The preparation of racemic, (S)- and (R)-1,2-O-(xanthen-9-ylidene)glycerol 17a, 20a and 23a and racemic, (S)- and (R)-1,2-O-(2,7-dimethylxanthen-9-ylidene)glycerol 17b, 20b and 23b is reported. The racemic derivatives 17a and 17b are converted into their stearate esters, which are then treated with dichloroacetic acid and pyrrole under mild conditions to give racemic 1-O-stearyl-glycerol 25 in good yield. The xanthen-9-yldene and 2,7-dimethylxanthen-9-yldene residues are incorporated into 9,9-di(pyrrol-2-yl)xanthene 36 and 2,7-dimethyl-9,9-di(pyrrol-2-yl)xanthene 37. These by-products are easily removed by treatment with iron(III) chloride in diethyl ether solution. What are believed to be enantiomerically pure (R)- and (S)-1-O-stearyl-glycerol 28 and 5 are similarly prepared in good yields from (S)- and (R)-1,2-O-(xanthen-9-yldene)glycerol 20a and 23a.

Introduction

(S)- and (R)-2,3-O-Isopropylideneglyceraldehyde 1 and 2 are valuable chiral building blocks that are both relatively easy to prepare\(^1,2\) in high enantiomeric excess. This is also true of (R)- and (S)-1,2-O-isopropylideneglycerol 3 and 4 which may readily be obtained\(^1\) by the sodium borohydride reduction of the corresponding glyeraldehyde derivatives 1 and 2. Recently, in connection with our work on the synthesis of phosphatidyl-

In the 1960s, in connection with our studies on the synthesis of oligoribonucleotides, we found that the methoxymethylene protecting group, as in 2',3'-O-(methoxymethylene)uridine 7, was one of two orders of magnitude more labile to acidic hydrolysis than the isopropylidene group in the corresponding uridine derivative 8a. However, the methoxymethylene group is chiral and its use in glycerol chemistry would lead to undesirable mixtures of diastereoisomers. Shortly afterwards, Hampton et al.\(^8\) reported that 2',3'-O-cyclopentylidene-, -cycloheptylidene- and -cyclooctylidene-uridine (9a, 9b and 9c, respectively) undergo hydrolysis in 0.01 mol dm\(^{-3}\) hydrochloric acid at 26 °C ca. 5, 7 and 8 times more rapidly than does 2',3'-O-isoprop-

ydeneuridine 8a. On the other hand, 2',3'-O-(pentan-3-yldiene)\(^4\) and 2',3'-O-(2,4-dimethylpentan-3-yldiene)\(^9\) uridine (8b and 8c, respectively) have been found to be ca. 2 and 7 times more stable to acidic hydrolysis than is 2',3'-O-isopropylidene-

uridine 8a. Presumably the intermediate oxonium ions (or carbocations) involved in the hydrolysis of compounds 8b and 8c are destabilized by steric hindrance. It is likely that there is a similar explanation for the fact\(^\dagger\) that 2,2-diphenyl-1,3-dioxolane 10b is considerably more stable to acidic hydrolysis than is 2,2-dimethyl-1,3-dioxolane 10a. However, the lability of the diphenylmethylene protecting group can easily be increased by the introduction of electron-donating aromatic substituents. Thus we have very recently shown\(^11\) that 2',3'-O-[di(p-anisyl)-methylene]uridine\(\dagger\) 11 is more than twice as labile as is 2',3'-O-isopropylideneuridine 8a in trifluoroacetic acid–water–methanol (1:2:7 v/v) solution at 30 °C. We have further shown\(^11\) that, under the same conditions of acidic hydrolysis, 2',3'-O-(xanthen-9-yldiene) and 2',3'-O-(2,7-dimethylxanthen-9-yldiene)-uridine (12a and 12b, respectively) are ca. 5 and 20 times more labile than is 2',3'-O-isopropylideneuridine 8a. We now report the preparation of both racemic and optically active 1,2-O-(xanthen-9-yldene) and 1,2-O-(2,7-dimethylxanthen-9-yldiene) derivatives of glycerol.

