Synthesis of 2-Amino-1,4-dihydro-4-quinolinones and Diaminomethylene Meldrum's Acids Derivatives as Potential Potassium Channel Openers

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Starting from 5-bismethylthiomethylene Meldrum's acid, the synthesis of 5-diaminomethylene Meldrum's acids and 2-aminoquinolone derivatives, structurally related to potassium channels openers pinacidil and diazoxide, is described.

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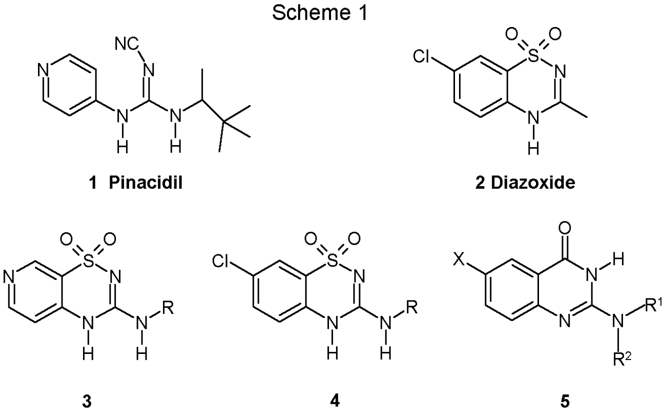
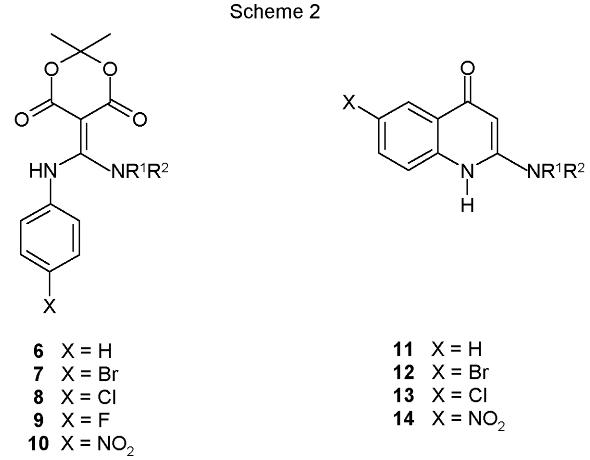
Potassium channels represent a very diversified group of ionic channels [1]. Many hypotensive or myorelaxant agents such as aprikalim, cromakalim, minoxidil sulfate, pinacidil (**1**) or diazoxide (**2**) have the properties to open the subtype of potassium channels called ATP-sensitive potassium channels or K_{ATP} channels [2]. Using the bioisosterism concept [3], the structural elements of compounds **1** and **2** were mixed. Products **3** and **4** resulting from this concept were found to be powerful inhibitors of insulin secretion [4]. Some compounds **3**, being more potent on the pancreatic than on the vascular smooth muscle tissue, are tissue selective K_{ATP} channel openers [4]. In a first publication [5] we applied the bioisosteric exchange of the sulfamide moiety by the chemically related amide group, and some products **5** possess interesting biological properties (Scheme 1).

Scheme 1



In the chemical structure of compounds **1-5** (Scheme 1), like in that of other potassium channel openers, it is possible to observe the presence of an electron deficient aromatic ring (pyridine or halobenzene), the presence of a lipophilic substituent (in the 3-position of the thiadiazine heterocycles **3** and **4**, in the 2-position of the quinazoline heterocycle **5** or in the *N*-position of the *N*-alkyl-*N*'-aryl-*N*''-cyanoguanidine **1**) and the presence of an electronegative site (iminonitrile, amide or sulfonamide group). Therefore, we decided to apply the bioisosteric exchange of the sulfonamide or amide moiety by the chemically related oxo group as well as the exchange of a *N*-cyano group by a Meldrum's moiety

Scheme 2



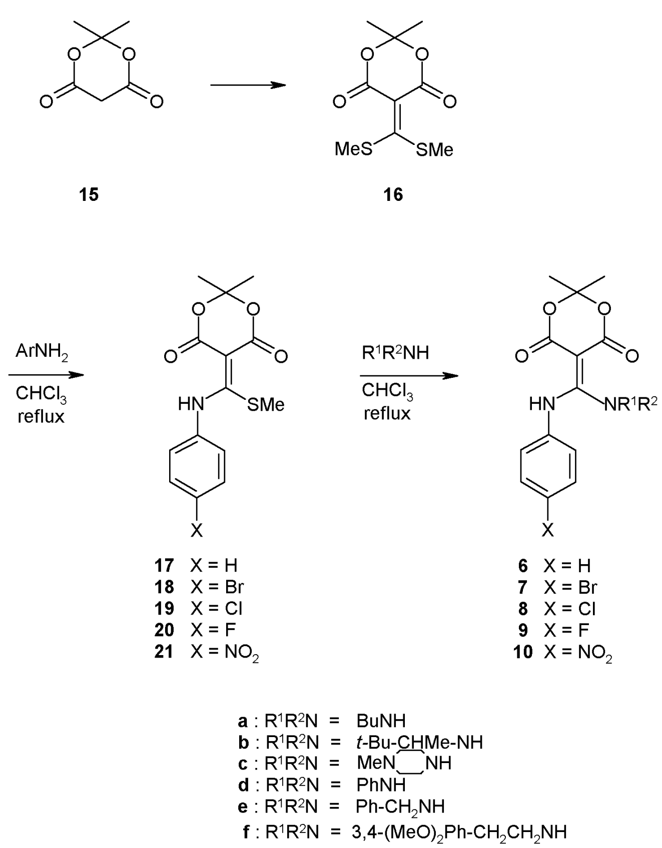
a : R^1R^2N = BuNH
b : R^1R^2N = *t*-Bu-CHMe-NH
c : R^1R^2N = MeN⌴NH
d : R^1R^2N = PhNH
e : R^1R^2N = Ph-CH_2NH
f : R^1R^2N = 3,4-$(MeO)_2$Ph-CH_2CH_2NH
g : R^1R^2N = 3,4,5-$(MeO)_3$PhCONHNH
h : R^1R^2N = 4-ClPhCONHNH
i : R^1R^2N = H_2NNH
j : R^1R^2N = Me_2C=N-NH

(Scheme 2). We use also a nitro or halobenzene (X = F, Cl, Br) as an electron deficient aromatic ring, with the aim at obtaining a compound with a better activity and/or a better tissue selectivity.

In this paper, we describe the synthesis of diaminomethylene Meldrum's acids **6-10** considered as pinacidil analogs and the synthesis of 2-amino-4-quinolones **11-14** considered as analogs of compounds **2-5** (Scheme 2).

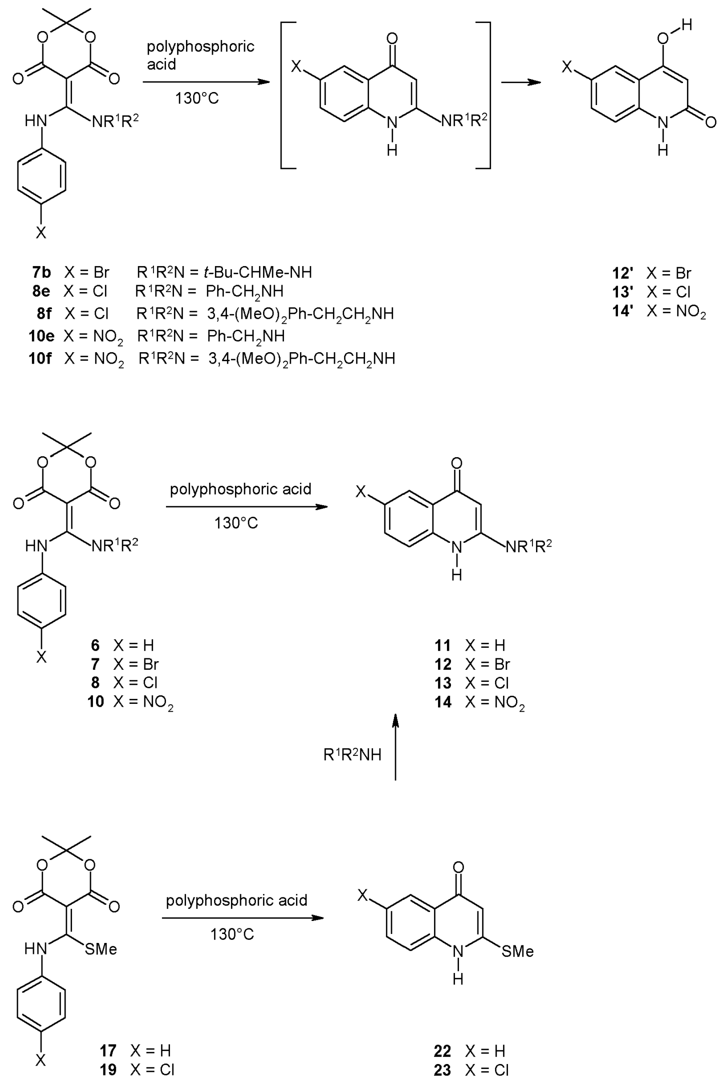
Antimicrobial properties of 4-oxoquinoline-3-carboxylic acids are well known [6a] and those of 3-amino-4-quinolones have been studied [6b]. However, only few publications deal with diaminomethylene derivatives of Meldrum's acid and with 2-amino-4-quinolones. A general method for the synthesis of diaminomethylene derivatives of Meldrum's acid (**15**) consists in starting from compound **16** [7a,b] whose reaction with two different amines can be conducted sequentially [8]. By using this method, products **6-10** were easily obtained; interestingly, it was not necessary to use a catalyst such as mercuric chloride [8,9,10] to perform the condensation between compounds **17-21** and aromatic or aliphatic amines (Scheme 3).

Scheme 3



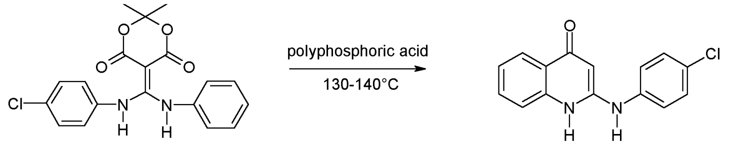
Heating compounds **6-10** in polyphosphoric acid is a first way to synthesize 2-amino-4-quinolones **11-14**, but variable yields (see Table 3, method H) were obtained, and this treatment of diaminomethylene Meldrum's derivatives **7b**, **8e**, **8f**, **10e** and **10f** only yield quinoline-2,4-diones **12'**, **13'**, **14'** (Scheme 4). Another way leading to 2-amino-quinolones **11-14** was to react 2-methylthio-4-quinolones **22**, **23** with amines (Table 3, method I). The latter compounds **22**, **23** were obtained in good yields by heating Meldrum's derivatives **17**, **19** in polyphosphoric acid (Scheme 4).

