Improved method for the synthesis of 1- or 3-acyl-sn-glycerols

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Summary
Optically active 1- or 3-acyl-sn-glycerols were synthesized from 2,3- or 1,2-isopropylidene-n-glycerols, respectively. The 2,3- or 1,2-isopropylidene-n-glycerols were condensed with appropriate long saturated or unsaturated fatty acids and the resulting acyl isopropylidene compounds were treated with dimethylboronbromide at ~50°C to give the title compounds. The keto cleavage of acyl isopropylidene-n-glycerols by dimethylboronic acid to produce the long 1- or 3-acyl-n-sn-glycerols was effective and gave good yields (70–90%). The reaction conditions were mild and there was no acyl migration, as shown by optical rotation of the monoacyl-n-sn-glycerols. The synthesis of 2,3-isopropylidene-n-m-glycerol was improved to give an overall yield of 40% from L-arabinose. L-Arabinose was first converted to its 1,1'-diethylmercapto derivative and then condensed with 2-methoxypropene to yield 1,1'-diethyl-mercapto-4,5-isopropylidene-L-arabinose. Oxidation of this compound with sodium periodate followed by reduction with sodium borohydride under alkaline conditions yielded 2,3-isopropylidene-n-m-glycerol \([\alpha]_{D}^{20} = -14.9^\circ\), neat (Lit. \(85^\circ\)), neat; 14 \([\alpha]_{D}^{20} = -10.8^\circ\); methanol C, 16.9). The optical purity of isopropylidene-n-m-glycerols was determined as benzoyl derivatives on a high performance liquid chromatographic column packed with a chiral stationary phase. – Kodali, D. R. Improved method for the synthesis of 1- or 3-acyl-sn-glycerols. J. Lipid Res. 1987. 28: 464 – 469.

Supplementary key words
monoacylglycerols • isopropylidene-n-glycerols • dimethylboronbromide • keto cleavage • enantiomeric separation

The general intermediates required for the chemical synthesis of optically active mono-, di-, and triacylglycerols and various phospholipids are 1,2-isopropylidene-n-glycerol and 2,3-isopropylidene-n-glycerol. Both these compounds are equally important as they provide access to the 3- or 1-hydroxy positions of n-glycerol.

The synthesis of optically active 1- or 3-acyl-sn-glycerols can be accomplished by the keto cleavage of the corresponding 2,3- or 1,2-isopropylidene-n-glycerol acyl derivatives. The acid hydrolysis of isopropylidene com-

The fatty acids lauric, palmitic, stearic, behenic, lignoceric, oleic, and linoleic acids and 1(1)-arabinose were purchased from Sigma Chemical Company (St. Louis, MO). Ethanethiol, DCC, DMAP, PTS, zinc chloride, sodium borohydride, and 2-methoxypropene were purchased from Aldrich Chemical Company (Milwaukee, WI). The solvents used were HPLC grade from Fisher Scientific Company (Medford, MA), except carbon tetrachloride, N,N-dimethylformamide, and dichloromethane which were Gold Label from Aldrich Chemical Company (Milwaukee, WI).

The melting temperatures were determined as peak transition temperatures on a Perkin-Elmer (Norwalk, CT) DSC-2 differential scanning calorimeter. The optical rotations were taken on an automatic polarimeter, Autopol-I1 (Rudolph Research, Flanders, NJ).

The purities of the intermediates and the final compounds were checked by TLC and HPLC. The structures of the final compounds were confirmed by \(^{1}H\) and \(^{13}C\) nuclear magnetic resonance spectroscopy. The analytical TLC was done on silica gel GHLF 250 micron plates, and the preparative TLC was done on Silicagel GF 100µm plates (Analtech, Newark, DE). The boric acid-impregnated TLC plates were prepared by the immersion of the TLC plates in 2.5% boric acid solution. The plates were air-dried and activated at 100°C for 1 hr. NMR spectra were recorded on a Bruker 200 MHz spectrometer with chemical shifts reported in parts per million relative to tetramethylsilane as internal standard.

HPLC was done on a Varian 5000 liquid chromatograph (Varian Associates, Palo Alto, CA), connected to a...
Fig. 1. Reaction sequence for the synthesis of 1-acyl-sn-glycerol from L-(+)-arabinose.

