SYNTHESIS AND ANTIMYCOTIC ACTIVITY OF NEW 2-CHLORO-3-(2-NITRO)ETHYL- AND (2-NITRO)VINYLQUINOLINES

Zoltán Cziáky[1*], Ferenc Korodi[1], László Frank[1] and Irén Czink[2]

[1]Alkaloida Chemical Company Ltd, Tiszavasvári, P. O. Box 1, H-4440, Hungary
[2]Department of Chemotherapy, Institute of Pharmacology, University Medical School, H-4440 Debrecen, Hungary

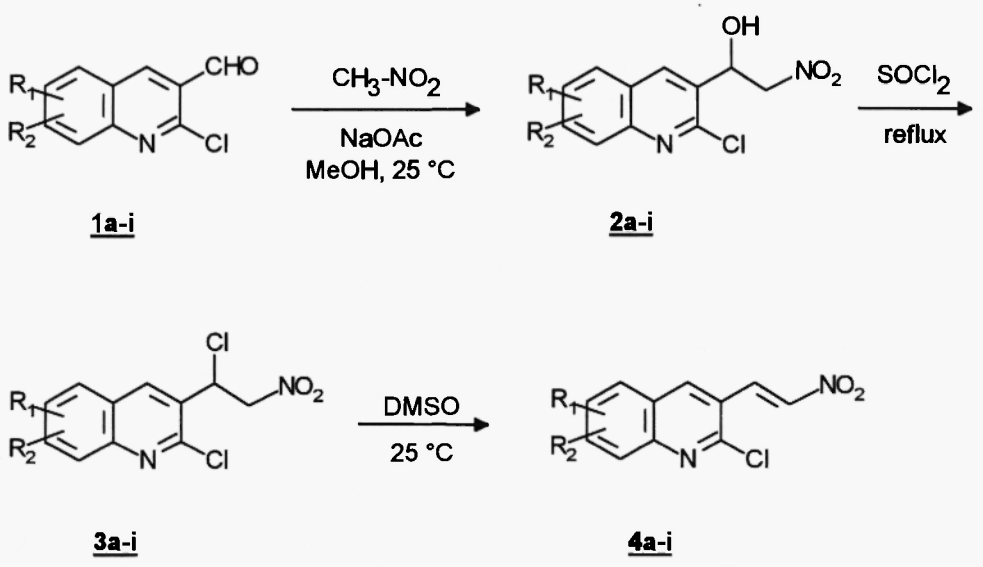
Abstract: 2-Chloro-3-(2-nitro)ethyl- and (2-nitro)vinylquinolines have been synthesized and tested *in vitro* for their antimycotic activity against *Aspergillus fumigatus*, *Trichophyton mentagrophytes*, *Microsporum gypseum*, *Epidermophyton floccosum* and *Candida albicans*. Several compounds exhibited strong inhibition to microorganisms.

INTRODUCTION

It is known that the aryl-(1-hydroxy-2-nitro)ethane derivatives (1, 2) as well as aryl-β-nitro-alkenes (3-5) often posses remarkable antimycotic activity. These types of aryl compounds can be prepared using the nitroaldol (or *Henry*) reaction, which is one of the classical C-C bond forming reactions (6-8), starting from the appropriate aryl-carboxaldehyde and nitroalkane. 2-Chloroquinoline-3-carboxaldehydes (9, 10) are suitable starting materials for the synthesis of new quinoline derivatives having similar structures. In this paper the synthesis and antimycotic activity of 2-chloro-3-(1-hydroxy-2-nitro)ethylquinolines **2**, 2-chloro-3-(1-chloro-2-nitro)ethylquinolines **3** and 2-chloro-3-(2-nitro)vinylquinolines **4** is reported.

RESULTS AND DISCUSSION

Indian authors have reported on the reaction of 2-chloro-6,7-diethoxyquinoline-3-carboxaldehyde with nitromethane in methanol in the presence of sodium acetate at room temperature (11). They have found that condensation occurred and the product was assigned as the corresponding nitrovinyl derivative. In another publication (12) the structure of the product of a similar transformation was assigned as 2-chloro-3-(1-hydroxy-2-nitro)ethylquinoline. In order to solve this discrepancy, we have carried out the reaction of 2-chloroquinoline-3-carboxaldehydes **1a-i** with nitromethane under the above mentioned conditions. We have found that the product was the appropriate 3-(1-hydroxy-2-nitro)ethylquinoline derivative **2** (53-87 %) in every case (Scheme).



