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Preparation and Reactions of Some Cyclic Orthoester Derivatives

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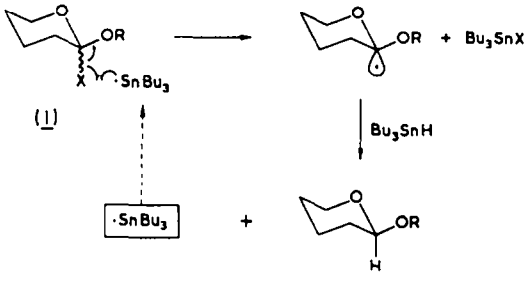
Abstract: Deprotonation of the alkoxysulphone (5) followed by quenching with diphenyl disulphide yields the dithioorthoester (6) and not the expected ketene monothioacetal (7). Attempts at orthoester exchange of (6) with decanol with a variety of reagents lead to ring opened products. Quenching of the anion derived from (5) with sulphuryl chloride or bromine leads respectively to the chloride (19) and bromide (20). Solvolysis of these halides leads to formation of sulphinate esters.

In connection with a project aimed at the design of synthetically useful stereoselective radical reactions[1] we have become interested in the reactions of pyramidal[2] 2-alkoxytetrahydropyran-2-yl radicals and their potential applications in carbohydrate chemistry. We wish to report here some novel reactions encountered in the course of our search for potentially large scale preparations of precursors for these radicals.

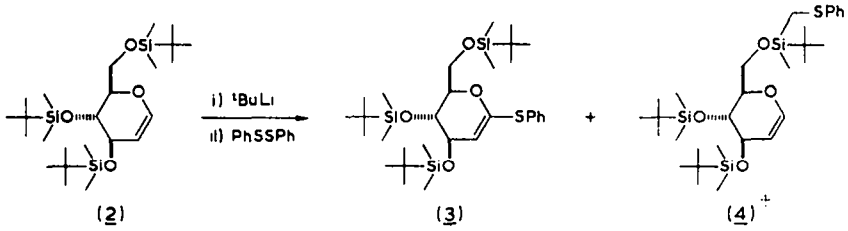
The successful use[3] of organotin reagents in conjunction with glycosyl halides and pseudohalides as an entry into glycosyl radicals on a preparative scale led us to the conclusion that 2-alkoxytetrahydropyran-2-yl radicals in general and 1-alkoxylglycos-1-yl radicals in particular ought to be available by a similar treatment of a 2-alkoxy-2-halogenotetrahydropyran or related compounds illustrated in scheme 1.



X = halogen, SPh, SMe, NO_2, SePh

Scheme 1

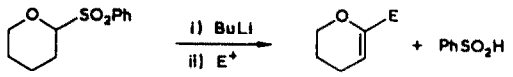
Reports[4] by Ferrier on the free radical bromination of glucose pentaacetate and related compounds with N-bromosuccinimide in tetrachloromethane suggest that bromination occurs predominantly at the 5 position (glucose numbering) and so rule out the most obvious entry into (1) (X = halogen). Thus we decided to look at methods for the preparation of (1) with phenylthio or methylthio as the radical labile group. Early attempts at the preparation of systems related to (1) (X = SMe) via S-alkylation of thionolactones in the presence of a suitable alcohol and via Pummerer reactions (X =SPh) of 1-phenylsulphinyl glycosides again in the presence of a suitable alcohol failed and so we turned to the preparation of (1) (X = SPh) by the addition of alcohols to 1-phenylthioglycals. Thus, following reports by Nicolaou[5] and Sinaÿ[6] on the regioselective deprotonation of 3,4,6-tri-O-t-butyldimethylsilylglucal (2) with t-butyllithium according to the general procedure of Boeckman[7] for the formation of cyclic vinyl ether carbanions, and a report by Hanessian[8] using Schlosser's base for a similar purpose, we reacted(2) with t-butyllithium and quenched with diphenyl disulphide (Scheme 2). After aqueous work and flash chromatography on silica the desired product (3) was isolated,but only in 15% yield. A second product (4) containing the phenylthio group in one of the protecting groups was isolated in 19% yield indicating that deprotonation in one of the protecting groups was competing with vinyl ether carbanion formation and this coupled with the low yield of (3) caused us to abandon this route. The various other possibilities suggested by Hanessian[8,9] and Sinaÿ[6,9] involving preparation of 1-tri-n-butylstannylglycals followed by trans-metallation with n-butyllithium were considered but not applied in favour of an apparently simpler scheme involving the use of 1-arylsulphonylglycals. Ley has demonstrated[10] that 2-phenylsulphonyltetrahydropyran is cleanly deprotonated with n-butyllithium and that following quenching of the carbanion with a range of electrophiles elimination of phenylsulphinic acid occurs to give 2-substituted-5,6-dihydropyrans (Scheme 3). Furthermore Sinaÿ has reported[11] studies on the deprotonation/alkylation of 1-phenylsulphonylglycosides indicating that any model studies ought eventually to be applicable in the carbohydrate field.



