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# *O*-Benzylidene Derivatives of D-Arabinose Diethyl and Dipropyl Dithioacetal*

*János Kuszmann*[A] *and Eszter Gács-Baitz*[B]

[A] Institute for Drug Research, P.O.B. 82, 1325-Budapest, Hungary.
[B] Central Research Institute for Chemistry, Hungarian Academy of Sciences, P.O.B. 17, 1525-Budapest, Hungary.

Benzylidenation of D-arabinose diethyl and dipropyl dithioacetals with $\alpha,\alpha$-dimethoxytoluene in the presence of *p*-toluenesulfonic acid has been studied in detail. Under kinetic control the two terminal dioxolan-type 4,5-*O*-(*R*)- and 4,5-*O*-(*S*)-benzylidene diastereomers are formed first which are in equilibrium with each other. In the thermodynamic phase of the reaction the corresponding dioxan-type 3,5-*O*-(*R*)-benzylidene isomer is formed too, but all three monobenzylidene isomers are gradually converted into the four possible dioxolan-type 2,3 : 4,5-di-*O*-benzylidene diastereomers. The dioxan-type 2,4 : 3,5-di-*O*-benzylidene isomer was present only in trace amounts. When benzaldehyde was used as reagent in the presence of hydrochloric acid or zinc chloride only the 2,3 : 4,5-di-*O*-benzylidene diastereomers were formed. Partial hydrolysis of the dibenzylidene derivatives yielded the corresponding 2,3-*O*-benzylidene diastereomers. Structures, including the chirality of the benzylidene groups, were determined by n.m.r. spectroscopy. A mechanism suggested for the reaction was partially supported by equilibration studies.

## Introduction

We have described[1–3] the rearrangement of 2,4-*O*-benzylidene-D-*xylo*- and -D-*ribo*-hex-5-enitols into *C*-glycosylbenzene derivatives on acetolysis and investigated the influence of different substituents on this reaction. In order to study the role of the chirality of C 2 on this rearrangement we decided on the synthesis of the 2,4-*O*-benzylidene D-*arabino* isomer (4), which should be obtainable upon partial hydrolysis of the 2,4 : 3,5-di-*O*-benzylidene derivative (3) (see Scheme 1).

## Results and Discussion

Despite the fact that the first synthesis of 2,3 : 4,5-*O*-benzylidene-L-arabinose diethyl dithioacetal was already described by Huebner *et al.*[4] in 1950 and an improved method for both the L- and the D-isomer (19) by Zinner *et al.*[5] in 1966, the configuration of the benzylidene groups has not been established so far. Even the location of the two benzylidene groups, i.e. their dioxolan-type structure, was proved only indirectly, as on partial hydrolysis of (19) the 2,3-*O*-benzylidene derivative (21) was obtained, the structure of which was elucidated by oxidation with periodate,[4] and lead tetraacetate.[5] However, as will be shown in this paper, mono-*O*-benzylidene isomers can undergo rearrangement under acidic conditions, whereupon an equilibrium occurs of the corresponding dioxan and dioxolan isomers. Accordingly the arrangement of the *O*-benzylidene group which remains after hydrolysis is not necessarily the same as that in the original molecule.

More recently Grindley *et al.*[6] reported the synthesis of the 2,4-(*R*) : 3,5-(*R*)-di-*O*-benzylidene derivative (3) and established its structure by X-ray crystallography. Partial hydrolysis of (3) could give the required 2,4-*O*-benzylidene derivative (4), if no rearrangement takes place simultaneously. For checking this possibility the synthesis of (3) was attempted, but met with difficulties. In the original paper[6] $\alpha,\alpha$-dimethoxytoluene was used as reagent (2·4 equiv.), *N*,*N*-dimethylformamide as solvent (no amount was given) and *p*-toluenesulfonic acid [5 mole % based on (1)] as catalyst for the conversion of (1) into (3). The reaction was carried out at 75–80°C and 2·66 kPa for 3 h. As at this diminished pressure $\alpha,\alpha$-dimethoxytoluene is already distilled off, in our experiments the pressure was kept at 4 kPa. This essentially should not influence the reaction as the methanol, which is formed during the reaction, is removed under this pressure too. When the reaction mixture was worked up as described[6] the obtained syrup contained according to $^1$H n.m.r., besides the four bis-dioxolan diastereomers (*S*,*S*) (17), (*R*,*R*) (19), (*R*,*S*) (23) and (*S*,*R*) (25), the dioxan-type 3,5-mono-*O*-(*R*)-benzylidene isomer (13) in the ratio of 3 : 6 : 4 : 7 : 2. No signals† of the bis-dioxan isomer (3) could be detected; consequently it can be present only in traces. From this mixture crystalline (19) could be

* Dedicated to Professor S. J. Angyal on the occasion of his 80th birthday.

† The n.m.r. signals of the benzylidene protons of (3) appear in $CDCl_3$ solution at 5·67 and 6·22 ppm, and are shifted in ($D_6$)benzene solution to 5·32 and 6·23 ppm, whereas the signals of the benzylidene protons of the obtained mixture appeared between 5·75 and 6·12 ppm in $CDCl_3$, and were shifted to 5·77–6·27 ppm in ($D_6$)benzene solution.

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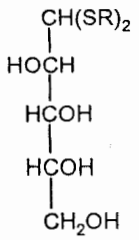
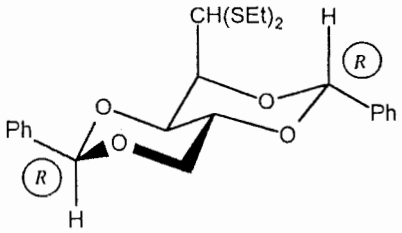


(1) R = Et
(2) R = Pr



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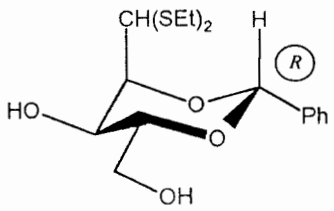
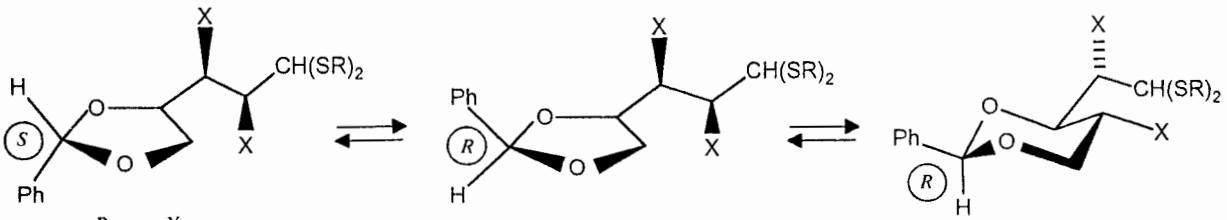