\(\dagger\) In this paper, p-anisyl is used for p-methoxyphenyl.
Results and discussion

The key reagents required for the preparation of 1,2-O-(xanthen-9-ylidene) and 1,2-O-(2,7-dimethylxanthen-9-ylidene) derivatives are the 9,9-dichloroxanthenes 14a,b and the corresponding 9,9-dimethoxoxyanthenes 15a,b. Following a literature procedure, 9,9-dichloroxanthene 14a was prepared (Scheme 1, step i) in virtually quantitative yield by heating commercially available xanthen-9-one 13a with thionyl chloride, under reflux, in the presence of a catalytic amount of DMF. Treatment of 9,9-dichloroxanthene 14a with sodium methoxide in methanol–THF (Scheme 1, step ii) gave 9,9-dimethoxy-

![Scheme 1 Reagents and conditions: i, SOCl₂, DMF, reflux; ii, NaOMe, MeOH, THF, 0 °C to room temp.](image)

xanthene 15a in 94.5% overall yield for the two steps. In the same way, 9,9-dichloro-2,7-dimethylxanthene 14b and 9,9-dimethoxy-2,7-dimethylxanthene 15b were prepared 11 from 2,7-dimethylxanthen-9-one 13b in virtually quantitative and 91% overall yield, respectively. 2,7-Dimethylxanthen-9-one 13b itself was prepared from commercially available di-(2,7-dimethylxanthen-9-ylidene)glycerol derivatives 16 in 81% yield. In the same way, racemic 1,2-(2,7-dimethylxanthen-9-ylidene)glycerol 17b was prepared (Scheme 2, step ii) in 94.5% overall yield for the two steps. In the presence of a catalytic quantity of CSA, in pyridine solution (Scheme 3a) gave 1,2:5,6-di-O-(xanthen-9-ylidene)-di-mannitol 19a, which was isolated as a crystalline solid in 84.5% yield. In the same way, di-mannitol 18 reacted with 9,9-dichloro-2,7-dimethylxanthene 14b to give its 1,2:5,6-bis-O-(2,7-dimethylxanthen-9-ylidene) derivative 19b in 81% isolated yield. Oxidative cleavage of 1,2:5,6-di-O-(xanthen-9-ylidene)-di-mannitol 19a was effected either with lead(iv) acetate 18 in ethyl acetate or with sodium metaperiodate 2 in THF. In both cases, the putative intermediate gyceraldehyde derivative was reduced with sodium borohydride (Scheme 3a, step iv) to give (S)-(1,2-(xanthen-9-ylidene)glycerol 20a as a crystalline solid in 81 and 94% isolated yield, respectively, based on the di-mannitol derivative 19a. 1,2:5,6-Bis-O-(2,7-dimethylxanthen-9-ylidene)-di-mannitol 19b was similarly treated with sodium metaperiodate and the putative intermediate aldehyde was reduced with sodium borohydride to give (S)-(2,7-dimethylxanthen-9-ylidene)glycerol 20b, which was isolated as a crystalline solid in 69% yield for the two steps. As indicated in Table 1 (entries nos. 1 and 2, respectively), compounds 20a and 20b are both dextrorotatory.

![Scheme 2 Reagents and conditions: i, CSA, MeCN, room temp., 4h.](image)

Like (S)-1,2-O-isopropylidenglycerol 14a, (S)-1,2-O-(xanthen-9-ylidene)glycerol 20a and (S)-1,2-O-(2,7-dimethylxanthen-9-ylidene)glycerol 20b may both be prepared from di-mannitol 18. Treatment of di-mannitol with 9,9-dichloroxanthene 14a in pyridine solution (Scheme 2b) gave the putative intermediate aldehyde 19a in 81.5% yield. Oxidative cleavage of 1,2:5,6-di-O-(xanthen-9-ylidene)-di-mannitol 19a was effected with lead(IV) acetate 18 in ethyl acetate or with sodium metaperiodate 2 in THF. In both cases, the putative intermediate gyceraldehyde derivative was reduced with sodium borohydride (Scheme 3a, step iv) to give (S)-(1,2-(xanthen-9-ylidene)glycerol 20a as a crystalline solid in 81 and 94% isolated yield, respectively, based on the di-mannitol derivative 19a. 1,2:5,6-Bis-O-(2,7-dimethylxanthen-9-ylidene)-di-mannitol 19b was similarly treated with sodium metaperiodate and the putative intermediate aldehyde was reduced with sodium borohydride to give (S)-(2,7-dimethylxanthen-9-ylidene)glycerol 20b, which was isolated as a crystalline solid in 69% yield for the two steps. As indicated in Table 1 (entries nos. 1 and 2, respectively), compounds 20a and 20b are both dextrorotatory.