(2) (3) (4)†

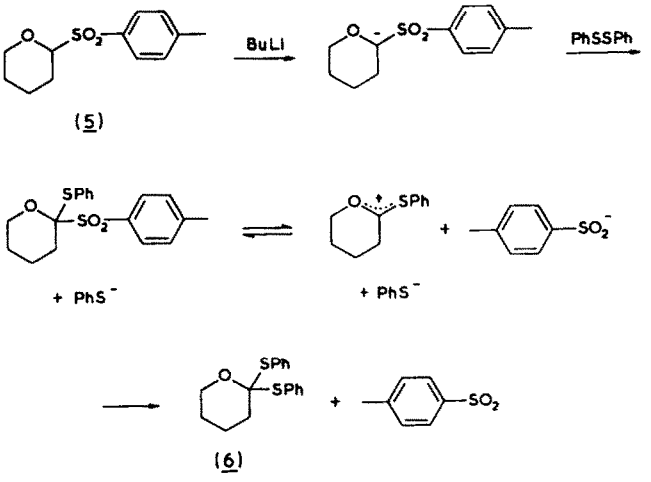
Scheme 2

† No attempt was made to determine which of the three protecting groups was undergoing deprotonation, although in Scheme 2 we represent it as the least hindered primary one for simplicities sake



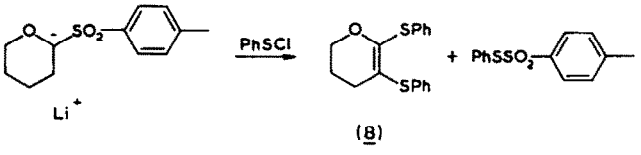
Scheme 3

Thus dihydropyran was reacted with 4-toluenesulphinic acid to give the arylsulphonyltetrahydropyran (5) in 81% isolated yield. Deprotonation of (5) in THF with n-butyllithium at -78 °C followed by quenching with diphenyl disulphide, aqueous workup and chromatography gave the dithioorthoester (6) as a white crystalline solid in 62% yield and not the expected ketene monothioacetal (7). A possible mechanism for the formation of (6) is outlined in scheme 4 although it is also possible to write an electron transfer mechanism of the $S_{RN}1$ type.



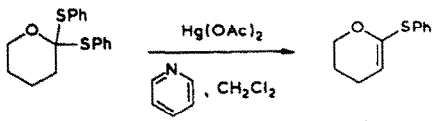
Scheme 4

We considered that replacement of diphenyl disulphide with phenylsulphenyl chloride as electrophile might lead to (7); however quenching of the lithium salt of (5) with this latter reagent gave 2,3-bisphenylthio-5,6-dihydropyran (8) as the only pyranoid product, isolated in 23% yield and phenylthio 4-toluenesulphonate in 56% yield (Scheme 5). Evidently (7) was formed in the reaction but underwent attack by phenylsulphenyl chloride followed by loss of hydrogen chloride.



Scheme 5

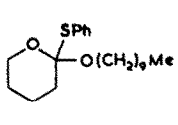
Ketene monothioacetal (7) was eventually prepared by reaction of (6) with mercuric acetate and pyridine in dichloromethane (Scheme 6).



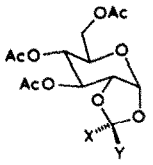
(6) (7)

