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New Compounds

Hydroxyamino sugar derivatives: sugar nitrones

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Abstract

We describe in this paper the preparation of 46 new sugar nitrone derivatives and their antibacterial activity against *Escherichia coli* and *Bacillus subtilis*.

Keywords: Nitrones; Carbohydrates; Antibacterial

Nitrones are very useful synthons, as upon reduction they afford hydroxylamines [1], upon cycloaddition oxazolidines and can rearrange to amides [2]. Carbohydrate derivatives bearing a nitrone function were first prepared in our laboratory [3]. They result from the reaction of a keto or aldehydo sugar with a *N*-alkylhydroxylamine [4].

We report here on the preparation of 46 new N-glycosyl nitrones (Figs. 1–4) obtained from the condensation of an aldehyde with a hydroxyamino sugar [5,6]. The acidic hydrolysis of the acetonide protection will be described elsewhere.

The nitrones **1–45** were submitted to antibacterial screening tests against *Escherichia coli* and *Bacillus subtilis* as part of a systematic screening program. Compound **46** was not tested. The results are listed in Table 1. They show a poor antibacterial activity, except for compound **32** which presents a MIC of 50 μg/ml for both *E. coli* and *B. subtilis* (Table 1).

The synthetic route explored here led to di- and trisaccharide derivatives, linked through a nitrone function [7].

1. Experimental

All chemicals are from commercial grade Fluka and Merck. The melting points were observed on a Mettler FP 52 apparatus. The optical rotations were measured in chloroform on a Schmidt-Haensch polarimeter. The UV spectra were observed on a Uvikon 810 spectrophotometer. The IR spectra were obtained on a Perkin-Elmer

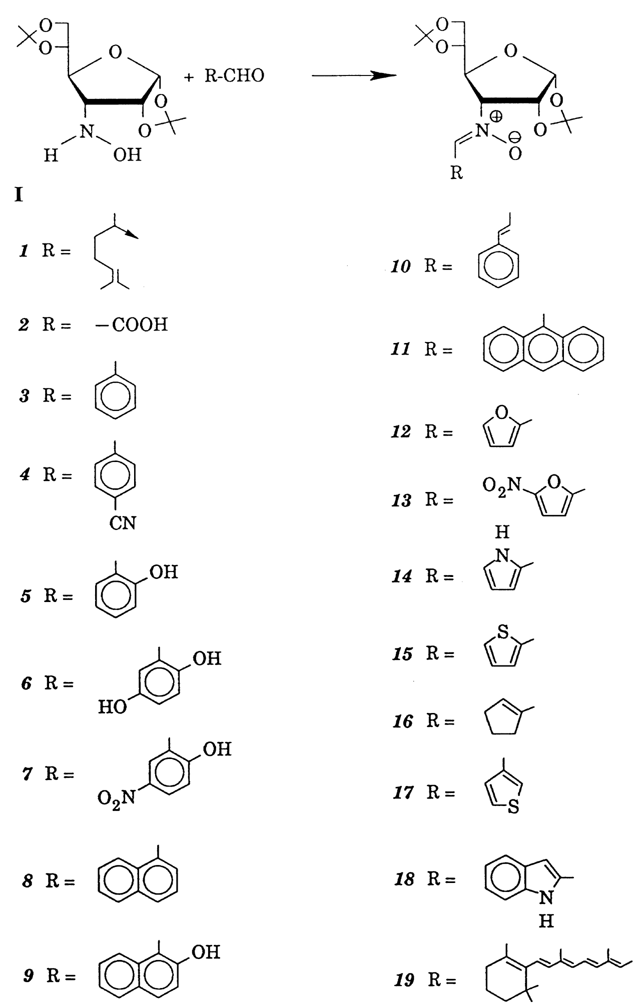

Fig. 1.