Like (R)-1,2-O-isopropylidenglycerol 14b, (R)-1,2-O-(xanthen-9-ylidene)glycerol 23a and (R)-1,2-O-(2,7-dimethylxanthen-9-ylidene)glycerol 23b may both be prepared (Scheme 3b) from l-aspartic acid 21. Thus l-aspartic acid was first heated, under reflux, with a slight excess of 9,9-dimethoxoxyanthen-9-one 15a in the presence of a catalytic quantity of CSA in dry acetonitrile (Scheme 3b, step v) to give its 5,6-O-(xanthen-9-ylidene) derivative 22a. Following the addition of an excess of lithium carbonate, the products were treated first with aqueous hydrogen peroxide and then with lead(iv) acetate (steps vi and ii, respectively) to give the putative (S)-2,3-O-(xanthen-9-ylidene)glyceraldehyde. Reduction with sodium borohydride (step iv) gave (R)-1,2-O-(xanthen-9-ylidene)glycerol 23a, which was isolated as a crystalline solid in 41.5% overall yield. In the same way, (R)-1,2-O-(dimethylxanthen-9-ylidene)glycerol 23b was prepared from l-aspartic acid 21 by the same four-step process via intermediate 22b, and was isolated as a crystalline solid in 32% overall yield. Compounds 23a and 23b are both laevorotatory (Table 1, entries nos. 3 and 4, respectively) and their specific rotations are very nearly equal and opposite to those of their respective enantiomers (entries nos. 1 and 2).

Table 1 Specific rotations of glycerol derivatives

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compound</th>
<th>[α]D°deg cm² g⁻¹</th>
<th>(ethanol)/g 100 cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20a</td>
<td>+15.7</td>
<td>1.5</td>
</tr>
<tr>
<td>2</td>
<td>20b</td>
<td>+18.2</td>
<td>1.5</td>
</tr>
<tr>
<td>3</td>
<td>23a</td>
<td>-15.3</td>
<td>1.5</td>
</tr>
<tr>
<td>4</td>
<td>23b</td>
<td>-18.2</td>
<td>1.5</td>
</tr>
</tbody>
</table>

The key reagents required for the preparation of 1,2-O-(xanthen-9-ylidene) and 1,2-O-(2,7-dimethylxanthen-9-ylidene) derivatives are the 9,9-dichloroxanthenes 14a,b and the corresponding 9,9-dimethoxoxyanthenes 15a,b. Following a literature procedure, 9,9-dichloroxanthene 14a was prepared (Scheme 1, step i) in virtually quantitative yield by heating commercially available xanthen-9-one 13a with thionyl chloride, under reflux, in the presence of a catalytic amount of DMF. Treatment of 9,9-dichloroxanthene 14a with sodium methoxide in methanol–THF (Scheme 1, step ii) gave 9,9-dimethoxy-
conditions indeed. When a ca. 0.15 mol dm$^{-3}$ solution of the intermediate stearate ester 24a in dichloromethane was treated with dichloroacetic acid (ca. 4 mol equiv.) and pyrrole 16 (ca. 5 mol equiv.) at room temperature, rapid unblocking occurred and, following work-up of the products after 15 min, racemic 1-O-stearoylglycerol 25 was isolated as a pure crystalline solid in 80% overall yield. The other product was identified as 9, di(pyrryl-2-yl)xanthenne 36 (see below and Experimental section). It seemed desirable that the lipid product 25, which would be expected to undergo acyl migration under mildly basic conditions, should be isolated without recourse to column chromatography. This was achieved by treating a solution of the products (i.e., compounds 25 and 36) with an excess of iron(III) chloride in diethyl ether solution. In this way, the xanthene derivative 36 was quantitatively removed (see below) and a dark brown solid precipitate was obtained. Following the same procedure (Scheme 4a), racemic 1,2-O-(2,7-dimethylxanthen-9-yldiene)glycerol 17b was also converted into racemic 1-O-stearoylglycerol 25, which was isolated in 85% overall yield. The xanthene by-product 37 (see below) was again removed by the iron(III) chloride precipitation method.

