The synthesis of triphenylene-based discotic mesogens New and improved routes

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The synthesis of triphenylene-based discotic mesogens
New and improved routes

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The synthesis of discotic liquid crystal materials based on the triphenylene core normally involves the preparation of hexahydroxytriphenylene. This has traditionally been accomplished by a chloranil promoted trimerization of 1,2-dimethoxybenzene followed by demethylation of the hexamethoxytriphenylene produced. Hexahydroxytriphenylene is subsequently alkylated to give the required derivative. The overall yield of this three step procedure is low and it is difficult to perform on a large scale. It is herein shown that a modified procedure using iron III chloride instead of chloranil yields hexa-alkoxytriphenylenes in a single step. The reaction is high yielding and can be performed on a large scale. This also provides a better route than those currently available for making the unsymmetrically substituted triphenylenes required in the synthesis of polymeric discotic liquid crystals. Some related elaborations of the triphenylene nucleus are also discussed.
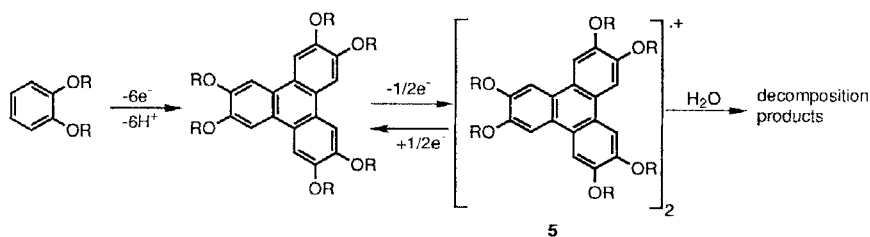
1. Introduction

Since Chandrasekhar's paper [1] reporting the first observation of a discotic liquid crystal material there has been an ever increasing interest in the preparation of new discotic mesogens. Studies of the basic physics and research into the potential applications of discotic liquid crystals has, however, been held back by synthetic difficulties which have restricted the availability of the requisite large amounts of highly pure materials.

Arguably the most widely synthesized discotic mesogens are those based on a hexasubstituted triphenylene nucleus. Their synthesis traditionally involves the oxidative trimerization of 1,2-dimethoxybenzene (veratrole) 1 in 67 per cent sulphuric acid using the quinone chloranil as oxidant [2, 3]. This reaction is more or less limited to the production of hexamethoxytriphenylene 2 and if, for example, hexahexyloxy-triphenylene (HAT6) 4 is required, it is necessary to replace the alkoxy groups. The methyl groups can be removed either by using hydrogen bromide/acetic acid or boron tribromide. The resulting hexahydroxytriphenylene is then alkylated with hexyl bromide (scheme 1). Although the chloranil/sulphuric acid mixture can be used to trimerize 1,2-dihexyloxybenzene directly, the yield of HAT6 obtained is low and purification requires repeated chromatography and repeated recrystallization. For this reason the indirect route via compounds 2 and 3 is usually more economical. The need to replace the alkoxy substituent in the 'chloranil' route is, however, a wasteful step and synthesis of hexa-alkoxytriphenylenes in this way involves two lengthy chromatographic separations (firstly to separate compound 2 from chloranil and secondly to purify the final product); this makes the whole process rather time consuming and

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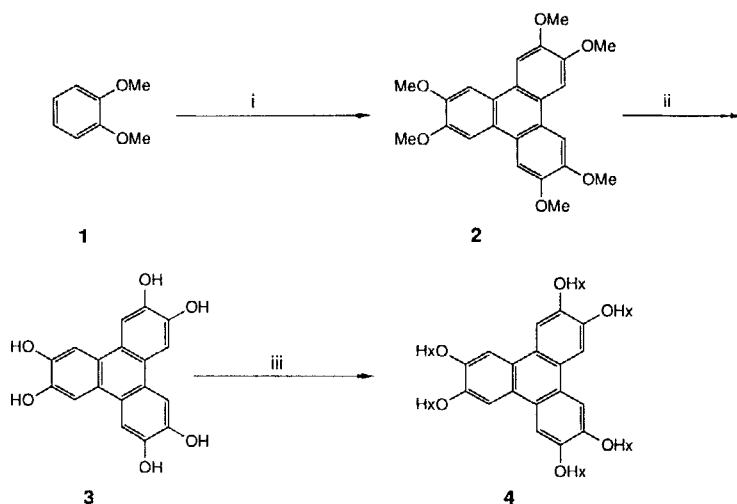
Scheme 1. The 'chloranil' route to hexahexyloxytriphenylene. Reagents: (i) 67 per cent H_2SO_4, chloranil; (ii) HBr/HOAc or BBr_3; (iii) HxBr, base.