Scheme 4

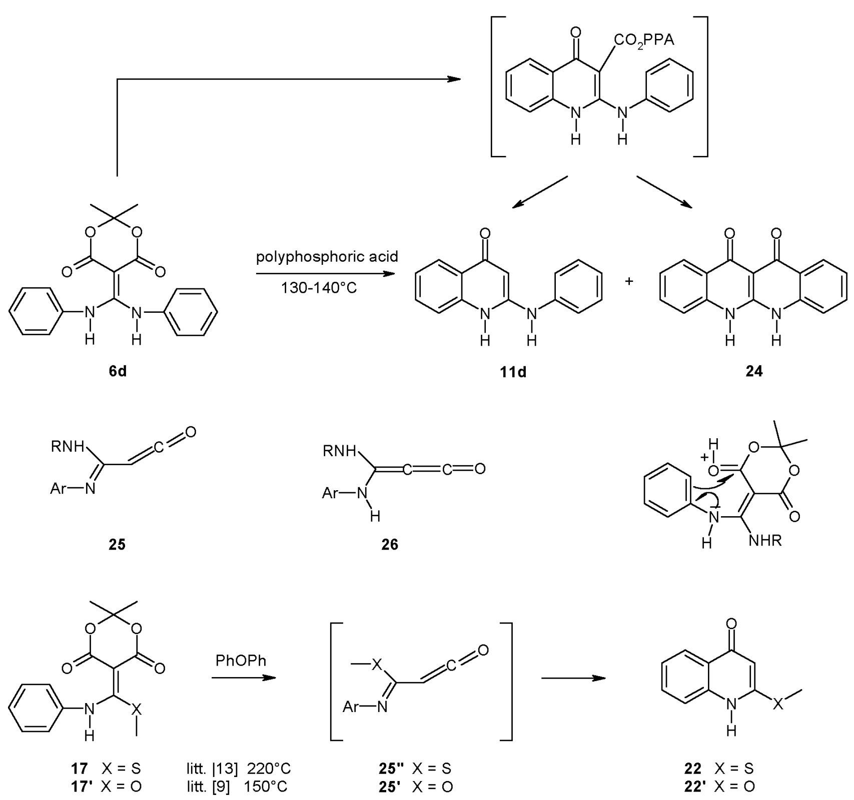


It is to be noticed that cyclization of the Meldrum's derivative **8d** mainly yields the quinolone **11k** (Scheme 5). The polyphosphoric acid cyclizations were usually performed at 130-140 °C by using only 4 grams of dehydrating agent for about 10 mmoles of compound **6-10**. When these ratios of reagents were used with the dianilino Meldrum's derivative **6d**, product **11d** was obtained as the major compound. However, by using a higher amount of polyphosphoric acid (10 grams for 10 mmoles of **6d**), a 45/55 mixture of compounds **11d** and **24** was obtained (Scheme 6). This result seems to indicate that, at the low temperature utilized for these reactions in polyphosphoric acid, other intermediates than imidoylketenes (**25**) or methyleneketenes (**26**) [11] could explain the ring closure reactions (Scheme 6). In analog cyclizations giving **22** or **22'**, performed in diphenyl ether, compound **17'** was thought to gives intermediates **25'** at 150 °C [9], and compound **17** was thought to yield **25''** at 220 °C [13].

Scheme 5



Scheme 6

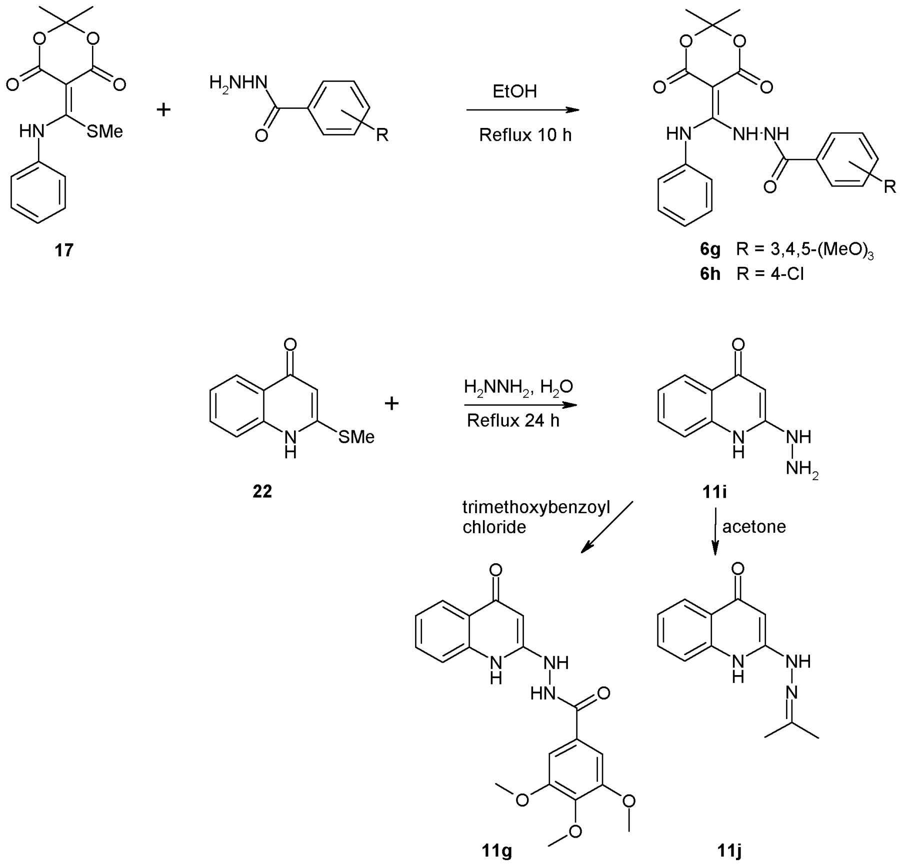


Some reactions performed in the hydrazine/hydrazide series are described in Scheme 7. These products were synthesized in order to extend the structure of the compounds submitted to biological investigation. It is to be noticed that good yields without side reaction were obtained during the condensation of aryl hydrazides with Meldrum's acid **17**.

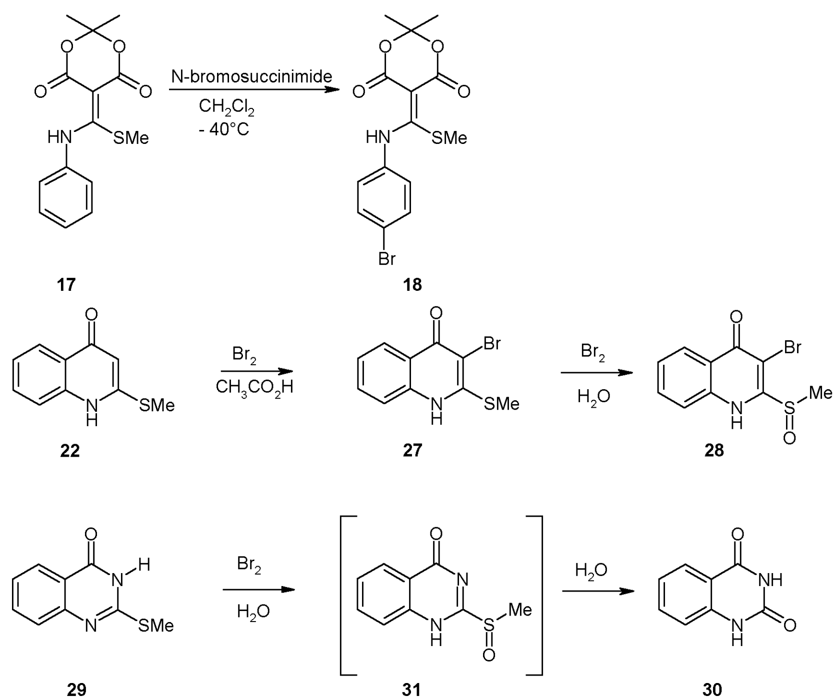
We have submitted compounds **17** and **22** to the action of bromine in water or in acetic acid in order to test their reactivity. In these conditions, whatever the temperature, a polybromination of Meldrum's derivative **17** occurred. A selective bromination of aryl amines can be realized by using *N*-bromosuccinimide [14-16]; by using this reagent, polybromination of **17** was still observed at room temperature, but by working at -40 °C, only compound **18** was obtained (Scheme 8). On the other hand, quinolone **22** reacted with one equivalent of bromine to give 86 % of pure product **27**. A second equivalent of bromine can then oxidize the thioether group [17], giving sulfoxide **28** (Scheme 8). In the quinazolinone series, bromine oxidation of compound **29** yielded the hydrolyzed product **30**, without isolation of sulfoxide **31** [5] (Scheme 8).

The reaction of carbon disulfide with Meldrum's acid **15** yields compound **16**. As an alternate way to this synthesis we have checked the reaction of heterocycle **15** with other reagents: condensation of Meldrum's acid with dicyclohexylcarbodiimide has been described [18] and its reaction with iminoethers is well documented. Starting from urea **32**, we synthesized the corresponding carbodiimide **33** following the method of Apple [19], and isourea **34** was obtained [20,21] by using triethyloxonium fluoroborate [22,23]. Whatever the conditions, a reaction between compounds **33** or **34** and Meldrum's acid was never observed. It is also known that Meldrum's acid reacts with isocyanates [24] or acylisothiocyanates [25], and that malonic derivatives, instead of Meldrum's acid, react with isothiocyanates

Scheme 7



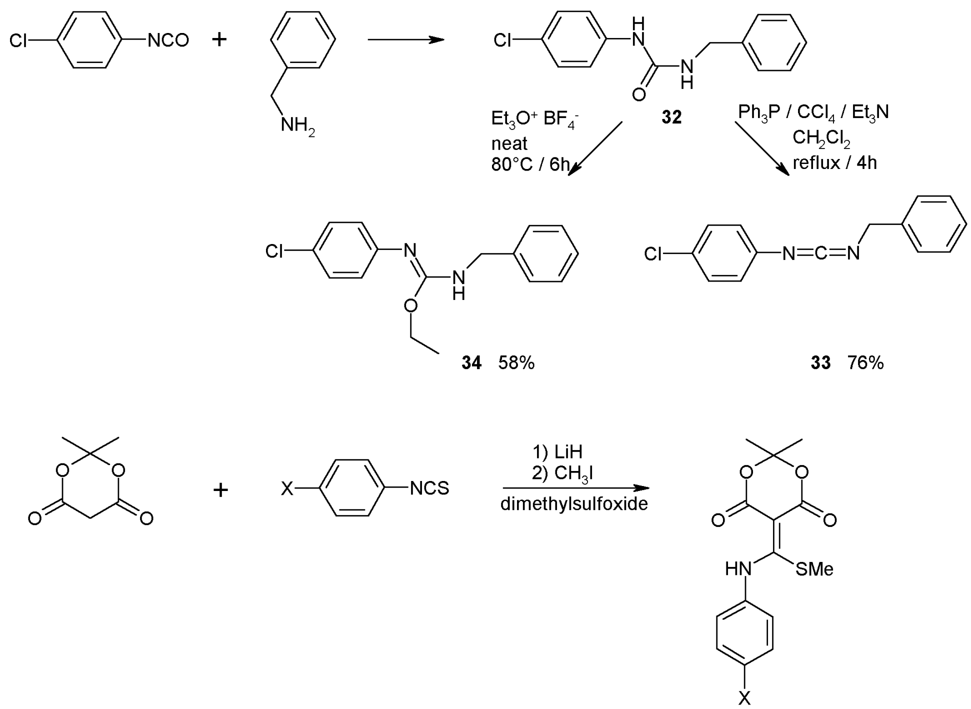
Scheme 8



[26,27]. Condensation of Meldrum's acid with phenyl or chlorophenyl isothiocyanates was then performed giving compounds **17** and **19** in medium yield (Scheme 9).

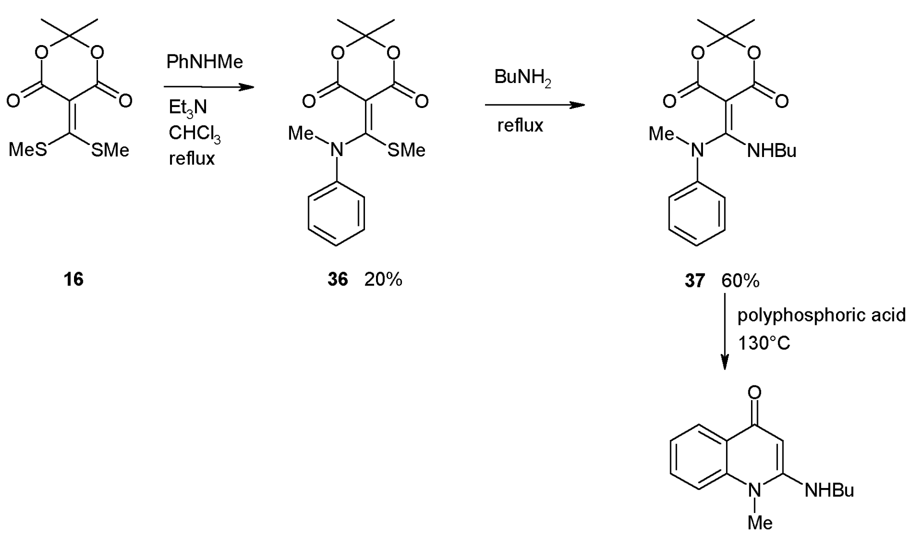
A very important feature of the potassium channel openers **2**, **3** and **4** shown in Scheme 1, is the presence of the NH group in the 4 position of the thiadiazine ring. Thus, the ultra-violet spectrum of the butylamino compound **11a** was compared to the spectrum of its *N*-methyl analog **35**. The strong analogy between the two spectra (Figure1) seems to indicate that, in methanol solution, quinolone **11a** mainly exists as a 1*H*-quinoline-4-one tautomer **11a** rather than as the 4-quinolinol tautomer **11a'** (see Figure 1) [28]. Compound **35** was prepared in the way described in Scheme 10.

