SYNTHESIS OF NEW 1-HEPTA-O-BENZOYL-β-D-LACTOSYL-3-ARYL THIOCARBAMIDES

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ABSTRACT

A series of new 1-hepta-O-benzoyl-β-D-lactosyl-3-aryl thiocarbamides have been synthesized by the interaction of hepta-O-benzoyl-β-D-lactosyl isothiocyanate with aryl amines. The identities of these new N-lactosides have been established on the basis of usual chemical transformations and IR, NMR and Mass spectral studies.

Key words: 1-hepta-O-benzoyl-β-D-lactosyl-3-aryl thiocarbamides, Aryl Amine, N-lactoside, IR, NMR, Mass.

INTRODUCTION

Thiocarbamides and their derivatives show strong antimicrobial activity and are also versatile reagent in organic synthesis1. Although they have been known from long ago to be biologically active2-4. Their varied biological features are still of great scientific interest. Some derivatives of these possess antituberculosis, anticancer, antitumor, antipyretic activities5,6.

In view of applications of thiocarbamides and its derivatives in medicinal chemistry and in many other ways, we herein report the synthesis of several 1-hepta-O-benzoyl-β-D-lactosyl-3-aryl thiocarbamides (4a-g) by the condensation of hepta-O-benzoyl-β-D-lactosyl isothiocyanate (2) with aryl amines (3a-g). The required lactosyl isothiocyanate was prepared by the reaction of hepta-O-benzoyl-α-D-lactosyl bromide (1) with lead thiocyanate7 (Scheme 1).

Scheme 1
P. T. Agrawal and S. P. Deshmukh: Synthesis of New 1-Hepta-O-Benzoyl-\(\beta\)-D-lactosyl-3-aryl thiocarbamides (4 a-g) (Scheme 2) (Table 1)

A mixture of hepta-O-benzoyl-\(\beta\)-D-lactosyl isothiocyanate (2) (0.005, 5.5 g in 35 mL) and (0.005 M, 0.46 g) of aryl amines (3a-g) in 30 mL of benzene was refluxed for 3 h while monitoring by TLC. After completion of the reaction, the solvent was triturated with petroleum ether (60-80°C) to afford a white solid (4 a-g). The products were purified from acetone- petroleum ether.

4a. m.p. 128-132°C; yield 76%, [\(\alpha\)]\(28^D\) +190\(^0\) (c, 1.1 in CHCl\(_3\)); IR (KBr): 3458 cm\(^{-1}\) (NH), 3066 cm\(^{-1}\) (Ar-H), 1729 cm\(^{-1}\) (C=O), 1271 cm\(^{-1}\) (C-N), 1176 cm\(^{-1}\) (C-O), 1096 cm\(^{-1}\) (C=S), 1068, 909 cm\(^{-1}\) (characteristic of lactose), 708 cm\(^{-1}\) (monosubstituted benzene); \(^1\)H NMR (ppm) : \(\delta 8.05-7.18\) (40H, m, aromatic protons), 5.91-3.79 (16H, m, 14 lactosyl protons, 2-NH protons); Mass (m/z): 1204 (M\(^{+}\)), 1145 (M-CH\(_3\)COOH), 1100 (M-CH\(_3\)COOH CH\(_2\)CO), 1052 (HBL\(^{+}\)), 579 (TBG\(^{+}\)), 391 (TBG\(^{+}\)-C\(_{12}\)H\(_{12}\)O\(_2\)), 335 (TBG-C\(_{14}\)H\(_{12}\)O\(_4\)), 105 (C\(_6\)H\(_5\)CO\(^{+}\)); Anal. Calcd for C\(_{68}\)H\(_{56}\)O\(_{17}\)N\(_2\)S: C, 67.77; H, 4.65; N, 2.32; S, 2.65%; Found: C, 67.70; H, 4.59; N, 2.30; S, 2.60%.