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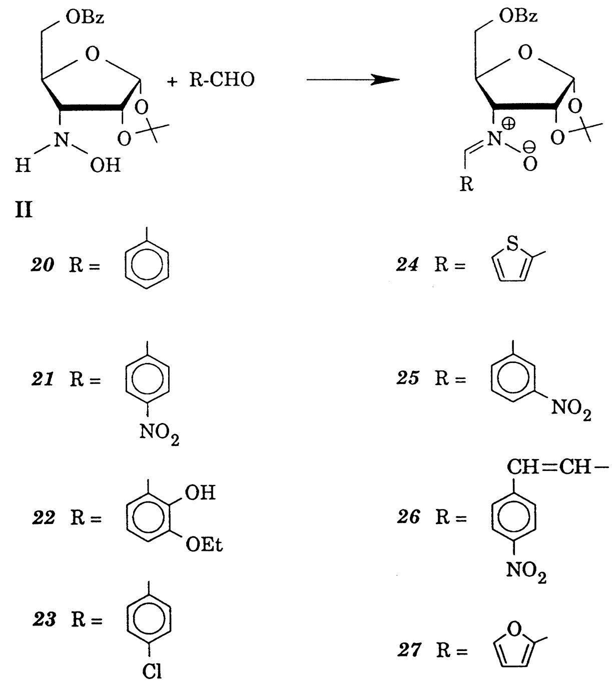

Fig. 2.

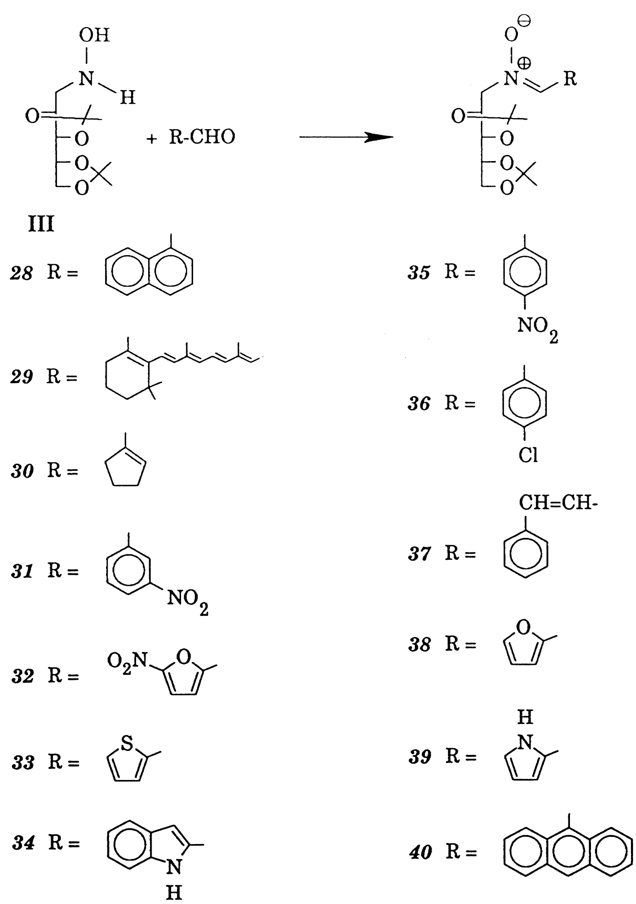

Fig. 3.

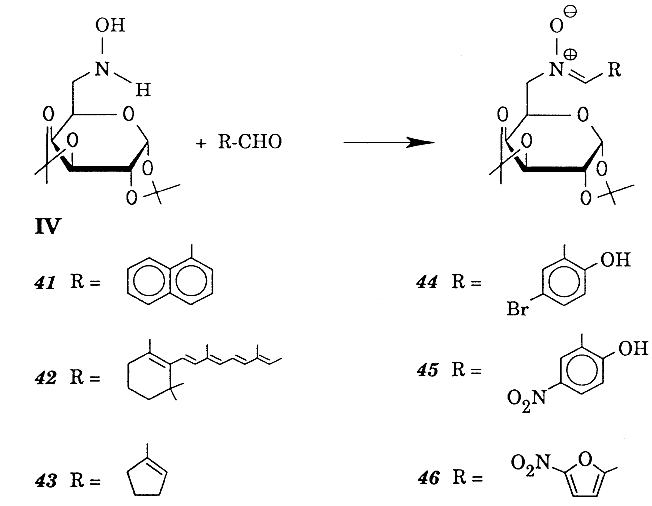

Fig. 4.