Scheme 6

Having thus obtained (7) we attempted its transformation into a monothioorthoester by treatment with 1-decanol in dry dichloromethane with a variety of acid catalysts including camphor 10-sulphonic acid, 4-toluenesulphonic acid, Amberlite IR-120(H) and glacial acetic acid. In no case were we able to isolate any of the desired product (9); thiophenol being liberated in all reactions. On carrying out analogous reactions in deuteriochloroform and following by ^{13}C-NMR spectroscopy it was possible to observe a peak at δ 111.6 ppm which we interpret as the C-2 signal in (9). The ^{13}C NMR chemical shifts of the orthoester carbons in (10) and (11) are δ 117.9 ppm and δ 118.25 ppm respectively[12] and so in reasonable agreement with this assumption. Evidently the acid catalysed addition of alcohols to the ketene-monothioacetal (7) does not permit the isolation of monothioorthoesters such as (9) and so we turned our attention to orthoester exchange reactions using the readily available (6) as substrate. Treatment of (6) with mercuric chloride and pyridine in dichloromethane in the presence of decanol gave two products identified as (12) (24%) and (13) (11%) but no (9). Treatment of (6) first with triethyloxonium tetrafluoroborate in dichloromethane and then with decanol gave (13) (16%) and (14) (22%) but again no (9). Triphenylmethyl tetrafluoroborate, decanol and (6) gave a good yield (72%) of triphenylmethyl thiophenate but once again no (9) The isolation of decyl esters (10)-(12) can be taken as reasonable evidence for the formation of (9) and as an indication of its instability under the reaction conditions. Simple monothioorthoesters have been prepared[13] by aluminium chloride catalysed exchange reactions of n-butyl mercaptan with triethylorthoesters but are reported to be highly sensitive to the reaction conditions. More complex monothioorthoesters (10) and (11) have been prepared and isolated and shown to be readily hydrolysed[12,14] Okuyama has studied[15] the hydrolysis of mixed O,S-orthoesters and finds that they are subject to spontaneous fragmentation with preferential cleavage of the carbon-sulphur bond in (15) suggesting that (9) might be less stable than (6). Finally in this context we note the failure of Khouri and Kaloustian[16] to isolate (17) from the reaction of (16) with sodium methanethiolate under conditions in which (18) was readily isolable

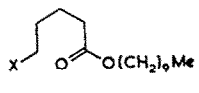


(9)

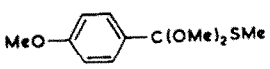


(10) X = Me, Y = S–C6H5

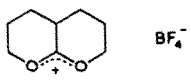
(11) X = S–C6H5, Y = Me



(12) X = Cl
(13) X = SPh
(14) X = O(CH2)9Me



(15)



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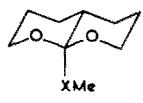
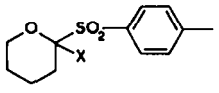
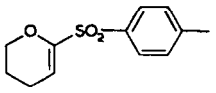


(17) X = S
(18) X = O

Given the evident difficulties in the preparation and isolation of even simple monothioorthoesters we turned our attention to the preparation of 2-alkoxy-2-arylsulphonyltetrahydropyrans with a view to the formation of radicals via a controlled reductive desulphonylation possibly with lithium naphthalenide. Thus treatment of the lithium salt of (5) with sulphuryl chloride in THF at -78 °C gave the 2-chloro-2-(4'-toluenesulphonyl)-tetrahydropyran (19) in 40% isolated yield as a colourless crystalline solid, 4-toluenesulphonyl chloride (22%) and a small amount (≈5%) of the alkoxyvinylsulphone (21). Attempts at the preparation of bromide (20) by quenching of the lithium salt of (5) with N-bromosuccinimide were unsuccesful; the major products being 4-toluenesulphonyl bromide and the alkoxyvinylsulphone (21), however quenching of the same anion with bromine gave the crystalline bromide (20) in 67% yield

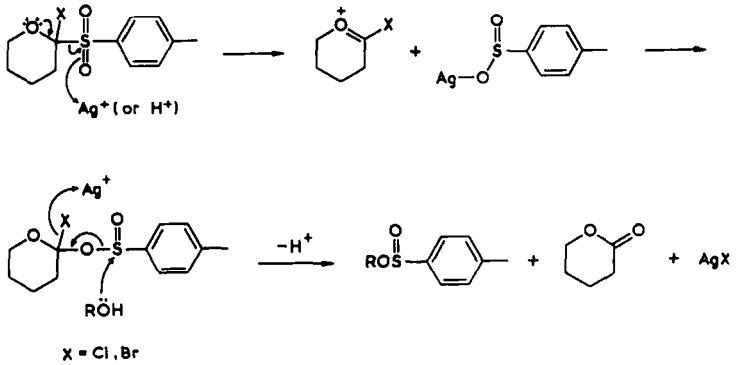


(19) X=Cl
(20) X=Br



(21)

Although it is reasonably well known[17] that α-arylsulphonyl groups strongly retard S_N2 reactions due to a combination of steric and field effects[18] and that only very good leaving groups are displaced[19] we considered that this lack of reactivity might be offset by the presence of the α-oxygen in (19) and (20) and that it should be possible to induce an S_N1 type mechanism In the event reaction of chloride (19) with n-decanol in dichloromethane in the presence of silver(I) triflate gave not the expected 2-arylsulphonyl-2-alkoxytetrahydropyran but decyl 4-toluenesulphinate in 71% yield. Similarly solvolysis of bromide (20) in methanol with a catalytic quantity of camphor 10-sulphonic acid gave methyl 4-toluenesulphinate as the major product (75%). Clearly a completely different mechanism to the one expected is operating and in scheme 7 we suggest that this may involve co-ordination of Ag^+(or H^+) to the sulphonate oxygen followed by rearrangement to a tetrahydropyran-2-yl sulphinate ester followed by reaction with the alcohol.