Scheme 2. The 'electrochemical' route to hexa-alkoxytriphenylenes.

limits the overall scale of production. In our experience it is not easy to prepare more than about 10 g of the pure mesogen in a single batch.

An alternative route (scheme 2) which has been explored is electrochemical oxidation [4–7]. For example, Bechgaard and Parker have shown that anodic oxidation of veratrole in trifluoroacetic acid/dichloromethane with tetrabutylammonium tetrafluoroborate as the supporting electrolyte gives hexamethoxytriphenylene 2. The anode potential required to bring about the reaction is also sufficiently positive to remove an electron from the triphenylene and so the observed product from such an oxidation is not the triphenylene itself, but the radical cation salt 5 ($R = Me$). Salts of this type are decomposed by reaction with nucleophiles such as water (which is in part the reason why such reactions are carried out in acidic solvents) and so the work-up procedure is crucial to the outcome of the reaction. However, if the mixture is worked up reductively a good yield of hexamethoxytriphenylene is obtained. Such a reductive work-up can be achieved either by chemical or electrochemical methods [6]. If the reaction is carried out under carefully controlled conditions, the radical cation salt 5 crystallizes out on the anode surface (electrocrystallization). The great advantage of the electrochemical route is that it is not limited to veratrole, but it seems that a wide range of 1,2-dialkoxybenzene derivatives can be trimerized in this way [6]. Its great disadvantage (at least in our experience) is that the reaction is slow and the work-up

relatively tedious, so that we have not succeeded in making more than c. 1 g quantities in this way and in most cases we do not regard it as a serious competitor to the 'chloranil' route.

2. Results and discussion

Another alternative oxidation reagent in these reactions is ferric chloride. Bengs *et al.* have described a reaction procedure in which 1,2-bishexadecyloxybenzene was treated with ferric chloride in 70 per cent sulphuric acid at 80°C, followed by an ice/water work-up, to give a 20 per cent yield of 2,3,6,7,10,11-hexakishexadecyloxytriphenylene [8] and have used a similar procedure for making mixed trimers in low but unspecified yield [8].

In our experience a modified form (scheme 3) of the 'ferric chloride' route is the method of choice. The low yields reported by Bengs *et al.*, may be a result of the rather unnecessarily strong acid and high temperature employed, but more probably relate to the work-up procedure which, as in the case of the electrochemical reactions, is crucial. Oxidation of veratrole can be achieved using c. 0·3 per cent (w/v) sulphuric acid in dichloromethane at 15–25°C for 2 h. The product is a dark green solid which is certainly an oxidized form of the triphenylene, most probably the radical cation salt **5**. This is then filtered off and reduced on the filter pad with methanol. Formaldehyde is liberated and hexamethoxytriphenylene obtained directly and virtually pure.

We have repeated this reaction using a range of different acids, but best yields were obtained using sulphuric (table). In truth, the HCl liberated as a byproduct in the reaction is probably the 'major' acid in all cases. A reasonable yield is obtained even if the acid is totally omitted.

This route to hexamethoxytriphenylene is both quicker and easier than any other route and has the advantage that it is easy to perform on a relatively large scale. It also has the advantage over the chloranil route that most 1,2-dialkoxybenzenes can be
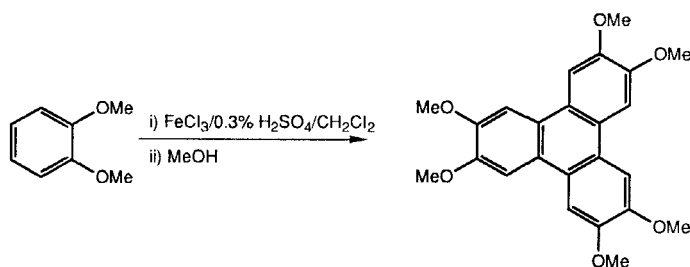
Scheme 3. The 'ferric chloride' route to hexamethoxytriphenylene.

