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ON THE STERIC COURSE OF THE ADDITION OF DIALLYLZINC ONTO α,β-DIALKOXY CHIRAL CARBONYL COMPOUNDS STEREOSPECIFIC SYNTHESIS OF 2,6-DIDEOXYSUGARS OF THE L-SERIES

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The synthesis of the 2,6-dideoxy sugars L-digitoxose (14), 2-deoxy-L-fucose (15) and L-mycarose (16) from the C_4 and C_5 chiral synthons (1), (2) and (3), through the intermediacy of the C_7 adducts (4), (8) and (12), obtained by erythro addition of diallylzinc onto (1), (2) and (3), is reported

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A recent report[1] on the preparation of 2,6-dideoxy-D-arabino- and D-ribohexose through the intermediacy of chiral hept-1-en-4,5,6-triols, from which the sugar framework is generated by ozonolysis, prompted us to present our synthesis of 2,6-dideoxysugars of the L-series, involving, as intermediates, heptentriols isomeric of those mentioned above, prepared,however, in a different way The work we are reporting on originates from studies on the steric course of the addition of carbon nucleophiles onto the carbonyl carbon of the C_4 and C_5 chiral products (1)[2], (2)[3] and (3)[4], bearing in the α and β positions oxygen substituents embedded in a pentacyclic ketal framework Previous observations[5] indicated that with the cyclohexyliden analogs of (1) and (2) allylmagnesium bromide in THF gives rise to the erythro and threo adducts in ca 6 4 and 2.8 ratios, respectively, whereas saturated Grignard reagents[6,7] react with the methylketone (3) or with its cyclohexyliden derivative in ether or THF to give adducts with threo stereochemistry relative to the newly formed bond Due to the relevance this type of chemical operation holds in organic synthesis[8] as a means for stereocontrolled chain elongation we have been investigating further the steric course of the addition of carbon nucleophiles onto the chiral synthons (1), (2) and (3), and we report here on the results of this study and on the synthetic applications of the products obtained

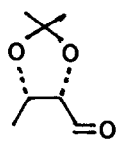
Thus, the methyl ketone (3) was reacted with $BrMgCH_2CH=CH_2$ in ether, at -78°C, to give (80%) an adduct, $[\alpha]_D^{20}$ -7 7 (c 1, $CHCl_3$), shown to be a single product by chromatographic (tlc and glc analysis) and spectroscopic (^{1}H-nmr spectrum) criteria This compound was assigned the structural

formula (12), with erythro stereochemistry, relative to positions 4 and 5, since, upon hydrolysis (20% aqueous acetic acid) (80%) it gave the (4S,5S,6S) triol (13), $[\alpha]_D^{20}$ -13.5 (c 1,$CHCl_3$), converted, in turn, by ozonolysis in MeOH and Me_2S treatment, into 2,6-dideoxy-3-C-methyl-L-ribo hexose (16) (L-mycarose), m.p. 126-129°C (from $CHCl_3$), $[\alpha]_D^{20}$ -29 (c 1, water) (equilibrium 24 h), being these data well in agreement with those of an authentic sample.[9] The same clean erythro mode of addition was observed reacting (3) with diallylzinc, prepared from 1.5M $BrMgCH_2CH=CH_2$ in ether and $ZnCl_2$ solution,[10] being the adduct (12) the sole reaction product. At variance with the above mentioned methyl ketone (3), the two aldehydes (1) and (2) gave with diallylzinc in ether a significant change in the stereochemistry of the addition respect to $BrMgCH_2CH=CH_2$ in the same solvent. Indeed, the erythro aldehyde (1) gives rise with diallylzinc in ether, at -78°C, to a C_7 adduct, shown to contain,by glc, ca. 95% of a compound, subsequently isolated in pure form by SiO_2 column chromatography as an oil, $[\alpha]_D^{20}$ -11.4 (c 1, EtOH), in ca. 70% yield. The latter material was assigned structural formula (4) since on acid hydrolysis it gave the triol (6), $[\alpha]_D^{20}$ 20.1 (c 1, EtOH), converted by ozonolysis and Me_2S treatment, into 2,6-dideoxy-L-ribo hexose (14) (L-digitoxose), m.p. 103°C, $[\alpha]_D^{20}$ -47.8 (c 0.8, water) (equilibrium), well in agreement with the lit.[11] data (^{1}H-nmr, see TABLE). The threo aldehyde (2) behaves similarly, giving with diallylzinc, as above, the product of erythro addition. Indeed, from (2), at -78°C, a crude C_7 adduct, shown to be ca. 95% pure by glc,was obtained in ca. 75% yield. SiO_2 column chromatography yielded pure (8), oil, $[\alpha]_D^{20}$ -7.2 (c 1, EtOH), hydrolysed to (10), $[\alpha]_D^{20}$ -1.4 (c 1, EtOH), giving, in turn, on ozonolysis, 2,6-dideoxy-L-lyxohexose (15) (2-deoxy-L-fucose), m.p. 102-103°C, $[\alpha]_D^{20}$ -132 (c 0.68, acetone), in agreement with the lit.[12] data (^{1}H-nmr, see TABLE).