1a-i 2a-i

3a-i 4a-i

a: R_1=H, R_2=H

b: R_1=7-Me, R_2=H

c: R_1=6-OMe, R_2=H

d: R_1=7-OMe, R_2=H

e: R_1=6-Cl, R_2=H

f: R_1=7-Cl, R_2=H

g: R_1=6-OMe, R_2=7-OMe

h: R_1=5-Cl, R_2=7-Cl

i: R_1=7-Cl, R_2=8-Me

Scheme

The structure of compounds 2a-i was determined on the basis of their ^{1}H-NMR and MS spectra (Table 2). The formation of 2-chloro-3-(2-nitro)vinylquinolines 4 was not observed in these reactions even if the reaction mixtures were acidified. The most probable reason of this fact may be that the protonation of the hydroxyl group (the first step of the dehydration) does not occur because of the higher basicity of the nitrogen atom in the quinoline ring. Pyridine-3-carboxaldehyde was reported to react with nitromethane similarly (13, 14).

Our efforts to dehydrate the alcohols 2 (methanesulfonyl chloride - triethylamine (15, 16) or phosphorous pentoxide (17)) to 2-chloro-3-(2-nitro)vinylquinolines 4 have failed, but they were found to be accessible by an indirect way. The reaction of alcohols 2a-i with thionyl chloride at reflux temperature gave the chloro-derivatives 3a-i in 43-97 % yields, which readily lost hydrogen chloride when they were stirred in dimethylsulfoxide at 25 °C overnight to give 2-chloro-3-(2-nitro)vinylquinolines 4a-i in 35-90 % yields. These vinylquinolines proved to be *trans* isomers exclusively on the basis of the ^{1}H-^{1}H coupling constant of their -CH=CH- unit (14 Hz). The physical and spectral data of the compounds are listed in Table 1 and Table 2.

Table 1. Physical data of compounds 2, 3 and 4 prepared.

Compound	Yield [%]	M.p. [°C]	Formula	Analysis calcd./found C [%]	H [%]	N [%]
2a	70	150-152[a]	$C_{11}H_9ClN_2O_3$	52.29/52.15	3.59/3.64	11.09/11.01
2b	53	137-139	$C_{12}H_{11}ClN_2O_3$	54.05/54.18	4.16/4.08	10.50/10.55