Scheme 7

In conclusion we consider that although we have not achieved our primary objective of preparing compounds likely to be ready precursors for 2-alkoxy-tetrahydropyran-2-yl radicals we have discovered some novel modes of reactivity of α-arylsulphonyltetrahydropyrans and their derivatives. We are currently pursuing our primary aim by an approach involving the decarboxylation of ulusonic acid ethers.

Acknowledgements: We thank Professor S V Ley, Imperial College London for helpful discussion, the SERC for financial assistance and Nuffield Foundation for an equipment grant.

Experimental

General : Melting points are uncorrected and were determined with a Kofler hot stage apparatus. Optical rotations were measured in chloroform with an Optical Activity AA-10 polarimeter. IR spectra were recorded as chloroform solutions with a Perkin-Elmer 983 spectrophotometer. Mass spectra were obtained on a VG 7070F/H spectrometer. ^{1}H-NMR spectra were obtained on Varian VXR-400, XL-200 and Jeol PMX 60 spectrometers in deuteriochloroform solutions. ^{13}C-NMR spectra were obtained on Varian VXR-400 or XL-200 instruments (at 100.6 MHz and 50 MHz respectively). Chemical shifts (δ) are in p.p.m. downfield from tetramethylsilane as internal standard. All solvents were purified and dried by standard methods.

Reaction of 3,4,6-tri-O-t-butyldimethylsilyl-D-glucal with t-butyllithium and diphenyl disulphide.

t-Butyllithium in hexane (1.53 M, 1.47 cm^3, 2.25 mmol) was added dropwise to a solution of 3,4,6-tri-O-t-butyldimethylsilyl-D-glucal (1.00g, 2.05 mmol) in THF (0.17 cm^3, 2.05 mmol) and 40-60 petroleum ether (1 cm^3) under nitrogen at -78 °C The reaction mixture was then allowed to warm to 0 °C and stirred for 1 hr before treatment with diphenyl disulphide (0.45 g, 2.06 mmol) in THF (1 cm^3). After a further 1 hour at 0 °C the reaction was diluted with water and ether extracted (3 x 25 cm^3). The combined extracts were washed with water, dried over magnesium sulphate, filtered and evaporated to dryness to give a pale yellow syrup (1.12 g). Chromotography on silica gel (eluent: diethyl ether-40-60 petroleum ether 1:20) gave 1-phenylthio-3,4,6-tri-O-t-butyl-dimethylsilyl-D-glucal (3) as a colourless oil (0.18 g, 0.3 mmol, 15%) with $[\alpha]_D$ = -2° (c=1); ν_{max}: 3029, 2940, 2892, 2854, 1640, 1475, 1440, 1254, 1087, 1004, 842, 781, 705, 670 cm^{-1}; ^{1}H-NMR δ (400 MHz): 7.39 (2H, m, ArH), 7.26 (2H, m, ArH), 7.18 (1H, m, ArH), 5.23 (1H, d, J = 5Hz, H-2), 4.10 (1H, m), 3.99 (1H,m), 3.85 (3H, m),0.90 (9H, s), 0.87 (9H, s), 0.86 (9H, s) 0.1-0.01 (18H. m). Further elution afforded the glucal (4) as a colourless oil (0.23 g, 0.39 mmol, 19%) with $[\alpha]_D$ = -25° (c = 1); ν_{max}: 3030, 2939, 2892, 2851, 1645, 1465, 1254, 1087, 1004, 840, 780, 707, 670 cm^{-1}; ^{1}H-NMR (400 MHz) δ: 7.22 (4H, m, ArH), 7.07 (1H, m, ArH), 6.27(1H, d, J = 6Hz),(H-1),4.63 (1H,t, H-2), 4.02-3.99 (2H, m), 3.85-3.79 (2H, m) 3.77 (1H, m), 2.29 (1H, m, SiCH$_2$SPh), 2.20 (1H, m, SiCH$_2$SPh), 0.94 (9H, s, t-Bu), 0.83 (9H, s, t-Bu), 0.82 (9H, s, t-Bu), 0.18 (3H, s, Me), 0.04 (12H, m, 4 x Me).