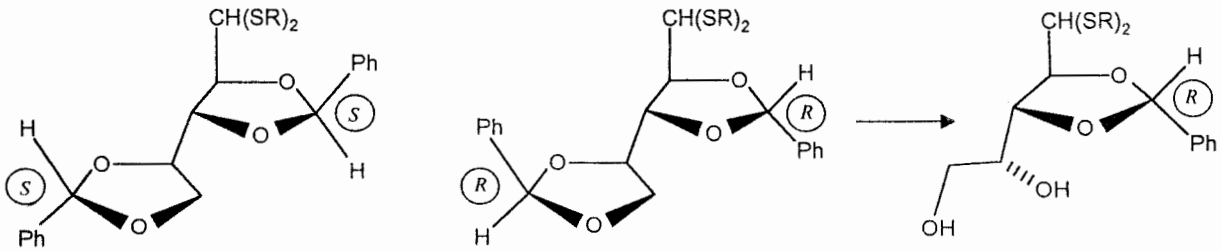
(4)



| | R | X |
|---|---|---|
| (5) | Et | OH |
| (6) | Et | OAc |
| (7) | Pr | OH |
| (8) | Pr | OAc |

| | R | X |
|---|---|---|
| (9) | Et | OH |
| (10) | Et | OAc |
| (11) | Pr | OH |
| (12) | Pr | OAc |

| | R | X |
|---|---|---|
| (13) | Et | OH |
| (14) | Et | OAc |
| (15) | Pr | OH |
| (16) | Pr | OAc |

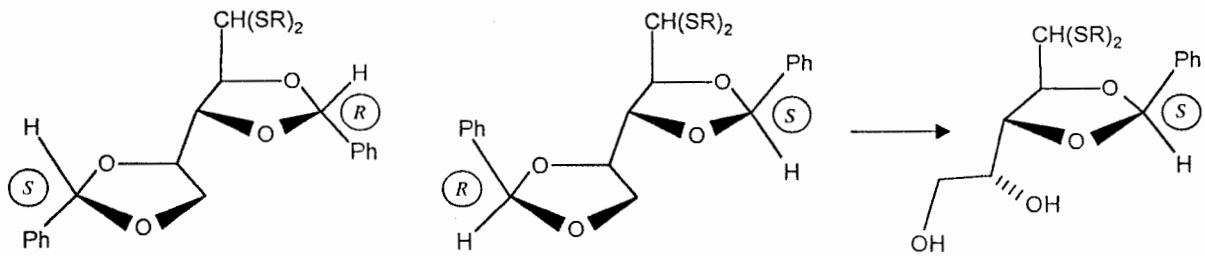


(17) R = Et
(18) R = Pr

(19) R = Et
(20) R = Pr

(21) R = Et
(22) R = Pr

+ +



(23) R = Et
(24) R = Pr

(25) R = Et
(26) R = Pr

(27) R = Et
(28) R = Pr

Scheme 1

isolated in a combined yield of 26·3% and proved to be identical with the dibenzylidene-D-arabinose diethyl dithioacetal already described.[5] Column chromatography of the mother liquor afforded (3) in a yield of 0·06% (in lit.[6] a yield of 12% was reported), an unseparable mixture of (17) and (23) (30%), pure (25) (29%) and finally the crystalline (13) (9%).

Partial hydrolysis of (19) and (25) was carried out according to the literature[4,5] (EtOH/AcOH/$H_2O$/reflux) and afforded the expected 2,3-(*R*) (21) and 2,3-(*S*) (27) diastereomers, respectively.

In further experiments, we tried to slow down the reaction by applying rather a catalytic amount of *p*-toluenesulfonic acid and carrying out the reaction at 60°C. Under these conditions the starting material was consumed in 3 h, and formed complex mixtures of mono- and di-*O*-benzylidene derivatives which were separated by column chromatography (68 and 22%). The mixture of the three mono-*O*-benzylidene derivatives could be separated after acetylation and gave the 4,5-(*S*) (6), 4,5-(*R*) (10) and 3,5-(*R*) (14) isomers in yields of 21·5, 28·2 and 25%, respectively. Zemplén deacetylation afforded (5), (9) and (13), respectively. The fact, that in the first, kinetically controlled step the dioxan-type 3,5-*O*-isomer (13) is formed in a yield of at least 25%, but the bis-dioxan-type isomer is present only in traces in the final product, means that under thermodynamic conditions (13) must undergo a rearrangement into the 2,3-*O*- or 4,5-*O*-isomers and these are gradually converted into the four 2,3:4,5-di-*O*-benzylidene diastereomers. The mechanism of this rearrangement will be discussed later.

Theoretically (13) could be converted into the bis-dioxan-type isomer (3) on treatment with $\alpha,\alpha$-dibromotoluene in pyridine[7] as no rearrangement reaction should occur under basic conditions. However, no reaction took place even at reflux for 10 h. This is probably due to the sterically strained disfavoured system of (3) in which the bulky dithioacetal group occupies an axial position, and not to the lack of reactivity of the hydroxy groups in (13), as they were acetylated under normal conditions affording diacetate (14).

For seeking conditions which meet the requirements of kinetic control, we turned our attention to the original benzylidenation method,[4,5] which converted (1) into (19) in 44% yield by using benzaldehyde and HCl gas at 0°C. As this isomer crystallizes directly from the reaction mixture, the composition of the mother liquor was investigated, but only the presence of the three other 2,3:4,5-di-*O*-benzylidene diastereomers (17), (23) and (25) could be detected. The isomer composition is probably shifted towards (19) because of the insolubility of this isomer in the reaction mixture. For this reason (1) was treated with benzaldehyde in the presence of zinc chloride at room temperature, whereupon a homogeneous reaction mixture was obtained. Investigation of this mixture by n.m.r. revealed the presence of five di-*O*-benzylidene isomers, namely (17), (19), (23), (25) and one with an unknown structure (ArC**H**: 5·90+5·87 ppm) in the ratio of 1:24:6:8:2. From this mixture only the main component could be isolated in a yield of 25·5% and proved to be identical with (19).