It is noteworthy that the 2,7-dimethylxanthen-9-yldiene derivative 24b did not appear to undergo more rapid dichloroacetic acid–pyrrole promoted unblocking than the simple xanthen-9-yldiene derivative 24a. Therefore, if unblocking is to be effected in this way, there appears to be no obvious advantage in using the 2,7-dimethylxanthen-9-yldiene rather than the more easily accessible unsubstituted xanthen-9-yldiene protecting group. For this reason, the enantiomeric (S)- and (R)-1,2-O-stearoylglycerols 5 and 28 were prepared from the corresponding (R)- and (S)-1,2-O-(xanthen-9-yldiene)glycerols 23a and 20a (Schemes 4b and 4c, respectively) by exactly the same procedure as was used for the preparation of the racemic material 25 (Scheme 4a). (R)-(−)-1-O-Stearoylglycerol 28 [[$[\alpha]$]$_{D}$] = −3.68 (c 4.1, CH$_2$N$_2$) and (S)-(−)-1-O-stearoylglycerol 5 [[$[\alpha]$]$_{D}$] = +3.64 (c 4.1, CH$_2$N$_2$) were thereby prepared and isolated in 77 and 79% overall yield, respectively. It appears from the specific rotation data that the present approach to the preparation of (R)- and (S)-1-O-stearoylglycerol 5 and 28 leads to material of even greater enantiomeric purity than was obtained previously.

The procedure for the dichloroacetic acid–pyrrole-promoted removal of the xanthen-9-yldiene protecting group is essentially the same as the procedure that we recommended 16 some 15 years ago for the removal of the 9-phenylxanthen-9-yl 17 and related (e.g., 4,4’-dimethoxytrityl) 18 protecting groups from alcoholic hydroxy functions. Thus, when a 9-phenylxanthen-9-y1 ether 29 (Scheme 5a) is treated with dichloroacetic acid and pyrrole, the 9-phenylxanthen-9-yl cation 30 is generated and then rapidly and irreversibly quenched by pyrrole to give 2-O-phenylxanthen-9-ylpyrrole 31. The suggested mechanism for the removal of the xanthen-9-yldiene protecting group, which is illustrated in Scheme 5b for an acyclic acetal 32, is somewhat more complicated. The cation 33 generated initially would perhaps be expected to be as stable as the 9-phenylxanthen-9-yl cation inasmuch as the mesomeric effect of an alkoxy group (OR$^+$) is generally unlikely to be smaller than that of a phenyl group. The monopyrrol-2-yl intermediate 34, formed by the reaction between cation 33 and pyrrole, would be expected to fragment very rapidly indeed under the reaction conditions to give cation 35. This intermediate 35, which is stabilized by the mesomeric effect of the pyrrol-2-yl residue, would be expected to be more stable than the 9-phenylxanthen-9-yl cation 30. Although we have not so far obtained any supporting experimental evidence, the inductive effect of the methyl substituents in the 2,7-dimethylxanthen-9-yldiene protecting group (as in 17b) would be expected to facilitate the transformations indicated in Scheme 5.

The two di(pyrryl-2-yl) derivatives 36 and 37 were both obtained as pure crystalline compounds and were fully characterized. Racemic 1-O-stearoyl-2,3-O-(xanthen-9-yldiene)glycerol 24a was treated with an excess each of dichloroacetic acid and pyrrole in dichloromethane solution at room temperature. Following fractionation of the products, the di(pyrryl-2-yl) derivative 36 was isolated as a colourless crystalline solid in

Scheme 4  
**Reagents and conditions:** i, CH$_3$(CH$_2$)$_3$COCl, 1-methylimidazole, CH$_2$Cl$_2$, room temp., 90 min; ii, (a) pyrrole, Cl$_2$CHCOOH, CH$_2$Cl$_2$, room temp., 15 min; (b) FeCl$_3$, Et$_2$O, room temp.

Scheme 5  
**Reagents:** i, pyrrole, Cl$_2$CHCO$_2$H, CH$_2$Cl$_2$.

92% yield. The latter compound was also prepared from 9,9-dimethoxyxanthene 15a and obtained in 74% isolated yield. In the same way, 2,7-dimethyl-9,9-di(pyrrol-2-yl)xanthene 37 was prepared both from racemic 1,2-O-(2,7-dimethylxanthene-9-ylidene)-3-O-stearoylglycerol 24b and 9,9-dimethoxy-2,7-dimethoxynthrene 15b and isolated in 82 and 64% yield, respectively. When solutions of each of these di(pyrrol-2-yl) derivatives 36 and 37 were treated with a threefold excess of iron(III) chloride in dry diethyl ether solution, dark coloured solid precipitates were obtained and, in both cases, none of the starting material remained in the ethereal solution. No attempt has so far been made to characterize these precipitated solids.

In conclusion, we believe that (R)- and (S)-O-(xanthan-9-ylidene)glycerol (23a and 20a, respectively) have several distinct advantages as building blocks for the preparation of chiral glycerol derivatives over the corresponding commercially available isopropylidene compounds (3 and 4, respectively).
Not only are they crystalline and ultraviolet-absorbing but, following the required transformation or transformations, the xanthen-9-yldene protecting group can be removed under very mild conditions indeed.