2-(4'-Toluenesulphonyl)tetrahydro-2H-pyran (5) 3,4-Dihydro-2H-pyran (1.62 g, 19.2 mmol) was added dropwise to a stirred solution of 4-toluenesulphinic acid (3.00 g, 19.2 mmol) in dry dichloromethane (125 cm^3) at room temperature under nitrogen. After stirring for 2 hr at room temperature the solvent was removed in vacuo and the crude product recrystallised from diethyl ether - 40-60 petroleum ether to give the title compound (5) as transparent needles (3.75 g, 15.6 mmol, 81%) with mp 66-68 °C; ν_{max}: 2945, 2852, 1598, 1440, 1318 1301, 1144, 1114, 1081, 1034, 1001, 904,880, 630 cm^{-1}; ^{1}H-NMR (200 MHz) δ: 7.78 (2H, d, J = 8H, ArH), 7.34 (2H, d, J = 8Hz, ArH), 4.36 (1H, dd, J = 3.2, 9.2 Hz, H-2), 4.10 (1H, m, H-6), 3.44 (1H m, H-6), 2.43 (3H, s, ArCH$_3$), 2.12-1.49 (6H, m); m/z: 139, 123, 91, 85. (Found: C, 59.9; H, 6.6; S, 13.3 calc. for $C_{12}H_{16}O_3S$: C, 60.0; H, 6.7; S, 13.3%)

2,2-(Bisphenylthio)tetrahydropyran (6). A solution of the sulphone (5) (5.00 g, 20.8 mmol) in dry THF (20 cm^3) cooled to -78 °C under nitrogen was treated dropwise with n-butyllithium in hexane (2.5 M, 9.15 cm^3, 22.9 mmol). After 15 mins at -78 °C solid diphenyl disulphide (5.00 g, 22.9 mmol) was added portionwise and the mixture allowed to come to room temperature over 2 hrs. The reaction mixture was poured into saturated sodium hydrogencarbonate solution and ether extracted (3 x 25 cm^3). The combined extracts were dried over magnesium sulphate and evaporated in vacuo to give a pale yellow syrup which was purified by chromatography on silica gel (eluent: diethyl ether - 40-60 petroleum ether 2:100) to give the dithioorthoester (6) (3.88 g, 12.9 mmol, 62%) as a white crystalline solid with mp 60-62 °C (ether - petroleum ether) ν_{max}:2985, 2939, 2865, 1578, 1471, 1436, 1114, 1094, 1057, 1014, 914, 873, 837 cm^{-1}; ^{1}H-NMR (200 MHz) δ: 7.64 (4H, m, ArH), 7.30 (6H, m, ArH), 4.06 (2H, t, J = 5.6Hz, H-6), 1.99-1.44 (6H, m); ^{13}C-NMR (50 MHz) δ: 135.1, 128.4, 128.3, 99.2 (C-2), 64.6, 35.7, 24.4, 20.5; m/z: 194 (MH^+ - SPh), 110, 85. (Found: C, 67.5; H, 6.0; S, 20.8, calc. for $C_{17}H_{18}OS_2$, C, 67.5; H, 6.0; S, 21.2%).

2,3-(Bisphenylthio)-5,6-dihydropyran (8). 2.5 M n-Butyllithium (1.75 cm^3, 4.37 mmol) was added dropwise at -78 °C to a stirred solution of sulphone (5) (1.00 g, 4.16 mmol) in THF (15 cm^3) under nitrogen. After 20 mins at -78 °C phenylsulphenyl chloride (0.66 g, 4.85 mmol) was added and the mixture allowed to warm to room temperature. After 2 hrs further phenylsulphenyl chloride (0 66 g, 4.58 mmol) was added and after a further 20 mins the reaction was quenched and worked up as for (6) to give a yellow oil (1.62 g) which was purified by column chromatography (silica gel, eluent: diethyl ether - petroleum ether 40-60 2:98) to give the dihydropyran (8) as a colourless oil (0.28 g 0 93 mmol, 23%) with ν_{max}:3052, 2932, 2872, 1578, 1471, 1438, 1324, 1218, 1150, 1094, 1074, 1044, 1024, 937, 743, 690 cm^{-1}; ^{1}H-NMR (200 MHz) δ: 7.42-7.14 (10H, m, ArH), 4.05 (2H, t, J = 2Hz, H-6), 2.31 (2H, t, J = 6.5 Hz, H-4), 1.92 (2H, m, H-5); ^{13}C-NMR (50 MHz) δ: 154.5 (C-2), 131.4, 129.0, 127.8, 127.2, 125.9, 106.6 (C-3), 68.6, 28 0, 23 7; m/z 300.0631 (M^+, calc. for $C_{17}H_{16}OS_2$ 300.0643), 191 (M-SPh), 135, 109, 91 Further elution yielded phenyl 4'-toluenethiosulphonate as a white crystalline solid (0.62 g, 2.36 mmol, 56%) with mp 77-78 °C (ether - petroleum ether), lit [20] mp 77-78 °C, ν_{max}:3206, 1591, 1324, 1141, 1027, 810, 650 cm^{-1}; ^{1}H-NMR (60 MHz) δ: 7.60-7.04 (9H, m, ArH), 2.41 (3H, s, $ArCH_3$). (Found. C, 58.9; H, 4.5, calc. for $C_{13}H_{12}O_2S_2$: C, 59.1; H, 4.6%).