According to the literature,[8] the formation of benzylidene dialkyl dithioacetals can be influenced by changing the alkyl substituents; for example, in the case of D-ribose a crystalline 2,4-*O*-benzylidene acetal can be obtained in a yield of 79% only from the dipropyl mercaptal,[9] while the ethyl mercaptal gives an unseparable mixture of different isomers. For checking the influence of the alkyl substituent on the formation of the benzylidene acetals in the case of the D-arabinose mercaptals, the dipropyl dithioacetal[10] (2) was prepared. Reaction of (2) with benzaldehyde in dioxan–HCl gave a mixture (50% yield) of four di-*O*-benzylidene isomers, from which the 2,3-(*S*):4,5-(*R*)-isomer (26) could be separated by column chromatography in a yield of 4·3%. According to n.m.r. data it is very probable that the mixture of the other three isomers contains the (*S*,*S*) (18), (*R*,*R*) (20) and (*R*,*S*) (24) diastereomers. This was supported by the fact that on partial hydrolysis only the corresponding 2,3-*O*-(*R*)- (22) and 2,3-*O*-(*S*)-benzylidene (28) isomers could be detected in, and isolated from, the reaction mixture. Similar results were obtained when benzaldehyde–zinc chloride were used as reagents.

When the reaction was carried out in *N*,*N*-dimethylformamide with $\alpha,\alpha$-dimethoxytoluene in the presence of *p*-toluenesulfonic acid [5 mole % based on (2)] at 75–80°C and 4 kPa for 3 h, the same four 2,3:4,5-di-*O*-benzylidene diastereomers (18), (20), (24) and (26) were formed in almost equal amounts, and (26) could be isolated in a yield of 24·5%.

The use of less forcing conditions (catalytic amount of *p*-toluenesulfonic acid, 60°C, 5 h) resulted in a mixture containing, besides the di-*O*-benzylidene isomers mentioned above, two dioxolan-type mono-*O*-benzylidene derivatives, namely the 4,5-(*S*)- (7) and the 4,5-(*R*)-isomer (11), as well as one dioxan-type compound, namely the 3,5-(*R*)-isomer (15). The last three compounds could be isolated in yields of 8, 17 and 16%, respectively. When the reaction time was shortened to 2 h, only (7) (27%) and (11) (29%) could be detected in, and isolated from, the reaction mixture. For structure elucidation by n.m.r., compounds (7), (11) and (15) were converted into their diacetates (8), (12) and (16), respectively.

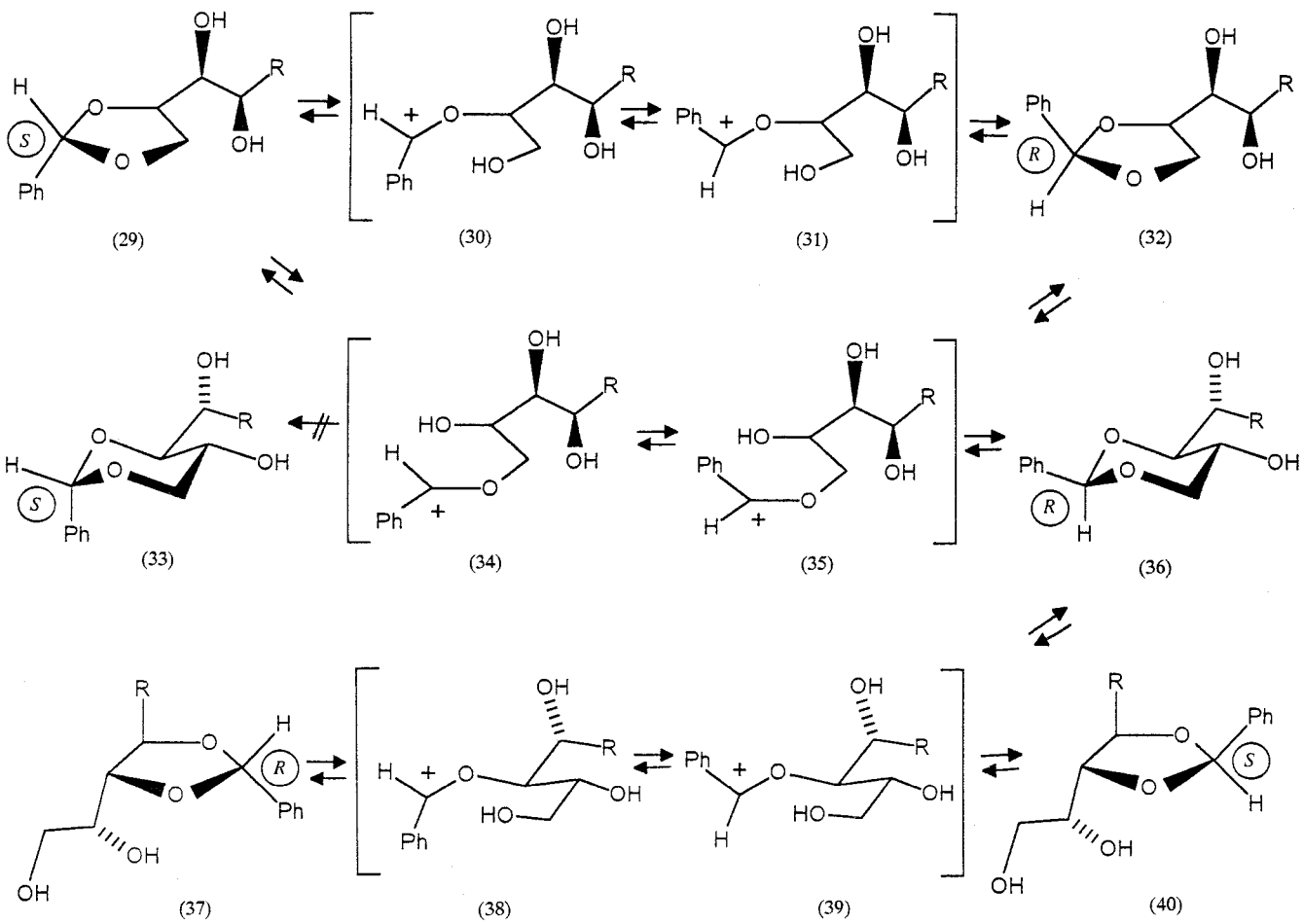
To get a deeper insight into the reaction mechanism, the isomerization of the dioxolan-type 4,5-*O*-benzylidene diastereomers was investigated in chloroform solution in the presence of a catalytic amount of acid. In the case of the diethyl dithioacetals (5) and (9) the reaction was followed by n.m.r., while for the propyl derivatives (7) and (11) t.l.c. was used. In both cases an approximately 1:1 equilibrium mixture of the corresponding diastereomers could be detected,

but the $R \rightarrow S$ conversion was a much faster process than the $S \rightarrow R$ isomerization. As a side-reaction a slow hydrolysis to benzaldehyde and the corresponding mercaptal took place too.