**Experimental**

Mps were measured with a Büchi melting point apparatus and are uncorrected. 1H NMR spectra were measured at 360 and 400 MHz with Bruker AM 360 and Avance 400 spectrometers. 13C NMR spectra were measured at 90.6 and 100.6 MHz, respectively, with the same spectrometers. Chemical shifts are given in ppm relative to tetramethylsilane, and J-values are given in Hz. UV absorption spectra were measured with a Perkin-Elmer Lambda spectrometer. Optical rotations were measured with a Perkin-Elmer 343 polarimeter, and [α]D-values are given in units of 10°/d cm−2 g−1. Merck silica gel 60 F254 plates (Art 5715 and 5642), which were developed in solvent mixtures.

**9.9-Dimethoxyxanthenes 15a**

Xanthen-9-one 13a (19.6 g, 0.10 mol), DMF (0.5 cm3) and thionyl dichloride (40 cm3) were heated together, under reflux, for 4 h. The remaining thionyl dichloride was removed by distillation at atmospheric pressure, followed by evaporation under reduced pressure. The residue was then distilled; methanol was dried by heating, under reflux, over calcium hydride and was then distilled; toluene was dried by heating, under reflux, over phosphorus pentoxide and was then distilled; acetonitrile and pyridine were dried by heating, under reflux, over sodium wire and was then distilled; thionyl dichloride (40 cm3) was added dropwise over a period of 30 min and in an atmosphere of nitrogen to a cooled (ice-water-bath), stirred solution of di(±)-camphor-10-sulfonic acid (0.010 g) in dry acetonitrile (5.00 g, 25.2 mmol), followed by well mixed and the products were evaporated to dryness under reduced pressure and the residue was co-evaporated with dry toluene (2 × 10 cm3) to give a pink solid (6.10 g), which was assumed to be 9,9-dichloro-2,7-dimethoxynanthene 14b. A solution of this material (6.10 g) in dry THF (50 cm3) was added dropwise over a period of 30 min and in an atmosphere of nitrogen to a cooled (ice-water-bath), stirred solution of methanolic sodium methoxide (ca. 4.3 mol dm−3; 25 cm3, ca. 0.11 mol). The reactants were allowed to warm to room temperature and, after a further period of 1 h, the products were concentrated to dryness under reduced pressure. The residue was dissolved in dichloromethane (100 cm3) and the solution was washed with saturated aq. sodium hydrogen carbonate (3 × 100 cm3). The combined aqueous washings were back-extracted with dichloromethane (2 × 100 cm3). The combined organic layers were dried (MgSO4) and evaporated under reduced pressure to give the title compound 15b (5.50 g, 91%) as a yellow solid [Found, in material recrystallized from ethanol–tritylamine (99 : 1 v/v): C, 75.5; H, 6.7. C9H8O3 requires C, 75.53; H, 6.71%; mp 81–82 °C, δH (CDCl3) 2.40 (6 H, s), 2.92 (6 H, s), 7.08 (2 H, d, J = 8.3), 7.21 (2 H, d, J = 8.3), 7.50 (2 H, s), δC (CDCl3) 20.91, 51.84, 96.94, 116.19, 118.16, 126.98, 131.09, 132.64, 151.45.

(±)-1,2-O-(Xanthen-9-yldiene)glycerol 17a

A solution of glycerol 16 (0.74 cm3, 10.1 mmol) and 9,9-dimethoxyxanthene 15a (1.21 g, 5.00 mmol) in dry acetonitrile (10 cm3) was evaporated under reduced pressure. A solution of the residue and (±)-camphor-10-sulfonic acid (0.010 g) in dry acetonitrile (20 cm3) was stirred in an atmosphere of argon at room temperature. After 4 h, triethylamine (0.1 cm3) was added and the products were evaporated under reduced pressure. A solution of the residue in dichloromethane (20 cm3) was washed with saturated aq. sodium hydrogen carbonate (2 × 10 cm3). The dried (MgSO4) organic layer was concentrated under reduced pressure and the residue was fractionated by short-column chromatography on silica gel: the appropriate fractions, which were eluted with dichloromethane–methanol (99 : 1 v/v), were combined, and evaporated under reduced pressure to give the title compound 17a [Found, in material recrystallized from ethyl acetate–petroleum spirit: C, 70.8; H, 5.2. C9H8O3 requires C, 71.10, H, 5.22%] as a colourless solid (1.10 g), mp 94–96 °C; Rf 0.52 (system A): 4-methoxyphenol (EtOH)/nm 288 (ε/dm3 mol−1 cm−1) 3680; δH ([CD3]2SO) 3.74 (2 H, m), 4.06 (1 H, t, J = 7.9), 4.38 (1 H, dd, J = 6.3 and 7.9), 4.62 (1 H, m), 5.15 (1 H, t, J = 5.6), 7.29 (4 H, m), 7.48 (2 H, m), 7.72 (1 H, dd, J = 1.3 and 7.8), 7.89 (1 H, dd, J = 1.3 and 7.8); δC ([CD3]2SO) 61.07, 67.37, 78.49, 100.24, 116.17, 116.44, 123.23, 128.45, 128.35, 126.46, 127.02, 130.05, 130.22, 150.65, 151.15.

