Tetrahedron Letters No. 52, pp 5353 - 5356, 1972. Pergamon Press. Printed in Great Britain.

BRANCHED-CHAIN SUGARS BY REACTION OF ULOSES WITH α-METALATED ISOCYANOACETIC ESTERS

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(Received in UK 3 November 1972; accepted for publication 30 November 1972)

Marked interest in the synthesis and chemistry of branched-chain sugars and nucleosides has in the past led to the application of modified Wittig reagents to ketoses to afford a large number of unsaturated branched-chain carbohydrates.[2]

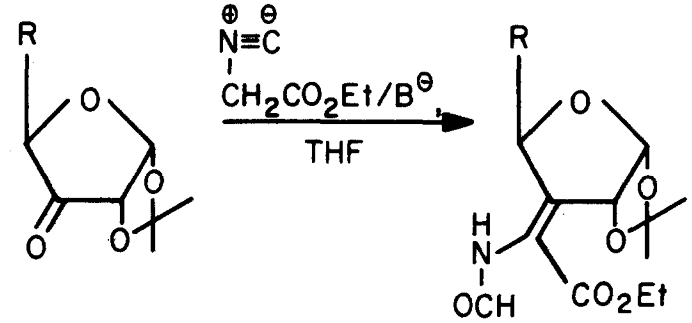
Schöllkopf[3] has pointed out that carbon-carbon double bonds can also be formed by reaction of α-metalated isocyanoacetic esters with ketones and aldehydes. The products are β-substituted α-formylaminoacrylates which can enter into a wide range of reactions.

We now describe the preparation of some novel branched-chain unsaturated carbohydrates from suitably protected uloses and ethyl isocyanoacetate in the presence of base. These unsaturated compounds have been converted into a variety of saturated carbohydrate derivatives. Some of these conversions are described.

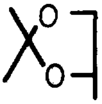
To the ulose *1* (1.72 g, 4 mmoles) and ethyl isocyanoacetate (452 mg, 4 mmoles) in dry THF (10 ml), sodium hydride (200 mg, 4.1 mmoles, 50% suspension in oil, washed with hexane) was slowly added with stirring. After 6 hr at 25° the THF was removed *in vacuo* and water (50 ml) and acetic acid (0.5 ml) added to the residue. The solution was extracted ($CHCl_3$, 3 x 50 ml), the chloroform washed with sodium bicarbonate solution and removed to leave an oil which crystallized from methanol to give *3* as colourless needles[4] (1.74 g), m.p. 184-186°, $[\alpha]_D^{25}$+158°.

Compound *4*, obtained from *2* in a similar manner, had m.p. 130-132°, $[\alpha]_D^{25}$+148°.

Both *3* and *4* could be hydrogenated by refluxing with Raney nickel in ethanol to give *5*, m.p. 171-173°, $[\alpha]_D^{22}$+57°, and *7*, m.p. 146-147°, $[\alpha]_D^{23}$+71°, respectively. Hydrogenolysis of *5* over Adams catalyst in acetic acid gave *6* as an oil from which a brosylate *8*, m.p. 141-142°, $[\alpha]_D^{23}$+29° was prepared. The 5,6-isopropylidene group of *7* was selectively removed (10% aqueous H_2SO_4, 2 hr, 25°) and the product oxidized with periodate to an aldehyde which was reduced with sodium borohydride to give a product from which a brosylate identical to *8* could be prepared. An X-ray analysis[5] on *8* established the *R*-configuration for the branched-chains



1. R = TrOCH$_2$–

2. R = 

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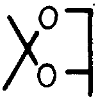
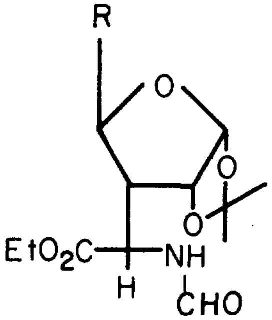
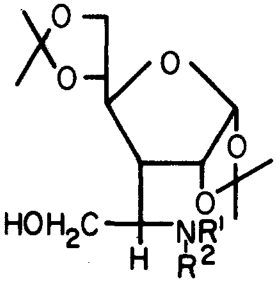
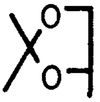
4. R = 





5. R = TrOCH$_2$–

6. R = HOCH$_2$–

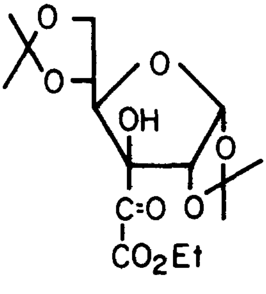
7. R = 

8. R = *p*–BrPhSO$_2$OCH$_2$–

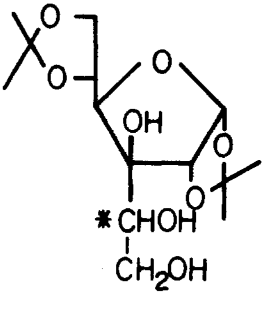
9. R^1 = CHO, R^2=H

10. R^1 = R^2 = H

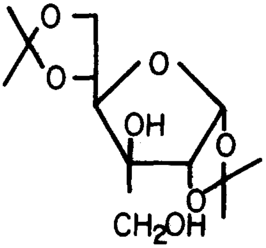
11. R^1,R^2 = *o*–HOPhCH =



12.



13, 14. * = *R* or *S*



15.

in *5*, *6*, *7* and *8*, and assuming that *cis*-hydrogenation had taken place from the β- face of *3* and *4*, it follows that the unsaturated derivatives *3* and *4* must have (*E*)-stereochemistry.

Partial reduction of *7* with LAH in ether gave *9*, m.p. 95-97°, $[\alpha]_D^{22}$ +26°, which could be hydrolyzed with hydrazine acetate[6] to give *10* as an oil from which an *N*-salicylidene derivative[7] *11*, m.p. 156-157°, $[\alpha]_D^{22}$ +129°, was prepared. The O.R.D. curve (EtOH, *c* = 0.0002) of *11* exhibited a positive Cotton effect with extrema $[\phi]_{333}$ +8840, $[\phi]_{300}$ −3655, and is another example of those sugar derivatives for which the correlation between the sign of the Cotton effect and the configuration of the carbon atom bearing the salicylidene moiety no longer holds.[8]

Osmium tetroxide oxidation of *4* gave *12* as an oil, $[\alpha]_D^{22}$ +76°, in *ca.* 60% yield. Reduction of *12* with LAH in ether gave an epimeric mixture of *13* and *14* which could be separated by chromatography on silica to give an oil $[\alpha]_D^{23}$ +25° and a slower moving crystalline compound m.p. 92.5-93.5°, $[\alpha]_D^{23}$ +20°. The configuration at the α-carbon atom of the branched-chain of the two crystalline epimers has yet to be determined. Both *13* and *14* reacted with periodate (1:1 mol equiv) to give an aldehyde which yielded the known[9] compound *15* on reduction with sodium borohydride.

Further work on the chemistry of *3*, *4* and their derivatives and on the preparation of nucleosides from these novel branched-chain carbohydrate derivatives is in progress and will be reported elsewhere.

REFERENCES AND NOTES

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