Yield of hexamethoxytriphenylene by the ferric chloride route as a function of acid catalyst (0·3 per cent w/v) added.

Acid	Yield per cent
Trifluoroacetic	73
Triflic	78
Chlorosulphonic	76
Concentrated sulphuric	86
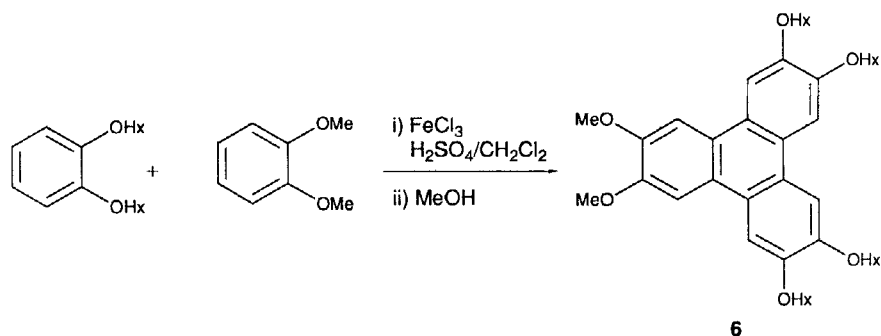
Scheme 4.   Modification of the ferric chloride route to produce asymmetric derivatives for the synthesis of polymeric discotic liquid crystals.
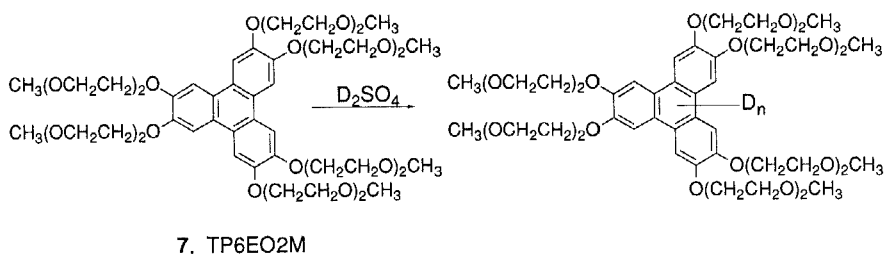
7, TP6EO2M

Scheme 5.   Ring deuteriation of TP6EO2M.

trimerized directly to give good yields (HAT3, 77 per cent, HAT4, 65 per cent, HAT6, 65 per cent, HAT8, 60 per cent, HAT9, 55 per cent). Another advantage which we have found with this route is that it can be used for mixed trimerization reactions. In the example shown in scheme 4 the yield of the tetrahexyloxy derivative is not high, but the products are easy to separate, and once again the reactions are easy to perform on a large scale providing an easier route of access to monomers for making polymeric discotic systems than those previously described in the literature [9, 10].

One limitation to the ferric chloride route is that it does not work for ethyleneoxy substituted triphenylenes. Hence, in the synthesis of lyotropic discotic systems such as TP6EO2M **7**, (see scheme 5), it provides a more convenient route to making the hexamethoxytriphenylene precursor, but it does not obviate the need to substitute the alkoxy groups [3, 11]. An attempted oxidative cyclisation of 1,2-di(1,4,7-tri-oxaoctyl)benzene failed. In our work on this system however, a more efficient route has been developed for the synthesis of TP6EO2M from hexahydroxytriphenylene (see experimental section). It has also proved necessary to synthesize this compound deuteriated on the aromatic nucleus and in the end chains. One method for obtaining ring-deuteriated material was that described by Luz and co-workers [12]. In this the hexamethoxy compound **2** is demethylated using DBr/DOAc to give partially deuteriated **3** (scheme 1) which can be subsequently alkylated. This procedure works, but is expensive and time consuming. A much simpler method is to directly deuteriate the methoxy substituted system in strong acid [13, 14]. When TP6EO2M is dissolved in D_2SO_4, deuteriation and decomposition occur at comparable rates, but with limited reaction times a good yield of partially ring-deuteriated compound is obtained (scheme 5).
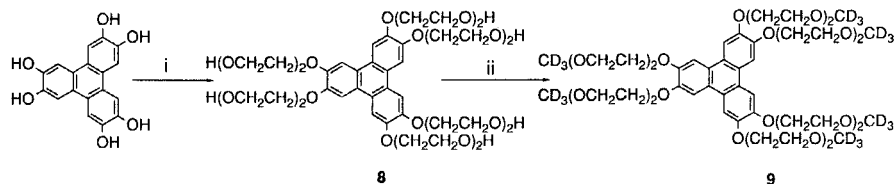
Scheme 6. Synthesis of end-chain deuteriated TP6EO2M. Reagents: (i) $BrCH_2CH_2OCH_2CH_2OPy$, K_2CO_3, EtOH; (ii) H^+; (iii) CD_3I, base. Py = tetrahydropyranyl.

