mp 87°C; IR (CHCl3) (υN-H) 3316, (υC=O)1687, (υC,N) 1257 cm⁻¹; ¹H NMR (DMSO+CDCl3, 400 MHz) δ 1.85(m, 2H), 3.305 (m, 4H), 3.46(m, 4H), 4.03(m, 4H), 6.76(broad signal (NH, s-trans)), 7.04(broad signal (NH, s-cis)); ¹³C NMR (DMSO+CDCl3, 75 MHz) δ 28.45, 41.40, 43.08, 57.37, 58.12, 60.76, 156.13, 156.34; HRMS (M+Na⁺) calecd for C9H11Cl2N2NaO4 309.0385, found 309.0373.

3.6-Diazoctylene-1,8-bis(N-cyclohexylcarbamate) (3c).

White solid; mp 81.2°C; IR (CHCl3) (υN-H) 3329, (υC=O)1683, (υC,N) 1224 cm⁻¹; ¹H NMR (DMSO+CDCl3, 300 MHz) δ 1.06-1.68(m, 20H), 3.28(s, 4H), 3.37-3.56(m, 10H), 4.01(t, 3JH,H= 4.5Hz, 4H), 7.10(d, 3JH,H= 6Hz (NH)); ¹³C NMR (DMSO+CDCl3, 75 MHz) δ 24.81, 25.22, 32.85, 49.60, 69.23, 70.03, 155.47; HRMS (M+Na⁺) calecd for C9H10Cl2N2NaO4 423.2471, found 423.2467.

3.6-Diazocyctylene-1,8-bis(N-propylcarbamate) (3d).

White solid; mp 95.9°C; IR (CHCl3) (υN-H) 3322, (υC=O)1684, (υC,N) 1254 cm⁻¹; ¹H NMR (DMSO+CDCl3, 400 MHz) δ 0.89(t, 3JH,H= 8Hz, 8H), 1.50(sextuplet, 3JH,H= 8Hz, 4H), 3.05(m, 4H), 3.61(s, 4H), 3.65(t, 3JH,H= 4Hz, 4H), 4.16(t, 3JH,H= 4Hz, 4H), 5.78(broad signal (NH, s-trans)), 6.11(broad signal (NH, s-cis)); ¹³C NMR (DMSO+CDCl3, 75 MHz) δ 11.22, 22.82, 42.29, 63.08, 69.29, 72.60, 156.39; HRMS (M+Na⁺) calecd for C11H22N2NaO5S 343.1845, found 343.1845.

3.6-Diazoctylene-1,8-bis(N-butylcarbamate) (3e).

White solid; mp 56.8°C; IR (CHCl3) (υN-H) 3314, (υC=O)1683, (υC,N) 1259 cm⁻¹; ¹H NMR (DMSO+CDCl3, 400 MHz) δ 0.85(t, 3JH,H= 6Hz, 6H), 1.255(sextuplet, 3JH,H= 8Hz, 4H), 1.37 (quintet, 3JH,H= 8Hz, 4H), 2.97(q, 3JH,H= 8Hz, 4H), 3.52(s, 4H), 3.555(m, 4H), 4.05(t, 3JH,H= 4Hz, 4H), 6.46(broad signal (NH, s-trans)), 6.84(broad signal (NH, s-cis)); ¹³C NMR (DMSO CDCl3, 75 MHz) δ 13.66, 19.57, 31.64, 40.08, 60.49, 62.99, 69.96 115.89, 156.26; HRMS (M+Na⁺) calecd for C15H32N2NaO6 371.58, found 371.2145.
3,6-Dioxaoctylene-1,8-bis(N-2-chloroethylcarbamate) (3f).
White solid; mp 61.6°C; IR (CHCl₃) (υN-H) 3303, (υC=O) 1692, (υC-N) 1256 cm⁻¹; ¹H NMR (DMSO+CDCl₃, 400 MHz) δ 3.43 (m, 4H), 3.51-3.59 (m, 12H), 4.11 (m, 4H), 6.62 (broad signal (NH, s-trans)), 6.95 (broad signal (NH, s-cis)); ¹³C NMR (DMSO+CDCl₃, 75 MHz) δ 30.17, 35.29, 50.60, 67.18, 70.31, 162; HRMS (M+Na⁺) calc for C₁₂H₂₂Cl₂N₂NaO₆ 383.0753, found 383.0746.

REFERENCES