Varian UV-50 detector and a Hewlett-Packard 3390A integrator. The following conditions, column, and solvent system were used for the analysis of the monoacylglycerols. The column used was a 4.6 mm x 25 cm Altex C18 bonded (Rainin Instrument Co., Inc., Woburn, MA) with a flow rate of 1.2 ml/min. UV absorption detection was at 215 nm. The solvents used were a gradient elution changing from an initial composition of water-isopropanol-acetonitrile-tetrahydrofuran 23:5:65:15 (v/v) over 30 min to a final composition of 0:70:27:0 (v/v). The following conditions, column, and solvent system were used for the optical purity determination of the enantiomeric isopropylidene-sn-glycerol. The column used was 'Chiralcel-OB' 4.6 mm x 25 cm (J. T. Baker Chemical Company, Phillipsburg, NJ) with a flow rate of 0.5 ml/minute. The UV absorption detection was at 229 nm and the solvent system was an isocratic elution of a mixture of hexane-isopropanol 95:5 (v/v).

1,2-Isopropylidene-sn-glycerol was synthesized from D-mannitol by the procedure of Baer and Fisher (4) as modified by Eibl (5).

Dimethylboronbromide was prepared according to the procedure reported in the literature (6). In brief, equimolar quantities of borontribromide and tetramethyltin were allowed to react under an inert atmosphere (argon). The resulting dimethylboronbromide was distilled and stored at ~20°C as a 2.5 M solution in dichloromethane under argon until used.

SYNTHESIS

1,1'-Diethylmercapto-L-arabinose (I)

Zinc chloride (75 g) was dissolved in ethanethiol (250 ml) by stirring at 10°C and L-(+)-arabinose (90 g) was added to this reaction mixture in portions of 15 g by vigorous stirring. After the addition was complete, the reaction mixture was left at room temperature for 5 hr. By this time the L-arabinose was completely converted to its 1,1'-diethylmercapto derivative as shown by TLC (ethyl acetate-methanol 10:3). The unreacted ethanethiol was removed under reduced pressure. The product was dissolved in the minimum amount of methanol (~250 ml) and filtered. Crushed ice (1 kg) was added to the filtrate with stirring and the white crystalline solid that precipitated was filtered and dried. The product was pure; however, it was crystallized from ethanol-water 50:50 (v/v) at 0°C yielding 146 g (95%); mp 127°C [α]_D^22 = +11.2° (methanol C, 5).
1,1'-Diethylmercapto-4,5-isopropylidene-L-arabinose (II)

1,1'-Diethylmercapto-L-arabinose 25.6 g (0.1 mol) was dissolved in dry N,N-dimethylformamide (100 ml) and the temperature was brought to 0-5°C. Drierite (2 g) and PTS (200 mg) were added to the reaction mixture followed by 2-methoxypropene 7.2 g (0.1 mol) dropwise with stirring. The reaction was stirred for 15 min after the addition was complete and monitored by TLC (CHCl₃ - CH₂OH 6:1). As the TLC showed the presence of some starting material, an additional 2.9 g (0.04 mol) of 2-methoxypropene was added dropwise and stirred for 1 hr. By this time, the reaction was complete and was stopped by the addition of 5 g of sodium carbonate and stirred for 10 min and filtered. The filtrate was poured on crushed ice. The precipitate produced was filtered and air-dried. The product was pure by TLC; however, it was crystallized from isopropyl ether (100 ml, at 0°C). mp 77°C, (Lit. ref. 7 mp 75.6°C); yield 24 g (81%) \( [\alpha]_D^20 = +7.5^\circ \) (methanol C, 8.5) (Lit. ref. 7, \( [\alpha]_D^26 = +7.6^\circ \) methanol C, 8.5).

2,3-Isopropylidene-sn-glycerol (III)

