Synthesis of Methyl Derivatives of New Polycyclic Systems of 4*H*-Furo[3,2-*g*]pyrrolo[3,2,1-*ij*]quinolin-4-one, of 1*H*,5*H*- and 3*H*,5*H*-Benzofuro[5,6,7-*ij*]quinolizin-5-one

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Received December 23, 1992

The synthesis of new tetracyclic 4*H*-furo[3,2-*g*]pyrrolo[3,2,1-*ij*]quinolin-4-ones, **15-17**, 1*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-ones, **18-20**, and 3*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-ones, **21-23** is described. The planarity of the structure of benzofuroquinolizin-5-one **18** was determined by X-ray single-crystal analysis.

J. Heterocyclic Chem., **30**, 715 (1993).

It is well-known that psoralens, such as 8-methoxypsoralen (8-MOP) and 5-methoxypsoralen (5-MOP) are employed in the treatment of some skin diseases characterized by hyperproliferative conditions [1]. This therapeutic approach, called PUVAtherapy due to the combination of drug administration and UVA irradiation of the skin, shows good efficacy, especially in the treatment of some resistant forms of psoriasis and in the early stage of *mycosis fungoides*. However, some adverse side-effects are observed: *i.e.*, short-term side-effects, such as skin phototoxicity and immune system depression, and long-term ones, such as the risk of cataract and skin cancer [2,3].

In order to reduce the above-mentioned side-effects and at the same time to maintain the same therapeutic effects as psoralen, a number of bioisosters of furocoumarin structure have been prepared and tested, such as pyrrolocoumarins [4] and furoquinolinones [5], both showing promising photochemical behaviour.

Recently, we reported the synthesis of some 9-hydroxy derivatives of pyrrolo[3,2,1-*ij*]quinolin-4-one as potential photochemical agents, obtained by exploiting the regiospecificity of the cyclization of 7-hydroxy-8-(2',3'-dibromopropyl)quinolin-2-ones [6].

Now, in order to obtain new and more extended polyheterocyclic systems such as furo[3,2-*g*]pyrrolo[3,2,1-*ij*]quinolinones, in which some skeletal features of psoralens and their bioisosters still appear [5-7], we considered to start from the above pyrroloquinolinones, as useful synthons, and annulating a further furan ring on them.

In this connection, the well known synthetic method [7-8] of building the furan ring through Claisen rearrangement of easily available 9-allyloxypyrroloquinolinones, bromination of the *ortho*-rearranged allyl moiety, and successive alkaline cyclization seemed to be a useful pathway. However, although performed under mild conditions, the bromination reaction gave electrophilic substitution on the pyrrole ring [9], together with addition to the allylic double bond [10].

Alternatively, keeping in mind the above-mentioned regiospecific cyclization of pyrroloquinolinones [6], in which an *ortho*-dibromopropyl residue reacts exclusively with the adjacent lactamic nitrogen, cyclizing a pyrrole

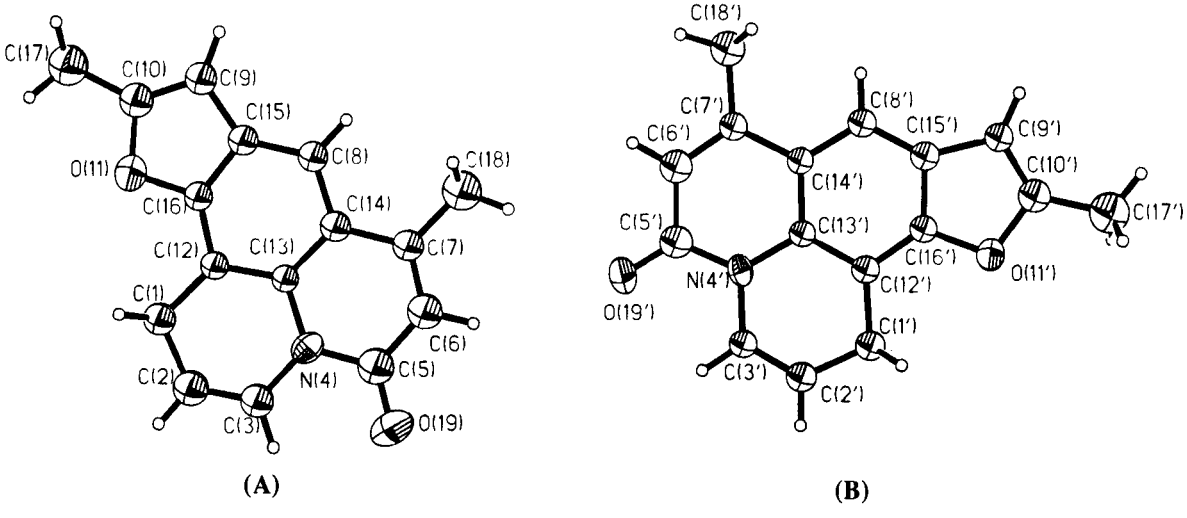
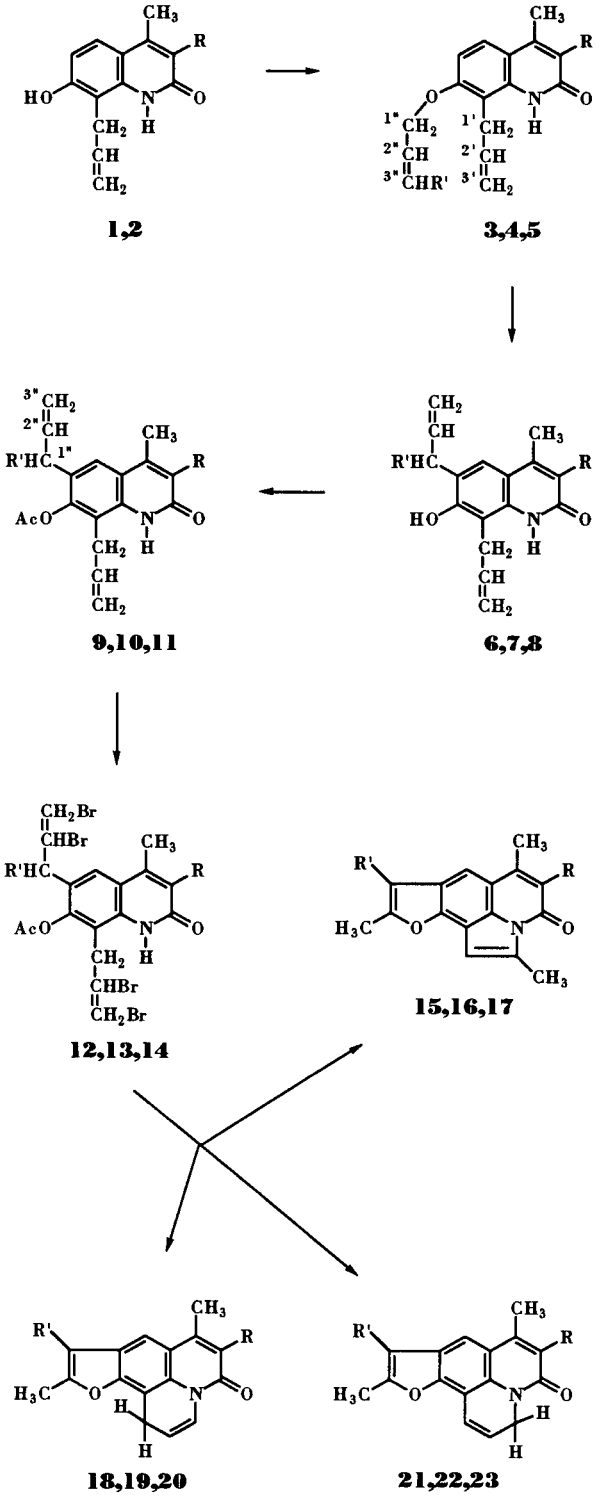