Scheme 9

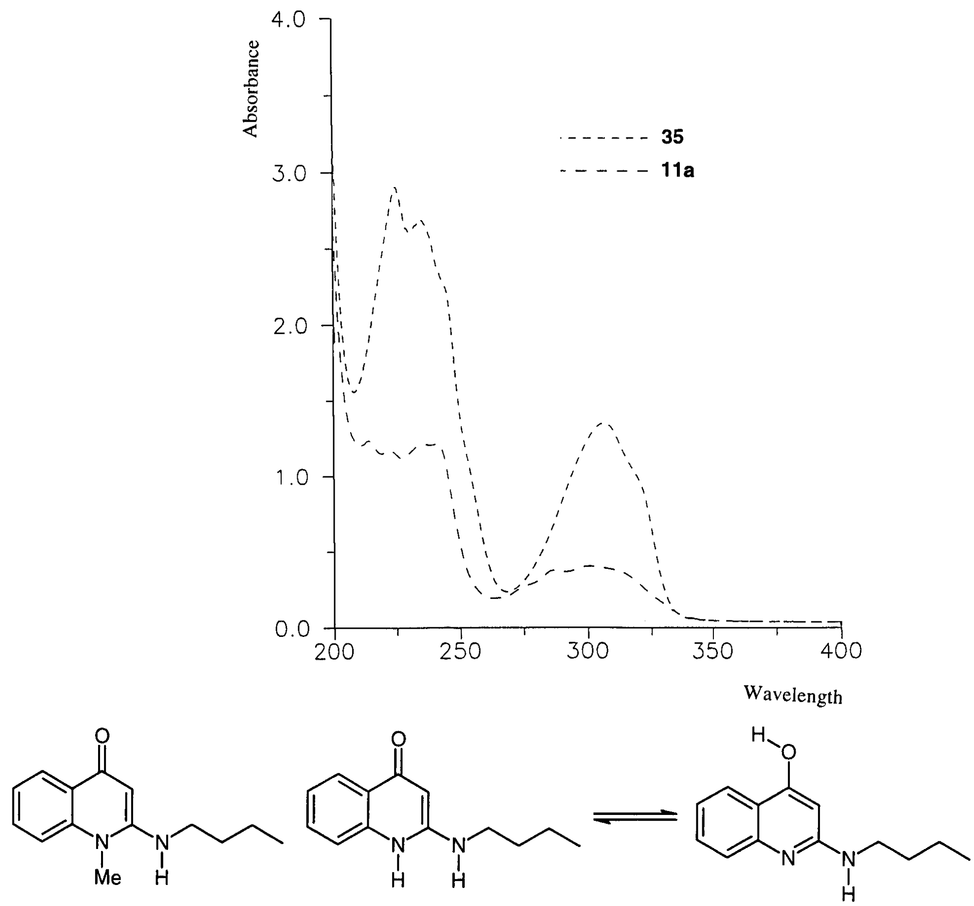


17 X = H 55%
19 X = Cl 54%

Scheme 10



35 50%



35 11a 11a'

Figure 1. Ultra-violet Spectra of Butylamino Quinoles **11a** and **35**.

Table 1

Elemental Analyses of Synthesized Compounds, % Calcd./Found

N°	Formula	C	H	N
6a	$C_{17}H_{22}N_2O_4$	64.13	6.97	8.80
		64.01	7.02	8.78
6c	$C_{18}H_{23}N_3O_4$	62.59	6.71	12.17
		62.51	6.95	12.36
6d	$C_{19}H_{18}N_2O_4$	67.45	5.36	8.28
		67.72	5.35	8.07
6e	$C_{20}H_{20}N_2O_4$	68.17	5.72	7.95
		68.46	5.82	7.85
6f	$C_{23}H_{26}N_2O_6$ [a]	64.78	6.15	6.57
		65.22	6.17	6.55
6g	$C_{23}H_{25}N_3O_8$	58.59	5.34	8.91
		58.72	5.43	8.88
6h	$C_{20}H_{18}ClN_3O_5$	57.77	4.36	10.10
		57.86	4.44	10.13
7a	$C_{17}H_{21}BrN_2O_4$ [a]	51.40	5.33	7.05
		50.72	5.31	7.04
7b	$C_{19}H_{25}BrN_2O_4$	53.66	5.92	6.59
		53.85	5.78	6.55
7c	$C_{18}H_{22}BrN_3O_4$	50.95	5.23	9.90
		51.04	5.30	9.71

Table 1 (continued)

N°	Formula	C	H	N
7d	$C_{19}H_{17}BrN_2O_4$	54.69	4.11	6.71
		54.91	4.23	6.54
7e	$C_{20}H_{19}BrN_2O_4$ [a]	55.70	4.44	6.50
		55.06	4.43	6.80
7f	$C_{23}H_{25}BrN_2O_6$	54.66	4.99	5.54
		54.41	4.99	5.51
8a	$C_{17}H_{21}ClN_2O_4$	57.87	6.00	7.94
		58.05	6.09	8.05
8b	$C_{19}H_{25}ClN_2O_4$	59.92	6.62	7.36
		59.80	6.51	7.25
8c	$C_{18}H_{22}ClN_3O_4$ [a]	56.92	5.84	11.06
		56.34	5.97	11.11
8d	$C_{19}H_{17}ClN_2O_4$ [a]	61.21	4.60	7.51
		61.79	4.65	7.49
8e	$C_{20}H_{19}ClN_2O_4$	62.10	4.95	7.24
		62.00	4.91	7.38
8f	$C_{23}H_{25}ClN_2O_6$	59.94	5.47	6.08
		60.06	5.51	5.88
9a	$C_{17}H_{21}FN_2O_4$	60.70	6.29	8.33
		60.64	6.63	8.39
9b	$C_{19}H_{25}FN_2O_4$	62.62	6.91	7.69
		62.61	6.94	7.93

Table 1 (continued)

N°	Formula	C	H	N
9c	$C_{18}H_{22}FN_3O_4$ [a]	59.50	6.10	11.56
		59.01	6.13	11.33
9d	$C_{19}H_{17}FN_2O_4$	64.04	4.81	7.86
		64.31	4.91	7.89
9e	$C_{20}H_{19}FN_2O_4$	64.86	5.17	7.56
		65.04	5.20	7.56
9f	$C_{23}H_{25}FN_2O_6$	62.15	5.67	6.30
		62.01	5.76	6.40
10a	$C_{17}H_{21}N_3O_6$	56.19	5.83	11.56
		56.30	5.92	11.50
10b	$C_{19}H_{25}N_3O_6$	58.30	6.44	10.74
		58.17	6.50	10.68
10c	$C_{18}H_{22}N_4O_6$	55.38	5.68	14.35
		55.54	5.67	14.44
10d	$C_{19}H_{17}N_3O_6$	59.53	4.47	10.96
		59.79	4.41	10.84
10e	$C_{20}H_{19}N_3O_6$	60.45	4.82	10.57
		60.20	4.80	10.42
10f	$C_{23}H_{25}N_3O_8$	58.59	5.34	8.91
		58.35	5.30	8.73
11c	$C_{14}H_{17}N_3O$	69.11	7.04	17.27
		68.99	7.17	17.26
11d	$C_{15}H_{12}N_2O$ [a]	76.25	5.12	11.86
		75.81	5.91	11.52
11e	$C_{16}H_{14}N_2O$	76.78	5.64	11.19
		76.82	5.79	11.10
11f	$C_{19}H_{20}N_2O_3$ [a]	70.35	6.21	8.64
		69.52	7.20	8.47
11g	$C_{19}H_{19}N_3O_5$, H_2O	58.91	5.46	10.85
		59.12	5.72	11.00
11i	$C_9H_9N_3O$, $1.5H_2O$	53.46	5.98	20.78
		53.60	5.71	20.55

Table 1 (continued)

N°	Formula	C	H	N
11j	$C_{12}H_{13}N_3O$	66.96	6.09	19.52
		66.68	6.43	19.52
11k	$C_{15}H_{11}ClN_2O$	66.55	4.10	10.35
		66.87	3.83	10.55
12a	$C_{13}H_{15}BrN_2O$, H_2O [a]	49.86	5.47	8.94
		50.43	5.33	9.05
12c	$C_{14}H_{16}BrN_3O$	52.19	5.01	13.04
		52.28	5.34	12.84
12f	$C_{19}H_{19}BrN_2O_3$ [a]	56.59	4.75	6.95
		56.08	5.21	6.82
13a	$C_{13}H_{15}ClN_2O$, H_2O [a]	58.10	6.38	10.42
		58.57	6.34	10.52
13c	$C_{14}H_{16}ClN_3O$	60.54	5.81	15.13
		60.79	5.62	14.77
14a	$C_{13}H_{15}N_3O_3$, H_2O	55.91	6.14	15.04
		55.92	6.17	14.64
14c	$C_{14}H_{16}N_4O_3$	58.33	5.59	19.43
		57.96	5.21	19.18
24	$C_{16}H_{10}N_2O_2$, 0.5 H_2O	70.84	4.09	10.33
		71.22	4.07	10.27
27	$C_{10}H_8BrNOS$	44.46	2.98	5.18
		44.06	3.01	5.06
28	$C_{10}H_8BrNO_2S$ [a]	41.97	2.82	4.89
		41.59	3.30	4.76
32	$C_{14}H_{13}ClN_2O$	64.50	5.03	10.74
		64.60	4.94	10.69
35	$C_{14}H_{18}N_2O$	73.01	7.88	12.16
		72.67	7.99	12.55

[a] Due to purification difficulties caused by a lack of solubility, we were not able to obtain a good elemental analysis for this compound; the nmr spectra are however consistent with the structure proposed.

Table 2

Yields and Physical Properties of Meldrum's Derivatives

N°	X	R^1R^2N	Method	Temperature (time, hours)	Yields %	MP °C	IR (KBr) ν cm^{-1}
6a	H	*n*-BuNH	A	60 (4)	93	161 (ether)	3100, 1650, 1590, 1500, 1470
6c	H	1-methyl piperazinyl	C	60 (5)	94	195 (acetone)	3100, 1705, 1650, 1605, 1510, 1495
6d	H	PhNH	D	60 (7)	82	155 (methyl alcohol)	3120, 1635, 1580, 1505, 1450
6e	H	$PhCH_2NH$	D	60 (5)	67	121-123 (methyl alcohol)	3650, 3080, 1670, 1635, 1590, 1500, 1450
6f	H	3,4-$(MeO)_2$Ph-CH_2CH_2NH	D	60 (5)	92	105 (methyl alcohol)	3400, 1655, 1635, 1595, 1590, 1540, 1515, 1450
6g	H	3,4,5-$(MeO)_3$Ph-CONHNH	E	78 (10)	72	208 (methyl alcohol)	3500, 3250, 1695, 1680, 1645, 1620, 1590, 1530, 1495, 1450
6h	H	*p*-ClPh-CONHNH	E	78 (10)	77	(210) (methyl alcohol)	3450, 3250, 1690, 1640, 1595, 1550, 1520, 1485
7a	Br	*n*-BuNH	A	60 (12)	91	88-90 (ethyl alcohol)	3270, 1675, 1635, 1580, 1545, 1490
7b	Br	*t*-BuCHMeNH	B	60 (12)	84	120-121 (ethyl alcohol)	3300, 1650, 1620, 1575, 1530, 1490, 1455
7c	Br	1-methyl piperazinyl	C	60 (8)	98	195-197 (acetone)	1700, 1645, 1630, 1600, 1565, 1485, 1440
7d	Br	PhNH	D	60 (16)	80	143-145 (ethyl alcohol)	1650, 1600, 1575, 1520, 1490, 1450
7e	Br	$PhCH_2NH$	D	60 (8)	100	175-177 (ethyl alcohol)	3280, 1660, 1630, 1590, 1570, 1520, 1485, 1450

Table 2 (continued)