*The Mechanism of the Reaction*

According to all these results it can be assumed that independently of the nature of the dithioacetal substituent the terminal dioxolan-type isomers (29) and (32) are formed in an equilibrium during the kinetic phase of the reaction (see Scheme 2). Their interconversion can take place either by protonation at O 5 and subsequent ring cleavage, affording the oxybenzyl cations (30) and (31), respectively, which are rotamers. Alternatively, protonation at O 4 and subsequent ring cleavage would lead to the rotamers (34) and (35), which are potential intermediates for the dioxolan → dioxan isomerization. It is quite obvious that, from the theoretically possible two dioxan diastereomers (33) and (36), only the latter is formed in the thermodynamic phase of the reaction, as the axial arrangement of the phenyl group in (33) should be energetically disfavoured. The reason why in chloroform solution in the presence of acid only the (29) ⇄ (32) interconversion, but not the formation of the dioxan-type isomer (36), could be observed is probably the hydrolytic side-reaction, which is certainly much faster for the terminal oxybenzyl cation than for the non-terminal one. The dioxan-type isomer (36), formed in the thermodynamic phase of the reaction, is gradually transformed almost completely into the bis-dioxolan diastereomers. This rearrangement can take two pathways, either via intermediates (34) and (35), forming the 4,5-dioxolan diastereomers (29) and (32), or via the rotamers (38) and (39), which are formed by protonation of O 5 and subsequent ring fission. Attack of the 2-OH group on the oxybenzyl cation of these rotamers should yield the 2,3-*O*-benzylidene diastereomers (37) and (40), respectively, which would be immediately converted into the dioxolan-type bis-dibenzylidene diastereomers. As no water is present in the reaction mixture, hydrolysis of any intermediate (the side-reaction observed in chloroform solution) is excluded.

Further support for this mechanism was obtained when the dioxan-type 3,5-*O*-benzylidene isomer (15) was treated with $\alpha,\alpha$-dimethoxytoluene under the forcing conditions used for the benzylidenation of (2)




Scheme 2

[see method *(a)*], as even in this case only the mixture of the four dioxolan-type 2,3 : 4,5-di-*O*-benzylidene diastereomers (18), (20), (24) and (26) was formed.

*Structure Elucidation of the O-Benzylidene Isomers by N.M.R.*

Assignment of the protons of the carbohydrate skeleton followed from homonuclear decoupling experiments. Connectivities between identified protons and protonated carbons were obtained by HECTOR experiments. $^1H$ and $^{13}C$ n.m.r. data are collected in Tables 1 and 2. Designations H 5a and H 5b, when C 5 is incorporated in a ring, correspond to $\alpha$ and $\beta$ orientations, respectively. H 5a and H 5b were distinguished by their vicinal couplings with H 4 and by the different nuclear Overhauser effects with the ring protons. The n.O.e. difference method was also applied to establish the chirality of the benzylidene group of the dioxolan-type isomers. Selective irradiation of H 1 showed enhancement on the resonance of H 3 and that of the benzylidene proton of the 2,3-*O*-(*R*)-benzylidene isomers (19) and (21)–(23). No such nuclear Overhauser effects were observed for those isomers (17) and (25)–(28) where this group had the *S* configuration. The same holds for the 4,5-*O*-benzylidene group, since, in the case of its *R* configuration (9), (10), (12), (19), (25) and (26), irradiation of the acetal proton enhanced the intensity of H 4 and H 5a, while for the *S* configuration (5),