Figure 1. Molecular structure of **18** showing the two formula molecules of the asymmetric unit.

Scheme



1: R = H
2: R = CH_3
3,6,9,12,15,18,21: R = R' = H
4,7,10,13,16,19,22: R = CH_3, R' = H
5,8,11,14,17,20,23: R = R' = CH_3

Table 1

uv Data of the Synthesized Compounds [a]

Compound		Molar absorptivity
4*H*-Furo[3,2-*g*]pyrrolo[3,2,1-*ij*]quinolin-4-one		
	246 (max)	24500
15	337 (max)	14400
	365 [b]	8900
	242 (max)	23600
16	335 (max)	15000
	365 [b]	9600
	254 (max)	22900
17	336 (max)	15700
	365 [b]	9500
1*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-one		
	233 (max)	30900
18	239 (max)	36400
	269 (max)	22800
	365 (maz)	6800
	234 (max)	30900
	240 (max)	31300
19	271 (max)	22000
	319 (max)	8200
	365 [b]	7300
	236 (max)	23300
	242 (max)	31100
20	272 (max)	21800
	320 (max)	8000
	365 [b]	7100
3*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-one		
	242 (shoulder)	45700
	249 (max)	60500
21	325 (max)	9700
	365 (max)	7400
	379 (max)	5900
	243 (shoulder)	41400
	249 (max)	51500
22	322 (max)	11200
	360 (max)	8600
	365 [b]	7800
	378 (max)	7100
	246 (shoulder)	44200
	251 (max)	54700
23	324 (max)	11000
	365 (max)	8300
	380 (max)	7100

[a] Ethanol 95% solution. [b] The most used wavelength in photochemical and photobiological experiments.

ring, we planned to carry out double cyclization starting from 6,8-dibromopropylpyrroloquinolinone derivatives **9-11**. In fact, considering that the 8-dibromopropyl moiety exclusively engages lactamic nitrogen to form the pyrrole ring [6], the 6-dibromopropyl residue necessarily engages the 7-hydroxyl group, giving the fourth desired furan ring.

This synthetic pathway furnished the new 4*H*-furo[3,2-*g*]pyrrolo[3,2,1-*ij*]quinolin-4-ones **15-17**. However, a concurrent cyclization reaction also occurred, leading to the formation of two kinds of closely correlated benzofuroquinolizinone isomers as co-products, both deriving from

Table 2

^{1}H NMR Spectra

4*H*-furo[3,2-*g*]pyrrolo[3,2,1-*ij*]chinolin-4-ones

Compound	H-1	H-5	H-7	H-8	Me-2	Me-5	Me-6	Me-8	Me-9
15	6.51 q $J_{1,Me-2}$ = 1.3	6.41 q $J_{5,Me-6}$ = 1.1	7.41 *s*	6.29 q $J_{8,Me-9}$ = 1.2	2.77 d $J_{Me-2,1}$ = 1.3	–	2.50 d $J_{Me-6,Me-5}$ = 1.1	–	2.43 d $J_{Me-9,8}$ = 1.2
16	6.64 q $J_{1,Me-2}$ = 1.2	–	7.58 *s*	6.48 q $J_{8,Me-9}$ = 1.1	2.83 d $J_{Me-2,1}$ = 1.2	2.24 q $J_{Me-5,Me-6}$ = 0.8	2.49 q $J_{Me-6,Me-5}$ = 0.8	–	2.52 d $J_{Me-9,8}$ = 1.1
17	6.68 q $J_{1,Me-2}$ = 1.3	–	7.56 *s*		2.86 d $J_{Me-2,1}$ = 1.3	2.24 q $J_{Me-5,Me-6}$ = 0.8	2.44 q $J_{Me-6,Me-5}$ = 0.8	2.28 q $J_{Me-8,Me-9}$ = 0.9	2.58 q $J_{Me-9,Me-8}$ = 0.9

1*H*,5*H*-Benzofuro[5,6,7-*ij*]chinolizin-5-ones

Compound	H-1	H-2	H-3	H-6	H-8	H-9	Me-6	Me-7	Me-9	Me-10
18	3.83 dd $J_{1,2}$ = 3.7 $J_{1,3}$ = 2.0	5.48 dt $J_{2,3}$ = 8.6 $J_{2,1}$ = 3.7	7.66 dt $J_{3,2}$ = 8.6 $J_{3,1}$ = 2.0	6.39 q $J_{6,Me-7}$ = 1.0	7.52 *s*	6.42 q $J_{9,Me-10}$ = 1.1		2.43 d $J_{Me-7,6}$ = 1.0	–	2.48 d $J_{Me-10,9}$ = 1.1
19	3.84 dd $J_{1,2}$ = 3.8 $J_{1,3}$ = 2.1	5.49 dt $J_{2,3}$ = 8.6 $J_{2,1}$ = 3.8	7.72 dt $J_{3,2}$ = 8.6 $J_{3,1}$ = 2.1	–	7.57 *s*	6.38 q $J_{9,Me-10}$ = 1.0	2.24 q $J_{Me-6,Me-7}$ = 0.7	2.43 q $J_{Me-7,Me-6}$ = 0.7	–	2.46 d $J_{Me-10,9}$ = 1.0
20	3.83 dd $J_{1,2}$ = 3.1 $J_{1,3}$ = 2.1	5.49 dt $J_{2,3}$ = 8.6 $J_{2,1}$ = 3.1	7.73 dt $J_{3,2}$ = 8.6 $J_{3,1}$ = 2.1	–	7.47 *s*	–	2.25 q $J_{Me-6,Me-7}$ = 0.7	2.46 q $J_{Me-7,Me-6}$ = 0.7	2.17 q $J_{Me-9,Me-10}$ = 0.9	2.38 q $J_{Me-10,Me-9}$ = 0.9