N°	X	R^1R^2N	Method	Temperature (time, hours)	Yields %	MP °C	IR (KBr) ν cm^{-1}
7f	Br	3,4-$(MeO)_2$Ph-CH_2CH_2NH	D	60 (12)	92	114-117 (ethyl alcohol)	3250, 1650, 1630, 1575, 1540, 1520, 1490, 1470
8a	Cl	*n*-BuNH	A	60 (5)	72	99 (ether)	3095, 1675, 1645, 1600, 1590
8b	Cl	*t*-BuCHMeNH	B	60 (12)	53	116 (ether)	3280, 1665, 1650, 1595, 1575, 1535, 1495, 1460
8c	Cl	1-methyl piperazinyl	C	60 (5)	82	193 (ether)	3550, 2950, 1690, 1645, 1610, 1570, 1495
8d	Cl	PhNH	D	60 (7)	65	151 (methyl alcohol)	3500, 3100, 1670, 1620, 1590, 1490, 1450
8e	Cl	PhCH_2NH	D	60 (6)	87	152-156 (methyl alcohol)	1670, 1630, 1590, 1575, 1490, 1450
8f	Cl	3,4-$(MeO)_2$Ph-CH_2CH_2NH	D	60 (6)	75	100-103 (methyl alcohol)	3500, 3150, 1665, 1635, 1595, 1585, 1495
9a	F	*n*-BuNH	A	60 (12)	81	83-85 (ether)	3275, 1660, 1630, 1600, 1540, 1510, 1465
9b	F	*t*-BuCHMeNH	B	60 (8)	72	127-128 (ethyl alcohol)	3300, 1670, 1640, 1600, 1550, 1510, 1470
9c	F	1-methyl piperazinyl	C	60 (48)	87	190-192 (acetone)	3480, 1700, 1630, 1610, 1575, 1510, 1460
9d	F	PhNH	D	60 (48)	68	135-136 (ethyl alcohol)	3280, 1670, 1640, 1600, 1590, 1525, 1505, 1450
9e	F	PhCH_2NH	D	60 (8)	100	148-149 (ethyl alcohol)	3280, 1655, 1635, 1605, 1585, 1535, 1510, 1450
9f	F	3,4-$(MeO)_2$Ph-CH_2CH_2NH	D	60 (8)	96	103-104 (ethyl alcohol)	3300, 1675, 1645, 1605, 1590, 1555, 1510, 1465
10a	NO_2	*n*-BuNH	A	60 (8)	87	116 (ethyl alcohol)	3280, 1675, 1640, 1605, 1595, 1540, 1515, 1470
10b	NO_2	*t*-BuCHMeNH	B	60 (8)	80	146-147 (ethyl alcohol)	3280, 1655, 1645, 1605, 1595, 1540, 1515, 1460
10c	NO_2	1-methyl piperazinyl	C	60 (8)	61	>200 (methyl alcohol)	1700, 1640, 1615, 1595, 1575, 1520, 1490, 1440
10d	NO_2	PhNH	D	60 (8)	88	152 (ethyl alcohol)	1670, 1635, 1605, 1590, 1520, 1450
10e	NO_2	PhCH_2NH	D	60 (8)	100	150 (ethyl alcohol)	3300, 1655, 1635, 1605, 1595, 1520, 1495, 1455, 1445
10f	NO_2	3,4-$(MeO)_2$Ph-CH_2CH_2NH	D	60 (8)	100	131-132 (ethyl alcohol)	3250, 1655, 1635, 1605, 1595, 1515, 1455
16					33	118 (ether) (119-121 [7a,b])	3010, 1730, 1680, 1280
17	H		F		55	148 (methyl alcohol)	3200, 3010, 1710, 1670, 1280, 1210
			G	60 (1)	85	(153 [8])	
18	Br		G	60 (1)	88	128-130(methyl alcohol) (143 [8])	3300, 1720, 1650, 1590, 1550, 1495
19	Cl		F		54	137 (methyl alcohol)	3500, 3100, 1715, 1660
			G	60 (1.5)	85	(143 [8])	
20	F		G	60 (0.5)	93	148-152 (methyl alcohol)	3200, 3160, 1715, 1660, 1600, 1550, 1505, 1435
21	NO_2		G	60 (12)	70	128-129 (methyl alcohol)	1710, 1660, 1610, 1580, 1545, 1510

The structures of the new products were established by elemental analysis and spectral data. Due to purification difficulties caused by a lack of solubility, we were not able to obtain a good elemental analysis for some compounds; the nmr spectra were however consistent with the structures proposed. Preliminary biological results indicate that some of the synthesized compounds act on pancreatic as well as on the vascular smooth muscle tissue and appear to adopt, at least in part, the pharmacological profile of potassium channel openers (data not shown). However, the exact mechanism of action remains to be elucidated.

EXPERIMENTAL

Melting points were measured on an 'Electrothermal' apparatus and are uncorrected. The ir spectra were recorded on a 'Perkin-

Table 3

Yields and Physical Properties of 1,4-Dihydro-4-quinolones

N°	X	R^1R^2N	Method	Yields %	MP °C	IR (KBr) ν cm^{-1}
11a	H	*n*-BuNH	H	80	221 (189 [29])	3270, 3100, 1670, 1660, 1615, 1515, 1460
11c	H	1-methylpiperazinyl	I	55	273	3450, 1635, 1595, 1540, 1500
11d	H	PhNH	H	51	> 310	3080, 1655, 1600, 1500, 1450
11e	H	$PhCH_2NH$	I	62	248	3250, 3200, 1650, 1600, 1500, 1460
11f	H	3,4-$(MeO)_2PhCH_2CH_2NH$	H	80	236	3275, 3100, 1670, 1640, 1610, 1510, 1455
11g	H	3,4,5-$(MeO)_3PhCONHNH$		76	274	3150, 1675, 1640, 1620, 1590, 1520, 1495, 1470
11i	H	H_2NNH	I	65	224	3240, 1660, 1625, 1610, 1500, 1460
11j	H	$Me_2C{=}NNH$		100	254	3100, 1625, 1595, 1580, 1565, 1495, 1475, 1460
11k	H	4-ClPh	H	25	> 320	3250, 3200, 1640, 1605, 1500, 1460
12a	Br	*n*-BuNH	H	60	280-284	3250, 1660, 1620, 1530, 1470
12c	Br	1-methylpiperazinyl	H	40	308-310	3225, 1620, 1580, 1540, 1480
12f	Br	3,4-$(MeO)_2PhCH_2CH_2NH$	H	50	230-235	3320, 1665, 1620, 1610, 1540, 1480
13a	Cl	*n*-BuNH	H	63	250-255	3300, 3180, 1660, 1590, 1520, 1460
13c	Cl	1-methylpiperazinyl	H	20	280-285	3250, 3200, 1640, 1590, 1550, 1470
14a	NO_2	*n*-BuNH	H	20	> 310	3275, 1650, 1620, 1540, 1460
14b	NO_2	*t*-BuCHMeNH	H	9	> 310	3300, 1660, 1620, 1550, 1460
14c	NO_2	1-methylpiperazinyl	H	16	> 310	3275, 1640, 1620, 1560, 1480
22	H		J	78	225 (222 [8], 225 [10])	3280, 1640, 1580, 1500, 1460
23	Cl		J	80	259-260 (257 [8])	3280, 1640, 1575, 1530, 1490, 1465
24	H		H	51	>300	3060, 1640, 1620, 1580
27	H			86	249	3250, 1620, 1600, 1575, 1540, 1490
28	H			95	247	3230, 1640, 1620, 1575, 1540, 1490
35	H	*n*-BuNH (N_1-Me)		step 1:20 step 2:60 step 3:50	155	3280, 1650, 1620, 1580, 1560

Table 4

NMR Spectra of Meldrum's Derivatives

N°	^{1}H NMR δ ppm (deuteriochloroform)	^{13}C NMR δ ppm (deuteriochloroform)
6a	0.81 (t, J = 6.5 Hz, 3H), 1.11-1.36 (m, 2H), 1.36-1.57 (m, 2H), 1.73 (s, 6H, $H_{7,8}$), 2.77 (q, J = 6.5 Hz, 2H), 7.18 (d, J = 8.3 Hz, 2H, H_{11}), 7.23-7.31 (m, 1H, H_{13}), 7.33-7.46 (m, 2H, H_{12}), 10.09 (bs, 1H, NH), 11.44 (bs, 1H, NH)	13.5, 19.7, 26.3 ($C_{6,7}$), 31.4, 45.5, 74.7 (C_5), 102.6 (C_2), 124.8 (C_{11}), 126.6 (C_{13}), 129.5 (C_{12}), 138.2 (C_{10}), 161.8 (C_9), 167.0 ($C_{4,6}$)
6c	1.72 (s, 6H, $H_{7,8}$), 2.27 (s, 3H), 2.42 (t, J = 4.9 Hz, 4H), 3.32 (t, J = 4.9 Hz), 7.10 (d, J = 7.3 Hz, 2H, H_{11}), 7.20-7.30 (m, 1H, H_{13}), 7.33-7.44 (m, 2H, H_{12}), 9.52 (bs, 1H, NH)	26.5 ($C_{7,8}$), 45.9, 50.4, 53.2, 76.2 (C_5), 102.4 (C_2), 124.2 (C_{11}), 126.8 (C_{13}), 129.8 (C_{12}), 139.2 (C_{10}), 163.8 (C_9), 165.0 ($C_{4,6}$)
6d	1.78 (s, 6H, $H_{7,8}$), 6.80-7.06 (ArH), 11.87 (bs, 2H, NH)	26.4 ($C_{7,8}$), 75.2 (C_5), 103.1 (C_2), 124.0 (C_{11}), 125.9 (C_{13}), 128.7 (C_{12}), 136.4 (C_{10}), 159.0 (C_9), 167.1 ($C_{4,6}$)
6e	1.71, 1.73 (2s, 6H, $H_{7,8}$), 4.01 (d, J = 5.5 Hz, 1H, NCH_2), 4.56 (d, J = 6.2 Hz, 1H, N-CH_2), 6.98-7.08 (m, 1H), 7.11-7.45 (m, 9H, H_{11}, H_{12}, ArH), 10.52 (bs, 1H, N*H*-CH_2), 11.56 (bs, 1H, N*H*-Ar)	26.2 and 26.3 ($C_{7,8}$), 48.4 and 49.3 (N-CH_2), 74.5 and 75.0 (C_5), 102.4 and 102.8 (C_2), 125.1 (C_{11}), 126.5 and 127.2 (ArH), 126.9 (C_{13}), 128.1 and 128.2 (ArH), 128.9 and 129.2 (ArH), 129.5 (C_{12}), 136.3 (C_{10}), 137.2 and 137.8 (Ar), 161.9 and 164.3 (C_9), 166.9 ($C_{4,6}$)
6f	1.61 (s, 1H, N*H*-Ar), 1.71 (s, 6H, $H_{7,8}$), 2.69 (t, J = 6.6 Hz, 2H, 3.05 (q, J = 6.1 Hz, 2H), 3.84 (s, 6H), 6.55 (bs, 1H), 6.60 (d, J = 8 Hz, 1H), 6.77 (d, J = 8 Hz, 1H), 7.17 (d, J = 7.9 Hz, 2H, H_{11}), 7.21-7.32 (m, 1H, H_{13}), 7.34-7.46 (m, 2H, H_{12}), 10.18 (bs, 1H, N*H*-CH_2)	26.3 ($C_{6,7}$), 35.5, 47.4, 56.0, 74.8 (C_5), 102.7 (C_2), 111.4, 112.0, 120.9, 124.8 (C_{11}), 126.7 (C_{13}), 129.6 (C_{12}), 130.1, 138.3 (C_{10}), 148.1, 149.1, 162.0 (C_9), 166.9 ($C_{4,6}$)
6g	1.74 (s, 6H, $H_{7,8}$), 3.74 (s, 6H), 3.84 (s, 3H), 6.35 (s, 2H), 7.18-7.42 (m, 5H, H_{11}, H_{12}, H_{13}), 3.27/7.73/11.37/11.77 (bs, 3H, NH)	26.3 ($C_{7,8}$), 56.3, 60.9, 74.2 (C_5), 103.5 (C_2), 104.2, 124.7 (C_{11}), 125.9 (C_{13}), 127.3, 129.7 (C_{12}), 137.6 (C_{10}), 141.6, 153.1, 163 (C_9), 165.2, 166.7 ($C_{4,6}$)
6h	1.73 (s, 6H, $H_{7,8}$), 7.03 (d, J = 8.3 Hz, 2H), 7.17-7.31 (m, 5H, H_{11}, H_{12}, H_{13}), 7.35 (d, J = 8.3 Hz, 2H), 3.26/7.71/11.42/11.79 (bs, 3H, NH)	26.3 ($C_{7,8}$), 74.1 (C_5), 103.5 (C_2), 124.8 (C_{11}), 127.5 (C_{13}), 128.5 (C_{12}), 128.9, 129.0, 129.9, 137.4 (C_{10}), 139.1, 163.0 (C_9), 164.4, 166.7 ($C_{4,6}$)
7a	0.84 (t, J = 7.3 Hz, 3H), 1.17-1.39 (m, 2H), 1.39-1.60 (m, 2H), 1.72 (s, 6H, $H_{7,8}$), 2.73-2.85 (m, 2H), 7.06 (dt, J = 8.7, 2.5 Hz, 2H, H_{11}), 7.51 (dt, J = 8.7, 2.5 Hz, 2H, H_{12}), 10.11 (bs, 1H, NH), 11.40 (bs, 1H, NH)	13.5, 19.7, 26.2 ($C_{6,7}$), 31.4, 45.8, 74.8 (C_5), 102.7 (C_2), 119.7 (C13), 126.1 (C_{11}), 132.6 (C_{12}), 137.4 (C_{10}), 162.0 (C_9), 166.9 ($C_{4,6}$)
7b	0.83 (s, 9H), 0.92 (d, J = 6.6 Hz, 3H), 1.73 (s, 6H, $H_{7,8}$), 2.92-3.11 (m, 1H), 7.10 (dt, J = 8.7, 2.5 Hz, 2H, H_{11}), 7.54 (dt, J = 8.7, 2.5 Hz, 2H, H_{12}), 10.13 (d, J = 9.7 Hz, 1H N*H*-CH, 2.75/11.41 (2 bs, 1H, N*H*-Ar)	14.6, 25.9, 26.2 ($C_{7,8}$), 35.8, 58.6, 74.8 (C_5), 102.7 (C_2), 120.3 (C_{13}), 126.3 (C_{11}), 132.8 (C_{12}), 137.9 (C_{10}), 162.2 (C_9), 167 ($C_{4,6}$)

