SHORT PAPER

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A facile method for the synthesis of hepta-O-acetyl-β-D-lactosyl substituted benzoates†

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Hepta-O-acetyl-β-D-lactosyl substituted benzoates were synthesised by the condensation of acetobromolactose with substituted benzoic acids in DMF at room temperature in the presence of Et_3N.

Keywords: hepta-O-acetyl-β-D-lactosyl substituted benzoates

In recent years, a steadily increasing research effort has centred on the production of glycosyl esters and glycosides because these compounds have been shown to possess many different biological activities.[1,2] The synthesis of these compounds has been widely reported[3–7] including that of lactosides.[8–12] However, the synthesis of lactosyl ester has not been reported. Here we describe a new simple, mild and stereospecific method for the synthesis of lactosyl esters in the presence of Et_3N. The results are listed in Scheme 1 and Table 1.

Table 1 Yields m.p. and ^{1}H NMR spectra of compounds **3a–3g**

Compd	Ar	Yield/%	m.p./°C	^{1}H NMR (H-1 ppm) ($J_{1,2}$Hz)
3a	2-FC_6H_4	58	92–93	5.89 (8.1)
3b	3-FC_6H_4	62	90–92	5.82 (7.6)
3c	4-FC_6H_4	59	94–96	5.85 (7.8)
3d	2,3,4,5-F_4C_6H	65	88–89	5.86 (7.5)
3e	C_6H_5	64	90–91	5.82 (7.9)
3f	4-$NO_2C_6H_4$	70	105–106	5.86 (7.9)
3g	4-$C_2H_5OC_6H_4$	52	97–98	5.87 (7.7)

Lactosyl benzoates (**3a–3g**) were readily prepared by the condensation of acetobromolactose (**1**) with substituted benzoic acids (**2**) with a slight excess of Et_3N at room temperature. The best results were obtained with DMF as the solvent and 1.2 equivalent of Et_3N. The use of ethyl acetate or acetonitrile instead of DMF greatly reduced the yields. The operation of this method is very easy, and the products were purified by simple crystallisation from ethanol in good yields.

The IR data for the lactosyl benzoates has the characteristic absorption of the lactose units in the range of 900–910,1000–1100 and 1200–1300 cm^{-1}.[13] The coupling constants of the anomeric protons of the lactosyl benzoates ranged from 7.5 to 8.1 Hz, and indicated that the glycosidic linkage between lactose units and benzoic acid had the β-configuration.[14,15]

Experimental

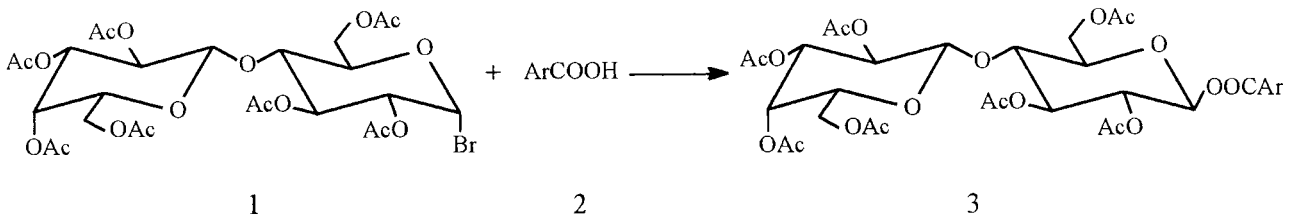
Melting points were determined on a Laboratory Devices Mel-temp apparatus and are uncorrected. The IR spectra (KBr) were recorded on a NICOLET 170SX FT-IR spectrophotometer; the ^{1}H NMR was obtained on a Varian Mercury-VX300 NMR spectrometer for sample in $CDCl_3$ solution with TMS as internal reference. The mass spectra were taken on a ZAB-3F mass spectrometer. The elemental analysis was determined on a Carlo Erba 1106 elementary analyzer. 2,2′,3,3′,4′,6,6′-Hepta-O-acetyl-α-D-lactosyl bromide was prepared according to the literature.[16] Substituted benzoic acids were obtained commercially, and were not purified before use.

General procedure: A solution of the substituted benzoic acid **(2)** (2.0mmol), freshly prepared hepta-O-acetyl-α-D-lactosyl bromide (**1**) (2.0mmol), Et_3N (2.4mmol) in DMF (20ml) was stirred at room temperature for 6–8h. It was then evaporated under reduced pressure to remove DMF. Ether (20ml) was added, filtered and the filtrate was evaporated under reduced pressure to afford the crude lactosyl benzoates (**3a–3g**). The products are purified by crystallisation from ethanol.