Deuteriation of the end chains of TP6EO2M is more difficult, but has been achieved using the reaction sequence shown in scheme 6, details of which are discussed in the experimental section.

3. Experimental

3.1. Synthesis of 2,3,6,7,10,11-hexamethoxytriphenylene 2 (ferric chloride route)

Veratrole (23 g, 0·166 mol) was added slowly to a well stirred suspension of iron III chloride (81 g, 0·5 mol) in dichloromethane (500 ml) and concentrated sulphuric acid (1·6 g). As the veratrole was added, hydrogen chloride gas was given off and the temperature rose until the dichloromethane was boiling. The reaction mixture was stirred for a further 2 h and then filtered. Methanol was carefully added to the solid on the filter pad which changed colour from dark green to grey with copious washings. Heat and formaldehyde were liberated and it is advised that this step is performed in a well ventilated fume cupboard. The remaining solid was dried under vacuum to yield hexamethoxytriphenylene 2 as a grey solid (19·7 g, 86 per cent), mp > 300°C, δ_H (CDCl$_3$) 7·80 (6 H, s, ArH), 4·13 (18 H, s, CH$_3$O).

3.2. Synthesis of 1,2-dihexyloxybenzene

Bromohexane (4·92 ml, 0·0375 mol) was added to a vigorously stirred solution of catechol (1·1 g, 0·01 mol) and potassium carbonate (6·2 g) in ethanol (100 ml) under nitrogen. The reaction mixture was stirred under reflux for 16 h and filtered through Celite with copious washings of ethanol. The filtrate was concentrated *in vacuo* and subjected to column chromatography on silica, eluting with 1 : 1 dichloromethane: light petroleum to give the product as a pale yellow oil (2·6 g, 95 per cent), δ_H (CDCl$_3$) 6·88 (s, 4 H, ArH), 3·97 (t, 4 H, OCH$_2$), 1·81 (m, 4 H, OCH$_2$CH$_2$), 1·33–1·49 (m, 12 H, CH$_2$), 0·97 (t, 6 H, CH$_3$).

In a similar manner were prepared: 1,2-dipropyloxybenzene (reaction time 4·5 h, yield 89 per cent); 1,2-dibutyloxybenzene (4·5 h, 91 per cent); 1,2-dioctyloxybenzene (16 h, 79 per cent, mp 24°C, lit. [15] 23–26°C); 1,2-dinonyloxybenzene (8 h, 86 per cent, mp 37°C, lit. [15] 37°C).

3.3. Synthesis of 2,3,6,7,10,11-hexahexyloxytriphenylene [HAT6, 4] (ferric chloride route)

1,2-Dihexyloxybenzene (1·5 g, 0·0055 mol) was added to a vigorously stirred suspension of iron III chloride (2·66 g, 0·0165 mol) in dichloromethane (20 ml) with concentrated sulphuric acid (2 drops). The reaction occurred with vigorous evolution of gas and was quenched with methanol (60 ml) after 45 min. The reaction mixture was filtered and the filtrate concentrated *in vacuo* to give a black solid which was subjected

to column chromatography, eluting with 1 : 1 dichloromethane : light petroleum to give the product as a pale yellow solid which was recrystallized from ethanol ($1 \cdot 09$ g, 73 per cent) C–D 67°C, D–I $99 \cdot 5^\circ$C. (lit. [16] 68°C, 97°C) δ_H (CDCl$_3$) $7 \cdot 83$ (s, 6 H, ArH), $4 \cdot 23$ (t, 12 H, OCH$_2$), $1 \cdot 94$ (m, 12 H, OCH$_2$CH$_2$), $1 \cdot 41$–$1 \cdot 56$ (m, 36 H, CH$_2$), $0 \cdot 93$ (t, 18 H, CH$_3$).