Table 4 (continued)

N°	^{1}H NMR δ ppm (deuteriochloroform)	^{13}C NMR δ ppm (deuteriochloroform)
7c	1.63 (s, 6H, $H_{7,8}$), 2.39 (bs, 3H), 2.56 (bs, 4H), 3.45 (bs, 4H), 6.96 (d, J = 8.4 Hz, 2H, H_{11}), 7.42 (d, J = 8.4 Hz, 2H, H_{12}), 9.71 (bs, 1H, NH)	26.6 ($C_{7,8}$), 45.4 (bs), 49.8 (bs), 53.3 (bs), 74.9 (C_5), 102.6 (C_2), 119.6 (C_{13}), 125.2 (C_{11}), 132.6 (C_{12}), 138.3 (C_{10}), 163.0 (C_9), 164.5 ($C_{4,6}$)
7d	1.78 (s, 6H, $H_{7,8}$), 2.70 (bs, 1H, NH), 6.78 (dt, J = 8.7, 2.5 Hz, 2H, H_{11}), 6.82-6.91 (m, 2H), 6.92-7.08 (m, 3H), 7.12 (dt, J = 8.7, 2.5 Hz, 2H, H_{12})	26.4 ($C_{7,8}$), 75.3 (C_5), 103.2 (C_2), 119.1 (C_{13}), 124.0, 125.4 (C_{11}), 126.9, 128.9, 131.7 (C_{12}), 135.5, 136.1 (C_{10}), 159.1 (C_9), 166.9 ($C_{4,6}$)
7e	1.73 (s, 6H, $H_{7,8}$), 2.86 (bs, 1H, NH), 4.04 (d, J = 5.7 Hz, 2H), 6.98-7.10 (m, 4H, H_{11}, ArH), 7.23-7.35 (m, 3H, ArH), 7.49 (d, J = 8.6 Hz, 2H, H_{12}), 10.56 (bs, 1H, NH)	26.3 ($C_{7,8}$), 49.5, 75.1 (C_5), 102.9 (C_2), 120.1 (C_{13}), 126.4 (C_{11}), 127.1, 128.2, 129.0, 132.6 (C_{12}), 135.9, 136.9 (C_{10}), 162.1 (C_9), 166.9 (C_4)
7f	1.70 (s, 6H, $H_{7,8}$), 2.72 (t, J = 6.8 Hz, 2H), 3.06 (q, J = 6.3 Hz, 2H), 3.85 (s, 6H), 6.58 (d, J = 2 Hz, 1H), 6.63 (dd, J = 8,2 Hz, 1H), 6.79 (d, J = 8 Hz, 1H), 7.03 (dt, J = 8.7, 2.5 Hz, 2H, H_{11}), 7.52 (dt, J = 8.7, 2.5 Hz, 2H, H_{12}), 2.70/10.18/11.38 (3 bs, 2H, NH)	26.2 ($C_{7,8}$), 35.4, 47.7, 55.9, 74.9 (C_5), 102.7 (C_2), 111.4, 111.9, 119.7, 120.8 (C_{13}), 126.0 (C_{11}), 129.9, 132.6 (C_{12}), 137.3 (C_{10}), 148.1, 149.1, 162.0 (C_9), 166.7 ($C_{4,6}$)
8a	0.83 (t, J = 7.1 Hz, 3H), 1.17-1.39 (m, 2H), 1.39-1.58 (m, 2H), 1.72 (s, 6H, $H_{7,8}$), 2.72-2.85 (m, 2H), 7.12 (dt, J = 8.7, 2.5 Hz, H_{11}), 7.37 (dt, J = 8.7, 2.5 Hz, 2H, H_{12}), 10.40 (bs, 1H, NH), 11.43 (bs, 1H, NH)	13.5, 19.7, 26.2 ($C_{6,7}$), 31.4, 45.7, 74.7 (C_5), 102.8 (C_2), 125.8 (C_{11}), 129.6 (C_{12}), 132.0 (C_{13}), 136.8 (C_{10}), 162.0 (C_9), 166.9 ($C_{4,6}$)
8b	0.83 (s, 9H), 0.91 (d, J = 6.6 Hz, 3H), 1.73 (s, 6H, $H_{7,8}$), 2.92-3.10 (m, 1H), 7.15 (dt, J = 8.6, 2.4 Hz, 2H, H_{11}), 7.38 (dt, J = 8.6, 2.4 Hz, 2H, H_{12}), 10.14 (d, J = 10.1 Hz, 1H, N*H*-CH), 3.15/11.42 (2 bs, 1H, N*H*-Ar)	14.6, 25.9, 26.2 ($C_{7,8}$), 35.8, 58.6, 74.8 (C_5), 102.7 (C_2), 126.1 (C_{11}), 129.9 (C_{12}), 132.6 (C_{13}), 137.4 (C_{10}), 162.3 (C_9), 167.0 ($C_{4,6}$)
8c	1.72 (s, 6H, $H_{7,8}$), 2.71 (s, 3H), 3.15 (bs, 4H), 3.49 (bs, 4H), 6.98 (d, J = 8.5 Hz, 2H, H_{11}), 7.36 (d, J = 8.5 Hz, 2H, H_{12}), 10.19 (bs, 1H, NH)	26.5 ($C_{7,9}$), 43.6, 47.4, 52, 75.7 (C_5), 103(C_2), 124.3 (C_{11}), 130.3 (C_{12}), 132.8 (C_{13}), 136.5 (C_{10}), 163.4 (C_9), 166.7 ($C_{4,6}$)
8d	1.78 (s, 6H, $H_{7,8}$), 3.05 (bs, 1H, NH), 6.74-6.91 (m, 2H), 6.80 (dt, J = 8.7, 2.4 Hz, 2H, H_{11}), 6.91-7.11 (m, 3H), 6,97 (dt, J = 8.7, 2.4 Hz, 2H, H_{12}), 11.84 (bs, 1H, NH)	26.4 ($C_{7,8}$), 75.3 (C_5), 103.2 (C_2), 124.0, 125.1 (C_{11}), 126.3, 128.7, 128.9 (C_{12}), 131.4 (C_{13}), 135.0, 136.1 (C_{10}), 159.1 (C_9), 167.0 ($C_{4,6}$)
8e	1.73 (s, 6H, $H_{7,8}$), 2.98 (bs, 1H, NHAr), 4.03 (d, J = 5.7 Hz, 2H), 6.99-7.07 (m, 2H), 7.09 (dt, J = 8.9, 2.6 Hz, 2H, H_{11}), 7.22-7.31 (m, 3H), 7.33 (dt, J = 8.9, 2.6 Hz, 2H, H_{12}), 10.57 (bt, J = 5.7 Hz, 1H, N*H*-CH_2)	26.3 ($C_{7,8}$), 49.4, 75.1 (C_5), 102.9 (C_2), 126.1 (C_{11}), 127.1, 128.2, 129.0, 129.6 (C_{12}), 132.4 (C_{13}), 135.9 (C_{17}), 136.4 (C_{10}), 162.1 (C_9), 166.9 ($C_{4,6}$)
8f	1.70 (s, 6H, $H_{7,8}$), 2.72 (t, J = 6.7 Hz, 2H), 3.05 (q, J = 6.2 Hz, 2H), 3.85 (s, 6H), 6.58 (d, J = 1.9 Hz, 1H), 6.63 (dd, J = 8.1, 1.9 Hz, 1H), 6.79 (d, J = 8.1, 1H), 7.09 (dt, J = 8.8, 2.5 Hz, 2H, H_{11}), 7.37 (dt, J = 8.8, 2.5 Hz, 2H, H_{12}), 10.20 (bs, 1H, N*H*-CH_2), 11.42 (bs, 1H, N*H*-Ar)	26.2 ($C_{7,8}$), 35.4, 47.7, 55.9, 74.9 (C_5), 102.8 (C_2), 111.4, 111.9, 120.8, 125.8 (C_{11}), 129.7 (C_{12}), 129.9, 132.1 (C_{13}), 136.8 (C_{10}), 148.1, 149.1, 162.1 (C_9), 166.8 ($C_{4,6}$)
9a	0.83 (t, J = 7.2 Hz, 3H), 1.14-1.37 (m, 2H), 1.37-1.58 (m, 2H), 1.73 (s, 6H, $H_{7,8}$), 2.69-2.82 (m, 2H), 7.03-7.23 (m, 4H, $H_{11,12}$), 10.12 (bs, 1H, NH), 11.43 (bs, 1H, NH)	13.5, 19.7, 26.2 ($C_{7,8}$), 31.4, 45.5, 74.6 (C_5), 102.7 (C_2), 116.4 (d, J = 23 Hz, C_{12}), 126.7 (d, J = 8 Hz, C_{11}), 134.2 (d, J = 3 Hz, C_{10}), 161.0 (d, J = 246 Hz, C_{13}), 162.0 (C_9), 167.0 ($C_{4,6}$)
9b	0.82 (s, 9H), 0.89 (d, J = 6.6 Hz, 3H), 1.72 (s, 6H, $H_{7,8}$) , 2.88-3.05 (m, 1H), 7.05-7.26 (m, 4H, H_{11}, H_{12}), 10.14 (d, J = 10.1 Hz, 1H, N*H*-CH), 2.90/11.42 (2 bs, 1H, N*H*-Ar)	14.7, 25.9, 26.2 ($C_{7,8}$), 35.6, 58.3, 74.6 (C_5), 102.6 (C_2), 116.6 (d, J = 24 Hz, C_{12}), 126.9 (d, J = 9 Hz, C_{11}), 134.7 (d, J = 3 Hz, C_{10}), 161.3 (d, J = 248 Hz, C_{13}), 162.3 (C_9), 167.0 ($C_{4,6}$)
9c	1.58 (s, 6H, $H_{7,8}$), 2.39 (bs, 3H), 2.57 (bs, 4H), 3.48 (bs, 4H), 6.93-7.13 (m, 4H, H_{11}, H_{12}), 9.72 (bs, 1H, NH)	26.5 ($C_{7,8}$), 45.4 (bs), 49.3 (bs), 53.3 (bs), 74.5 (C_5), 102.5 (C_2), 116.3 (d, J = 24 Hz, C_{12}), 125.8 (d, J = 10 Hz, C_{11}), 135.1 (C_{10}), 160.9 (d, J = 248 Hz, C_{13}), 163.5 (C_9), 164.4 ($C_{4,6}$)
9d	1.79 (s, 6H, $H_{7,8}$), 2.76 (bs, 1H, NH), 6.70 (dt, J = 8.6, 2.7 Hz, 2H, H_{12}), 6.78-6.91 (m, 4H, H_{11}, ArH), 6.91-7.10 (m, 3H)	26.4 ($C_{7,8}$), 75.2 (C_5), 103.1 (C_2), 115.5 (d, J = 24 Hz, C_{12}), 124.3, 125.9 (d, J = 9 Hz, C_{11}), 126.3, 128.8, 132.5 (d, J = 3 Hz, C_{10}), 136.2, 159.4 (C_9), 160.4 (d, J = 247 Hz, C_{13}), 167.0 ($C_{4,6}$)
9e	1.73 (s, 6H, $H_{7,8}$), 4.01 (d, J = 5.6 Hz, 2H), 6.97-7.18 (m, 6H, H_{11}, H_{12}, ArH), 7.22-7.34 (m, 3H, ArH), 10.56 (bt, J = 5.6 Hz, 1H, N*H*- CH_2), 11.53 (bs, N*H*-Ar)	26.2 ($C_{7,8}$), 49.2, 74.9 (C_5), 102.8 (C_2), 116.4 (d, J = 23 Hz, C_{12}), 127.0 (d, J = 8 Hz, C_{11}), 127.1, 128.1, 129.0, 133.7 (d, J = 3 Hz, C_{10}), 136.1, 161.2 (d, J = 248 Hz, C_{13}), 162.2 (C_9), 166.9 ($C_{4,6}$)
9f	1.70 (s, 6H, $H_{7,8}$), 2.70 (t, J = 6.7 Hz, 2H), 3.02 (q, J = 6.3 Hz, 2H), 3.85 (s, 6H), 6.56 (d, J = 2 Hz, 1H), 6.61 (dd, J = 8.1, 2 Hz, 1H), 6.78 (d, J = 8.1 Hz, 1H), 7.04-7.22 (m, 4H, H_{11}, H_{12}), 2.68/10.16/11.40 (bs, 2H, NH)	26.2 ($C_{7,8}$), 35.5, 47.4, 55.9, 74.7 (C_5), 102.7 (C_2), 111.4, 112.0, 116.5, (d, J = 23 Hz, C_{12}), 120.8, 126.7 (d, J = 9 Hz, C11), 130.0, 134.2 (d, J = 3 Hz, C_{10}), 148.1, 149.1, 161.0 (d, J = 247 Hz, C_{13}), 162.2 (C_9), 166.9 ($C_{4,6}$)
10a	0.86 (t, J = 7.2 Hz, 3H), 1.21-1.43 (m, 2H), 1.47-1.66 (m, 2H), 1.74 (s, 6H, $H_{7,8}$), 2.82-2.94 (m, 2H), 7.26 (d, J = 8.9 Hz, 2H, H_{11}), 8.29 (dt, J = 8.9, 2.5 Hz, H_{12}), 10.34 (bs, 1H, NH), 11.66 (bs, 1H, NH)	13.5, 19.7, 26.3 ($C_{7,8}$), 31.5, 46.6, 75.7 (C_5), 103.2 (C_2), 123.0 (C_{11}), 125.3 (C_{12}) , 144.3 (C_{10}), 144.9 (C_{13}), 162.2 (C_9), 166.8 ($C_{4,6}$)
10b	0.87 (s, 9H), 1.02 (d, J = 6.6 Hz, 3H), 1.74 (s, 6H, $H_{7,8}$), 2.93-3.13 (m, 1H), 7.33 (dt, J = 9, 2.5 Hz, 2H, H_{11}), 8.30 (dt, J = 9.0, 2.5 Hz, 2H, H_{12}), 10.30 (d, J = 10.2 Hz, 1H, N*H*-CH), 2.88/11.63 (2 bs, 1H, NH Ar)	14.3, 26.0, 26.3 ($C_{7,8}$), 36.3, 59.8, 75.7 (C_5), 103.1 (C_2), 123.3 (C_{11}), 125.1 (C_{12}), 145.0 (C_{10}), 145.3 (C_{13}), 162.6 (C_9), 166.9 ($C_{4,6}$)
10c	1.70 (s, 6H, $H_{7,8}$), 2.62 (s, 3H), 3.02 (bs, 4H), 3.59 (bs, 4H), 7.18 (d, J = 8.7 Hz, 2H, H_{11}), 8.23 (d, J = 8.7 Hz, 2H, H_{12})	26.8 ($C_{7,8}$), 43.8, 47.2, 52.4, 75.5 (C_5), 103.2 (C_2), 122.4 (C_{11}), 125.4 (C_{12}), 144.5 (C_{10}), 145.3 (C_{13}), 163.3 (C_9), 164.2 ($C_{4,6}$)
10d	1.79 (s, 6H, $H_{7,8}$), 6.89-7.14 (m, 7H, H_{11}, ArH), 7.90 (dt, J = 9.1, 2.5 Hz, 2H, H_{12}), 2.75/12.05/12.14 (3 bs, 2H, NH)	26.5 ($C_{7,8}$), 76.1 (C_5), 103.6 (C_2), 123.3, 123.6 (C_{11}), 124.3 (C_{12}), 126.8, 129.4, 136.2, 142.3 (C_{10}), 144.6 (C_{13}), 159.2 (C_2), 167 ($C_{4,6}$)
10e	1.74 (s, 6H, $H_{7,8}$), 4.11 (d, J = 5.6 Hz, 2H), 7.02-7.11 (m, 2H), 7.27 (dt, J = 9.1, 2.5 Hz, 2H, H_{11}), 7.26-7.34 (m, 3H), 8.27 (dt, J = 9.1, 2.5 Hz, 2H, H_{12}), 2.69/10.74/11.74 (3 bs, 2H, NH)	26.3 ($C_{7,8}$), 50.2, 75.9 (C_5), 103.3 (C_2), 123.4 (C_{11}), 125.3 (C_{12}), 127.2, 128.5, 129.1, 135.4, 144.0 (C_{10}), 145.1 (C_{13}), 162.3 (C_9), 166.7 ($C_{4,6}$)