3*H*,5*H*-Benzofuro[5,6,7-*ij*]chinolizin-5-ones

Compound	H-1	H-2	H-3	H-6	H-8	H-9	Me-6	Me-7	Me-9	Me-10
21	6.93 dt $J_{1,2}$ = 10.2 $J_{1,3}$ = 2.2	6.07 dt $J_{2,1}$ = 10.2 $J_{2,3}$ = 3.7	4.92 dt $J_{3,2}$ = 3.7 $J_{3,1}$ = 2.2	6.36 q $J_{6,Me-7}$ = 1.1	7.49 *s*	6.53 bs	–	2.47 d $J_{Me-7,6}$ = 1.1	–	2.46 bs
22	6.92 dt $J_{1,2}$ = 10.2 $J_{1,3}$ = 2.2	6.06 dt $J_{2,1}$ = 10.2 $J_{2,3}$ = 3.8	4.94 dd $J_{3,2}$ = 3.8 $J_{3,1}$ = 2.2	–	7.54 *s*	6.34 bs	2.27 bs	2.45 bs	–	2.45 bs
23	6.91 dt $J_{1,2}$ = 10.2 $J_{1,3}$ = 2.2	6.05 dt $J_{2,1}$ = 10.2 $J_{2,3}$ = 3.7	4.94 dd $J_{3,2}$ = 3.7 $J_{3,1}$ = 2.2	–	7.42 *s*	–	2.28 q $J_{Me-6,Me-7}$ = 0.7	2.48 q $J_{Me-7,Me-6}$ = 0.7	2.15 q $J_{Me-9,Me-10}$ = 0.9	2.37 q $J_{Me-10,Me-9}$ = 0.9

Table 3

Atomic Coordinates (x10^4) and Equivalent Isotropic Displacement Coefficients (Å^2 x10^3)

	x	y	z	U(*)
C(1)	4538 (12)	10608 (4)	6172	52 (3)
C(2)	4950 (15)	10091 (4)	6803 (9)	63 (3)
C(3)	4877 (13)	9442 (4)	6659 (9)	56 (3)
N(4)	4291 (10)	9175 (3)	5883 (7)	48 (3)
C(5)	4315 (15)	8488 (4)	5782 (8)	68 (3)
C(6)	3647 (12)	8240 (5)	5008 (8)	63 (3)
C(7)	3125 (13)	8620 (4)	4381 (8)	49 (2)
C(8)	2644 (13)	9788 (3)	3840 (8)	44 (2)
C(9)	2371 (12)	11063 (4)	3470 (7)	52 (2)
C(10)	2763 (13)	11576 (4)	3956 (8)	58 (3)
O(11)	3397 (8)	11378 (3)	4747 (7)	58 (2)
C(12)	3871 (11)	10300 (3)	5393 (7)	40 (2)
C(13)	3775 (11)	9617 (3)	5239 (7)	36 (2)
C(14)	3174 (12)	9346 (3)	4476 (8)	46 (2)
C(15)	2734 (12)	10473 (3)	3950 (7)	45 (2)
C(16)	3349 (11)	10685 (4)	4715 (7)	41 (2)
C(17)	2734 (15)	12315 (4)	3859 (8)	81 (3)
C(18)	2595 (14)	8324 (4)	3571 (8)	76 (3)
O(19)	4723 (11)	8132 (3)	6388 (7)	98 (3)
C(1')	1855 (11)	4115 (4)	3709 (7)	45 (2)
C(2')	2487 (12)	4630 (3)	4296 (8)	47 (2)
C(3')	2408 (12)	5271 (3)	4170 (7)	39 (2)
N(4')	1730 (9)	5551 (3)	3413 (7)	41 (2)
C(5')	1693 (13)	6232 (4)	3365 (8)	56 (2)
C(6')	1059 (12)	6494 (4)	2572 (8)	54 (2)
C(7')	551 (11)	6114 (3)	1922 (6)	40 (2)
C(8')	99 (12)	4969 (4)	1366 (7)	41 (2)
C(9')	-167 (11)	3698 (3)	966 (7)	41 (2)
C(10')	160 (12)	3177 (4)	1442 (7)	53 (3)
O(11')	770 (8)	3362 (2)	2243 (6)	50 (2)
C(12')	1254 (11)	4427 (4)	2910 (7)	39 (2)
C(13')	1180 (11)	5120 (3)	2777 (7)	35 (2)
C(14')	616 (11)	5392 (3)	2014 (6)	35 (2)
C(15')	178 (11)	4292 (4)	1463 (7)	42 (2)
C(16')	750 (11)	4051 (4)	2236 (7)	37 (2)
C(17')	109 (12)	2449 (4)	1311 (8)	81 (3)
C(18')	-52 (12)	6433 (4)	1122 (7)	60 (3)
O(19')	2113 (10)	6594 (2)	3949 (6)	75 (3)

(*) Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor.