**Table 1. $^1H$ n.m.r. data for solutions of *O*-benzylidene-D-arabinose mercaptal derivatives in $CDCl_3$**

| Compound | Chemical shifts ($\delta$) | | | | | | | Coupling constants (Hz) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | H 1 | H 2 | H 3 | H 4 | H 5a | H 5b | =CHPh | $J_{1,2}$ | $J_{2,3}$ | $J_{3,4}$ | $J_{4,5a}$ | $J_{4,5b}$ | $J_{5a,5b}$ |
| (3) | 4·56 | 4·59 | 4·40 | 4·37 | 3·89 | 4·32 | 6·22; 5·67 | 8·0 | 5·7 | [A] | [A] | [A] | 10·1 |
| (5) | 4·04 | 3·80 | 4·15 | 4·29 | 4·09 | 4·30 | 5·92 | 9·1 | 1·5 | 7·0 | 6·8 | [A] | 8·5 |
| (6) | 4·07 | 5·41 | 5·78 | 4·25 | 4·15 | 3·96 | 5·96 | 7·0 | 3·4 | 7·1 | 6·7 | 7·0 | 8·5 |
| (8) | 4·05 | 5·40 | 5·78 | 4·25 | 4·14 | 3·96 | 5·96 | 7·0 | 3·5 | 7·0 | 6·4 | 7·2 | 8·5 |
| (9) | 4·02 | 3·79 | 4·09 | 4·26 | 4·15 | 4·30 | 5·80 | 9·1 | 1·5 | 7·8 | 6·6 | 3·8 | 8·3 |
| (10) | 3·97 | 5·37 | 5·76 | 4·28 | 4·02 | 4·13 | 5·79 | 7·0 | 3·3 | 6·8 | 7·0 | 4·5 | 8·5 |
| (12) | 3·94 | 5·35 | 5·76 | 4·27 | 4·02 | 4·13 | 5·79 | 7·0 | 3·3 | 6·8 | 7·0 | 4·5 | 8·5 |
| (13) | 4·12 | 3·96 | 4·12 | 4·10 | 3·65 | 4·35 | 5·52 | [A] | 2·8[B] | [A] | 10·5 | 4·5 | 10·5 |
| (14) | 4·16 | 5·24 | 4·51 | 4·88 | 3·64 | 4·40 | 5·52 | 10·7 | 2·1 | 9·9 | 10·0 | 5·3 | 10·4 |
| (16) | 4·13 | 5·21 | 4·51 | 4·88 | 3·65 | 4·40 | 5·52 | 10·6 | 2·1 | 9·9 | 10·0 | 5·3 | 10·4 |
| (17) | 4·05 | 4·59 | 4·48 | 4·46 | 4·26 | 4·10 | 6·05; 5·98 | 4·2 | 5·0 | [A] | 6·5 | 5·0 | 8·5 |
| (19) | 3·95 | 4·50 | 4·43 | 4·28 | 4·14 | 4·32 | 6·12; 5·78 | 4·3 | 5·0 | 7·6 | 6·2 | 3·6 | 8·7 |
| (21) | 4·10 | 4·51 | 4·36 | 3·81 | 3·79 | 3·81 | 6·12 | 5·2 | 5·2 | 5·4 | [A] | 6·3 | 11·0 |
| (22) | 4·06 | 4·50 | 4·35 | 3·81 | 3·73 | 3·81 | 6·10 | 5·0 | 5·0 | 6·0 | [A] | 6·5 | 11·0 |
| (23) | 4·11 | 4·55 | 4·46 | 4·47 | 4·31 | 4·13 | 6·13; 6·03 | 4·8 | 7·1 | [A] | 6·0 | 5·2 | 8·5 |
| (25) | 3·85 | 4·59 | 4·36 | 4·41 | 4·19 | 4·32 | 5·96; 5·81 | 3·5 | 5·0 | 8·0 | 6·5 | 3·6 | 8·5 |
| (26) | 3·81 | 4·57 | 4·36 | 4·40 | 4·19 | 4·33 | 5·96; 5·80 | 3·5 | 5·0 | 8·0 | 6·5 | 3·5 | 8·4 |
| (27) | 4·04 | 4·57 | 4·26 | 3·85 | 3·73 | 3·85 | 5·88 | 4·0 | 5·1 | 7·5 | [A] | 6·5 | 11·0 |
| (28) | 4·00 | 4·56 | 4·27 | 3·85 | 3·73 | 3·85 | 5·89 | 4·5 | 5·2 | 7·6 | [A] | 6·5 | 11·0 |

[A] Not determined. [B] $J_{2,OH} = 5·2$ Hz.

**Table 2. $^{13}C$ n.m.r. data for solutions of *O*-benzylidene-D-arabinose mercaptal derivatives in $CDCl_3$**

| Compound | Chemical shifts ($\delta$) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | C 1 | C 2 | C 3 | C 4 | C 5 | =**C**HPh | **C**H$_3$CO | CH$_3$**C**O |
| (3) | 50·60 | 75·90[A] | 76·80[A] | 67·60 | 69·10 | 97·00; 102·20 | | |
| (5) | 55·55 | 70·72 | 70·04 | 76·30 | 68·39 | 103·66 | | |
| (6) | 51·68 | 72·57 | 71·21 | 74·77 | 67·59 | 103·83 | 20·76; 21·01 | 169·76; 169·78 |
| (8) | 52·18 | 72·61 | 71·19 | 74·74 | 67·58 | 103·80 | 20·75; 20·99 | 169·74; 169·76 |
| (9) | 55·58 | 71·21 | 70·12 | 76·50 | 68·46 | 104·46 | | |
| (10) | 51·66 | 72·27 | 71·07 | 74·16 | 67·11 | 104·30 | 20·82; 21·07 | 169·73; 169·83 |
| (12) | 52·23 | 72·38 | 71·11 | 75·23 | 67·13 | 104·32 | 20·87; 21·11 | 169·77; 169·90 |
| (13) | 54·42 | 69·81 | 80·00 | 61·43 | 71·11 | 100·92 | | |
| (14) | 50·94 | 69·75 | 77·22 | 62·65 | 68·01 | 101·57 | 2×20·67 | 169·77; 170·18 |
| (16) | 51·43 | 69·87 | 77·31 | 62·70 | 68·08 | 101·68 | 2×20·71 | 169·83; 170·22 |
| (17) | 52·98 | 83·90 | 79·27 | 76·11 | 68·47 | 103·92; 104·47 | | |
| (19) | 53·54 | 83·68 | 80·35 | 77·07 | 68·58 | 104·67; 104·68 | | |
| (21) | 53·70 | 80·29 | 82·32 | 72·53 | 64·43 | 104·30 | | |
| (22) | 54·29 | 82·22 | 80·46 | 72·59 | 63·53 | 104·39 | | |
| (23) | 53·21 | 82·87 | 79·99 | 76·78 | 67·74 | 103·92; 104·47 | | |
| (25) | 53·02 | 84·14 | 79·46 | 76·39 | 68·82 | 104·49; 104·51 | | |
| (26) | 53·53 | 84·10 | 79·56 | 76·47 | 68·86 | 104·52; 104·54 | | |
| (27) | 53·41 | 83·51 | 78·86 | 72·06 | 63·98 | 104·21 | | |
| (28) | 53·92 | 83·44 | 78·94 | 72·09 | 64·02 | 104·25 | | |

[A] These assignments could be reversed.

(6), (8), (17) and (23) irradiation of the acetal proton enhanced the signal intensity of H 5b only.

For the structure elucidation of the dioxan-type isomer (15) the n.m.r. data of its diacetate (16) were used. Spectral comparison with the parameters found for (14) showed striking similarities for both the ring carbons and the protons. A common feature of compounds (13), (14) and (16), possessing six-membered dioxan-type rings, is the characteristic coupling value of the *trans*-diaxial protons ($^3J_{4,5a}$ = 10–10·5 Hz).

## Experimental

*General Methods*

Organic solutions were dried with $Na_2SO_4$ and concentrated under diminished pressure. Optical rotations were carried out at 20°C on 1% solutions in $CHCl_3$ if not stated otherwise. T.l.c. was performed on Kieselgel 60 $F_{254}$ with EtOAc/hexane mixtures (*A* 1:1, *B* 1:2, *C* 1:3, *D* 1:4, *E* 1:5, and *F* 1:10), with detection by using u.v. light and/or 1:1 0·1 M $KMnO_4$/1 M $H_2SO_4$ at 200°C. For column chromatography Kieselgel 60 was used. $^1H$ and $^{13}C$ n.m.r. spectra were recorded with a Varian XL-400 spectrometer at 400 MHz ($^1H$) and 100 MHz ($^{13}C$) on solutions in $CDCl_3$ (internal $Me_4Si$) if not stated otherwise. Signal multiplicities of the $^{13}C$ n.m.r. spectra were obtained from DEPT experiments. N.m.r. data for all isolated compounds are summarized in Tables 1 and 2. For the determination of the isomer ratio the intensity of the benzylidene proton was used.