2-Phenylthio-5,6-dihydro-4H-pyran (7). Mercuric acetate (1 17 g, 3.67 mmol) was added to a stirred solution of the dithioorthoester (6) (2.22 g, 7.34 mmol) and pyridine (0.58 g, 7.34 mmol) in dry dichloromethane (20 cm^3) at room temperature and the mixture heated to reflux for 15 mins. The mixture was allowed to cool and the solvent evaporated in vacuo. The residue was suspended in diethyl ether (10 cm^3) and the precipitate removed by filtration. The filtrate was concentrated to dryness and the residual oil purified by chromatography (diethyl ether 40-60 petroleum ether 1.5:100) to afford the ketene monothioacetal (7) as a colourless oil (0.88 g, 4.58 mmol, 62%) with ν_{max}:2932, 2871, 1625, 1578, 1475, 1338, 1067, 1037, 897 cm^{-1}; ^{1}H-NMR (200 MHz) δ: 7.34-7.14 (5H, m), 5.35 (1H, t, J = 4Hz, H-3), 4.05 (2H, t, J = 5.2Hz, H-6), 2.15 (2H, m, H-4), 1.85 (2H, m, H-5), lit[7] H^1-NMR δ: 7.37 (5H), 5.40 (1H), 4.10 (2H), 2.40-1.47 (4H); ^{13}C-NMR δ: 146.5 (C-2), 134.6, 128.8, 128.5, 126.2, 109.4 (C-3), 68.2, 22.0, 21.7; m/z: 192.0620 (M^+, calc. for $C_{11}H_{12}OS$: 192.0609), 110, 109, 83, 77.

Decyl 5-chloropentanoate (12) and decyl 5-(phenylthio)pentanoate (13)

Mercuric chloride (0.045 g, 0.17 mmol) was added to a stirred solution of 2,2'-(bisphenylthio)tetrahydropyran (6) (0.100 g, 0.33 mmol) and 1-decanol (0.052 g, 0.33 mmol) in dry dichloromethane (2.5 cm^3) and pyridine (0.026 g, 0 33 mmol). After 24 hr at room temperature the solvent was removed in vacuo and the residue purified by preparative t.l.c. (silica gel; diethyl ether - 40-60 petroleum ether 1:99) to afford the chloro ester (12) (0.022 g, 0 079 mmol, 24%) as a colourless oil; ν_{max}:2919, 2852, 1722, 1461, 1354, 1188, 1134, 1071, 897, 643 cm^{-1}; ^{1}H-NMR (200 MHz) δ: 4.07 (2H, t, J = 6.6Hz, $-OCH_2-$), 3.55 (2H, t, J = 6.2Hz, H-5), 2.35 (2H, t, J = 6Hz, H-2), 1.81 (4H, m, H-4, H-5), 1.62 (2H, m, $-OCH_2CH_2$), 1.27 (14H, brs) , 0.88 (3H, t, J = 6.6Hz); m/z 277.1946 (MH^+, calc. for $C_{15}H_{30}O_2Cl$: 277.1956), 137, 119, 101,85. The more polar component, obtained as a colourless oil, was characterised as the phenylthio ester (13) (0.013 g, 0.037 mmol, 11%); ν_{max}:2919, 2852, 1722, 1441, 1181, 1144, 1084, 1041 cm^{-1}; ^{1}H-NMR (200 MHz) δ: 7.32-7.27 (5H, m, ArH), 4.05 (2H, t, J = 6.8Hz-OCH_2), 2.93 (2H, t, J = 7Hz, H-5), 2.32(2H, t, J = 7Hz, H-2), 1.85-1.70 (6H, m), 1.26 (14H, br s), 0.88 (3H, t, J = 7Hz); m/z: 350.2295 (M^+, calc. for $C_{21}H_{34}O_2S$: 350 2279), 193, 101, 85.

Decyl 5-(phenylthio)pentanoate (13) and decyl 5-(decyloxy)pentanoate (14).