Table 4

Bond Lengths (Å)

C(1)-C(2)	1.48(1)	C(1')-C(2')	1.48(1)
C(1)-C(12)	1.48(1)	C(1')-C(12')	1.50(1)
C(2)-C(3)	1.32(1)	C(2')-C(3')	1.31(1)
C(3)-N(4)	1.43(2)	C(3')-N(4')	1.44(1)
N(4)-C(5)	1.39(1)	N(4')-C(5')	1.37(1)
N(4)-C(13)	1.42(1)	N(4')-C(13')	1.40(1)
C(5)-C(6)	1.43(2)	C(5')-C(6')	1.46(2)
C(5)-O(19)	1.25(1)	C(5')-O(19')	1.23(1)
C(6)-C(7)	1.32(1)	C(6')-C(7')	1.35(1)
C(7)-C(14)	1.46(1)	C(7')-C(14')	1.46(1)
C(7)-C(18)	1.48(2)	C(7')-C(18')	1.50(1)
C(8)-C(14)	1.41(1)	C(8')-C(14')	1.40(1)
C(8)-C(15)	1.39(1)	C(8')-C(15')	1.37(1)
C(9)-C(10)	1.33(1)	C(9')-C(10')	1.32(1)
C(9)-C(15)	1.44(1)	C(9')-C(15')	1.46(1)
C(10)-O(11)	1.42(2)	C(10')-O(11')	1.42(1)
C(10)-C(17)	1.49(1)	C(10')-C(17')	1.48(1)
O(11)-C(16)	1.39(9)	O(11')-C(16')	1.38(8)
C(12)-C13)	1.39(1)	C(12')-C(13')	1.41(1)
C(12)-C(16)	1.39(1)	C(12')-C(16')	1.37(1)
C(13)-C(14)	1.42(1)	C(13')-C(14')	1.41(1)
C(15)-C(16)	1.38(2)	C(15')-C(16')	1.40(1)

Table 5

Bons Angles (°)

C(2)-C(1)-C(12)	111.0(7)	C(2')-C(1')-C(12')	110.6(7)
C(1)-C(2)-C(3)	123.9(12)	C(1')-C(2')-C(3')	125.2(10)
C(2)-C(3)-N(4)	122.4(11)	C(2')-C(3')-N(4')	122.3(9)
C(3)-N(4)-C(5)	118.1(9)	C(3')-N(4')-C(5')	116.5(9)
C(3)-N(4)-C(13)	119.3(7)	C(3')-N(4')-C(13')	118.8(6)
C(5)-N(4)-C(13)	122.6(10)	C(5')-N(4')-C(13')	124.7(10)
N(4)-C(5)-C(6)	116.2(10)	N(4')-C(5')-C(6')	114.5(10)
N(4)-C(5)-O(19)	118.7(11)	N(4')-C(5')-O(19')	122.8(11)
C(6)-C(5)-O(19)	124.6(9)	C(6')-C(5')-O(19')	122.7(8)
C(5)-C(6)-C(7)	124.6(9)	C(5')-C(6')-C(7')	124.6(8)
C(6)-C(7)-C(14)	119.0(10)	C(6')-C(7')-C(14')	118.2(9)
C(6)-C(7)-C(18)	121.1(8)	C(6')-C(7')-C(18')	120.6(7)
C(14)-C(7)-C(18)	119.8(9)	C(14')-C(7')-C(18')	121.2(8)
C(14)-C(8)-C(15)	121.0(10)	C(14')-C(8')-C(15')	120.3(9)
C(10)-C(9)-C(15)	106.2(10)	C(10')-C(9')-C(15')	107.2(9)
C(9)-C(10)-O(11)	112.7(8)	C(9')-C(10')-O(11')	112.4(8)
C(9)-C(10)-C(17)	135.0(11)	C(9')-C(10')-C(17')	134.4(11)
O(11)-C(10)-C(17)	112.3(9)	O(11')-C(10')-C(17')	113.4(9)
C(10)-O(11)-C(16)	103.9(8)	C(10')-O(11')-C(16')	104.5(7)
C(1)-C(12)-C(13)	125.2(8)	C(1')-C(12')-C(13')	123.6(9)
C(1)-C(12)-C(16)	121.7(7)	C(1')-C(12')-C(16')	122.0(7)
C(13)-C(12)-C(16)	113.0(9)	C(13')-C(12')-C(16')	114.3(9)
N(4)-C(13)-C(12)	118.0(9)	N(4')-C(13')-C(12')	119.2(9)
N(4)-C(13)-C(14)	118.8(7)	N(4')-C(13')-C(14')	119.0(7)
C(12)-C(13)-C(14)	123.2(9)	C(12')-C(13')-C(14')	121.8(9)
C(7)-C(14)-C(8)	122.8(10)	C(7')-C(14')-C(8')	121.2(9)
C(7)-C(14)-C(13)	118.7(9)	C(7')-C(14')-C(13')	118.9(8)
C(8)-C(14)-C(13)	118.5(7)	C(8')-C(14')-C(13')	119.8(7)
C(8)-C(15)-C(9)	137.4(11)	C(8')-C(15')-C(9')	137.7(10)
C(8)-C(15)-C(16)	115.8(9)	C(8')-C(15')-C(16')	117.1(9)
C(9)-C(15)-C(16)	106.8(7)	C(9')-C(15')-C(16')	105.1(7)
O(11)-C(16)-C(12)	121.2(9)	O(11')-C(16')-C(12')	122.6(9)
O(11)-C(16)-C(15)	110.4(9)	O(11')-C(16')-C(15')	110.8(8)
O(12)-C(16)-C(15)	128.4(7)	O(12')-C(16')-C(15')	126.6(7)

the annulation of a six-membered dihydropyridine ring. This side-reaction was not predictable, since a six member annulation had not previously been observed in the most commonly used building method of the furan ring in the synthesis of furocoumarin derivatives [7,8,10]. However, the mechanism of this reaction may easily be explained. Assuming that a six-membered tetrahydropyridine ring formation first occurs, later dehydrohalogenation reaction involving the surviving bromine-2 and either H-1 or H-3

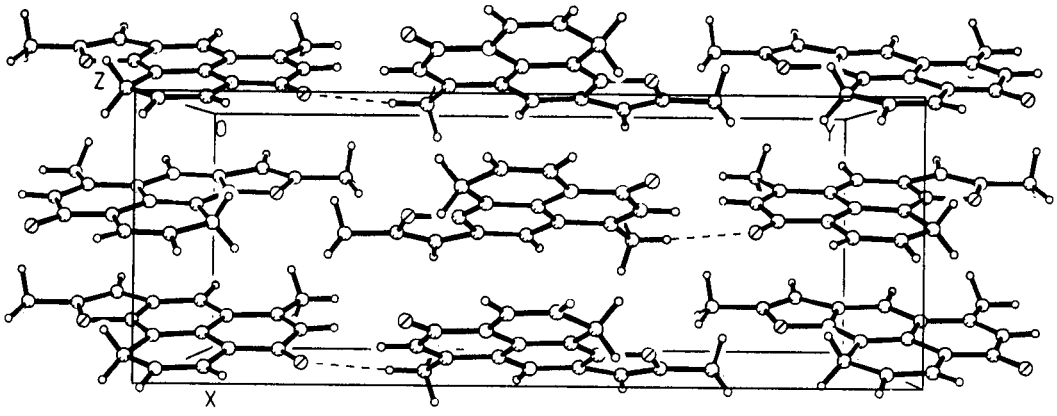


Figure 2. The contents of the unit cell.

atoms to the same extent, gives rise to the two kinds of benzofuroquinolizinone derivatives, carrying respectively a C(1)-C(2) or C(2)-C(3) double bond.