2c	74	140-142	$C_{12}H_{11}ClN_2O_4$	50.99/50.93	3.92/3.99	9.91/9.92
2d	87	152-154 dec.	$C_{12}H_{11}ClN_2O_4$	50.99/50.86	3.92/3.87	9.91/9.97
2e	84	137-139	$C_{11}H_8Cl_2N_2O_3$	46.02/45.90	2.81/2.92	9.76/9.79
2f	87	95-97	$C_{11}H_8Cl_2N_2O_3$	46.02/46.15	2.81/2.88	9.76/9.70
2g	60	207-208 dec.	$C_{13}H_{13}ClN_2O_5$	49.93/49.93	4.19/4.10	8.96/8.91
2h	81	152-154	$C_{11}H_7Cl_3N_2O_3$	41.09/41.23	2.19/2.22	8.71/8.81
2i	67	168-170	$C_{12}H_{10}Cl_2N_2O_3$	47.86/47.90	3.35/3.33	9.30/9.34
3a	83	126-128	$C_{11}H_8Cl_2N_2O_2$	48.73/48.58	2.97/2.90	10.33/10.23
3b	70	102-104	$C_{12}H_{10}Cl_2N_2O_2$	50.55/50.50	3.54/3.58	9.82/9.88
3c	67	147-149	$C_{12}H_{10}Cl_2N_2O_3$	47.86/47.75	3.35/3.33	9.30/9.34
3d	58	134-135	$C_{12}H_{10}Cl_2N_2O_3$	47.86/47.81	3.35/3.27	9.30/9.25
3e	67	136-138	$C_{11}H_7Cl_3N_2O_2$	43.24/43.20	2.31/2.36	9.17/9.22
3f	75	124-126	$C_{11}H_7Cl_3N_2O_2$	43.24/43.37	2.31/2.30	9.17/9.14
3g	97	251-253	$C_{13}H_{12}Cl_2N_2O_4$	47.15/47.10	3.65/3.69	8.46/8.40
3h	43	94-96	$C_{11}H_6Cl_4N_2O_2$	38.86/38.96	1.78/1.71	8.24/8.22
3i	58	142-144	$C_{12}H_9Cl_3N_2O_2$	45.10/45.16	2.84/2.88	8.77/8.74
4a	85	201-202 dec.	$C_{11}H_7ClN_2O_2$	56.31/56.27	3.01/2.89	11.94/11.90
4b	61	187-189 dec.	$C_{12}H_9ClN_2O_2$	57.96/57.90	3.65/3.71	11.27/11.26
4c	76	208-210 dec.	$C_{12}H_9ClN_2O_3$	54.46/54.44	3.43/3.48	10.58/10.53
4d	87	236-238 dec.	$C_{12}H_9ClN_2O_3$	54.46/54.33	3.43/3.50	10.58/10.51
4e	89	218-220 dec.	$C_{11}H_6Cl_2N_2O_2$	49.10/49.21	2.25/2.17	10.41/10.36
4f	90	195-197 dec.	$C_{11}H_6Cl_2N_2O_2$	49.10/48.98	2.25/2.33	10.41/10.32
4g	35	247-248 dec.	$C_{13}H_{11}ClN_2O_4$	52.98/53.11	3.76/3.71	9.51/9.60
4h	37	193-195 dec.	$C_{11}H_5Cl_3N_2O_2$	43.53/43.59	1.66/1.55	9.23/9.09
4i	57	176-178 dec.	$C_{12}H_8Cl_2N_2O_2$	50.91/51.09	2.85/2.80	9.89/9.77