*Reaction of (1) with α,α-Dimethoxytoluene*

*(a)* A solution of (1)[11] (12·8 g, 50 mmol) and *p*-toluenesulfonic acid (0·5 g, 2·5 mmol) in dimethylformamide (40 ml) and α,α-dimethoxytoluene (18·2 g, 120 mmol) was stirred for 3 h at 75–80°C at 4 kPa, then cooled, poured into ice-cold $NaHCO_3$ solution (3%, 300 ml), and the mixture extracted with ether (3×200 ml). The combined extracts were washed with water (100 ml), dried and concentrated to a syrup (21 g), which according to $^1H$ n.m.r. contained four bis-dioxolan diastereomers (17), (19), (23) and (25) (ArC**H**: 6·13+6·03; 6·12+5·78; 6·04+5·98; and 5·95+5·82 ppm) as well as the dioxan derivative (13) (ArC**H**: 5·52 ppm) in the ratio of 3:6:4:7:2. This syrup was dissolved in hot EtOH (15 ml), and the solution was kept for 3 days at 5°C. The formed crystals were filtered off and washed with EtOH to give 2,3-(*R*):4,5-(*R*)-di-*O*-benzylidene-D-arabinose diethyl dithioacetal (19) (4·7 g, 21·7%) m.p. 104–106°C, $[\alpha]_D$ +10°; (lit.[5] m.p. 103–105°C, $[\alpha]_D$ +12·6°).

The residue obtained on concentration of the EtOH filtrate was submitted to column chromatography (solvent *F*). Fraction A ($R_F$ 0·60), on concentration and treatment with hexane gave (3) (15 mg, 0·06%), m.p. 171–172°C, having n.m.r. spectra identical with those published in lit.:[6] m.p. 173–174°C.

Fraction B ($R_F$ 0·55), on concentration, gave a syrup which on treatment with EtOAc/hexane afforded a further crop of (19) (1·0 g, 4·6%). The syrup obtained on concentration of the filtrate (6·5 g, 30%) contained according to n.m.r., besides traces of (19), 2,3-(*S*):4,5-(*S*)-di-*O*-benzylidene-D-arabinose diethyl dithioacetal (17) and 2,3-(*R*):4,5-(*S*)-di-*O*-benzylidene-D-arabinose diethyl dithioacetal (23) in the ratio of 3:4; these compounds could not be separated.

Fraction C ($R_F$ 0·45) on concentration gave *2,3-(S):4,5-(R)-di-O-benzylidene-D-arabinose diethyl dithioacetal* (25) (6·2 g, 29%) as a syrup, $[\alpha]_D$ +55·3° (Found: C, 63·8; H, 6·6; S, 14·7. $C_{23}H_{28}O_4S_2$ requires C, 63·9; H, 6·5; S, 14·8%).

Elution was continued with solvent *B* to give, on concentration of the fractions having $R_F$ 0·30, *3,5-O-(R)-benzylidene-D-arabinose diethyl dithioacetal* (13) (1·55 g, 9%), m.p. 128–129°C (acetone/hexane), $[\alpha]_D$ −72° (Found: C, 55·7; H, 7·2; S, 18·6. $C_{16}H_{24}O_4S_2$ requires C, 55·8; H, 7·0; S, 18·6%).

*(b)* A solution of (1) (5·1 g, 20 mmol) and *p*-toluenesulfonic acid (20 mg) in α,α-dimethoxytoluene (6·6 g, 44 mmol) and dimethylformamide (20 ml) was stirred for 3 h at 60°C and 4 kPa. The mixture was processed as described for *(a)*. The semisolid residue, obtained on concentration of the ether solution, showed on t.l.c. (solvent *C*) two set of spots ($R_F$ 0·85–0·70 and 0·35–0·20) which were separated by column chromatography, and proved to be mixtures of dibenzylidene (1·9 g, 22%) and monobenzylidene derivatives, respectively. Evaporation of the latter fraction gave a solid residue (4·7 g, 68%), containing according to n.m.r. (5), (9) and (13) in the ratio of 1:1·4:1. As the last two isomers had almost identical $R_F$ values, the mixture was acetylated with $Ac_2O$ (10 ml) in pyridine (20 ml) to give a semisolid residue (6 g) after the usual workup. This was submitted to column chromatography (solvent *B*). The fractions having $R_F$ 0·7, on evaporation, gave *2,4-di-O-acetyl-3,5-O-(R)-benzylidene-D-arabinose diethyl dithioacetal* (14) (1·5 g, 25%), m.p. 91–93°C (ether/hexane), $[\alpha]_D$ +4° (Found: C, 56·0; H, 6·6; S, 14·9. $C_{20}H_{28}O_6S_2$ requires C, 56·0; H, 6·6; S, 15·0%).

The fractions having $R_F$ 0·55, on evaporation, gave *2,3-di-O-acetyl-4,5-O-(S)-benzylidene-D-arabinose diethyl dithioacetal* (6) (1·3 g, 21·5%) as a syrup, $[\alpha]_D$ +16° (Found: C, 56·1; H, 6·7; S, 14·8. $C_{20}H_{28}O_6S_2$ requires C, 56·0; H, 6·6; S, 15·0%).

The fractions having $R_F$ 0·45, on evaporation, gave *2,3-di-O-acetyl-4,5-O-(R)-benzylidene-D-arabinose diethyl dithioacetal* (10) (2·3 g, 38·2%), m.p. 88–90°C, $[\alpha]_D$ +18° (Found: C, 56·1; H, 6·6; S, 14·9. $C_{20}H_{28}O_6S_2$ requires C, 56·0; H, 6·6; S, 15·0%).

*4,5-O-(S)-Benzylidene-D-arabinose Diethyl Dithioacetal (5)*

To a solution of (6) (0·43 g) in methanol (10 ml), M sodium methoxide (0·05 ml) was added. After 24 h at room temperature the solution was concentrated to give (5) (0·29 g, 84%), m.p. 72–74°C (acetone/hexane), $[\alpha]_D$ −33°, $R_F$ 0·25 (solvent *B*) (Found: C, 55·7; H, 7·1; S, 18·5. $C_{16}H_{24}O_4S_2$ requires C, 55·8; H, 7·0; S, 18·6%).