Table 4 (continued)

N°	^{1}H NMR δ ppm (deuteriochloroform)	^{13}C NMR δ ppm (deuteriochloroform)
10f	1.71 (s, 6H, $H_{7,8}$), 2.79 (t, J = 6.5 Hz, 2H), 3.12 (q, J = 5.8 Hz, 2H), 3.86 (s, 6H), 6.63-6.71 (m, 2H), 6.81 (s, 6H), 6.63-6.71 (m, 2H), 6.81 (d, J = 8.8 Hz, 1H), 7.22 (d, J = 9 Hz, 2H, H_{11}), 8.28 (d, J = 9 Hz, 2H, H_{12}), 2.81/10.37/11.60 (bs, 2H, NH)	26.3 ($C_{7,8}$), 35.6 (C_{17}), 48.7, 55.9, 75.7 (C_5), 103.3 (C_2), 111.6, 112.1, 120.9, 122.9 (C_{11}), 125.4 (C_{12}), 129.5, 144.2 (C_{10}), 144.9 (C_{13}), 148.3, 149.2, 162.3 (C_9), 166.8 ($C_{4,6}$)
16	1.75 (s, 6H, $H_{7,8}$), 2.66 (s, 6H)	21.5, 26.9 ($C_{7,8}$), 103.2 (C_5), 103.4 (C_2), 160.2 ($C_{4,6}$), 192.9 (C_9)
17	1.77 (s, 6H, $H_{7,8}$), 1.80 (s, 1H, NH), 2.28 (s, 3H), 7.28-7.52 (m, 5H, H_{11}, H_{12}, H_{13})	19.0, 26.5 ($C_{7,8}$), 86.5 (C_5), 103.3 (C_2), 125.5 (C11), 128.2 (C_{13}), 129.7 (C_{12}), 137.5 (C_{10}), 164.2 (C_9), 178.3 ($C_{4,6}$)
18	1.77 (s, 6H, $H_{7,8}$), 1.78/3.25 (bs, 1H, NH), 2.33 (s, 3H), 7.21 (d, J = 8.4 Hz, 2H, H_{11}), 7.59 (d, J = 8.4 Hz, H_{12})	19.1, 26.4 ($C_{7,8}$), 86.8 (C_5), 103.4 (C_2), 121.9 (C_{13}), 127.1 (C_{11}), 133.8 (C_{12}), 136.4 (C_{10}), 164.1 (C_9), 175.1 ($C_{4,6}$)
19	1.61 (s, 1H, NH), 1.77 (s, 6H, $H_{7,8}$), 2.32 (s, 3H), 7.27 (dt, J = 8.7, 2.4 Hz, H_{11}), 7.43 (dt, J = 8.7, 2.4 Hz, 2H, H_{12})	
20	1.77 (s, 6H, $H_{7,8}$), 1.78/3.25 (bs, 1H, NH), 2.33 (s, 3H), 7.17-7.27 (m, 2H, H_{11}), 7.49-7.63 (m, 2H, H_{12})	18.9, 25.4 ($C_{7,8}$), 86.3 (C_5), 103.3 (C_2), 116.6 (d, J = 23 Hz, C_{12}), 127.5 (d, J = 9 Hz, C_{11}), 133.3 (d, J = 3 Hz, C_{10}) , 161.9 (d, J = 248 Hz, C_{13}), 164.1 (C_9), 175.7 ($C_{4,6}$)
21	1.78/3.48 (bs, 1H, NH), 1.79 (s, 6H, $H_{7,8}$), 2.34 (s, 3H), 7.54 (d, J = 8.9 Hz, 2H, H_{11}), 8.34 (d, J = 8.9 Hz, 2H, H_{12})	
36	1.73 (bs, 6H), 2.55 (s, 3H), 3.65 (s, 3H), 7.36 (dd, J = 7.9 Hz, 2H), 7.41-7.52 (m, 3H)	