In a similar manner were prepared: 2,3,6,7,10,11-hexapropyloxytriphenylene, HAT3 (77 per cent), C–I $176 \cdot 5^\circ$C, (lit. [16] 177°C); 2,3,6,7,10,11-hexabutyloxytriphenylene, HAT4 (65 per cent), C–D 88°C, D–I $143 \cdot 5^\circ$C, (lit. [16] $88 \cdot 6^\circ$C, $145 \cdot 6^\circ$C); 2,3,6,7,10,11-hexaoctyloxytriphenylene, HAT8 (60 per cent), C–D $65 \cdot 8^\circ$C, D–I $84 \cdot 8^\circ$C, (lit. [16] $66 \cdot 8^\circ$C, $85 \cdot 6^\circ$C); 2,3,6,7,10,11-hexanonyloxytriphenylene, HAT9 (55 per cent), C–D $56 \cdot 5^\circ$C, D–I 78°C, (lit. [16] 57°C, $77 \cdot 6^\circ$C).

3.4. *Synthesis of 2,3-dimethoxy-6,7,10,11-tetrahexyloxytriphenylene* **6**

A solution of 1,2-dihexyloxybenzene (10 g, $0 \cdot 036$ mol) and veratrole (10 g, $0 \cdot 074$ mol) in dichloromethane (40 ml) was added to a stirred mixture of iron III chloride (70 g, $0 \cdot 434$ mol) and concentrated sulphuric acid (1 ml) in boiling dichloromethane (250 ml), at such a rate that gentle reflux was maintained. The mixture was stirred for a further 1 h and poured into methanol (400 ml). The dichloromethane was removed *in vacuo* and the solid filtered off and purified by column chromatography on silica, eluting with benzene. The white solid was recrystallized from dichloromethane/methanol to give the product ($2 \cdot 7$ g, 22 per cent), mp 102°C. δ_H (CDCl$_3$) $7 \cdot 84$ (s, 2 H, ArH), $7 \cdot 82$ (s, 2 H, ArH), $7 \cdot 76$ (s, 2 H, ArH), $4 \cdot 24$ (m, 8 H, OCH$_2$), $4 \cdot 11$ (s, 6 H, OCH$_3$) $1 \cdot 99$ (m, 8 H, OCH$_2$CH$_2$), $1 \cdot 40$–$1 \cdot 60$ (m, 24 H, CH$_2$), $0 \cdot 94$ (m, 12 H, CH$_3$). Elemental analysis: found, C (76·6 per cent), H (9·4 per cent); C$_{44}$H$_{64}$O$_6$ requires C (76·7 per cent), H (9·4 per cent).

3.5. *Improved procedure for the synthesis of 2,3,6,7,10,11-hexa-(1,4,7-trioxa-octyl)triphenylene 7 (TP6EO2M)*

2,3,6,7,10,11-Hexahydroxytriphenylene ($1 \cdot 11$ g, $0 \cdot 0034$ mol) was added, under nitrogen, to 1-bromo-2-(2-methoxyethoxy)ethane ($5 \cdot 1$ g, $0 \cdot 028$ mol) in ethanol (82 ml). Potassium carbonate ($5 \cdot 27$ g) was added and the mixture was well stirred under reflux in an atmosphere of nitrogen for 20 h. The mixture was allowed to cool before being filtered through Celite and the filtrate evaporated *in vacuo* to give the crude product. This material was purified by column chromatography on Kieselgel, eluting first with dichloromethane followed by 2 per cent methanol in dichloromethane and finally with 4 per cent methanol in dichloromethane. Repeated recrystallization of the product from ether at 0°C gave pure TP6EO2M as white needles ($1 \cdot 05$ g, 37 per cent) mp $53 \cdot 4$–$53 \cdot 7^\circ$C (lit. [3] 51–53°C). δ_H (CDCl$_3$) $7 \cdot 88$ (s, 6 H, ArH), $4 \cdot 00$, $4 \cdot 40$ (both t, 12 H, OCH$_2$CH$_2$O), $3 \cdot 60$, $3 \cdot 80$ (both m, 12 H, OCH$_2$CH$_2$), $3 \cdot 40$ (s, 18 H, OCH$_3$).