*4,5-O-(R)-Benzylidene-D-arabinose Diethyl Dithioacetal (9)*

Deacetylation of (10) (0·43 g) was carried out as described above to give (9) (0·30 g, 88%), m.p. 93–94°C (acetone/hexane), $[\alpha]_D$ −67°, $R_F$ 0·20 (solvent *B*) (Found: C, 55·8; H, 7·1; S, 18·6. $C_{16}H_{24}O_4S_2$ requires C, 55·8; H, 7·0; S, 18·6%).

*3,5-O-(R)-Benzylidene-D-arabinose Diethyl Dithioacetal (13)*

Deacetylation of (14) (0·43 g) was carried out as described above to give (13) (0·34 g, 92%).

*Reaction of (1) with Benzaldehyde-Zinc Chloride*

A suspension of freshly fused $ZnCl_2$ (3 g) in benzaldehyde (10 ml) was stirred for 30 min, then (1) (2·6 g) was added. Stirring was continued for 48 h, then the reaction mixture was poured into a mixture of $CHCl_3$ (20 ml), water (20 ml) and $K_2CO_3$ (4 g). The organic solution was separated, washed with water, dried, concentrated and the benzaldehyde distilled off at 1·5 Pa. The semisolid residue obtained was boiled with hexane (40 ml), and the hot solution was decanted from the undissolved syrup, which according to t.l.c. contained mostly monobenzylidene derivatives. The hexane solution on t.l.c. (solvent *F*) showed two sets of spots ($R_F$ *c.* 0·55 and *c.* 0·45) and contained according to $^1H$ n.m.r. five di-*O*-benzylidene isomers, namely (17), (19), (23), (25) and one further isomer (ArC**H**: 5·90+5·87 ppm), in the ratio of 1:24:6:8:2. The hexane solution was concentrated to 20 ml and was decanted from the separated oil. On further concentration to 5 ml

and cooling, compound (19) (1·1 g, 25·5%) was obtained, identical with that described above. No further isomer could be separated by column chromatography of the mother liquor.

*Reaction of (1) with Benzaldehyde–HCl*

A stream of HCl was passed into a stirred and cooled (0°C) slurry of (19) (2·5 g) in benzaldehyde (10 ml). After 5 min a turbid solution was obtained which solidified after 10 min and, after dilution with hexane, was filtered to give (19) (1·8 g, 42%), identical with that described above. The filtrate was evaporated, the residue dissolved in $CHCl_3$, washed with aq. 4% $NaHCO_3$ solution and water, dried, evaporated and benzaldehyde was removed at 1·5 Pa. The residue (2 g, 46%) contained according to n.m.r. the four bis-dioxolan diastereomers (17), (19), (23) and (25) in the ratio of 8:10:1:1.

*2,3-(R)-O-Benzylidene-D-arabinose Diethyl Dithioacetal (21)*

A solution of (19) (2·9 g) in EtOH (95 ml), water (25 ml) and AcOH (75 ml) was boiled for 1 h and was then concentrated. Water and subsequently EtOH were evaporated from the residue which solidified on cooling and was isolated by filtration with hexane to give (21) (1·9 g, 82%), m.p. 100–102°C (EtOH/water), $[\alpha]_D$ +21°, $R_F$ 0·50 (solvent *A*) (lit.[5] m.p. 102–103°C, $[\alpha]_D$ +24·6°).

*2,3-O-(S)-Benzylidene-D-arabinose Diethyl Dithioacetal (27)*

Partial hydrolysis of (25) (1·5 g) was carried out as described for (21) to give after column chromatography (solvent *A*) (27) (0·8 g, 67%) as a *syrup*, $[\alpha]_D$ +59°, $R_F$ 0·40 (solvent *A*) (Found: C, 55·6; H, 7·2; S, 18·5. $C_{16}H_{24}O_4S_2$ requires C, 55·8; H, 7·0; S, 18·6%).

*Reaction of (2) with Benzaldehyde–HCl*

To a stirred solution of (2)[10] (2·84 g) in benzaldehyde (10 ml) and dioxan (10 ml) conc. HCl (10 ml) was added at 0°C. Stirring was continued for 30 min; then the mixture was poured onto ice, extracted with $CHCl_3$, and the organic solution was washed with aq. 4% $NaHCO_3$ solution and water. The residue obtained on concentration of the dried solution was submitted to column chromatography (solvent *F*). The fraction having $R_F$ *c.* 0·6, on concentration, gave a syrup (2·1 g, 45·6%) which according to n.m.r. contained three 2,3:4,5-di-*O*-benzylidene diastereomers [ArC**H**: 6·13+6·02 (18), 6·12+5·78 (20), and 6·04+5·99 ppm (24)] in the ratio of 2:3:1; these compounds could not be separated by further chromatography. The fraction having $R_F$ 0·45, on concentration, gave *2,3-(S):4,5-(R)-di-O-benzylidene-D-arabinose dipropyl dithioacetal* (26) (0·2 g, 4·3%) as a syrup, $[\alpha]_D$ +55° (ArC**H**: 5·96+5·80 ppm) (Found: C, 65·1; H, 7·1; S, 13·8. $C_{25}H_{32}O_4S_2$ requires C, 65·2; H, 7·0; S, 13·9%).

*Reaction of (2) with Benzaldehyde–Zinc Chloride*

The reaction of (2) (5·6 g) with benzaldehyde (20 ml) and $ZnCl_2$ (6 g) was performed as described for (1). The residue of the concentrated $CHCl_3$ solution was submitted to column chromatography (solvent *F*). The fraction having $R_F$ 0·6, on concentration, gave a syrup (4·3 g, 46·7%) containing the same three dibenzylidene isomers in a similar ratio as described for the previous reaction. The fraction having $R_F$ 0·45, on concentration, gave (26) (1·5 g, 16·3%).

*Reaction of (2) with α,α-Dimethoxytoluene*

(a) The reaction of (2) (5·6 g) was carried out as described for (1) [method *(a)*], and the residue obtained on concentration of the ether solution was submitted to column chromatography as described for the previous reaction. Concentration of the first fraction ($R_F$ 0·6) gave a syrup (4·5 g, 49%) containing the above-mentioned three 2,3:4,5-di-*O*-benzylidene diastereomers in a ratio of *c.* 1:1:1. Concentration of the second fraction ($R_F$ 0·45) afforded (26) (2·25 g, 24·5%).