(±)-1,2-O-(2,7-Dimethoxynanthene-9-yldiene)glycerol 17b

Glycerol 16 (0.37 cm3, 5.1 mmol), 9,9-dimethoxy-2,7-dimethoxynanthene 15b (0.81 g, 3.0 mmol) and (±)-camphor-10-sulfonic acid (5.10 g, 90%), mp 139–141 °C (lit. 13 C143 °C; δH (CDCl3) 2.45 (6 H, s), 7.35 (2 H, d, J = 8.5), 7.49 (2 H, dd, J = 2.2 and 8.7), 8.1 (2 H, d, J = 1.3); δC (CDCl3) 20.78, 117.66, 121.37, 125.95, 133.40, 135.85, 154.36, 177.30.

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acid (0.010 g) were allowed to react together in acetonitrile (20 cm³) solution as in the above preparation of (±)-1,2-O-(xanthene-9-ylidene)glycerol 17a. The products were worked up and chromatographed as the sodium borohydride (1.0 mmol) in dry pyridine (5 cm³) at room temperature. After 4 h, the products were concentrated under reduced pressure. The residue was dissolved in dichloromethane (20 cm³) and then sodium borohydride (0.227 g, 6.0 mmol) in absolute ethanol (5 cm³) was added. After a further period of 10 min, the products were filtered and the residue was washed with ethyl acetate (20 cm³). The combined filtrate and washings were added dropwise over a period of 15 min to a stirred solution of sodium borohydride (1.75 g, 46.3 mmol) in ethanol (115 cm³) at 0°C (ice–water-bath). After a further period of 1 h, sodium hydroxide pellets (0.80 g) and then 1.0 mol dm⁻³aq. sodium hydroxide (50 cm³) were added with continued stirring. The products were filtered and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 20 cm³) and the combined organic layers were concentrated to dryness (water-pump, followed by oil-pump). When petroleum spirit (100 cm³) was added to a solution of the residue in dichloromethane (20 cm³), the title compound 20a (2.58 g, 81%) [Found, in material recrystallized from ethyl acetate–petroleum spirit: C, 70.85; H, 5.1. C₇H₈O₈ requires C, 71.10; H, 5.22%] was obtained as a colourless solid, mp 105–107°C; Rₙ 0.52 (system A); [α]D₂⁰ +15.7° (c 1, ethyl acetate). The H¹ and ¹³C NMR spectra ([CD₃]₂SO) were identical with those indicated above for the racemic material.