[a] Llt. (12) M.p.: 134 °C.

Table 2. Spectral data of compounds **2**, **3** and **4** prepared.

Compound	^{1}H-NMR[a] [δ]	MS [rel. int., %]
2a	4.63(1H, dd, J_1=13 Hz, J_2=9 Hz); 5.03(1H, dd, J_1=13 Hz, J_2=2.5 Hz); 5.68(1H, m); 6.62(1H, d, J=4.5 Hz); 7.71(1H, m); 7.85(1H, m); 8.00(1H, m); 8.13(1H, m); 8.68(1H, s)	234(M^+, 33); 199(100); 187(27); 169(24); 152(90)
2b	2.52(3H, s); 4.63(1H, dd, J_1=13 Hz, J_2=9 Hz); 5.01(1H, dd, J_1=13 Hz, J_2=2.5 Hz); 5.66 (1H, m); 6.56(1H, d, J=4.5 Hz); 7.53 (1H, dd, J_1=8.5 Hz, J_2=1 Hz); 7.78(1H, d, J=1 Hz); 8.00(1H, d, J=8.5 Hz); 8.59(1H, s)	266(M^+, 7); 219(12); 205(100); 176(43); 169(38)
2c	3.93(3H, s); 4.62(1H, dd, J_1=13 Hz, J_2=9 Hz); 5.02(1H, dd, J_1=13 Hz, J_2=2.5 Hz); 5.70(1H, m); 6.61(1H, d, J=4.5 Hz); 7.50 (2H, m); 7.91(1H, d, J=9 Hz); 8.54(1H, s)	282(M^+, 34); 264(5); 235(13); 221(100); 186(27)
2d	3.96(3H, s); 4.64(1H, dd, J_1=13 Hz, J_2=9 Hz); 5.00(1H, dd, J_1=13 Hz, J_2=2.5 Hz); 5.68(1H, m); 6.63(1H, d, J=4.5 Hz); 7.32(1H, dd, J_1=8.5 Hz, J_2=1.5 Hz); 7.40(1H, d, J=1.5 Hz); 8.01(1H, d, J=8.5 Hz); 8.55(1H, s)	282(M^+, 32), 235(27); 222(100); 186(52); 158(53)
2e	4.58(1H, dd, J_1=13 Hz, J_2=9 Hz); 5.02(1H, dd, J_1=13 Hz, J_2=2.5 Hz); 5.64(1H, m); 6.68(1H, d, J=4.5 Hz); 7.80(1H, dd, J_1=8.5 Hz, J_2=1 Hz); 7.98(1H, d, J=8.5 Hz); 8.26(1H, d, J=1 Hz); 8.63(1H, s)	286(M^+, 18); 239(30); 225(100); 190(45); 161(94)
2f	4.68(1H, dd, J_1=13 Hz, J_2=9 Hz); 5.04(1H, dd, J_1=13 Hz, J_2=2.5 Hz); 5.69(1H, m); 6.70(1H, d, J=4.5 Hz); 7.22(1H, dd, J_1=8.5 Hz, J_2=2 Hz); 8.08(1H, d, J=2 Hz); 8.21(1H, d, J=8.5 Hz); 8.71(1H, s)	286(M^+, 17); 239(48); 226(100); 196(39); 190(58); 161(89)
2g	3.92(3H, s); 3.95(3H, s); 4.62(1H, dd, J_1=13 Hz, J_2=9 Hz); 4.99(1H, dd, J_1=13 Hz, J_2=2.5 Hz); 5.65(1H, m); 6.59(1H, d, J=4.5 Hz); 7.35(1H, s); 7.46(1H, s); 8.45(1H, s)	312(M^+, 2); 279(6); 251(17); 167(20); 149(100)
2h	4.65(1H, dd, J_1=13 Hz, J_2=9 Hz); 5.06(1H, dd, J_1=13 Hz, J_2=2.5 Hz); 5.66(1H, m); 6.78(1H, d, J=4.5 Hz); 8.03(1H, d, J=2.5 Hz); 8.11(1H, d, J=2.5 Hz); 8.73(1H, s)	320(M^+, 5); 275(17); 260(100); 230(33); 195(96)
2i	2.69(3H, s); 4.62(1H, dd, J_1=13 Hz, J_2=9 Hz); 5.04(1H, dd, J_1=13 Hz, J_2=2.5 Hz); 5.68(1H, m); 6.62(1H, d, J=4.5 Hz); 7.70(1H, d, J=9 Hz); 8.00(1H, d, J=9 Hz); 8.65(1H, s)	300(M^+, 32); 253(27); 239(100); 204(45); 175(53)
3a	5.58(1H, dd, J_1=15 Hz, J_2=8.5 Hz); 5.69(1H, dd, J_1=15 Hz, J_2=5.5 Hz); 6.11(1H, dd, J_1=8.5 Hz, J_2=5.5 Hz); 7.75(1H, m); 7.90(1H, m); 8.02(2H, m); 8.88(1H, s)	270(M^+, 10); 223(48); 199(24); 188(43); 152(100)

Table 2 (continued)