Table 5

NMR Spectra of 1,4-Dihydro-4-quinolones

N°	Solvant	^{1}H NMR δ ppm	^{13}C NMR δ ppm
11a	deuteriochloroform and 5% trifluoroacetic acid	0.95 (t, J = 7.3 Hz, 3H), 1.32-1.55 (m, 2H), 1.55-1.78 (m, 2H), 3.30 (t, J = 7.2 Hz, 2H), 6.28 (s, 1H, H_3), 7.42 (d, J = 8.1 Hz, 1H, H_8), 7.44 (t, J = 7.8 Hz, 1H, H_6), 7.71 (t, J = 7.8 Hz, 1H, H_7), 8.05 (d, J = 8.1 Hz, 1H, H_5), 9.89 (bs, 1H, NH)	13.3, 19.9, 30.4, 42.5, 91.1 (C_3), 116.3 (C_{4a}), 117 (C_8), 124.2 (C_5), 125.8 (C_6), 134.2 (C_7), 137.1 (C_{8a}), 154.5 (C_2), 165.9 (C_4)
11c	methanol-d_4	2.36 (s, 3H), 2.61 (bt, J = 5.1 Hz, 4H), 2.71 (bs, 1H, NH), 3.53 (bt, J = 5.1 Hz, 4H), 5.82 (s, 1H, H_3), 7.28 (dt, J = 6.9, 2 Hz, 1H, H_6), 7.49-7.64 (m, 2H, H_7, H_8), 8.09 (d, J = 8.2 Hz, 1H, H_5)	46.1, 47.7, 55.4, 93.4 (C_3), 118.4 (C_8), 123.8 (C_{4a}), 124.3 (C_6), 125.7 (C_5), 133 (C_7), 140.7 (C_{8a}), 157 (C_2), 179.7 (C_4)
11d	deuteriochloroform and 5% trifluoroacetic acid	6.60 (s, 1H, H_3), 7.31-7.45 (m, 3H, C_8, ArH), 7.45-7.64 (m, 4H, H_6, ArH), 7.76 (t, J = 7.9 Hz, 1H, H_7), 8.17 (d, J = 8.2 Hz, 1H, H_5), 8.80 (bs, 1H, NH), 8.97 (bs, 1H, NH), 8.97 (bs, 1H, NH)	92.4 (C_3), 117 (C_{4a}), 117.3 (C_8), 124.5 (C_5), 125.8 (Ar), 126.4 (C_6), 129.6 (Ar), 131.3 (Ar), 133.6 (Ar), 134.4 (C_7), 136.6 (C_{8a}), 153.7 (C_2), 167 (C_4)
11e	deuteriochloroform and 5% trifluoroacetic acid	4.55 (s, 2H), 6.33 (s, 1H, H_3), 7.25-7.48 (m, 6H, H_8, ArH), 7.43 (t, J = 7.9 Hz, 1H, H_6), 7.70 (dt, J = 7.9, 1.2 Hz, 1H, H_7), 8.06 (d, J = 8.2 Hz, 1H, H_5), 10.22 (bs, 1H, NH)	46.6, 91.2 (C_3), 116.3 (C_{4a}), 117.1 (C_8), 124.2 (C_5), 125.9 (C_6), 127.3 (Ar), 129.2 (Ar), 129.8 (Ar), 134.3 (C_7), 134.4 (Ar), 137.1 (C_{8a}), 154.7 (C_2), 166.4 (C_4)
11f	deuteriochloroform and 5% trifluoroacetic acid	2.94 (t, J = 6.3 Hz, 2H), 3.63 (t, J = 6.3 Hz, 2H), 3.82 (s, 3H), 3.87 (s, 3H), 6.17 (bs, 1H, H_3), 6.84 (s, 3H, ArH), 7.25 (d, J = 8.2 Hz, 1H, H_8), 7.43 (t, J = 7.8 Hz, 1H, H_6), 7.69 (t, J = 7.8 Hz, 1H, H_7), 8.06 (d, J = 8.2 Hz, 1H, H_5)	34.9, 44.6, 56.3, 56.9, 90.3 (C_3), 113 (Ar), 113.8 (Ar), 116.2 (C_{4a}), 116.9 (C_8), 122.7 (Ar), 124.2 (C_5), 125.9 (C_6), 131.4 (Ar), 134.3 (C_7), 137 (C_{8a}), 148 (Ar), 148.6 (Ar), 154.7 (C_2), 166.2 (C_4)
11g	deuteriochloroform and 5% trifluoroacetic acid	3.92 (s, 6H), 3.99 (s, 3H), 6.73 (s, 1H, H_3), 7.26 (s, 2H, Ar), 7.46 (t, J = 7.6 Hz, 1H, H_6), 7.54 (d, J = 8.7 Hz, 1H, H_8), 7.74 (t, J = 7.6 Hz, 1H, H_7), 7.97 (d, J = 8 Hz, 1H, H_5), 9.19 (bs, 1H, NH)	56.4, 61.6, 90.1 (C_3), 105.9 (Ar), 117 (C_8), 117.9 (C_{4a}),124.1 (C_5), 124.9 (Ar), 126.8 (C_6), 134.8 (C_7), 136.7 (C_{8a}), 142 (Ar), 153.3 (Ar), 155.3 (C_2), 167.6 (C_4), 170.6 (N-CO)
11i	dimethyl sulfoxide-d_6	5.69 (s, 1H, H_3), 7.23 (t, J = 7.6 Hz, 1H, H_7), 7.53 (td, J = 7.6, 1.5 Hz, 1H, H_6), 7.79 (d, J = 7.1 Hz, 1H, H_8), 7.98 (dd, J = 8.1, 1.5 Hz, 1H, H_5), 8.86 (bs, 1H, NH)	87.7 (C_3), 117.6 (C_8), 120.7 (C_{4a}), 122.8 (C_6), 123.8 (C_5), 131.2 (C_7), 138 (C_{8a}), 156.4 (C_2), 169.9 (C_4)
11j	deuteriochloroform	2 (s, 3H), 2.09 (s, 3H), 6.06 (s, 1H, H_3), 7.27 (t, J = 7.4 Hz, 1H, H_6), 7.57 (t, J = 7.4 Hz, 1H, H_7), 7.81 (d, J = 8.1 Hz, 1H, H_8), 8.02 (d, J = 7.9 Hz, 1H, H_5), 10.28 (bs, 1H, NH)	(dimethyl sulfoxide-d_6) 17.7, 24.9, 88.9 (C_3), 118 (C_8),122.1 (C_{4a}), 122.5 (C_6), 124.1 (C_5), 131 (C_7), 138.6 (C_{8a}), 151.7 (C_2, *C*Me_2), 172.6 (C_4)
11k	dimethyl sulfoxide-d_6	6.23 (s, 1H, H_3), 7.21 (td, J = 7.1, 1.8 Hz, 1H, H_7), 7.32 (d, J = 8.3 Hz, 2H, ArH), 7.45-7.61 (m, 2H, H_6, H_8), 7.75 (d, J = 8.3 Hz, 2H, ArH), 7.96 (d, J = 7.9 Hz, 1H, H_5)	
12a	deuteriochloroform and 5% trifluoroacetic acid	0.95 (t, J = 7.1 Hz, 3H), 1.30-1.53 (m, 2H), 1.58-1.78 (m, 2H), 3.34 (t, J = 7.2 Hz, 2H), 6.33 (s, 1H, H_3), 7.34 (d, J = 8.8 Hz, 1H, H_8), 7.77 (dd, J = 8.8, 1.8 Hz, 1H, H_7), 8.17 (d, J = 1.8 Hz, H_5)	
12c	deuteriochloroform and 5% trifluoroacetic acid	3.09 (bs, 3H), 3.22-3.54 (m, 2H), 3.71-4.04 (m, 4H), 4.19-4.54 (m, 2H), 6.66 (s, 1H, H_3), 7.57 (d, J = 8.9 Hz, 1H, H_8), 7.93 (dd, J = 8.9, 2 Hz, 1H, H_7), 8.36 (d, J = 2 Hz, 1H, H_5)	

Table 5 (continued)

N°	Solvant	^{1}H NMR δ ppm	^{13}C NMR δ ppm
12f	deuteriochloroform and 5% trifluoroacetic acid	2.95 (t, J = 6.6 Hz, 2H), 3.63 (t, J = 6.6 Hz, 2H), 3.85 (s, 3H), 3.89 (s, 3H), 6.16 (s, 1H, H_3), 6.89 (m, 3H, Ar), 7.20 (d, J = 8.8 Hz, 1H, H_8), 7.79 (dd, J = 8.8, 2.1 Hz, 1H, H_7), 8.21 (d, J = 2.1 Hz, 1H, H_5)	
13a	dimethyl sulfoxide-d_6	0.89 (t, J = 7.3 Hz, 3H), 1.25-1.43 (m, 2H), 1.43-1.64 (m, 2H), 3.10-3.26 (m, 2H), 5.55 (bs, 1H, H_3), 6.99 (bs, 1H, NH), 7.47 (bs, 2H, H_7, H_8), 7.84 (bs, 1H, H_6)	
13c	dimethyl sulfoxide-d_6	2.35 (s, 3H), 2.59 (m, 4H), 3.55 (m, 4H), 6.05 (bs, 1H, H_3), 7.45 (dd, J = 8.8, 2.3 Hz, 1H, H_7), 7.53 (d, J = 8.8 Hz, 1H, H_8), 7.87 (d, J = 2.3 Hz, 1H, H_5)	
14a	deuteriochloroform and 5% trifluoroacetic acid	0.97 (t, J = 7.1 Hz, 3H), 1.32-1.52 (m, 2H), 1.58-1.82 (m, 2H), 3.30-3.51 (m, 2H), 6.47 (bs, 1H, H_3), 7.68 (d, J = 9.1 Hz, 1H, H_8), 8.51 (dd, J = 9.1, 2.4 Hz, 1H, H_7), 8.93 (d, J = 2.4 Hz, 1H, H_5)	
14b	deuteriochloroform and 5% trifluoroacetic acid	1.0 (s, 9H), 1.30 (d, J = 6.5 Hz, 3H), 3.44-3.67 (m, 1H), 6.55 (bs, 1H, H_3), 6.98 (bd, J = 10 Hz, 1H, NH), 7.65 (d, J = 9.3 Hz, 1H, H_8), 8.52 (dd, J = 9.3, 2.4 Hz, 1H, H_7), 8.98 (d, J = 2.4 Hz, 1H, H_5)	
14c	dimethyl sulfoxide-d_6	2.41 (s, 3H), 2.52-2.82 (m, 4H), 3.53-3.93 (m, 4H), 6.16 (s, 1H, H_3), 7.59 (d, J = 8.8 Hz, 1H, H_8), 7.97 (bs, 1H, NH), 8.24 (d, J = 8.8 Hz, 1H, H_7), 8.76 (bs, 1H, H_5)	
22	deuteriochloroform and 5% trifluoroacetic acid	2.70 (s, 3H), 6.97 (s, 1H, H_3), 7.62 (t, J = 7.7 Hz, 1H, H_6), 7.73 (d, J = 8.3 Hz, 1H, H_8), 7.88 (t, J = 7.7 Hz, 1H, H_7), 8.21 (d, J = 8.3 Hz, 1H, H_5), 11.98 (bs, 1H, NH)	(dimethyl sulfoxide-d_6) 13.8, 104.8 (C_3), 117.4 (C_8), 123(C_{4a}, C_6), 124.9 (C_5), 131.6 (C_7), 140.7 (C_{8a}), 152.9 (C_2), 175.5 (C_4)
23	deuteriochloroform and 5% trifluoroacetic acid	2.71 (s, 3H), 6.95 (s, 1H, H_3), 7.69 (d, J = 9 Hz, 1H, H_8), 7.80 (dd, J = 9, 2.3 Hz, 1H, H_7), 8.08 (d, J = 2.3 Hz, 1H, H_5)	
24	deuteriochloroform and 5% trifluoroacetic acid	7.65 (t, J = 8.2 Hz, 2H, H_6), 7.79 (d, J = 8.2 Hz, 2H, H_8), 8.01 (t, J = 7.8 Hz, 2H, H_7), 8.47 (d, J =7.8 Hz, 2H, H_5), 9.2 (bs, 2 H, NH)	
27	dimethyl sulfoxide-d_6	2.76 (s, 3H), 7.41 (t, J = 7.6 Hz, 1H, H_6), 7.70 (td, J = 7.6, 1.5 Hz, 1H, H_7), 7.83 (d, J = 8.4 Hz, 1H, H_8), 8.11 (d, J = 8.2 Hz, 1H, H_5)	
28	dimethyl sulfoxide-d_6	3.05 (s, 3H), 7.48 (t, J = 7.6 Hz, 1H, H_6), 7.77 (td, J = 7.6 Hz, 1H, H_7), 8.16 (dd, J = 8.2, 1.6 Hz, 1H, H_8), 8.20 (d, J = 7.8 Hz, 1H, H_5)	39.6, 100.5 (C_3),119.8 (C_8), 124 (C_{4a}), 125 (C_6), 125.3 (C_5), 132.5 (C_7), 139.5 (C_2), 152.8 (C8a), 170.8 (C_4)
35	deuteriochloroform	0.91 (t, J = 7.4 Hz, 3H), 1.23-1.50 (m, 2H), 1.58-1.81 (m, 2H), 3.20-3.36 (m, 2H), 3.76 (s, 3H), 6.27 (s, 1H, H_3), 6.91 (bs, 1H, NH), 7.24 (d, J = 8.7 Hz, 1H, H_8), 7.33 (t, J = 8.7 Hz, 1H, H_6), 7.56 (t, J = 7.8 Hz, 1H, H_7), 8.10 (d, J = 7.8 Hz, 1H, H_5)	(deuteriochloroform and 5% trifluoroacetic acid) 13.3, 19.9, 30.7, 33 (NCH_3), 44.2, 90.4 (C_4), 115.6 (C_{4a}), 117.5 (C_8), 125.3 (C_5),125.8 (C_6), 134.8 (C_8), 139.6 (C_{8a}), 155.4 (C_2), 165.6 (C_4)

Elmer' 700 spectrometer and the nmr spectra on a Varian 'Gemini 2000' at 200 MHz for ^{1}H and 50 MHz for ^{13}C, using tetramethylsilane as an internal reference. Elemental analyses were performed by the «Service Central de Microanalyses» (CNRS, Vernaison, France).