Sodium periodate (64.2 g; 0.3 mol) was dissolved in distilled water (600 ml) and was chilled in an ice-salt bath to 0°C. To this solution, 29.6 g of 1,1'-diethylmercapto-4,5-isopropylidene-L-arabinose (0.1 mol) was added in portions over about 20 min while stirring. During the addition, the temperature was kept below 15°C. After the addition was complete, the reaction mixture was stirred for an additional 15 to 20 min. To the thick red reaction mixture, ethanol (1 liter) was added to precipitate sodium hydroxide (which was ~4.4) was adjusted to 8.0 by the addition of sodium hydroxide (10%) solution (~40-45 ml required). To the light yellow solution, 15.2 g of sodium borohydride (0.4 mol) was added in portions and was stirred for 30-40 min at room temperature. The reaction was stopped by the addition of 25 g of sodium chloride. The reaction mixture was diluted by the addition of 250 ml of distilled water and then extracted with chloroform repeatedly (3-4 times). The organic extracts were combined and washed with water and dried over sodium sulfate. The solvents were evaporated and the product was distilled under vacuum. 2,3-Isopropylidene-sn-glycerol distilled at 45°C (at ~0.25 mm), Lit. ref. 8, bp 94-95°C (15 mm), yield = 7.2 g (54.5%) \( [\alpha]_D^22 = -14.3^\circ \) (neat). Optical rotation was improved on redistillation to ~14.9° (neat). (Lit. ref. 8, \( [\alpha]_D^22 = -14.5^\circ \) neat; 14 \( [\alpha]_D^22 = -10.8^\circ \) methanol C, 16.9; 15 \( [\alpha]_D^22 = -13.4^\circ \) neat). 1H NMR (CDCl₃) δ1.36 (3H, s, CH₃), 1.44 (3H, s, CH₃), 2.79 (1H, broad s, OH), 3.7-4.2 (5H, m, 2CH₂O and CH₂O); 13C NMR (CDCl₃) δ25.30, 26.73 (C-(CH₃)₂), 63.07, 65.81, 76.27 (glycerol 2C_H₂ and C_H, 109.48 (C(CH₃)₂). The enantiomeric purity of the isopropylidene-sn-glycerols were determined as their benzoyl derivatives. The benzoyl derivatives of 1,2-isopropylidene-sn-glycerol, 2,3-isopropylidene-sn-glycerol, and racemic isopropylidene glycerol were synthesized by the condensation of equimolar amounts of isopropylidene compound with benzoic acid in the presence of DCC and DMAP. The compounds thus prepared were purified by preparative TLC (solvent system hexane-isopropyl ether 50:50, v/v). The optical rotation of 1,2-isopropylidene-3-benzoyl-sn-glycerol was \( [\alpha]_D^22 = +9.9^\circ \) (chboroform, C, 10), Lit. ref. 4, \( [\alpha]_D^22 = +12.3^\circ \) (neat) and that of 1-benzoyl-2,3-isopropylidene-sn-glycerol was \( [\alpha]_D^22 = -9.9^\circ \) (chloroform, C, 10). The 1H and 13C NMR spectra of the enantiomers and the racemic mixture were identical. 1H NMR (CDCl₃) δ1.40 (3H, s, C-CH₃), 1.47 (3H, s, C-CH₃), 3.80-4.50 (5H, m, C-2CH₂O and CH₂O), 7.40-8.10 (5H, m, -C₆H₅); 13C NMR (CDCl₃) δ28.39, 26.76 (C-(CH₃)₂) 65.06, 66.44, 73.75 (glycerol 2C_H₂O and CH₂O), 128.40, 129.73, 133.13 (°C₆H₅), 166.31 (carbonyl carbon).

Separate HPLC injections of 1,2-isopropylidene-3-benzoyl-sn-glycerol and 1-benzoyl-2, 3-isopropylidene-sn-glycerol (each 1 µg in 20 µl of hexane-isopropanol 80:20, v/v) gave single peaks with retention times (uncorrected) of 13.00 and 15.11 min, respectively (Fig. 2 A and B). The elution profile of the enantiomers from the racemic benzoyl isopropylidene glycerol (2 µg in 20 µl of hexane-isopropanol 80:20, v/v) coincided with the above retention times (Fig. 2 C).

The synthesis of 1-acyl-2,3-isopropylidene-sn-glycerols was accomplished by condensing 2,3-isopropylidene-sn-glycerol with an appropriate fatty acid in the presence of DMAP and DCC. 1,2-Isopropylidene-3-acyl-sn-glycerols were similarly prepared from 1,2 or 2,3-isopropylidene-sn-glycerol. The compounds thus synthesized are listed in Table 1 along with their physical data. A typical preparation procedure adopted for the synthesis of these compounds is given below.