Thus, according to the Scheme, the starting materials were the appropriately methylated 7-hydroxy-8-allylquinolin-2-ones **1,2** [6]. These compounds were condensed with allyl bromide or 1-chlorobut-2-ene to give the corresponding 7-*O*-allyl or 7-*O*-(1''-methylallyl) ethers, **3-5**, which by Claisen rearrangement gave 6,8-diallyl-7-hydroxyquinolin-2-ones, **6,7**, or 6-(1''-methylallyl)-8-allyl-7-hydroxyquinolin-2-one, **8**. The rearranged derivatives were then acetylated and brominated at room temperature to afford 6,8-dibromopropyl derivatives, **12-14**. By cyclization in alkaline medium, these compounds gave 4*H*-furo[3,2-*g*]pyrrolo[3,2,1-*ij*]quinolin-4-ones, **15-17**, 1*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-ones, **18-20**, and 3*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-ones, **21-23**.

These structures should be of interest from a photobiological point of view, owing to the above-mentioned resemblance to the furocoumarin skeleton and, particularly, to the same location of the potentially photoreacting double bond.

In addition, the uv absorption at higher λ of all types of compounds is strongly red-shifted with respect to that of the corresponding psoralens and the relative absorptivities are greatly enhanced; this fact may consequently lead to an improvement in the photoreactive behaviour of these compounds under uv-A irradiation. The uv data of the three series of compounds are summarized in Table 1.

Because planarity of the polycyclic structure is a prerequisite for good intercalation into duplex DNA, which affords the succesive photoreactive event, the planarity of the structure of furobenzoquinolizinones in particular was further investigated.

The planar structure of **18** was unequivocally established by X-ray crystal-structure analysis. Two formula molecules (A) and (B) make up the asymmetric unit (Figure 1); they overlap, the root mean square deviation being only 0.05 Å when the four-ring skeleton is fitted. In both molecules the skeleton is essentially planar (maximum deviation of 0.05 Å by C(5) in (A) and 0.06 Å by C(1') in (B)) and the π-electron system seems to be localized particularly on the C(2)-C(3) bond (1.32 (1) and 1.31 (1) Å, in (A) and (B), respectively). The shortest intermolecular interaction (O(19)---HC(18) (at ½-x, y, ½ + z) of 2.48 Å) is not an effective hydrogen bond, although the geometry looks appropriate (O(19)---HC(18)-C(18) angle of 174°) (Figure 2).

EXPERIMENTAL

Melting points (uncorrected) were determined using a Büchi-Tottoli SPM-20 capillary melting point apparatus. Analytical thin layer chromatography (tlc) was performed on pre-coated silica gel plates 60-F-254 (Merck; 0.25 mm), developing with ethyl acetate/cyclohexane mixture (35:65). Preparative column chromatography was performed using silica gel (Merck; 0.063-0.200 mm). The ^{1}H nmr spectra were recorded on a Varian Gemini-200 spectrometer with TMS as internal standard and deuteriochloroform as solvent, unless otherwise indicated. The relative peak areas and the decoupling experiments were in agreement with all assignments. The uv spectra were recorded on a Perkin-Elmer Lambda 15 UV/VIS spectrophotometer.

Allyl Ethers: **3**, **4** and **5**.

4-Methyl-7-allyloxy-8-allylquinolin-2-one (**3**).

A solution of 1.13 g (5.25 mmoles) of 4-methyl-7-hydroxy-8-allylquinolin-2-one (**1**) [6] in 200 ml of acetone was reacted with allyl bromide (1.41 g, 11.65 mmoles) in the presence of anhydrous potassium carbonate (30.0 g) by refluxing the mixture for 3 hours. After chilling the potassium carbonate was filtered off and washed with fresh acetone. The pooled filtrate and acetone washings were concentrated to dryness and the residue crystallized from methanol giving 1.25 g (93%) of 4-methyl-7-allyloxy-8-allylquinolin-2-one (**3**), mp 206°; ^{1}H nmr: δ 2.44 (d, 3H, Me-4, $J_{Me\text{-}4,3}$ = 1.1 Hz), 3.64 (dt, 2H, H-1', $J_{1',2'}$ = 5.7 and $J_{1',3'}$ = 1.7

Hz), 4.65 (dt, 2H, H-1'', $J_{1'',2''}$ = 5.0 and $J_{1'',3''}$ = 1.6 Hz), 5.00-5.13 (m, 2H, H-3'), 5.27-5.47 (m, 2H, H-3''), 5.84-6.15 (m, 2H, H-2' and H-2''), 6.38 (q, 1H, H-3, $J_{3,4\text{-Me}}$ = 1.1 Hz), 6.85 (d, 1H, H-6, $J_{6,5}$ = 9.0 Hz), 7.54 (d, 1H, H-5, $J_{5,6}$ = 9.0 Hz), 8.93 (broad s, 1H, NH).

Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.19; H, 6.57; N, 5.36.

In the same manner the following ethers were prepared:

3,4-Dimethyl-7-allyloxy-8-allylquinolin-2-one (**4**).

This compound was prepared from 3,4-dimethyl-7-hydroxy-8-allylquinolin-2-one (**2**) [6], mp 161° (methanol, 91%); ^{1}H nmr: δ 2.23 (q, 3H, Me-3, $J_{\text{Me-3,Me-4}}$ = 0.7 Hz), 2.43 (q, 3H, Me-4, $J_{\text{Me-4,Me-3}}$ = 0.7 Hz), 3.63 (dt, 2H, H-1', $J_{1',2'}$ = 5.6 and $J_{1',3'}$ = 1.8 Hz), 4.64 (dt, 2H, H-1'', $J_{1'',2''}$ = 5.0 and $J_{1'',3''}$ = 1.6 Hz), 4.99-5.13 (m, 2H, H-3'), 5.26-5.47 (m, 2H, H-3''), 5.84-6.04 (m, 1H, H-2'), 5.96-6.15 (m, 1H, H-2''), 6.84 (d, 1H, H-6, $J_{6,5}$ = 9.0 Hz), 7.57 (d, 1H, H-5, $J_{5,6}$ = 9.0 Hz), 8.82 (broad s, 1H, NH).

Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.72; H, 7.05; N, 5.02.

3,4-Dimethyl-7-(but-2'-enyloxy)-8-allylquinolin-2-one (**5**).

This compound was prepared from 3,4-dimethyl-7-hydroxy-8-allylquinolin-2-one (**2**) [6], mp 175° (methanol, 71%); ^{1}H nmr: δ 1.74 (dd, 3H, Me-3'', $J_{\text{Me-3'',3''}}$ = 6.1 and $J_{\text{Me-3'',2''}}$ = 1.1 Hz), 2.20 (s, 3H, Me-3), 2.41 (s, 3H, Me-4), 3.58 (dt, 1H, H-1', $J_{1',2'}$ = 5.7 and $J_{1',3'}$ = 1.8 Hz), 4.52-4.66 (m, 2H, H-1''), 4.97-5.11 (m, 2H, H-3'), 5.62-6.02 (m, 3H, H-2', H-2'' and H-3''), 6.83 (d, 1H, H-6, $J_{6,5}$ = 9.0 Hz), 7.55 (d, 1H, H-5, $J_{5,6}$ = 9.0 Hz), 8.64 (broad s, 1H, NH).

Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.04; H, 7.46; N, 4.79.

Claisen Rearrangement: **6,7** and **8**.

4-Methyl-6,8-dially-7-hydroxyquinolin-2-one (**6**).

A solution of 4-methyl-7-allyloxy-8-allylquinolin-2-one (**3**) (2.70 g, 10.57 mmoles) in *N,N*-diethylaniline (30 ml) was refluxed for 3 hours. The reaction mixture was cooled and *n*-hexane was added. The precipitate was collected, washing it many times with *n*-hexane and crystallized from methanol giving 1.89 g (70%) of 4-methyl-6,8-diallyl-7-hydroxyquinolin-2-one (**6**), mp 135°; ^{1}H nmr (tetradeuteriomethanol): δ 2.46 (d, 3H, Me-4, $J_{\text{Me-4,3}}$ = 1.1 Hz), 3.53 (broad d, 2H, H-1'', $J_{1'',2''}$ = 6.2 Hz), 3.62 (dt, 2H, H-1', $J_{1',2'}$ = 5.5 and $J_{1',3'}$ = 1.8 Hz), 5.02-5.28 (m, 4H, H-3' and H-3''), 5.87-6.15 (m, 2H, H-2' and H-2''), 6.39 (q, 1H, H-3, $J_{3,\text{Me-4}}$ = 1.1 Hz), 7.36 (s, 1H, H-5).

Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.23; H, 6.61; N, 5.38.

The following derivatives were prepared in an analogous manner:

3,4-Dimethyl-6,8-diallyl-7-hydroxyquinolin-2-one (**7**).

This compound was prepared from 3,4-dimethyl-7-allyloxy-8-allylquinolin-2-one (**4**), mp 152° (methanol, 71%); ^{1}H nmr (tetradeuteriomethanol): δ 2.23 (broad s, 3H, Me-3), 2.43 (broad s, 3H, Me-4), 3.52 (broad d, 2H, H-1'', $J_{1'',2''}$ = 6.12 Hz), 3.61 (dt, 2H, H-1', $J_{1',2'}$ = 5.5 and $J_{1',3'}$ = 1.8 Hz), 5.00-5.27 (m, 4H, H-3' and H-3''), 5.87-6.16 (m, 2H, H-2' and H-2''), 7.38 (s, 1H, H-5).

Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.70; H, 7.08; N, 5.11.

3,4-Dimethyl-6-(1''-methylallyl)-7-hydroxy-8-allylquinolin-2-one (**8**).

This compound was prepared from 3,4-dimethyl-7-(but-2'-enyloxy)-8-allylquinolin-2-one (**5**), mp 183° (methanol, 85%); ^{1}H nmr: δ 1.48 (d, 3H, Me-1'', $J_{\text{Me-1'',1''}}$ = 7.0), 2.23 (s, 3H, Me-3), 2.44 (s, 3H, Me-4), 3.59 (dt, 2H, H-1', $J_{1',2'}$ = 5.3 and $J_{1',3'}$ = 1.7 Hz), 3.71 (qd, 1H, H-1'', $J_{1'',\text{Me-1''}}$ = 7.0 and $J_{1'',2''}$ = 7.0), 5.00-5.40 (m, 4H, H-3' and H-3''), 5.87-6.22 (m, 2H, H-2' and H-2''), 7.40 (s, 1H, H-5).

Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.02; H, 7.44; N, 4.85.

7-Acetoxyquinolin-2-ones: **9, 10** and **11**.

4-Methyl-6,8-diallyl-7-acetoxyquinolin-2-one (**9**).

A solution of 1.50 g (5.87 mmoles) of 4-methyl-6,8-diallyl-7-hydroxyquinolin-2-one (**6**) in 30 ml of acetic anhydride was refluxed for 1 hour in the presence of anhydrous sodium acetate (1.0 g). The reaction mixture was cautiously diluted with 40 ml of water, refluxed for 10 minutes and poored into water (400 ml). The precipitate was collected, washed with abundant water and crystallized from methanol to give 1.58 g (90%) of 4-methyl-6,8-diallyl-7-acetoxyquinolin-2-one (**9**) mp 206°; ^{1}H nmr: δ 2.37 (s, 3H, MeCO-), 2.47 (d, 3H, Me-4, $J_{\text{Me-4,3}}$ = 1.1 Hz), 3.34 (broad d, 2H, H-1'', $J_{1'',2''}$ = 6.6 Hz), 3.46 (broad d, 2H, H-1', $J_{1',2'}$ = 5.6 Hz), 5.09-5.22 (m, 4H, H-3' and H-3''), 5.77-6.02 (m, 2H, H-2' and H-2''), 6.49 (q, 1H, H-3, $J_{3,\text{Me-4}}$ = 1.1 Hz), 7.47 (s, 1H, H-5), 8.85 (s, 1H, NH).

Anal. Calcd. for $C_{18}H_{19}NO_3$: C, 72.70; H, 6.44; N, 4.71. Found: C, 72.69; H, 6.32; N, 4.60.

In the same manner the following 7-acetoxy derivatives were obtained:

3,4-Dimethyl-6,8-diallyl-7-acetoxyquinolin-2-one (**10**).