5-[(Anilino)(4-methylpiperazino)methylene]-2,2-dimethyl-4,6-dioxo-1,3-dioxane (**6c**) (Method C).

A stirred mixture of *N*-methylpiperazine (3.8 ml, 3.4 g, 34 mmol) and of compound **17** (Method F or G) (5 g, 17 mmol) in chloroform (20 ml) was refluxed for 5 hours. The solvent was evaporated, then the residue was stirred in ether (50 ml). The solid was washed with ether, then recrystallized from acetone. Data are reported in Tables 1, 2 and 4.

5-[(Anilino)(4-chlorobenzoylhydrazino)methylene]-2,2-dimethyl-4,6-dioxo-1,3-dioxane (**6h**) (Method E).

A stirred mixture of 4-chlorobenzhydrazide (7.7 g, 45 mmol) and of compound **17** (Method F or G) (8.8 g, 30 mmol) in ethanol (25 ml) was refluxed for 10 hours. The precipitate was filtered from the hot solution, washed with ethanol, then recrystallized from ethanol. Data are reported in Tables 1, 2 and 4.

5-[(4-Bromophenylamino)(3,3-dimethyl-2-butylamino)methylene]-2,2-dimethyl-4,6-dioxo-1,3-dioxane (**7b**) (Method B).

A stirred mixture of 3,3-dimethyl-2-butylamine (4.25 g, 42 mmol) and of compound **18** (Method G) (11.2 g, 30 mmol) in chloroform (20 ml) was refluxed for 12 hours. Volatile compounds were removed under vacuum, then the residue was recrystallized from ethanol. Data are reported in Tables 1, 2 and 4.

5-[(Anilino)(4-chlorophenylamino)methylene]-2,2-dimethyl-4,6-dioxo-1,3-dioxane (**8d**) (Method D).

A stirred mixture of aniline (5 ml, 5.1 g, 55 mmol) and compound **19** (Method F or G) (9.8 g, 30 mmol) in chloroform (20 ml) was refluxed for 7 hours. The solvent was evaporated, then the residue was stirred in ether (50 ml). The solid was washed with ether, then recrystallized from methanol. Data are reported in Tables 1, 2 and 4.

5-[(Butylamino)(4-nitrophenylamino)methylene]-2,2-dimethyl-4,6-dioxo-1,3-dioxane (**10a**) (Method A).

A stirred mixture of butylamine (4.7 ml, 3.5 g, 48 mmol) and of compound **21** (Method G) (8.1 g, 24 mmol) in chloroform (40 ml) was refluxed for 8 hours. Volatile compounds were removed under vacuum, then the residue was recrystallized from ethanol. Data are reported in Tables 1, 2 and 4.

1,4-Dihydro-2-(4-methylpiperazino)-4-quinolinone (**11c**) (Method I).

A stirred mixture of *N*-methylpiperazine (33 ml, 29.8 g, 298 mmol) and of compound **22** (Method J) (5.8 g, 30 mmol) was refluxed for 24 hours. After cooling, acetone (60 ml) was added. The solid obtained was purified by washing with water, then with acetone. Data are reported in Tables 1, 3 and 5.

2-Phenylamino-1,4-dihydro-4-quinolinone (**11d**).

Polyphosphoric acid (6 g) was stirred at 140 °C and compound **6d** (Method D) (2.1 g, 6 mmol) was added. When the carbon dioxide evolution was complete (30 minutes), the mixture was allowed to cool at 100 °C and neutralized with 2 *N* sodium hydroxide. The solid obtained was washed with dilute hydrochloric acid then with water. The yellow powder was stirred in acetone then in ethanol. The insoluble quinolone **24** was collected by filtration and obtained in 51% yield. The organic phases were evaporated, giving 43% of compound **11d**. Data are reported in Tables 1, 3 and 5.

2-Benzylamino-1,4-dihydro-4-quinolinone (**11e**).

A stirred mixture of benzylamine (11.5 ml, 11.3 g, 105 mmol) and of compound **22** (Method J) (10 g, 52 mmol) was refluxed for 3 hours. After cooling, ethanol (25 ml) was added. The solid obtained was purified by washing with ether. Data are reported in Tables 1, 3 and 5.

1,4-Dihydro-2-hydrazino-4-quinolinone (**11i**).

A stirred mixture of hydrazine hydrate (200 ml, 206 g, 4.1 mol) and compound **22** (Method J) (50 g, 262 mmol) was refluxed for 24 hours. After cooling, the solution was dropped in icy cooled water (800 ml). The solid obtained was purified by washing with water.

1,4-Dihydro-2-(2-propylidenehydrazino)-4-quinolinone (**11j**).

A mixture of compound **11i (**1.75 g, 10 mmol) and acetone (30 ml) was stirred at 20 °C for 1 hour. The solid obtained was purified by washing with ether. Data are reported in Tables 1, 3 and 5.

6-Bromo-1,4-dihydro-2-(3,4-dimethoxyphenethylamino)-4-quinolinone (**12f**) (Method H).

Compound **7f** (Method D) (6 g, 12 mmol) was added to hot (130 °C), stirred, polyphosphoric acid (5 g). When the carbon dioxide evolution was complete, the mixture was allowed to cool to 100 °C and neutralized with 2 *N* sodium hydroxide. The solid obtained was washed with water and purified by stirring first in acetone then in ethanol. Data are reported in Tables 1, 3 and 5.

5-[(4-Chlorophenylamino)(methylthio)methylene]-2,2-dimethyl-4,6-dioxo-1,3-dioxane (**19**) (Method F).

Meldrum's acid (7.2 g, 50 mmol) was added to a suspension of lithium hydride (0.795 g, 100 mmol) in dimethyl sulfoxide (100 ml). The mixture was stirred 1 hour at room temperature under nitrogen then 4-chlorophenyl isothiocyanate (8.5 g, 50 ml) was added. After stirring for 12 hours, methyl iodide (3.2 ml, 7.1 g, 50 mmol) was added. After stirring for 4 hours, the mixture was poured into water (0 °C, 800 ml) and the solution was neutralized with 2 *N* hydrochloric acid. The solid obtained was washed with water then recrystallized from methanol. Data are reported in Tables 2 and 4.

5-[(4-Fluorophenylamino)(methylthio)methylene]-2,2-dimethyl-4,6-dioxo-1,3-dioxane (**20**) (Method G).

A stirred mixture of 4-fluoroaniline (23 ml, 27 g, 242 mmol) and of compound **16** [7a,b] (59.6 g, 240 mmol) in chloroform (240 ml) was refluxed for 0.5 hour. The solvent was evaporated then ether (150 ml) was added. The mixture was stirred for 1 hour and the solid was recrystallized from methanol. Data are reported in Tables 2 and 4.

6-Chloro-1,4-dihydro-2-methylthio-4-quinolinone (**23**) (Method J).

Polyphosphoric acid (6 g) was stirred at 130 °C, then compound **19** (Method F or G) (5 g, 15 mmol) was added. When the carbon dioxide evolution was complete, the mixture was allowed to cool to 100 °C. The solid obtained after neutralization with 2 *N* sodium hydroxide was washed with water and purified by refluxing in acetone. The product was not analyzed, but directly used for the next syntheses. Data are reported in Tables 3 and 5.

3-Bromo-1,4-dihydro-2-methylthio-4-quinolinone (**27**).

Bromine (2.6 ml, 8 g, 50 mmol) was added dropwise to a stirred solution of compound **22** (Method J) (9.6 g, 50 mmol) in acetic acid (200 ml). The mixture was stirred for 1 hour. The solid obtained was purified by washing with water. Data are reported in Tables 1, 3 and 5.

3-Bromo-1,4-dihydro-2-methylsulfinyl-4-quinolinone (**28**).

Bromine (0.5 ml, 1.6 g, 10 mmol) was added dropwise to a suspension of compound **27** (2.7 g, 10 mmol) in water (20 ml). The mixture was stirred for 1 hour. The solid obtained was washed with water. Data are reported in Tables 1, 3 and 5.

1-Benzyl-3-(4-chlorophenyl)urea (**32**).

A solution of 4-chlorophenylisocyanate (10 g, 65 mmol) in dichloromethane (60 ml) was added dropwise to a solution of benzylamine (7.1 ml, 7 g, 65 mmol) in dichloromethane (20 ml). The mixture was stirred for 1 hour. The solid obtained was washed with dichloromethane, giving 97 % of pure product **32**; mp 201 °C, ^{1}H nmr (deuteriochloroform): δ 4.47 (s, 2H), 7.10-7.60 (m, 9H) ppm. Elemental analyses are reported in Table 1.

1-Benzyl-3-(4-chlorophenyl)carbodiimide (**33**).

A mixture of urea **32** (16.3 g, 63 mmol), triphenylphosphine (24.3 g, 93 mmol), triethylamine (11.3 ml, 8.2 g, 81 mmol) and carbon tetrachloride (11.1 ml, 17.7 g, 115 mmol) in dichloromethane (100 ml) was refluxed for 4 hours (nitrogen). A part of solvents was evaporated then ether (50 ml) was added. The solid (triethylamine hydrochloride and triphenylphosphine oxide) was filtered and volatile compounds were evaporated. Ether (20 ml) and heptane (20 ml) were added and the solution was cooled (-40 °C) for 3 days ; the solid was filtered and volatile compounds were evaporated. These operations were repeated 3 times. Compound **33** was obtained as an oil (76 %) that was used directly in the next syntheses, ^{1}H nmr (deuteriochloroform): δ 4.44 (s, 2H), 6.70-7.50 (m, 9H) ppm.

1-Benzyl-3-(4-chlorophenyl)-O-ethylisourea (**34**).

Epichlorohydrin (5.1 ml, 6.1 g, 66 mmol) was added dropwise to a refluxing solution of boron trifluoride etherate (10.4 ml, 12 g, 85 mmol) in ether (25 ml) (nitrogen). The mixture was refluxed for 2 hours. The precipitate obtained was washed with ether (nitrogen), then urea **32** (14.8 g, 56.8 mmol) was introduced. The mixture was stirred at 80 °C for 6 hours. After cooling, ether (100 ml) was added. Triethylamine (10 ml, 7.3 g, 72 mmol) was added to the cooled (ice) mixture. The solid obtained was filtered and the solution was washed 3 times with water. The organic phases were dried (sodium sulfate) then evaporated giving 58 % of compound **34** (oil) which was used directly in the next syntheses. ^{1}H nmr (deuteriochloroform): δ 1.30 (t, J = 7.4 Hz, 3H), 4.26 (bs, 2H), 4.27 (q, J = 7.4 Hz, 2H), 6.80 (d, J = 8.9 Hz, 2H), 7.13-7.36 (m, 7H) ppm.

2-Butylamino-1,4-dihydro-1-methyl-4-quinolinone (**35**).

A stirred mixture of *N*-methylaniline (1.6 g, 15 mmol) and compound **16** [7a,b] (3.7 g, 15 mmol) in triethylamine (1.5 g, 15 mmol) and chloroform (10 ml) was refluxed for 48 hours. The solvent was evaporated, water (50 ml) was added and the suspension was stirred for 1 hour. The solid obtained was washed with water, then dried, giving product **36** (20 %). ^{1}H nmr (deuteriochloroform): δ 1.73 (bs, 6H), 2.55 (s, 3H), 3.65 (s, 3H), 7.36 (dd, J = 7.9 Hz, 2H), 7.41-7.49 (m, 3H) ppm.

This compound was added to butylamine (2 ml, 1.5 g, 20 mmol) and the mixture was refluxed for 24 hours. Volatile compounds were evaporated and the residue was washed with water, giving product **37** (60 %). This compound was added to hot (130 °C) stirred polyphosphoric acid (0.7 g). When the carbon dioxide evolution was complete, the mixture was allowed to cool at 100 °C, then neutralized with 2 *N* sodium hydroxide. The solid obtained was washed with water, giving product **35** (50 %). Data are reported in Tables 1, 3 and 5.

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