3.6. *Synthesis of ring deuteriated TP6EO2M*

TP6EO2M (207 mg, $2 \cdot 46 \times 10^{-4}$ mol) was added to sulphuric acid (98 per cent, 7 ml) in deuterium oxide (4 ml) and the solution was stirred under nitrogen for 40 h. The solution was diluted with water (12 ml) and neutralized with 50 per cent sodium hydroxide solution. Chloroform (3 × 50 ml) was used to extract the product. The combined extracts were dried (magnesium sulphate) and concentrated *in vacuo* to give 208 mg of crude product which was dried *in vacuo* before purification by column-chromatography on Kieselgel, eluting with 3 per cent methanol/chloroform, giving 170 mg of the deuteriated compound as a grey solid.

This solid was recrystallized from 50 per cent ether/light petroleum (30–40°C boiling range) to give deuteriated TP6EO2M (80 mg, 39 per cent) as pale grey needles. ^{1}H NMR (CDCl$_3$) gave a spectrum that was identical to that of the undeuteriated compound, but with the intensity of the aromatic singlet much reduced. From the ratio of the integrals the compound was found to be c. 60 per cent deuteriated.

3.7. *Synthesis of chain deuteriated TP6EO2M* 9

Since the ^{1}H NMR spectra of intermediates in this sequence showed them to be essentially pure (although highly coloured) and since some of them proved difficult to purify, the sequence was carried straight through to the TP6EO2M which was then purified by column chromatography and recrystallization. *p*-Toluene sulphonic acid (100 mg) was added to a cooled (solid CO$_2$–acetone), stirred mixture of dihydropyran (2·3 g, 0·028 mol) and 5-chloro-3-oxapentanol (3·1 g, 0·025 mol) in dry dichloromethane (1·5 ml). After 2 h, more dichloromethane was added, the solution washed with aqueous sodium bicarbonate, dried with magnesium sulphate and concentrated *in vacuo* to give the essentially pure tetrahydropyranyl derivative as a colourless oil (5·31 g, 100 per cent) δ_H (CDCl$_3$) 4·65 (m, 1 H, OC$\underline{H}$O), 3·4–4·0 (m, 10 H, OC$\underline{H}_2$ and C$\underline{H}_2$ Cl), 1·4–1·9 (m, 6 H, C$\underline{H}_2$).

A stirred mixture of this tetrahydropyranyl derivative (3·34 g, 0·016 mol), hexahydroxytriphenylene (650 mg, 0·002 mol), potassium carbonate (1·93 g) and ethanol (25 ml) was heated under reflux in an atmosphere of nitrogen for 90 h. The mixture was filtered, the residue was washed with chloroform and the combined filtrate and washings were evaporated *in vacuo*. The oil was repeatedly extracted with light petroleum and the black residue dried *in vacuo* to give the hexakistetrahydropyranyl compound as a black semi-solid (presumably as a mixture of all possible stereoisomers), (2·04 g, 76 per cent crude). δ_H (CDCl$_3$) 7·90 (br s, 6 H, Ar$\underline{H}$), 4·75 (m, 6 H, OC$\underline{H}$O), 4·43 (t, 12 H, ArOC$\underline{H}_2$), 3·4–4·1 (m, 48 H, C$\underline{H}_2$O), 1·4–1·9 (m, 36 H, C$\underline{H}_2$).

A portion of this product (500 mg) was treated with concentrated hydrochloric acid (2 ml), water (4 ml) and tetrahydrofuran (4 ml) under an atmosphere of argon for 18 h, the solvents were removed *in vacuo* and the residue was washed repeatedly with light petroleum and dried *in vacuo*. The alcohol **8** was then dissolved in dry dimethylformamide (10 ml). Sodium hydroxide (200 mg) was added to the stirred, cooled (solid CO$_2$–acetone) mixture under an atmosphere of nitrogen. It was allowed to warm to room temperature and d_3-methyl iodide (2·0 g) added. After a further 18 h at room temperature, tlc of the mixture showed that reaction was incomplete, and it was therefore heated at 50°C for 3 h. Water was added and the product isolated by chloroform extraction and purified by column chromatography and recrystallization to give the deuteriated TP6EO2M **9** as white needles, mp and ^{1}H NMR spectra identical to those previously reported (0·25 g, 74 per cent based in the crude tetrahydropyranyl derivative).

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