r-1,t-3-Bis-[(6-butyl-4-hydroxy-2-oxo-2H-pyran-3-yl)-oxomethyl]-c-2,t-4-bis-(4-chlorphenyl)-cyclobutan (**2e**)

Bestrahlungszeit von **1e**: 2h. Beige Kristalle, Schmp. 237°, Ausb.: 100%, d.Th. – $C_{36}H_{34}Cl_2O_8$ (665.6) Ber. C 65.0 H 5.15 Gef. C 64.0 H 4.96. – IR (KBr): 3430, 3090, 2960, 2860, 1720, 1635, 1605, 1560, 1550, 1490, 1445, 1430, 1385, 1350, 1250, 1200, 1105, 1095, 1035, 1015, 1000, 985, 965, 895, 855, 820, 760, 725, 710 cm^{-1}. – ^{1}H-NMR ($CDCl_3$): δ (ppm) = 16.08 (s, 2H, OH, austauschbar), 7.25–7.12 (m, 8H, aromat.), 5.73 (s, 2H, H-5'), 5.08–4.88 (m, 4H, H-1, H-2, H-3, H-4), 2.39 (t, 4H, J = 7 Hz, 2x -CH_2-C_3H_7), 1.62–1.56 (m, 4H, 2x -CH_2-CH_2-C_2H_5), 1.36–1.28 (m, 4H, 2x -$(CH_2)_2$-CH_2-CH_3), 0.92 (t, 6H, J = 7 Hz, 2x -$(CH_2)_3$-CH_3). – MS (70 eV/250°): m/z = 664/666 (8/6%, M^+), 454 (13), 452 (11), 345 (10), 332/334 (100/28), 333 (28), 331 (26), 247/249 (15/6), 221 (50), 195 (39), 165/167 (46/13), 137/139 (12/6), 127 (10). – UV (MeOH): λmax (log ε) = 203 (4.8), 225 (4.7), 316 (4.4), 402 (3.8).

Die Bestimmung der anticoagulativen Wirkung erfolgte wie beschrieben[6].

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Synthesis and Antimicrobial Activity of Some 2-(2-Nitroethenyl)naphthofuran and -benzofuran Derivatives

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Eingegangen am 20. September 1982

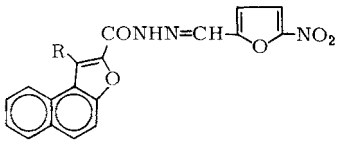
Some 2-(2-nitroethenyl)naphthofuran and 2-(2-nitroethenyl)benzofuran derivatives were synthesized and tested in vitro for antimicrobial activity. Only 2-(2-nitroethenyl)naphtho[2,1-*b*]furan exhibits appreciable activity against gram-positive and gram-negative bacteria.

0365-6233/83/1010-0849 $ 02.50/0

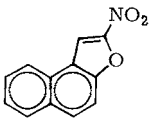
Synthese und antimikrobielle Wirkung einiger 2-(2-Nitrovinyl)-Naphthofuran- und -Benzofuran-Derivate

Einige 2-(2-Nitrovinyl)naphthofuran- und 2-(2-Nitrovinyl)benzofuran-Derivate wurden hergestellt und auf ihre antimikrobielle in vitro-Aktivität untersucht. Als einzige Verbindung zeigte 2-(2-Nitrovinyl)naphtho[2,1-b]furan eine signifikante Wirksamkeit gegen grampositive und gramnegative Bakterien.

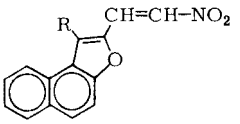
Previous research on the antimicrobial properties[1] of some naphtho[2,1-*b*]furan-2-carbohydrazones of 5-nitro-2-furaldeyde **1a–d** showed the important role of the R-substituents, particulary chlorine. These results together with the recently reported antiprotozoal activity of some related 2-nitro-naphtho[2,1-*b*]furan[2,3,4] **(2)** prompted us to extend our investigations in this area.



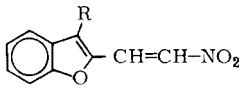
1a-d
R = H, Cl, OCH_3, CH_3



2



3a-d



4a, b

Since compound **2**, on behalf of the vinylogy principle, might be considered an extreme semplification of **1**, we have thought it to be of interest to synthesize the true vinylogues **3a–d**. We have also taken the occasion to prepare the more simple related derivatives **4a, b**.

These compounds have been prepared by a standard method, i.e. by condensing the appropriate aldehydo derivative with excess of nitromethane in presence of ammonium acetate[5].

All new derivatives have been tested for antimicrobial activity against Gram-positive bacteria *(Staphylococcus aureus, Bacillus subtilis)*, Gram-negative bacteria *(Pseudomonas aeruginosa, Proteus mirabilis, Escherichia coli)* and *Candida albicans*. The minimal inhibitory concentrations were determined by disk and agar dilution methods. Dimethylformamide was used as the solvent. Only 2-(2-nitroethenyl)naphtho[2,1-*b*]furan **(3a)**, the vinylogue of **2**, showed appreciable inhibitory effect; the MIC values were 150 µg/ml and 70–100 µg/ml against Gram-positive and Gram-negative bacteria, resp.

Experimental Part

Elementary analyses: Laboratory for microanalysis of the faculty of Pharmacy of the University of Pisa, Italy. *MP:* not corr., Electrothermal melting point apparatus. *Thin layer chromatography:* Baker Flex Silica-gel IB2-F, $CHCl_3$ eluent.

Table 1: *Analytical data of the nitrovinyl derivatives* **3a–d** *and* **4a,b**

Nr.	R	Formula	Calc. / Found	C	H	N	MP° (dec.) (*)	Yield %
3a	H	$C_{14}H_9NO_3$		70,3	3,80	5,8	165–167	61
				70,0	3,80	5,5	(A)	
3b	Cl	$C_{14}H_8ClNO_3$		61,4	2,95	5,1	189–194	87
				61,8	3,04	5,2	(A)	
3c	CH_3	$C_{15}H_{11}NO_3$		71,1	4,37	5,5	215–217	99
				71,2	4,14	5,4	(B)	
3d	OCH_3	$C_{15}H_{11}NO_4$		66,9	4,11	5,2	211–212	85
				67,0	4,04	5,1	(B)	
4a	OCH_3	$C_{11}H_9NO_4$		60,2	4,14	6,3	138–140	53
				59,8	4,14	6,3	(A)	
4b	Cl	$C_{10}H_6ClNO_3$		53,7	2,70	6,2	99–102	41
				54,1	2,53	5,9	(B)	

* Recrystallized form: A = ethanol, B = aceton-ethanol

Starting compounds

3-Chloro- and 3-methoxy-benzofuran-2-carboxyaldehyde[6], naphtho[2,1-*b*]furan-2-carboxyaldehyde and the analogue 1-methyl-[7], 1-chloro- and 1-methoxy- naphtho-2-carboxyaldehyde[8] were synthesized according to literature.

Nitrovinyl derivatives

General procedure: 3,5 mmole of the appropriate naphtho- and benzofuranaldehyde, 5 ml nitromethane, and 3,5 mmole ammonium acetate were heated gently under reflux for 1/4 h. On cooling, a brownorange precipitate slowly separated wich was crystallized from ethanol or from aceton-ethanol. Compound **4b** required a preliminary purification by column cromatography on silica gel (Eluent: ethyl acetate/petroleum ether 1/9).

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