Commercial 1 M triethyloxonium tetrafluoroborate in dichloromethane (0.50 cm^3, 0.5 mmol) was added to a stirred solution of the dithioorthoester (6) (0.15 g, 0.50 mmol) and 1-decanol (0.079g, 0.50 mmol) in dry dichloromethane (3 cm^3) at room temperature. After 36 hrs the solvent was evaporated in vacuo and the residue purified by preparative t.l.c. to afford the 5-phenylthio ester (13) (0.028 g, 0.08 mmol, 16%) identical with the above isolated product and the 5-decyloxy ester (14) (0.015 g, 0.038 mmol, 22%) as a colourless oil with ν_{max}:2919, 2852, 1722, 1461, 1375, 1171, 1107 cm^{-1}; ^{1}H-NMR (200 MHz) δ: 1.06 (2H, t, CO_2CH_2), 3.39 (4H, 2t, $-OCH_2-$), 2.34 (2H, t, H-2), 1.59 (8H, m), 1 23 (28H, m) 0.88 (6H, m).

2-Chloro-2-(4'-toluenesulphonyl)tetrahydropyran (19). A stirred solution of the anion of the sulphone (5) (0.80 g, 3.33 mmol) generated in the usual way was treated with sulphuryl chloride (0.414 g, 3.66 mmol). After 20 mins at -78 °C saturated sodium hydrogencarbonate solution (1 cm^3) was added and the mixture allowed to warm to room temperature and worked up in the usual way. The crude yellow syrup so obtained was purified by chromatography on silica gel(eluent: diethyl ether - 40-60 petroleum ether 3:7) to give firstly 4-toluenesulphonyl chloride (0.14 g, 0.73 mmol, 22%) with mp 70 °C, lit [21] mp 69-71 °C, and then the title compound (19) (0.36 g 1.31 mmol, 40%) as a white crystalline solid with mp 100-102 °C; ν_{max}: 2945, 1595, 1324, 1214, 1154, 1131, 1087, 1034, 897, 834, 814; ^{1}H-NMR (200 MHz) δ: 7.89 (2H, d, ArH), 7.35 (2H, d, ArH), 4.10-3.82 (2H, m, H-6), 2.46 (3H, s, $ArCH_3$), 2.31 (2H, m, H-3), 1.96 (2H, m, H-5), 1.66 (2H, m, H-4); ^{13}C-NMR δ: 145.7, 131.6, 130.0, 129.3, 113.7 (C-2), 66.2, 31.1, 23.6, 21.8, 18.4; m/z: 238 $(M-H)^+$, 139, 119 ($M- SO_2C_7H_7$), 91, 83, 36: (Found: C, 52.3; H, 5.4; Cl, 12 7; S, 12.0, calc. for $C_{12}H_{15}ClO_3S$: C, 52.3; H, 5.5; Cl, 12.9; S, 11.7%). Further elution afforded a white crystalline solid (0.1 g) which was found to be a 1:1 mixture of sulphone (5) and the sulphonyldihydropyran (21) by ^{1}H-NMR spectroscopy.

2-Bromo-2-(4'-toluenesulphonyl)tetrahydropyran (20) A stirred solution of sulphone (5) (1.00 g, 4 16 mmol) in dry diethyl ether (15 cm^3) at -78 °C under nitrogen was treated with n-butyllithium (4.58 mmol). After 20 mins at -78 °C bromine (0.665 g, 4.58 mmol) was added dropwise and the mixture allowed to warm tc room temperature. After 1 hr saturated sodium bicarbonate solution was added and the reaction mixture extracted with dichloromethane (2 x 25 cm^3). The combined

extracts were washed with 5% sodium thiosulphate solution, and then with sodium hydrogencarbonate, dried over magnesium sulphate, filtered and concentrated to low volume. The residual solution was diluted with 40-60 petroleum ether. On standing at room temperature the bromosulphone (20) was obtained as a colourless crystalline solid (0.89 g, 2.79 mmol, 67%), with mp 105-106 °C; ν_{max}:2939, 1595, 1325, 1154, 1084, 1064, 1034, 830, 650 cm^{-1}; ^{1}H-NMR (400 MHz) δ: 7.88 (2H, d, J = 8.6Hz, ArH), 7.33 (2H, d, J = 8.6 Hz, ArH), 4.04 (1H, m, H-6) 3.82 (1H, m, H-6), 2.44 (3H, s, $ArCH_3$), 2.42 (1H, m, H-3), 2 20 (1H, m, H-3), 1.95 (2H, m,H-5), 1.64 (2H, m, H-4); ^{13}C-NMR (100.6 MHz) δ: 145.6, 131.6, 130.0, 129.2, 113 7 (C-2), 67.5, 33.1, 23.4, 21.7, 19.2; m/z: 238 (M-HBr), 162.9769 (M- $SO_2C_7H_7$, calc for C_5H_8BrO: 162.9758), 139, 119, 91, 83. (Found C, 45.15; H, 4.7; Br, 25.0; S, 10.2, calc for $C_{12}H_{15}BrO_3S$: C, 45.15; H, 4.7; Br, 25.0 ; 10 0%).