Compound **3a**: IR: 2965, 1749, 1605, 1509, 1234, 1074, 901 cm^{-1}. ^{1}H NMR: δ (ppm) 1.97–2.16 (m, 21H, 7OAc), 3.72–3.93 (m, 3H, H-4, H-5 and H-5′), 4.05–4.17 (m, 3H, 2H-6′ and H-6), 4.46 (d, 1H, $J_{1',2'}$=7.2Hz, H-1′), 4.50 (m, 1H, H-6), 4.97 (m, 1H, H-2), 5.12 (m, 1H, H-3′), 5.22 (m, 1H, H-2′), 5.32 (m, 1H, H-3), 5.35 (m, 1H, H-4′), 5.89 (d, 1H, $J_{1,2}$=8.1Hz, H-1), 7.55–7.91 (m, 4H, ArH). MS (FAB) 757 (M+–1). Anal. Calcd. for $C_{33}H_{39}FO_{19}$ C 52.24; H 5.15; Found: C 52.42; H 5.09

Compound **3b**: IR: 2964, 1753, 1593, 1487, 1231, 1071, 908 cm^{-1}. ^{1}H NMR: δ (ppm) 1.95–2.13 (m, 21H, 7OAc), 3.66–3.87 (m, 3H, H-4, H-5 and H-5′), 4.08–4.23 (m, 3H, 2H-6′ and H-6), 4.44(d, 1H, $J_{1',2'}$=7.2Hz, H-1′), 4.52 (m, 1H, H-6), 4.94 (m, 1H, H-2), 5.13 (m, 1H, H-3′), 5.27 (m, 1H, H-2′), 5.33 (m, 1H, H-3), 5.36 (m, 1H, H-4′), 5.82 (d, 1H, $J_{1,2}$=7.6Hz, H-1), 7.21–8.06 (m, 4H, ArH).

Compound **3c**: IR: 2966, 1748, 1614, 1584, 1234, 1074, 901 cm^{-1}. ^{1}H NMR: δ (ppm) 1.97–2.15 (m, 21H, 7OAc), 3.74–3.90 (m, 3H, H-4, H-5 and H-5′), 4.05–4.17 (m, 3H, 2H-6′ and H-6), 4.46(d, 1H, $J_{1',2'}$=7.2Hz, H-1′), 4.50 (m, 1H, H-6), 4.96 (m, 1H, H-2), 5.11 (m,



1 2 3

Scheme 1

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

1H, H-3′), 5.24 (m, 1H, H-2′), 5.30 (m, 1H, H-3), 5.36 (m, 1H, H-4′), 5.85 (d, 1H, $J_{1,2}$=7.8Hz, H-1), 7.12–8.05 (m, 4H, ArH).

Compound **3d**: IR: 1754, 1630, 1529, 1223, 1051, 908 cm^{-1}. ^{1}H NMR: δ (ppm) 1.97–2.16 (m, 21H, 7OAc), 3.69–3.88 (m, 3H, H-4, H-5 and H-5′), 4.05–4.12 (m, 3H, 2H-6′ and H-6), 4.47 (d, 1H, $J_{1',2'}$=7.2Hz, H-1′), 4.50 (m, 1H, H-6), 4.97 (m, 1H, H-2), 5.11 (m, 1H, H-3′), 5.20 (m, 1H, H-2′), 5.32 (m, 1H, H-3), 5.36 (m, 1H, H-4′), 5.86 (d, 1H, $J_{1,2}$=7.5Hz, H-1), 7.61 (m, 1H, ArH).

Compound **3e**: IR: 1752, 1605, 1509, 1231, 1069, 901 cm^{-1}. ^{1}H NMR: δ (ppm) 1.95–2.16 (m, 21H, 7OAc), 3.72–3.91 (m, 3H, H-4, H-5 and H-5′), 4.02–4.17 (m, 3H, 2H-6′ and H-6), 4.46 (d, 1H, $J_{1',2'}$=7.2Hz, H-1′), 4.50 (m, 1H, H-6), 4.97 (m, 1H, H-2), 5.14 (m, 1H, H-3′), 5.24 (m, 1H, H-2′), 5.28 (m, 1H, H-3), 5.36 (m, 1H, H-4′), 5.82 (d, 1H, $J_{1,2}$=7.9Hz, H-1), 7.55–8.12 (m, 5H, ArH).

Compound **3f**: IR: 1753, 1609, 1532, 1227, 1052, 902 cm^{-1}. ^{1}H NMR: δ (ppm) 1.96–2.13 (m, 21H, 7OAc), 3.69–3.87 (m, 3H, H-4, H-5 and H-5′), 4.05–4.14 (m, 3H, 2H-6′ and H-6), 4.43 (d, 1H, $J_{1',2'}$=7.2Hz, H-1′), 4.53 (m, 1H, H-6), 4.89 (m, 1H, H-2), 5.11 (m, 1H, H-3′), 5.25 (m, 1H, H-2′), 5.33 (m, 1H, H-3), 5.38 (m, 1H, H-4′), 5.86 (d, 1H, $J_{1,2}$=7.9Hz, H-1), 7.92–8.33 (m, 4H, ArH).

Compound **3g**: IR: 2965, 1754, 1609, 1509, 1231, 1074, 904 cm^{-1}. ^{1}H NMR: δ (ppm) 1.98–2.16 (m, 21H, 7OAc), 3.72–3.94 (m, 3H, H-4, H-5 and H-5′), 4.06–4.17 (m, 3H, 2H-6′ and H-6), 4.44 (d, 1H, $J_{1',2'}$=7.2Hz, H-1′), 4.50 (m, 1H, H-6), 4.99 (m, 1H, H-2), 5.10 (m, 1H, H-3'), 5.22 (m, 1H, H-2′), 5.30 (m, 1H, H-3), 5.35 (m, 1H, H-4′), 5.87 (d, 1H, $J_{1,2}$=7.7Hz, H-1), 6.92–7.89 (m, 4H, ArH).

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