*(b)* Reaction of (2) (5·6 g) was carried out as described for (1) [method *(b)*]. The residue obtained on concentration of the ether solution contained according to t.l.c. mono- (3·2 g, 43%) and di-benzylidene derivatives (1·8 g, 20%) which were separated as mixtures by flash column chromatography (solvent *C*). The individual monobenzylidene isomers were separated by column chromatography (solvent *C*). Concentration of the first fraction ($R_F$ 0·50) gave on evaporation *4,5-O-(S)-benzylidene-D-arabinose dipropyl dithioacetal* (7) (0·6 g, 8%), m.p. 66–67°C (ether/hexane), $[\alpha]_D$ −46° (Found: C, 58·0; H, 7·6; S, 17·1. $C_{18}H_{28}O_4S_2$ requires C, 58·0; H, 7·6; S, 17·2%). Concentration of the second fraction ($R_F$ 0·35) afforded *4,5-O-(R)-benzylidene-D-arabinose dipropyl dithioacetal* (11) (1·25 g, 17%), m.p. 88–90°C (ether/hexane), $[\alpha]_D$ −78° (Found: C, 58·0; H, 7·7; S, 17·2. $C_{18}H_{28}O_4S_2$ requires C, 58·0; H, 7·6; S, 17·2%). The third fraction ($R_F$ 0·25), on concentration, gave *3,5-O-(R)-benzylidene-D-arabinose dipropyl dithioacetal* (15) (1·20 g, 16%), m.p. 140–142°C (ether/hexane), $[\alpha]_D$ −85° (Found C, 57·9; H, 7·5; S, 17·1. $C_{18}H_{28}O_4S_2$ requires C, 58·0; H, 7·6; S, 17·2%).

*(c)* When the same reaction was quenched after 2 h, the dibenzylidene isomers were present only in traces and the dioxan-type isomer (15) was absent too. The only two isomers which could be detected and separated were (7) (27%) and (11) (29%).

*Equilibration of the Monobenzylidene Isomers (5) and (9)*

This process was investigated by $^1H$ n.m.r. by using a 1% solution of the isomers in $CDCl_3$ and a catalytic amount of trifluoracetic acid. The time for obtaining a *c.* 1:1 equilibrium mixture was <10 min for (5), and *c.* 1·5 h for (9). This process was accompanied by a slow hydrolysis affording benzaldehyde and (1), which started to precipitate from the solution.

*Equilibration of the Monobenzylidene Isomers (7) and (11)*

To a solution of (7) (0·1 g) in $CHCl_3$ (10 ml) trifluoroacetic acid (10 μl) was added; samples were withdrawn at different time intervals, quenched with $Et_3N$ and the course of the reaction was followed by t.l.c. After 30 min, *c.* 50% of (7) was converted into (11). When isomer (11) was treated under identical conditions, *c.* 60 min were needed for a 50% conversion into (7).

*Acetylation of (7), (11) and (15)*

Acetylation of the isomers (0·2 g) was performed with acetic anhydride (0·5 ml) in pyridine (1 ml) to give the following compounds after the usual processing and purification by column chromatography (solvent *D*). *2,3-Di-O-acetyl-4,5-O-(S)-benzylidene-D-arabinose dipropyl dithioacetal* (8) (0·22 g, 90%), $[\alpha]_D$ +17° (Found: C, 57·8; H, 7·1; S, 14·0. $C_{22}H_{32}O_6S_2$ requires C, 57·9; H, 7·1; S, 14·0%). *2,3-Di-O-acetyl-4,5-O-(R)-benzylidene-D-arabinose dipropyl dithioacetal* (12) (0·2 g, 83%), $[\alpha]_D$ +18° (Found: C, 57·8; H, 7·1; S, 13·9. $C_{22}H_{32}O_6S_2$ requires C, 57·9; H, 7·1; S, 14·0%). *2,4-Di-O-acetyl-3,5-O-(R)-benzylidene-D-arabinose dipropyl dithioacetal* (16) (0·19 g, 77%), $[\alpha]_D$ 0° (Found: C, 57·9; H, 7·1; S, 13·9. $C_{22}H_{32}O_6S_2$ requires C, 57·9; H, 7·1; S, 14·0%).

*Reaction of (15) with α,α-Dimethoxytoluene*

Benzylidenation of (15) (0·37 g) was carried out as described for (2) [method *(a)*] to give a mixture of the four 2,3:4,5-di-*O*-benzylidene diastereomers (0·23 g, 50%) the n.m.r. spectrum of which was similar to that obtained from (2) according to method *(a)*. From this mixture (26) could be isolated by column chromatography (50 mg, 10%).

*2,3*-O-(S)-*Benzylidene*-D-*arabinose Dipropyl Dithioacetal (28)*

A solution of (26) (2·3 g) in EtOH (60 ml) and AcOH (45 ml) was boiled for 1 h and was then concentrated. Water and subsequently EtOH were evaporated from the residue which became partly crystalline and was filtered with ether to give fully hydrolysed (2) (0·3 g, 21·4%), m.p. 128–130°C. The residue obtained on concentration of the filtrate was purified by column chromatography (solvent *A*) to give (28) (1·1 g, 59%), m.p. 68–70°C, $[\alpha]_D$ +68°, $R_F$ 0·45. (Found: C, 57·9; H, 7·6; S, 17·1. $C_{18}H_{28}O_4S_2$ requires C, 58·0; H, 7·6; S, 17·2%).

*2,3*-O-(R)-*Benzylidene*-D-*arabinose Dipropyl Dithioacetal (22)*

A solution of the mixture of dibenzylidene isomers (3·3 g), obtained from the reaction of (2) with $\alpha,\alpha$-dimethoxytoluene according to method *(a)*, was hydrolysed as described for (28) to give after separation by column chromatography (solvent *A*) (22) (1·2 g, 45%), m.p. 108–110°C, $[\alpha]_D$ +19°, $R_F$ 0·55 (Found: C, 57·9; H, 7·6; S, 17·2. $C_{18}H_{28}O_4S_2$ requires C, 58·0; H, 7·6; S, 17·2%). Concentration of the fraction having $R_F$ 0·45 gave (28) (0·6 g, 22·5%).

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