When the two aldehydes (1) and (2) were reacted with $BrMgCH_2CH=CH_2$ in ether, at -78°C, the product of erythro addition were accompanied by ca. 30-35% of the isomers (5) and (9), respectively, arising by threo addition onto the carbonyl carbon. Indeed, when the mixture (4) + (5) was hydrolysed and the resulting mixture (6) + (7) was ozonised, as above, the L-ribo isomer (14) was obtained nearby ca. 30% of the L-arabino isomer (17), $[\alpha]_D^{20}$ -18.1 (c 1, water) (equilibrium)[13] (^{1}H-nmr, see TABLE), separated by repeated SiO_2 column chromatography with AcOEt-MeOH. Similarly, products (8) + (9), obtained from the threo aldehyde (2), once submitted to the above mentioned sequence, yielded, via (10) + (11), the expected L-lyxo isomer (15), nearby ca. 25% 2,6-dideoxy-L-xylohexose (18) (L-boivinose), m.p. 95-98°C, $[\alpha]_D^{20}$ -13.5 (c 1, acetone)[14] (^{1}H-nmr, see TABLE).

The results mentioned above thus indicate that the C_5 methyl ketone (3) adds diallylzinc or allylmagnesium bromide in ether to give the erythro adduct (12), exclusively. The same erythro preference is shown by the two aldehydes (1) and (2) during the addition of diallylzinc in ether, but with allylmagnesium bromide in ether the products of erythro and threo mode of addition appear in ca. 7:3 ratio. The last value is not too far from the 6:4 erythro: threo ratio

observed in the products in the addition of the same reagent in THF onto (1), but differs from the 2 8 ratio observed with the threo aldehyde (2) under the same conditions



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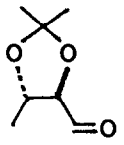

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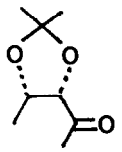

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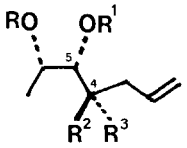
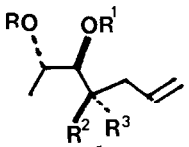
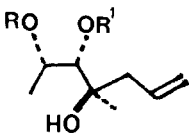


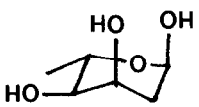
(4) R,R^1=>CMe_2, R^2= OH, R^3= H
(5) R,R^1=>CMe_2, R^2= H, R^3= OH
(6) R= R^1= R^3= H, R^2= OH
(7) R= R^1= R^2= H, R^3= OH



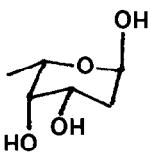
(8) R,R^1=>CMe_2, R^2= H, R^3= OH
(9) R,R^1=>CMe_2, R^2= OH, R^3= H
(10) R= R^1= R^2= H, R^3= OH
(11) R= R^1= R^3= H, R^2= OH



(12) R,R^1=>CMe_2
(13) R= R^1= H



(14)



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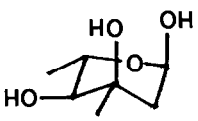

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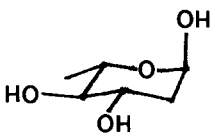

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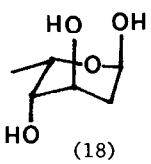

(18)

However, apart from the mechanistic significance of the above results, the present work represents a three steps, stereospecific facile synthesis of the 2,6-dideoxysugars of the L-series (14), (15) and (16) from the easily accessible, non-carbohydrate derived, chiral synthons (1), (2) and (3) Further synthetic applications of the stereochemically rich adducts (4), (8) and (12) are in progress

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TABLE ^{1}H-nmr data of compounds (14), (15), (17) and (18)[a,b,c]

comp.	H-1	H-2e	H-2a	H-3	H-4	H-5	Me	J(1,2e)	J(1,2a)	J(2a,2e)	J(3,2e)	J(3,2a)	J(3,4)	J(4,5)	J(5,Me)
(17)-α	5.07	1.81	1.41	3.6	2.73	3.64	1.11	1 4	3.6	12.8	5.0	11.7	9.0	9.2	6.2
(17)-β	4.61	1.92	1.28	3.32	2 70	3.11	1.15	2.0	9.7	12 6	5.0	11.8	8.6	9.0	6 2
(14)-β	4.90	1.79	1 46	3.83	2 97	3.60	1.11	2.1	9.5	13.5	3.6	2.7	3.0	9.4	6.2
(18)-β	4.90	1.55	1.69	3.83	3.08	3.87	1.I5	2.2	9.5	13.2	3.0	2.7	3.1	1.4	6.5
(15)-α	5.05	1.45	1.68	3 77	3.34	3.87	1.04	1.4	3.7	12.3	4 9	12.0	3.1	1.3	6.5
(15)-β	4.49	1 59	1.47	3.50	3.25	3 35	1.09	2.5	9.2	12.0	5.0	12.0	3 0	1.2	6 5

[a] chemical shifts in ppm from int. TMS, J in Hz [b] solvent: DMSO-d_6 + D_2O [c] the L-arabino and the L-lyxo compounds give rise in solution to a mixture of α and β-tautomers, whereas only the β tautomer is present in appreciable amount for the L-ribo and L-xylo compounds.

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• compound (6) shows $[\alpha]_D^{20}$ 20.15 (c 1, acetone), in ref.[1] the enantiomer of (6) leading to (+) (14) is reported to have $[\alpha]_D^{25}$ -19 3 in the same solvent