This compound was prepared from 3,4-dimethyl-6,8-diallyl-7-hydroxyquinolin-2-one (**7**) mp 232° (methanol, 92%); ^{1}H nmr: δ 2.24 (broad s, 3H, Me-3), 2.35 (s, 3H, MeCO-), 2.44 (broad s, 3H, Me-4), 3.33 (broad d, 2H, H-1'', $J_{1'',2''}$ = 6.7 Hz), 3.44 (broad d, 2H, H-1', $J_{1',2'}$ = 4.6 Hz), 5.07-5.20 (m, 4H, H-3' and H-3''), 5.78-6.02 (m, 2H, H-2' and H-2''), 7.48 (s, 1H, H-5), 8.89 (broad s, 1H, NH).

Anal. Calcd. for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.28; H, 6.72; N, 4.39.

3,4-Dimethyl-6-(1''-methylallyl)-7-acetoxy-8-allylquinolin-2-one (**11**).

This compound was prepared from 3,4-dimethyl-6-(1''-methylallyl)-7-hydroxy-8-allylquinolin-2-one (**8**) mp 209° (methanol, 93%); ^{1}H nmr: δ 1.35 (d, 3H, Me-1'', $J_{\text{Me-1'',1''}}$ = 7.0 Hz), 2.22 (s, 3H, Me-3), 2.35 (s, 3H, MeCO), 2.42 (s, 3H, Me-4), 3.40 (broad d, 2H, H-1', $J_{1',2'}$ = 5.4 Hz), 3.51 (broad q, 1H, H-1'', $J_{1'',\text{Me-1''}}$ = 7.0 Hz), 5.03-5.20 (m, 4H, H-3' and H-3''), 5.77-6.02 (m, 2H, H-2' and H-2''), 7.25 (s, 1H, H-5), 8.75 (broad s, 1H, NH).

Anal. Calcd. for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.68; H, 7.02; N, 4.19.

Bromination: **12, 13** and **14**.

4-Methyl-6,8-di(2',3'-dibromopropyl)-7-acetoxyquinolin-2-one (**12**).

An acetic solution (20 ml) containing the stoichiometric amount of bromine was dropped at room temperature during 20 minutes into an acetic solution (40 ml) of 1.45 g (4.87 mmoles) of 4-methyl-6,8-diallyl-7-acetoxyquinolin-2-one (**9**). After the addition was completed, the solution was further stirred for 30 minutes, the solvent was evaporated to dryness and the residue crystallized from methanol giving 2.9 g (96%) of 4-methyl-6,8-di(2',3'-

dibromopropyl)-7-acetoxyquinolin-2-one (**12**) mp 149°; ^{1}H nmr: δ 2.50 (s, 3H, MeCO), 2.52 (broad s, 3H, Me-4), 3.61-3.74 (m, 4H, H-1′ and H-1″), 3.90-4.11 (m, 4H, H-3′ and H-3″), 4.32-4.49 (m, 2H, H-2′ and H-2″), 6.54 (broad s, 1H, H-3), 7.66 (s, 1H, H-5), 11.27 (s, 1H, NH).

Anal. Calcd. for $C_{18}H_{19}Br_2NO_3$: C, 47.29; H, 4.19; Br, 34.96; N, 3.06. Found: C, 47.22; H, 4.09; Br, 34.92; N, 3.01.

The following dibromopropyl derivatives were prepared in an analogous manner:

3,4-Dimethyl-6,8-di(2′,3′-dibromopropyl)-7-acetoxyquinolin-2-one (**13**).

This compound was obtained from 3,4-dimethyl-6,8-diallyl-7-acetoxyquinolin-2-one (**10**) mp 129° (methanol, 91%); ^{1}H nmr: δ 2.31 (broad s, 3H, Me-3), 2.50 (broad s, 6H, Me-4 and MeCO), 3.49-4.09 (m, 8H, H-1′, H-1″, H-3′ and H-3″), 4.32-4.51 (m, 2H, H-2′ and H-2″), 7.69 (s, 1H, H-5), 10.86 (s, 1H, NH).

Anal. Calcd. for $C_{19}H_{21}Br_2NO_3$: C, 48.43; H, 4.49; Br, 33.92; N, 2.97. Found: C, 48.37; H, 4.41; Br, 33.82; N, 2.90.

3,4-Dimethyl-6-(1″-methyl-2″,3″-dibromopropyl)-7-acetoxy-8-(2′,3′-dibromopropyl)quinolin-2-one (**14**).

This compound was prepared from 3,4-dimethyl-6-(1″-methylallyl)-7-acetoxy-8-allylquinolin-2-one (**11**) mp 164° (methanol, 90%); ^{1}H nmr: δ 1.40 (d, 3H, Me-1″, $J_{Me\text{-}1'',1''}$ = 6.4 Hz), 2.31 (broad s, 3H, Me-3), 2.51 (broad s, 6H, Me-4 and MeCO-), 3.50-4.08 (m, 7H, H-1′, H-1″, H-3′ and H-3″), 4.41-4.54 (m, 2H, H-2′ and H-2″), 7.89 (s, 1H, H-5), 10.82 (s, 1H, NH).

Anal. Calcd. for $C_{20}H_{23}Br_2NO_3$: C, 49.50; H, 4.78; Br, 32.94; N, 2.89. Found: C, 49.46; H, 4.69; Br, 32.79; N, 2.81.

Cyclization: **15-23**.

2,6,9-Trimethyl-4*H*-furo[3,2-*g*]pyrrolo[3,2,1-*ij*]quinolin-4-one (**15**), 7,10-Dimethyl-1*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-one (**18**), 7,10-Dimethyl-3*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-one (**21**).

To an ethanolic solution (150 ml) of 1.00 g (1.62 mmoles) of 4-methyl-6,8-di(2′,3′-dibromopropyl)-7-acetoxyquinolin-2-one (**12**) an ethanolic 4% potassium hydroxide solution (40 ml) was added. The mixture was refluxed for 1.5 hours, chilled, diluted with twice its volume of water and acidified with diluted hydrochloric acid obtaining a solid, which was filtered. Three products were present in the crude precipitate (tlc), which were isolated by silica gel column chromatography, eluting with chloroform. From first fractions containing a single product (tlc) the solvent was evaporated obtaining 2,6,9-trimethyl-4*H*-furo[3,2-*g*]pyrrolo[3,2,1-*ij*]-quinolin-4-one (**15**) mp 160°, (methanol, 22%); ^{1}H nmr: see Table 2.

Anal. Calcd. for $C_{16}H_{13}NO_2$: C, 76.47; H, 5.22; N, 5.57. Found: C, 76.20; H, 5.33; N, 5.46.