(b) Water (1.0 cm³), sodium hydrogen carbonate (0.10 g, 1.2 mmol) and sodium metaperiodate (0.853 g, 4.0 mmol) were added to a stirred solution of 1,2,5,6-di-O-(xanthene-9-ylidene)-D-mannitol 19a (0.538 g, 1.00 mmol) in THF (10 cm³) at room temperature. After 4 h, the products were concentrated under reduced pressure. The residue was dissolved in dichloromethane (30 cm³) and the solution was washed with saturated aq. sodium hydrogen carbonate (2 × 30 cm³). The combined aq. layers were back-extracted with dichloromethane (2 × 20 cm³). The combined organic layers were dried (MgSO₄) and then sodium acetate (0.364 g, 2.0 mmol) in dry pyridine (5 cm³) was added in one portion to a stirred, cooled (ice–water-bath) mixture of 1,2,5,6-di-O-(xanthene-9-ylidene)−D-mannitol 19a (3.15 g, 5.85 mmol), sodium hydrogen carbonate (1.96 g, 23.3 mmol) and ethyl acetate (115 cm³). After 1 h, the products were filtered through a bed of Celite (20 g) and the residue was washed with ethyl acetate (30 cm³). The combined filtrate and washings were added dropwise over a period of 15 min to a stirred solution of sodium borohydride (1.75 g, 46.3 mmol) in ethanol (115 cm³) at 0°C (ice–water-bath). After a further period of 1 h, sodium hydroxide pellets (0.80 g) and then 1.0 mol dm⁻³aq. sodium hydroxide (50 cm³) were added with continued stirring. The products were filtered and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 20 cm³) and the combined organic layers were concentrated to dryness (water-pump, followed by oil-pump). When petroleum spirit (100 cm³) was added to a solution of the residue in dichloromethane (20 cm³), the title compound 20a (2.58 g, 81%) [Found, in material recrystallized from ethyl acetate–petroleum spirit: C, 70.85; H, 5.1. C₇H₈O₈ requires C, 71.10; H, 5.22%] was obtained as a colourless solid, mp 105–107°C; Rₙ 0.52 (system A); [α]D₂⁰ +15.7° (c 1, ethyl acetate). The H¹ and ¹³C NMR spectra ([CD₃]₂SO) were identical with those indicated above for the racemic material.
on silica gel: the appropriate fractions, which were eluted with dichloromethane–methanol (99:1 v/v), were combined, and evaporated under reduced pressure to give the title compound 20b as a colourless glass (0.230 g, 68%), which later solidified [Found, in material recrystallized from ethyl acetate–petroleum spirit: C, 72.2; H, 6.0. C₂₉H₂₇O₅ requires C, 72.47; H, 6.08%, mp 143–144 °C; R₂O₆ (system A): δH 18.2 (1.5, ethanol). The ¹H and ¹³C NMR spectra of this compound were identical with the corresponding spectra obtained from the racemic material 17b (see above).

(R)-(-)-2,3-O-(Xanthen-9-ylidene)glycerol 23a

A solution of L-ascorbic acid 21 (2.67 g, 15.2 mmol) and 9,9-dimethoxyxanthene 15a (4.5 g, 18.6 mmol) in dry acetonitrile (20 cm³) was evaporated under reduced pressure. The residue was redissolved in dry acetonitrile (40 cm³) and (±)-camphor-10-sulfonic acid (0.05 g, 0.22 mmol) was added. The reactants were heated, under reflux, in an atmosphere of nitrogen for 3 h. The cooled products were concentrated to half volume and were extracted with dichloromethane (3 × 15 cm³). The combined organic layers were washed with diethyl ether (2 × 15 cm³) and the residue was added to a stirred solution of (±)-1,2-stearoyl-2,3-O-(xanthen-9-ylidene)glycerol 23a in ethyl acetate, as in the above preparation of (R)-(−)-2,3-O-(xanthen-9-ylidene)glycerol 23a. Subsequent reactions withaq. hydrogen peroxide, lead(IV) acetate in ethyl acetate, and sodium borohydride in ethanol–ethyl acetate, as in the above preparation of (R)-(−)-2,3-O-(xanthen-9-ylidene)glycerol 23a and with the same stoichiometry, gave, after chromatography, the title compound 23b as a colourless solid (0.800 g, 32% overall yield) [Found, in material recrystallized from ethyl acetate–petroleum spirit: C, 72.4; H, 6.1. C₂₉H₂₇O₅ requires C, 72.47; H, 6.08%, mp 143–144 °C; R₂O₆ (system A): δH 18.2 (1.5, ethanol). The ¹H and ¹³C NMR spectra of this compound were identical with the corresponding spectra of the racemic material 17b (see above).

(R)-(-)-2,3-O-(2,7-Dimethylxanthen-9-ylidene)glycerol 23b

1. Ascorbic acid 21 (1.48 g, 8.4 mmol) was heated, under reflux, with 9,9-dimethoxy-2,7-dimethylxanthene 15b (2.7 g, 10.0 mmol) in the presence of (±)-camphor-10-sulfonic acid (0.02 g, 0.09 mmol) in dry acetonitrile (30 cm³) for 3 h as in the above preparation of (R)-(−)-2,3-O-(xanthen-9-ylidene)glycerol 23a.


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the same conditions described under (a) above. The physical properties (mp, $^1$H and $^{13}$C NMR spectra) of this material were identical with those obtained under (a) above, starting from (±)-1,2-O-(xanthen-9-yldiene)glycerol 17a.