3b	2.56(3H, s); 5.58(1H, dd, J_1=15 Hz, J_2=8.5 Hz); 5.69(1H, dd, J_1=15 Hz, J_2=5.5 Hz); 6.13(1H, dd, J_1=8.5 Hz, J_2=5.5 Hz); 7.58(1H, dd, J_1=8.5 Hz, J_2=1.5 Hz); 7.80(1H, d, J=1.5 Hz); 7.94(1H, d, J=8.5 Hz); 8.82(1H, s)	284(M^+, 20); 248(11); 237(63); 203(72); 166(100)
3c	3.94(3H, s); 5.54(1H, dd, J_1=15 Hz, J_2=8.5 Hz); 5.67(1H, dd, J_1=15 Hz, J_2=5.5 Hz); 6.12(1H, dd, J_1=8.5 Hz, J_2=5.5 Hz); 7.42(1H, d, J=2.5 Hz); 7.52(1H, dd, J_1=9 Hz, J_2=2.5 Hz); 7.93(1H, d, J=9 Hz); 8.78(1H, s)	300(M^+, 48); 264(23); 253(42); 219(97); 182(100)
3d	3.97(3H, s); 5.55(1H, dd, J_1=15 Hz, J_2=8.5 Hz); 5.64(1H, dd, J_1=15 Hz, J_2=5.5 Hz); 6.11(1H, dd, J_1=8.5 Hz, J_2=5.5 Hz); 7.40 (1H, dd, J_1=9 Hz, J_2=2.5 Hz); 7.43(1H, d, J=2.5 Hz); 7.96(1H, d, J=9 Hz); 8.74(1H, s)	300(M^+, 23); 264(11); 253(34); 219(100); 182(57)
3e	5.50(1H, dd, J_1=15 Hz, J_2=8.5 Hz); 5.62(1H, dd, J_1=15 Hz, J_2=5.5 Hz); 6.10(1H, dd, J_1=8.5 Hz, J_2=5.5 Hz); 7.89(1H, dd, J_1=9 Hz, J_2=2 Hz); 8.01(1H, d, J=9 Hz); 8.11(1H, d, J=2 Hz); 8.87(1H, s)	304(M^+, 20); 268(10); 257(55); 222(51); 186(100)
3f	5.53(1H, dd, J_1=15 Hz, J_2=8.5 Hz); 5.63 (1H, dd, J_1=15 Hz, J_2=5.5 Hz); 6.12(1H, dd, J_1=8.5 Hz, J_2=5.5 Hz); 7.29(1H, dd, J_1=8.5 Hz, J_2=2 Hz); 8.10(1H, d, J=8.5 Hz); 8.18(1H, d, J=2 Hz); 8.87(1H, s)	304(M^+, 5); 268(22); 257(24); 233(100); 223(41)
3g	3.94(3H, s); 3.96(3H, s); 5.51(1H, dd, J_1=15 Hz, J_2=8.5 Hz); 5.62(1H, dd, J_1=15 Hz, J_2=5.5 Hz); 6.08(1H, dd, J_1=8.5 Hz, J_2=5.5 Hz); 7.84(1H, s); 7.89(1H, s); 8.63(1H, s)	330(M^+, 8); 294(31); 259(100); 249(28); 229(18)
3h	5.60(1H, dd, J_1=15 Hz, J_2=8.5 Hz); 5.76(1H, dd, J_1=15 Hz, J_2=5.5 Hz); 6.20(1H, dd, J_1=8.5 Hz, J_2=5.5 Hz); 8.03(1H, d, J=2.5 Hz); 8.10(1H, d, J=2.5 Hz); 8.91(1H, s)	340(M^++2, 8); 302(17); 293(51); 267(75); 220(100)
3i	2.70(3H, s); 5.57(1H, dd, J_1=15 Hz, J_2=8.5 Hz); 5.65(1H, dd, J_1=15 Hz, J_2=5.5 Hz); 6.13(1H, dd, J_1=8.5 Hz, J_2=5.5 Hz); 7.72(1H, d, J=8.5 Hz); 7.91(1H, d, J=8.5 Hz); 8.88(1H, s)	318(M^+, 29); 282(41); 271(32); 235(100); 200(80)
4a	7.63(1H, m); 7.72(1H, d, J=14 Hz); 7.89(2H, m); 8.05(1H, m); 8.40(1H, s); 8.45(1H, d, J=14 Hz)	234(M^+, 33); 199(100); 187(46); 152(70)
4b	2.63(3H, s); 7.48(1H, dd, J_1=8.5 Hz, J_2=1.5 Hz); 7.70(1H, d, J=14 Hz); 7.78(1H, d, J=8.5 Hz); 7.83(1H, d, J=1.5 Hz); 8.30(1H, s); 8.41(1H, d, J=14 Hz)	248(M^+, 26); 213(100); 201(32); 183(23); 166(55)
4d	3.98(3H, s); 7.27(1H, dd, J_1=9 Hz, J_2=2.5 Hz); 7.33(1H, d, J=2.5 Hz); 7.69(1H, d, J=14 Hz); 7.77(1H, d, J=9 Hz); 8.31(1H, s); 8.45(1H, d, J=14 Hz)	264(M^+, 43); 229(100); 217(70); 199(37); 182(53)
4e	7.67(1H, d, J=14 Hz); 7.76(1H, dd, J_1=9 Hz, J_2=2.5 Hz); 7.86(1H, d, J=2.5 Hz); 7.99(1H, d, J=9 Hz); 8.29(1H, s); 8.40(1H, d, J=14 Hz)	268(M^+, 50); 233(100); 221(35); 186(96); 151(78)

Table 2 (continued)