2-(4'-Toluenesulphonyl)-3,4-dihydro-2H-pyran (21): Preparation of an Authentic Sample. The sulphone (5) (1.00 g, 4.16 mmol) was treated with n-butyllithium and bromine as described above to obtain crude bromosulphone (20) which was dissolved in chloroform (5 cm^3) and triethylamine (3 cm^3) and heated to reflux for 30 mins. After cooling the reaction mixture was poured into dilute hydrochloric acid and extracted with dichloromethane (2 x 25 cm^3). The combined extracts were dried over magnesium sulphate and evaporated to dryness. The residual solid was recrystallised from dichloromethane - 40-60 petroleum ether to give the vinylsulphone (21) (0.733 g, 3.08 mmol, 74%) with mp 124-127 °C; ν_{max}:2925, 2878, 1658, 1595, 1318, 1154, 1107, 1067, 1037, 900, 844, 810, 603 cm^{-1}; ^{1}H-NMR (200 MHz) δ: 7.83 (2H, d, J = 8.4Hz, ArH), 7.35 (2H, d, J = 8.4Hz, ArH), 6.13 (1H, t, J = 4Hz, H-3), 4.05 (2H, t, J = 5.2Hz, H-6), 2.44 (3H, s, $ArCH_3$), 2.23 (2H, m, H-4), 1.85 (2H, m, H-5); ^{13}C-NMR (100.6 MHz): 152.5, 144.5, 135.6, 129.6, 128.3, 68.3, 21.6, 21.1, 20.3; m/z 238.0641 (M^+,calc. for $C_{12}H_{14}O_3S$ 238.0664), 139, 123, 91, 85. (Found: C, 60.2; H, 5.8 calc for $C_{12}H_{14}O_3S$: C, 60.5; H, 5.9%).

Reaction of Chloride (19) with Decanol and Silver(I)Triflate. Silver trifluoromethanesulphonate (0.058 g, 0.23 mmol) was added to a solution of the chloride (19) (0.062 g, 0.23 mmol) and decanol (0.036 g, 0 23 mmol) in dry dichloromethane (1 cm^3) After 24 hr the reaction mixture was evaporated in vacuo and purified by chromatography on silica gel (eluent dichloromethane - 40-60 petroleum ether 1:1) to afford decyl 4'-toluenesulphinate (0.040 g, 0.14 mmol, 60%) as a colourless oil with ν_{max}: 2919, 2852, 1461, 1124, 1081, 1031, 937, 810 cm^{-1}; ^{1}H-NMR (200 MHz) δ:7.60 (2H, d, J = 6.6Hz, ArH), 7.34 (2H, d, J = 6.6Hz, ArH), 4.01 (1H, dt, J = 10, 7Hz,CH_2OSOAr), 3.60 (1H, dt, J = 10, 7Hz, CH_2OSOAr), 2.43 (3H, s, $ArCH_3$), 1.60 (2H, m, CH_2CH_2O), 1.24 (14H, br s), 0.88 (3H, t). (Found: C, 68.8; H, 9.3, calc for $C_{17}H_{28}O_2S$: C, 68.9; H, 9.5%).

Solvolysis of Bromide (20) in Methanol Camphor 10-sulphonic acid (5 mol%) was added to a solution of the bromide (20) (0.25 g, 0.78 mmol) in methanol (3 cm^3). The solution was heated to reflux for 10 mins, allowed to cool and the methanol removed in vacuo. The residue was purified by chromatography on silica gel (eluent: diethyl ether / 40-60 petroleum ether 3/7) to give first methyl 4'-toluenesulphinate (0.109 g, 0.64 mmol, 82%) with bp 100-104 °C at 1.0 mm Hg, lit [22] bp 86-88 °C at 0.4 mm Hg; ν_{max}: 2985, 2931, 1595, 1488, 1431, 1117, 1081, 974, 900, 810, 630 cm^{-1}; lit [22] ν: 1136 (film); ^{1}H-NMR(60MHz) δ: 7.59 (2H, d, J = 8Hz, ArH), 7.28 (2H, d, J = 8Hz, ArH), 3.50 (3H, s, OCH_3), 2.45 (3H, s, $ArCH_3$). Further elution yielded sulphone (21) (0.023 g, 0.1 mmol, 12%) identical with an authentic sample and finally methyl 5-hydroxypentanoate[23] as a colourless oil (0.064 g, 0.49 mmol, 62%) with ν_{max}: 3606, 3506, 2932, 2872, 1727, 1361, 1184, 1047 cm^{-1}; ^{1}H-NMR (400 MHz) δ: 3.69 (3H, s, OMe), 3.67 (2H, t, J = 6.4Hz, OCH_2), 2.37 (2H, m, CH_2CO_2), 1.76-1.60 (5H, m).

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