4b. m.p. 130-135°C; yield 79%, [\(\alpha\)]\(28^D\) +250\(^0\) (c, 1.11 in CHCl\(_3\)); IR (KBr): 3446 cm\(^{-1}\) (NH), 3068 cm\(^{-1}\) (Ar-H), 1728 cm\(^{-1}\) (C=O), 1271v (C-N), 1176 cm\(^{-1}\) (C-O), 1097 cm\(^{-1}\) (C=S), 1026, 909 cm\(^{-1}\) (characteristic of lactose), 710 cm\(^{-1}\) (monosubstituted benzene); \(^1\)H NMR (ppm) : \(\delta 8.04-7.17\) (39H, m, aromatic protons), 5.92-3.79 (16H, m, 14 lactosyl protons, 2 NH protons), 2.28 (3H, s, -CH\(_3\)); Mass (m/z): 1218 (M\(^{+}\) + 1), 1159 (M-CH\(_3\)COOH), 1052 (HBL\(^{+}\)), 579 (TBG\(^{+}\)), 391 (TBG\(^{+}\)-C\(_{12}\)H\(_{12}\)O\(_2\)), 335 (TBG-C\(_{14}\)H\(_{12}\)O\(_4\)), 105 (C\(_6\)H\(_5\)CO\(^{+}\)); Anal. Calcd for C\(_{68}\)H\(_{58}\)O\(_{17}\)N\(_2\)S: C, 67.98; H, 4.65; N, 2.29; S, 2.56%; Found: C, 67.88; H, 4.69; N, 2.28; S, 2.56%.
4e. m.p. 145-150°C; yield 88%, $[\alpha]^{28}_{D} +170^0$ (c, 1.11 in CHCl$_3$); IR (KBr): 3444 cm$^{-1}$ (NH), 2949 cm$^{-1}$ (Ar-H), 1728 cm$^{-1}$ (C=O), 1272 cm$^{-1}$ (C-N), 1176 cm$^{-1}$ (C-O), 1097 cm$^{-1}$ (C=S), 1026, 907 cm$^{-1}$ (characteristic of lactose), 710 cm$^{-1}$ (monosubstituted benzene); $^1$H NMR (ppm) : δ 8.05-7.18 (39H, m, aromatic protons), 5.93-3.77 (16H, m, 14 lactosyl protons, 2 NH protons); Mass (m/z) : 1238 (M$^+$), 1178 (M-CH$_3$COOH), 1052 (HBL$^+$), 579 (TBG$^+$), 391 (TBG$^+$ -C$_{12}$H$_{12}$O$_2$), 335 (TBG-C$_{14}$H$_{12}$O$_4$), 105 (C$_5$H$_3$CO$^+$); Anal. calcd for C$_{68}$H$_{55}$O$_{17}$N$_2$SCl: C, 65.85; H, 4.43; N, 2.25; S, 2.58%; Found: C, 65.80; H, 4.40; N, 2.23; S, 2.54%.

Table 1: 1-hepta-O-benzoyl-β-D-lactosyl-3-aryl thiocarbamides (4 a-g)

<table>
<thead>
<tr>
<th>Product</th>
<th>Melting point °C</th>
<th>% Yield</th>
<th>Analysis found (requires)</th>
<th>[α]$^{28}_{D}$ (c,0.15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>128-132</td>
<td>76</td>
<td>2.30 (2.32) 2.60 (2.65)</td>
<td>+190$^0$</td>
</tr>
<tr>
<td>4b</td>
<td>130-135</td>
<td>79</td>
<td>2.28 (2.29) 2.56 (2.56)</td>
<td>+250$^0$</td>
</tr>
<tr>
<td>4c</td>
<td>155-160</td>
<td>80</td>
<td>2.30 (2.29) 2.51 (2.56)</td>
<td>+140$^0$</td>
</tr>
<tr>
<td>4d</td>
<td>145</td>
<td>76</td>
<td>2.27 (2.29) 2.53 (2.56)</td>
<td>+180$^0$</td>
</tr>
<tr>
<td>4e</td>
<td>145-150</td>
<td>88</td>
<td>2.23 (2.25) 2.54 (2.58)</td>
<td>+170$^0$</td>
</tr>
<tr>
<td>4f</td>
<td>130</td>
<td>87</td>
<td>2.21 (2.25) 2.59 (2.58)</td>
<td>+140$^0$</td>
</tr>
<tr>
<td>4g</td>
<td>148</td>
<td>76</td>
<td>2.24 (2.25) 2.56 (2.58)</td>
<td>+170$^0$</td>
</tr>
</tbody>
</table>

RESULTS AND DISCUSSION

1-hepta-O-benzoyl-β-D-lactosyl-3-aryl thiocarbamides (4 a-g) were prepared by the condensation of 1-hepta-O-benzoyl-β-D-lactosyl isothiocyanate 2 with aryl amines (3a-g) in benzene medium for 3 h. Then, the solvent was distilled off and sticky residue obtained was triturated with petroleum ether (60-80°C) to afford a white solid (4a-g). The structure of the products were confirmed on the basis of IR, NMR and Mass spectral analysis. The specific rotation of the products were also recorded.

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REFERENCES