357 and the PMR spectra were observed on a Bruker SP200 apparatus. The antibacterial tests were performed according to Ref. [8].

One millimole of a hydroxyamino sugar [5,6] was allowed to react with an aldehyde in an appropriate solvent. When the reaction was completed (TLC), the mixture was evaporated to dryness and purified by column chromatography on silicagel 60F254 from Merck. The general synthetic conditions are shown in Table 2.

Melting points of compounds **1–46** are listed in Table 2. All the prepared sugar nitrones present elemental analysis, UV, IR, SM and PMR spectra in accordance with their structure (details may be obtained from the authors (GZL)).

Table 1
Antimicrobial activity in μg/ml

Nitrone	*E. coli*	*B. subtilis*	Nitrone	*E. coli*	*B. subtilis*
1	NA[a]	> 500	27	NA	NA
2	225	> 500	28	NA	250
5	NA	> 500	29	> 500	> 500
6	NA	> 500	30	NA	> 200
7	400	400	32	50	50
8	NA	NA	33	NA	NA
9	> 500	> 500	34	NA	> 400
11	> 500	> 500	35	NA	> 400
12	NA	NA	36	NA	> 400
13	400	400	37	175	NA
14	> 500	> 500	38	> 400	NA
15	> 500	> 500	39	NA	> 400
20	NA	> 500	40	125	125
22	200	200	41	NA	NA
23	400	400	43	> 400	> 400
24	> 400	> 400	44	NA	NA
25	NA	NA	45	400	400
26	NA	NA			

[a] NA, no activity.

Table 2
General synthetic conditions and melting points in °C

Nitrone	Solvent	Reaction temperature (°C)	Reaction time (h)	Yield (%)	M.p. (°C)
1	Methanol	65	0.5	65	83.7–85.3
2	Pyridine	20	12	87	129.0–129.7
3	Benzaldehyde	20	12	76	145.0–145.5
4	Toluene	110	5	55	183.4–185.5
5	Toluene	20	12	79	131.4–132.5
6	Toluene	110	2	75	230.6–230.7
7	Toluene	110	2	70	171.1–171.5
8	Toluene	110	2	70	159.3–162.5
9	Toluene	110	2	70	175.0–176.0
10	THF	20	12	68	159.0–160.0
11	Toluene	110	4	84	188.3–189.5
12	Furfuraldehyde	20	4	93	162.4–167.4
13	Toluene	110	2	80	119.0–121.1
14	Toluene	110	2	72	116.2–116.5
15	Toluene	110	2	85	129.6–130.9
16	Toluene	110	2	70	120.9–121.4
17	THF	20	12	82	45.9–46.0
18	Ethanol	75	12	95	82.5–83.3
19	Benzene	80	12	90	41.0–42.0
20	Benzaldehyde	20	12	60	118.2–119.2
21	Toluene	110	2	68	108.0–109.3
22	Toluene	110	2	60	100.5–103.1
23	Toluene	110	2	72	128.3–130.0
24	Toluene	110	2	82	50.9–52.4
25	Toluene	110	2	64	109.9–111.5
26	Toluene	110	2	77	62.0–63.5
27	Toluene	110	1	64	139.0–141.0
28	Toluene	110	2	78	104.5–106.5
29	Toluene	110	1	78	51.9–53.9
30	Toluene	110	3	39	117.2–119.2
31	Toluene	110	1	78	85.5–85.7
32	Toluene	110	0.5	85	147.1–148.7
33	Toluene	110	1	94	118.5–119.4
34	Toluene	110	2	61	247.5–248.5
35	Toluene	110	1	75	125.1–125.8
36	Toluene	110	1	73	138.2–139.9
37	Toluene	110	1	57	108.9–110.6
38	Toluene	110	1	90	114.6–115.3
39	Toluene	110	2	71	141.1–142.4
40	Toluene	110	2	38	226.0–228.0
41	Toluene	110	0.5	78	57.7–59.2
42	Toluene	110	1	40	53.4–54.3
43	Toluene	110	2	34	Syrup
44	Toluene	110	1	76	74.3–75.7
45	Toluene	110	1	98	71.9–73.6
46	Toluene	110	0.5	81	71.7–73.1

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