1-Behenoyl-2,3-isopropylidene-sn-glycerol (IV, \( n = 20 \))

2,3-Isopropylidene-sn-glycerol (132 mg; 1 mmol) was dissolved in carbon tetrachloride (15 ml). Behenic acid (375 mg; 1.1 mmol) and 122 mg of DMAP (1 mmol) were added to the solution with stirring. DCC (226 mg; 1.1 mmol) dissolved in carbon tetrachloride (10 ml) was added to the reaction mixture over about 10-15 min at room temperature. After the addition was complete the reaction mixture was stirred for 1.5 hr. The reaction was monitored by TLC (isopropyl ether-hexane 1:2) and was found to be complete by this time. The precipitated dicyclohexyl urea was filtered and washed with carbon tetrachloride. The filtrate was concentrated and purified by medium pressure column chromatography (9). The eluting sol-
The 1- or 3-acyl-sn-glycerols were obtained by the ketal cleavage of corresponding 2,3- or 1,2-isopropylidene compounds by dimethylboronbromide at -50°C. All the ketal cleavage reactions were carried out under an inert atmosphere of argon. A typical reaction procedure for ketal cleavage is given below for 1-behenoyl-sn-glycerol.

**1-Behenoyl-sn-glycerol (V, \( n = 20 \))**

1-Behenoyl-2,3-isopropylidene-sn-glycerol (454 mg; 1 mmol) dissolved in dichloromethane was placed in a 25-ml flask kept under argon. This solution was cooled to -50°C and dimethylboronbromide (2.5 M solution in dichloromethane, 2.5 ml) was added with stirring. The reaction was monitored by TLC (chloroform-acetone-methanol 95:4:1). After 2 hr the reaction was stopped by adding saturated aqueous sodium bicarbonate solution (3 ml) slowly with stirring. The reaction mixture was brought to room temperature and extracted with chloroform. Chloroform extracts were combined, washed with water, and dried over Na₂SO₄. The product, obtained after evaporating the solvent, was crystallized from diethyl ether (35 ml, at 0°C). Yield 344 mg (84%), mp 85.2°C \([\alpha]_D^2 = + 2.4^\circ\) (pyridine, C, 5). "H NMR (CDCl₃) \& 0.88 (3H, t, CH₃), 1.26-1.64 (38H, m, -(CH₂)₁₉), 2.35 (2H, t, OOC-CH₂), 3.6-4.2 (7H, m, 2C₂H₂O, CBO, 20H) ¹³C NMR (CDCl₃) 614.07, 22.71, 24.97, 29.18, 29.28, 29.38, 29.47, 29.72, 31.35, 34.23 (behenoyl C₆H₃ and (C₆H₄)₂₀), 63.46, 65.28, 70.42 (glycerol 2 C₂H₂ and C), 174.30 (carbonyl carbon).

Other 1-acyl-sn-glycerols and 3-acyl-sn-glycerols were synthesized similarly. They are listed in Table 2, along with their physical data. On boric acid-impregnated TLC plates (solvent system, chloroform-acetone 75:25, v/v) all the 1- or 3-monoacyl-sn-glycerols showed a single spot without any evidence of 2-monoacylglycerols. On HPLC, separate injections of each monoacylglycerol (75 µg) showed a single peak without any evidence of 2-monoacylglycerols.

**DISCUSSION**

This report describes a convenient synthesis of 1- or 3-acyl-sn-glycerols from 2,3- or 1,2-isopropylidene-sn-glycerols, respectively. The difficulty encountered during the synthesis of monoacyl-sn-glycerols is the removal of the protected isopropylidene group which becomes increasingly difficult with increasing acyl chain length and impractical with stearic acid or longer chains. Recently it was found that dimethylboronbromide is a very effective reagent for the cleavage of acyclic and cyclic acetals and ketals and does not affect the ester bonds (6). In the present effort to synthesize monoacyl-sn-glycerols, dimethylboronbromide was employed for the ketal cleavage and found to be devoid of all the side reactions associated with
TABLE 1. Physical data of 1,2-isopropylidene-3-acyl-sn-glycerols and 1-acyl-2,3-isopropylidene-sn-glycerols