4f	7.61(1H, dd, J_1=8.5 Hz, J_2=2 Hz); 7.68(1H, d, J=14 Hz); 7.81(1H, d, J=8.5 Hz); 8.06(1H, d, J=2 Hz); 8.37(1H, s); 8.42(1H, d, J=14 Hz)	268(M^+, 24); 233(100); 221(32); 186(71); 151(55)
4g	4.02(3H, s); 4.04(3H, s); 7.09(1H, s); 7.34(1H, s); 7.70(1H, d, J=14 Hz); 8.23(1H, s); 8.43(1H, d, J=14 Hz)	294(M^+, 31); 259(100); 247(16); 229(21); 212(25)
4h	7.70(1H, d, J=2 Hz); 7.74(1H, d, J=14 Hz); 7.97(1H, d, J=2 Hz); 8.42(1H, d, J=14 Hz); 8.69(1H, s)	302(M^+, 25); 267(100); 255(52); 237(42); 220(81)
4i	2.83(3H, s); 7.64(2H, m); 7.69(1H, d, J=14 Hz); 8.34(1H, s); 8.42(1H, d, J=14 Hz)	282(M^+, 45); 247(68); 217(40); 200(81); 164(100)

[a] compounds **2** and **3**: in DMSO-d_6, compounds **4**: in $CDCl_3$

PHARMACOLOGY

The quinoline derivatives **2**, **3** and **4** were evaluated for antimycotic activity against *Aspergillus fumigatus*, *Trichophyton mentagrophytes*, *Microsporum gypseum*, *Epidermophyton floccosum* and *Candida albicans*. On the basis of the antimycotic test results shown in Table 3, there is no clear-cut relationship between the electronic character of the substituents on the homoaromatic ring and the antimycotic activity of the compounds investigated. In case of compounds **2** it seemed, however, that the presence of a methoxy substituent on the homoaromatic ring is disadvantageous in terms of the activity. Therefore, methoxy substituted derivatives of compounds **3** and **4** were not subjected to antimycotic testing. It is not surprising, however, that the different types of side chain at the position 3 of the quinoline ring have an essential role on the activity. Comparing the MIC values of the compound having the same substituent on the homoaromatic ring, the activity of the compounds generally increases in the sequence of **2** < **4** < **3**. Some representatives of the 2-chloro-3-(1-chloro-2-nitro)ethylquinolines (**3e**, **3f**, **3i**) can be considered as potent as Ketoconazole against the microorganisms investigated and may serve as a basis for further synthetic and biological studies.

EXPERIMENTAL

M.p.'s were determined in open capillary tubes on a Büchi apparatus and are uncorrected. ^{1}H-NMR spectra were recorded on a Bruker WP-200 SY instrument at 200 MHz. TMS was used as internal standard. Chemical shifts are expressed in ppm. Mass spectra were scanned on a VG 7035 instrument in EI mode at 70 eV.

2-Chloroquinoline-3-carboxaldehydes **1a-i** were prepared according to previously described procedure (9).

Table 3. Results of antimycotic testing of compounds 2, 3 and 4.

Compound	MIC [μg/ml]				
	Aspergillus fumigatus	*Trichophyton mentagrophytes*	*Microsporum gypseum*	*Epidermophyton floccosum*	*Candida albicans*
2a	>100	12.5	25	50	100
2b	100	6.25	6.25	25	50
2c	>100	100	100	>100	>100
2d	>100	50	50	>100	>100
2e	>100	25	50	50	100
2f	50	25	50	25	50
2g	>100	>100	>100	>100	>100
2h	100	6.25	6.25	12.5	100
2i	>100	12.5	12.5	25	>100
3a	50	6.25	6.25	12.5	12.5
3e	25	3.12	3.12	12.5	25
3f	50	3.12	1.56	3.12	25
3h	>100	0.78	0.78	3.12	>100
3i	12.5	0.78	0.78	6.25	25
4a	>100	12.5	6.25	12.5	50
4e	100	6.25	6.25	25	50
4f	100	6.25	6.25	12.5	25
4h	>100	6.25	6.25	6.25	>100
4i	100	6.25	6.25	25	>100
Ketoconazole	12.5	3.12	3.12	3.12	12.5

2-Chloro-3-(1-hydroxy-2-nitro)ethylquinolines (2) General procedure

The corresponding 2-chloroquinoline-3-carboxaldehyde (1) (25 mmoles) was suspended in methanol (50 ml) and stirred with 50 mmoles of nitromethane and 50 mmoles of anhydrous sodium acetate at 25 °C for 24 h. The suspension was cooled to 0 °C, the solid material was filtered off, washed with water and dried. The crude product was crystallized from acetone - ethanol mixture.

