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Preliminary communication

A facile synthesis of *C*-glycosylbarbiturates

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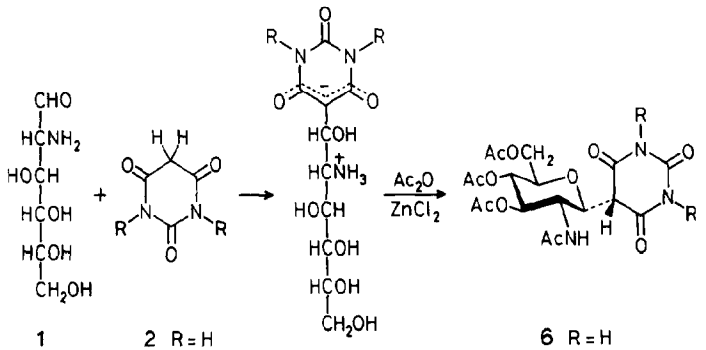
The discovery of *C*-nucleosides and their antibacterial and antitumor properties[1–3] has directed considerable attention to the development of synthetic routes to this class of compounds. Although many synthetic routes have been developed[4–6], they are generally very laborious and require the convenient protection and functionalization of the sugar precursor. We now report a facile synthesis of *C*-nucleoside derivatives of barbituric acids by reaction of some aldoses with barbituric or 1,3-dimethylbarbituric acid.

In this way, the reaction of these acids with 2-amino-2-deoxy-D-glucose, conducted in aqueous medium at 50°, yields the acyclic *C*-glycosides **4** {gradually dec. from 200°, $[\alpha]_D^{30}$ −7° (*c* 0.7, M NaOH); yield 70%}, and **5** {gradually dec. from 200°, $[\alpha]_D^{20}$ −19° (*c* 0.6, water); yield 85%}. The acetylation of these compounds takes place with dehydration, to give the cyclic *C*-nucleoside analogs **6** {m.p. 170–171°, $[\alpha]_{578}^{20}$ −35° (*c* 0.6, methanol); yield 55%} and **7** {m.p. 178–179°, $[\alpha]_{578}^{20}$ −35° (*c* 0.4, methanol); yield 63%}.



1 **2** R = H; **3** R = Me; **4** R = H; **5** R = Me; **6** R = H; **7** R = Me

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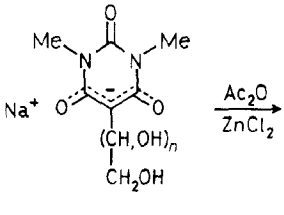
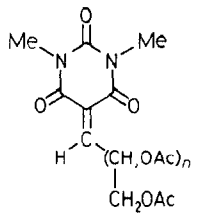
In a similar way, the reaction of the hexoses D-glucose, D-galactose, and D-mannose, and the pentoses D-arabinose and D-xylose, with 1,3-dimethylbarbituric acid and Na_2CO_3 in aqueous solution, at pH 7, gives the sodium 5-(alditol-1-yl)-1,3-dimethylbarbiturates **8**–**12**. The acetylation of these compounds takes place with dehydration between C-5 and C-1′, yielding the acetates **13**–**17** (see Table I). In the acetylation of **10**, the cyclic compound **18** {m.p. 160–161°, $[\alpha]_D^{20}$ −81° (*c* 1.6, chloroform); yield 16%} was also obtained.

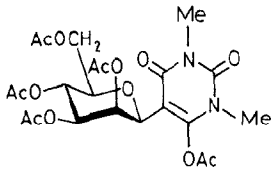
On the other hand, by heating an alkaline solution of **8**, sodium 5-β-D-glucopyranosyl-1,3-dimethylbarbiturate (**19**) {m.p. 195–196° (dec.), $[\alpha]_D^{25}$ −9° (*c* 0.4, water); yield 86%} was obtained. This compound was also obtained by warming a solution of **8** in Me_2SO.



8–**12**



13–**17**



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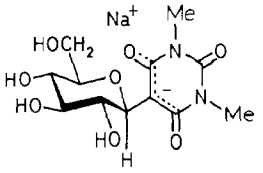

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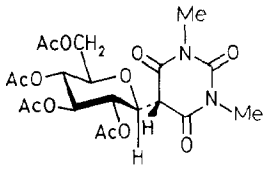

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TABLE I

SOME PROPERTIES OF COMPOUNDS **8**–**17**

Compound	n	*Configuration*	*M.p. (degrees)*	$[\alpha]_D^{20}$ *(degrees)*	*Yield (%)*
8	5	D-*glycero*-D-*ido*	183–185	−14 (*c* 0.5, water)	78
9	5	D-*glycero*-L-*manno*	185–186	+17 (*c* 2.9, water)	78
10	5	D-*glycero*-D-*talo*	(dec.) [a]	−34 (*c* 3.1, water)	80
11	4	D-*manno*	(dec.) [a]	−34 (*c* 2.0, water)	80
12	4	D-*ido*	(dec.) [a]	−24 (*c* 1.4, water)	70
13	4	D-*gluco*	130–131	+86 (*c* 1.3, chloroform)	76
14	4	D-*galacto*	159–160	+47 (*c* 1.4, chloroform)	85
15	4	D-*manno*	71–72	+39 (*c* 1.5, chloroform)	46
16	3	D-*arabino*	154–155	0 (*c* 1.7, chloroform)	93
17	3	D-*xylo*	136–137	+72 (*c* 3.7, chloroform)	75

[a] Gradually decomposes above 200°.

Its structure was confirmed by preparing its tetraacetate (**20**) {m.p. 177–178°, $[\alpha]_D^{20}$ −39° (*c* 1, chloroform); yield 57%} .

The structures assigned these compounds are in agreement with their elemental analyses and spectral data (u.v., i.r., and ^{1}H-n.m.r.).

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