<table>
<thead>
<tr>
<th>Compound</th>
<th>Rotation [α]D&lt;sup&gt;20&lt;/sup&gt;</th>
<th>Melting Point</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,2-Isopropylidene-3-acyl-sn-glycerols&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-Lauroyl-sn-glycerol (C12:0)</td>
<td>+ 4.90&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(neat)</td>
<td>10</td>
</tr>
<tr>
<td>3- Palmitoyl-sn-glycerol (C16:0)</td>
<td>− 1.2&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(CHCl&lt;sub&gt;3&lt;/sub&gt;, C, 10)</td>
<td>35.5&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>3-Behenoyl-sn-glycerol (C22:0)</td>
<td>− 1.2&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(CHCl&lt;sub&gt;3&lt;/sub&gt;, C, 10)</td>
<td>55</td>
</tr>
<tr>
<td>3-Lignoceroyl-sn-glycerol (C24:0)</td>
<td>− 1.0&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(CHCl&lt;sub&gt;3&lt;/sub&gt;, C, 10)</td>
<td>58</td>
</tr>
<tr>
<td>3- Oleoyl-sn-glycerol (C18:1)</td>
<td>+ 3.97&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(neat)</td>
<td>− 9.5</td>
</tr>
<tr>
<td>3- Linoleoyl-sn-glycerol (C18:2)</td>
<td>+ 3.76&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(neat)</td>
<td>− 20.7</td>
</tr>
</tbody>
</table>

1-Acyl-2,3-isopropylidene-sn-glycerols

<table>
<thead>
<tr>
<th>Compound</th>
<th>Rotation [α]D&lt;sup&gt;20&lt;/sup&gt;</th>
<th>Melting Point</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Stearyl-sn-glycerol (C18:0)</td>
<td>+ 1.3&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(CHCl&lt;sub&gt;3&lt;/sub&gt;, C, 10)</td>
<td>43</td>
</tr>
<tr>
<td>1-Behenoyl-sn-glycerol (C22:0)</td>
<td>+ 1.2&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(CHCl&lt;sub&gt;3&lt;/sub&gt;, C, 10)</td>
<td>54</td>
</tr>
</tbody>
</table>

<sup>a</sup>The solvent and the concentration of solute are given in parentheses.
<sup>b</sup>The number of carbon atoms and the double bonds present in the acyl chain are given in parentheses.
<sup>1</sup>Lit. [α]<sub>D</sub> = + 5.06° (neat) (Ref. 1).
<sup>2</sup>Lit. [α]<sub>D</sub> = + 4.95° (neat) (Ref. 1).
<sup>1</sup>Lit. mp = 33.0-34.5°C (Ref. 1). 2. Lit. [α]<sub>D</sub> = + 4.12° (neat) (Ref. 19).
<sup>5</sup>Due to less solubility, the rotation is measured at 30%.
<sup>1</sup>Lit. mp = 85.5°C (Ref. 3).

Acidic conditions. This method was very effective for the synthesis of the long acyl chain compounds (up to 24 carbons). There was no acyl migration as shown by the optical rotation of the final products. 2-Acylglycerols are produced during the acyl migration of 1- or 3-acyl-sn-glycerols (10). The 1- or 3-acyl-sn-glycerols can be separated from 2-acylglycerols by TLC on boric acid-impregnated plates (11) or on HPLC (3). However, in the present synthesis, the 1- or 3-acyl-sn-glycerols produced were found to be pure, with no 2-acylglycerols (TLC on boric acid-impregnated plates and HPLC) implying no acyl migration occurred during the synthesis. The yields of monoacyl-sn-glycerols were good. In particular, the dimethylboronbromide ketal cleavage reaction was very useful in the synthesis of very long chain acyl (>18 carbons) saturated or unsaturated monoacyl-sn-glycerols.

The synthesis of 1,2-isopropylidene-sn-glycerols has been reported by many workers (4, 5, 12-14). However, the synthesis of 2,3-isopropylidene-sn-glycerol is more difficult than that of its enantiomer (8, 12, 14, 15). In general we adopted the synthetic sequence of Kanda and Wells (8) for the preparation of 2,3-isopropylidene-

TABLE 2. Physical properties of 1- and 3-acyl-sn-glycerols

<table>
<thead>
<tr>
<th>Compound</th>
<th>Rotation [α]D&lt;sup&gt;20&lt;/sup&gt;</th>
<th>Melting Point</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-Acyl-sn-glycerols&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-Lauroyl-sn-glycerol (C12:0)</td>
<td>− 4.8&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(pyridine, C, 10)</td>
<td>63.0&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>3- Palmitoyl-sn-glycerol (C16:0)</td>
<td>− 3.9&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(pyridine, C, 10)</td>
<td>70.5&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>3-Behenoyl-sn-glycerol (C22:0)</td>
<td>− 2.7&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(pyridine, C, 10)</td>
<td>85.3&lt;sup&gt;g&lt;/sup&gt;</td>
</tr>
<tr>
<td>3-Lignoceroyl-sn-glycerol (C24:0)</td>
<td>− 2.6 to − 4.4&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(pyridine, C, 5)</td>
<td>89.9&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>3-Oleoyl-sn-glycerol (C18:1)</td>
<td>− 3.2&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(pyridine, C, 5)</td>
<td>50.5</td>
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<tr>
<td>3-Linoleoyl-sn-glycerol (C18:2)</td>
<td>− 2&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(pyridine, C, 10)</td>
<td>3.2</td>
</tr>
</tbody>
</table>