From the following fractions containing the second product (tlc) by evaporation of the solvent 7,10-dimethyl-1*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-one (**18**) was obtained, mp 213°, (methanol, 14%); ^{1}H nmr: see Table 2.

Anal. Calcd. for $C_{16}H_{13}NO_2$: C, 76.47; H, 5.22; N, 5.57. Found: C, 76.42; H, 5.28; N, 5.46.

Latest fractions containing the third product (tlc) by evaporation of the solvent gave 7,10-dimethyl-3*H*,5*H*-benzofuro[5,6,7-*ij*]-quinolizin-5-one (**21**), mp 181°, (methanol, 20%); ^{1}H nmr: see Table 2.

Anal. Calcd. for $C_{16}H_{13}NO_2$: C, 76.47; H, 5.22; N, 5.57. Found: C, 76.32; H, 5.26; N, 5.55.

In the same manner by alkaline cyclization and column chromatography the following compounds were obtained:

2,5,6,9-Tetramethyl-4*H*-furo[3,2-*g*]pyrrolo[3,2,1-*ij*]quinolin-4-one (**16**), 6,7,10-Trimethyl-1*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-one (**19**), 6,7,10-Trimethyl-3*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-one (**21**).

From 3,4-dimethyl-6,8-di(2′,3′-dibromopropyl)-7-acetoxyquinolin-2-one (**13**) the following compounds were obtained:

i) 2,5,6,9-Tetramethyl-4*H*-furo[3,2-*g*]pyrrolo[3,2,1-*ij*]quinolin-4-one (**16**).

This compound had mp 159° (methanol, 22%); ^{1}H nmr: see Table 2.

Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.89; H, 5.64; N, 5.43.

ii) 6,7,10-Trimethyl-1*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-one (**19**).

This compound had mp 194°, (methanol, 16%); ^{1}H nmr: see Table 2.

Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.77; H, 5.87; N, 5.25.

iii) 6,7,10-Trimethyl-3*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-one (**22**).

This compound had mp 169°, (methanol, 15%); ^{1}H nmr: see Table 2.

Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.89; H, 5.64; N, 5.43.

2,5,6,8,9-Pentamethyl-4*H*-furo[3,2-*g*]pyrrolo[3,2,1-*ij*]quinolin-4-one (**17**), 6,7,9,10-Tetramethyl-1*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-one (**20**), 6,7,9,10-Tetramethyl-3*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-one (**23**).

From 3,4-dimethyl-6-(1″-methyl-2″,3‴-dibromopropyl)-7-acetoxy-8-(2′,3′-dibromopropyl)quinolin-2-one (**14**) the following compounds were obtained:

i) 2,5,6,8,9-Pentamethyl-4*H*-furo[3,2-*g*]pyrrolo[3,2,1-*ij*]quinolin-4-one (**17**).

This compound had mp 231° (methanol, 29%); ^{1}H nmr: see Table 2.

Anal. Calcd. for $C_{18}H_{17}NO_2$: C, 77.39; H, 6.13; N, 5.01. Found: C, 77.65; H, 6.28; N, 5.14.

ii) 6,7,9,10-Tetramethyl-1*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-one (**20**).

This compound had mp 171°, (methanol, 18%); ^{1}H nmr: see Table 2.

Anal. Calcd. for $C_{18}H_{17}NO_2$: C, 77.39; H, 6.13; N, 5.01. Found: C, 77.68; H, 6.36; N, 5.22.

iii) 6,7,9,10-Tetramethyl-3*H*,5*H*-benzofuro[5,6,7-*ij*]quinolizin-5-one (**23**).

This compound had mp 189°, (methanol, 19%); ^{1}H nmr: see Table 2.

Anal. Calcd. for $C_{18}H_{17}NO_2$: C, 77.39; H, 6.13; N, 5.01. Found: C, 77.22; H, 6.12; N, 4.91.

X-ray Crystallography of **18**.

Pale orange crystals of **18** were obtained by recrystallization from methanol. A prismatic crystal of dimensions *ca.* 0.15 x 0.10 x 0.15 mm was mounted on a Siemens Nicolet R3m/V diffractometer, equipped with graphite monochromatized MoKα radiation (λ=0.71073 Å). Cell parameters were obtained from least-squares analysis of 50 high angle data ($2\theta > 23°$); 1634 independent reflections were collected in the range $4° < 2\theta < 45°$ using ω-2θ scan technique. The structure was solved by direct methods and all of the non-hydrogen atoms came out from the *E* map with the highest figure of merit. The hydrogens were included in calculated positions with a common, variable isotropic thermal factor; the quantity minimized in full-matrix least-squares refinement was $\Sigma w(| F_o | - | F_c |)^2$ with $w^{-1} = \sigma^2(F) + 0.0014 F^2$ and to ensure a good observation/variable ratio and to achieve convergence, only N and O atoms were refined anisotropically. The final *R* value was 0.050 for the 1011 unique reflections with $| F_o | > 3\sigma(F_o)$ (R_w = 0.055; GOF = 0.97). Difference map, calculated after the refinement, was essentially featureless, the largest peak being 0.21 e Å^{-3} and the largest hole -0.19 e Å^{-3}. The SHELXTL-Plus package [11] of computer programs was employed for the solution and refinement of **18**.

Crystal Data.

$C_{16}H_{13}NO_2$, M = 251.3, orthorhombic, space group $Pca2_1$, a = 7.500(4), b = 20.042(11), c = 16.084(8) Å, V = 2418(2) Å, Z = 8, D_c = 1.381 g/cm^3.

The final non-hydrogen atomic coordinates are given in Table 3 while bond distances and angles are given in Table 4 and 5, respectively. Additional data, including anisotropic thermal parameters, H atoms coordinates and a listing of the observed/calculated structure factors, are available from the authors.

An ORTEP view of **18** is shown in Figure 1, while Figure 2 shows the crystal-packing viewed along the *c*-axis.

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[10] A recent re-investigation of the synthesis of pyrrolo[3,2,1-*ij*]-quinolin-4-ones [6] allowed us to isolate in small amount 1*H*,5*H*- and 3*H*,5*H*-benzo[*ij*]quinolizin-5-ones as minor co-products.

[11] G. M. Sheldrick, SHELXTL-PLUS. An Integrated System for Solving, Refining and Displaying Crystal Structure from Diffraction Data for Nicolet R3m/V. University of Göttingen, Germany, 1987.