(5)-(+)-1-O-Stearoylglycerol 5

The experiment described under heading (a) above, for compound 25 was repeated on the same scale and with the same stoichiometry, starting from (5)-(+)-1,2-O-(xanthen-9-yldiene)glycerol 23a (0.811 g, 3.0 mmol). The intermediate trideutero(5)-1-O-stearoyl-2,3-O-(xanthen-9-yldiene)glycerol 26 (1.848 g) was obtained as a colourless solid.

This material (0.565 g) was converted into (5)-(+)-1-O-stearoylglycerol 5 (0.325 g, 79% overall yield). (Found, in material recrystallized from hexane: C, 69.9; H, 11.9). Calc. for C$_{37}$H$_{68}$O$_2$ (±)-1,2-O-(xanthen-9-yldiene)glycerol 26 (1.848 g) was obtained as a colourless solid.

This material (0.565 g) was converted into (5)-(+)-1-O-stearoylglycerol 5 (0.325 g, 79% overall yield). (Found, in material recrystallized from hexane: C, 69.9; H, 11.9). Calc. for C$_{37}$H$_{68}$O$_2$ (±)-1,2-O-(xanthen-9-yldiene)glycerol 26 (1.848 g) was obtained as a colourless solid.

(5)-(+)-1-O-Stearoylglycerol 28

The experiment described under heading (a) above was repeated on the same scale and with the same stoichiometry, starting from (5)-(+)-1,2-O-(xanthen-9-yldiene)glycerol 20a (0.487 g, 1.8 mmol). The intermediate trideutero(5)-1-O-stearoyl-2,3-O-(xanthen-9-yldiene)glycerol 27 (0.842 g) was obtained as a colourless solid.

This material (0.565 g) was converted into (5)-(+)-1-O-stearoylglycerol 28 (0.333 g, 77% overall yield) (Found, in material recrystallized from hexane: C, 69.9; H, 11.9). Calc. for C$_{37}$H$_{68}$O$_2$ (±)-1,2-O-(xanthen-9-yldiene)glycerol 27 (0.842 g) was obtained as a colourless solid.

9,9-Di(pyrrrol-2-yl)xanthene 36

(a) (±)-1-O-Stearoyl-2,3-O-(xanthen-9-yldiene)glycerol 24 (0.532 g, 1.0 mmol), the putative intermediate in one of the above preparations of (±)-1-O-stearoylglycerol 25, was dissolved in pyrrole-dichloromethane (1 : 9 v/v; 3.4 cm$^3$; ca. 4.9 mmol of pyrrole), and dichloroacetic acid–dichloromethane (1:9 v/v; 3.4 cm$^3$; ca. 4.1 mmol of dichloroacetic acid) was added to the stirred solution at room temperature. After 15 min, the products were partitioned between dichloromethane (15 cm$^3$) and saturated aq. sodium hydrogen carbonate (15 cm$^3$). The layers were separated. The organic layer was washed with saturated aq. sodium hydrogen carbonate, dried (MgSO$_4$), and evaporated under reduced pressure. The residue was fractionated by short-column chromatography on silica gel to give a colourless solid (0.462 g, 74%), identical in all respects (mp, $R_f$ (System B), $^1$H and $^{13}$C NMR) with the product 36 obtained above under heading (a).

2,7-Dimethyl-9,9-di(pyrrrol-2-yl)xanthene 37

A solution of anhydrous iron(III) chloride (0.487 g, 3.0 mmol) in dry diethyl ether (30 cm$^3$) was added to a stirred solution of 9,9-di(pyrrrol-2-yl)xanthene 36 (0.312 g, 1.0 mmol) in dry diethyl ether (10 cm$^3$) at room temperature. After 20 min, the resulting dark brown solid precipitate was collected by filtration, washed with diethyl ether (3 × 20 cm$^3$), and dried (yield 0.280 g). No remaining 9,9-di(pyrrrol-2-yl)xanthene 36 could be detected (by TLC) in the filtrate and washings.

Action of iron(III) chloride on 2,7-dimethyl-9,9-di(pyrrrol-2-yl)xanthene 37

A solution of anhydrous iron(III) chloride (0.487 g, 3.0 mmol) in dry diethyl ether (30 cm$^3$) was added to a stirred solution of 2,7-dimethyl-9,9-di(pyrrrol-2-yl)xanthene 37 (0.340 g, 1.0 mmol) in dry diethyl ether (10 cm$^3$) at room temperature. After 20 min, the resulting dark red solid precipitate was collected by filtration, washed with diethyl ether (3 × 20 cm$^3$), and dried (yield 0.290 g). No 2,7-dimethyl-9,9-di(pyrrrol-2-yl)xanthene 37 could be detected in the filtrate and washings.

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References