2-Chloro-3-(1-chloro-2-nitro)ethylquinolines (3) General procedure

The corresponding 2-chloro-3-(1-hydroxy-2-nitro)ethylquinoline (2) (20 mmoles) was suspended in thionyl chloride (30 ml) and refluxed for 15 min. By the end of this period the starting material had gone to solution.

After cooling, the thionyl chloride was removed in vacuum. The residue was suspended in ethyl acetate (25 ml) and was dissolved by neutralization with K_2CO_3 solution (10 %, w/v). The organic layer was dried with Na_2SO_4 and evaporated to the half of its volume and 10 ml of *n*-hexane was added. After cooling to 0 °C, the product was collected by filtration, washed with *n*-hexane and dried.

2-Chloro-3-(2-nitro)vinylquinolines (4) General procedure

The corresponding 2-chloro-3-(1-chloro-2-nitro)ethylquinoline (3) (15 mmoles) was dissolved in 20 ml of DMSO. The solution was stirred at 25 °C for 24 h and diluted with water (30 ml). The crystalline product was filtered off, washed with water, dried and crystallized from 2-butanone.

Antimycotic testing

The *in vitro* antifungal activity was assayed against *Aspergillus fumigatus*, *Trichophyton mentagrophytes*, *Microsporum gypseum*, *Epidermophyton floccosum* and *Candida albicans*. All compounds were dissolved in DMSO. Minimal inhibitory concentration (MIC) was evaluated by agar dilution in Sabouraud dextrose agar. Assays were performed in triplicate. MIC values were read after 48 h of incubation at 28 °C in the case of *Candida albicans* and after 288 h of incubation at 28 °C in the cases of the other microorganisms examined.

REFERENCES

1 Gy. Mikite, E. Jakucs, A. Kis-Tamás, F. Darvas and A. Lopata, *Pestic. Sci.* 13, 557 (1982)
2 A. Lopata, F. Darvas, K. Valkó, Gy. Mikite, E. Jakucs and A. Kis-Tamás, *Pestic. Sci.* 14, 513 (1983)
3 N. Latif, F. M. Asaad and N. S. Girgis, *Indian J. Chem., Sect B*, 20, 463 (1981)
4 N. Latif, N. Mishriky, N. S. Girgis and S. Arnos, *Indian J. Chem., Sect B*, 19, 301 (1980)
5 N. Latif, F. M. Asaad and H. Hosni, *Liebigs Ann. Chem.* 495 (1987)
6 L. Henry, *C. R. Acad. Sci. Paris*, 120, 1265 (1895)
7 C. A. Sprang and E. F. Degering, *J. Am. Chem. Soc.* 64, 1063 (1942)
8 D. Seebach, A. K. Beck, T. Mukhopadhyay and E. Thomas, *Helv. Chim. Acta* 65, 1101 (1982)
9 O. Meth-Cohn and B. Narine, *Tetrahedron Lett.* 2045 (1978)
10 O. Meth-Cohn, B. Narine and B. Tarnowski, *Tetrahedron Lett.* 3111 (1979)
11 B. Bhat and A. P. Bhaduri, *Indian J. Chem.* 21B, 729 (1982)
12 R. P. Srivastava, Neelima and A. P. Bhaduri, *Indian J. Chem.* 26B, 418 (1987)
13 F. Zymalkowski, *Arch. Pharm.* 12 (1958)
14 K. Irie, *Nippon Kagaku Kaishi* 150 (1983)
15 J. Melton and J. E. McMurry, *J. Org. Chem.* 40, 2138 (1975)
16 H. H. Baer and F. F. Z. Georges, *J. Org. Chem.* 41, 3474 (1976)
17 H. Wieland and E. Sakellarios, *Chem. Ber.* 52, 898 (1919)

Received August 13, 1995