1-Acyl-sn-glycerols

<table>
<thead>
<tr>
<th>Compound</th>
<th>Rotation [α]D&lt;sup&gt;20&lt;/sup&gt;</th>
<th>Melting Point</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Stearyl-sn-glycerol (C18:0)</td>
<td>+ 5.6&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(pyridine, C, 5)</td>
<td>76.8</td>
</tr>
<tr>
<td>1-Behenoyl-sn-glycerol (C22:0)</td>
<td>+ 2.4&lt;sup&gt;°&lt;/sup&gt;</td>
<td>(pyridine, C, 5)</td>
<td>85.2</td>
</tr>
</tbody>
</table>

<sup>a</sup>The solvent and the concentration of solute are given in parentheses.
<sup>b</sup>The number of carbon atoms and the double bonds present in the acyl chain are given in parentheses.
<sup>1</sup>Lit. [α]<sub>D</sub> = − 4.90° (pyridine, C, 10) (Ref. 1).
<sup>1</sup>Lit. [α]<sub>D</sub> = − 4.37° (pyridine, C, 7.8) (Ref. 1).
<sup>1</sup>Lit. mp = 54-55°C (Ref. 1); mp = 62°C (Ref. 3).
<sup>1</sup>Due to less solubility, the rotation is measured at 30°C.
<sup>1</sup>Lit. mp = 85.5°C (Ref. 3).
<sup>1</sup>The rotation varies from − 2.6 to − 4.4°.
<sup>1</sup>Lit. mp = 89.8°C (Ref. 3).
<sup>1</sup>Due to less solubility, the rotation is measured at 30°C.
<sup>1</sup>Lit. [α]<sub>D</sub> = − 3.39° (pyridine, C, 4.57) (Ref. 19).
The preparation of 1,1'-diethylmercapto-4,5-isopropylidene-L-arabinose was time-consuming with a reaction time of 3 days. We adopted new reaction procedures for the synthesis of 1,1'-diethylmercapto-L-arabinose and its isopropylidene derivative. The ketalization of 1,1'-diethylmethoxypropene in the presence of PTS (16). The idene-L-arabinose was time-consuming with a reaction hydride reduction of the ketals are unstable in the acidic medium, alkaline mercapto-L-arabinose is affected by the treatment of this resulted in the improved optical rotation of 2,3-isopropylidene-L-arabinose with opposite signs. The HPLC chromatogram of 2,3-isopropylidene-L-arabinose for this enantiomer has stronger diastereomeric interactions with the stationary phase than its enantiomer. The latter compound has stronger diastereomeric interactions with the stationary phase than its enantiomer. The separation factor (\(\alpha\)) for this enantiomeric pair is 1.54. Even though the 2,3-isopropylidene-L-arabinose showed slightly lower optical rotation (\(-14.9^\circ\)) than its enantiomer (\(+15.2^\circ\)), the benzoyl derivatives of these compounds showed the same optical rotation value (9.9°) with opposite signs. The HPLC chromatogram of these benzoyl derivatives, shown in Fig. 2 A and B, proves unequivocally the optical purity of the enantiomeric isopropylidene-L-arabinoses.

The 2,3-isopropylidene and 1,2-isopropylidene-L-arabinose were converted to the corresponding 1- or 3-acyl-L-arabinose derivatives by the condensation of an appropriate fatty acid in the presence of DMAP and DCC (18).

In conclusion, the dimethylboronbromide ketal cleavage procedure described here is very efficient, mild, does not induce any acyl migration, and is convenient for the synthesis of optically active long-chain saturated or unsaturated 1- or 3-acyl-L-arabinoses. An improved procedure for the synthesis of 2,3-isopropylidene-L-arabinose from L- (+)-arabinose is also described.

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