Synthesis and Structure−Activity Relationships of Carboxylated Chalcones: A Novel Series of *CysLT*$_1$ (LTD$_4$) Receptor Antagonists

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The synthesis and *CysLT*$_1$ antagonistic activities of a new series of 2-, 3-, and 4-(2-quinolinylmethoxy)- and 3- and 4-[2-(2-quinolinyl)ethenyl]-substituted, 2′-, 3′-, 4′-, or 5′-carboxylated chalcones are described. Structure−activity relationship studies indicate a preference for the presence of a negatively charged (acidic) moiety, although in some cases nitrile or ester analogues also exhibit moderate activity. The quinoline moiety may be substituted at either the 3- or the 4-position. Replacement of this heterocycle by other aromatic groups results in compounds with comparable affinities [2-(7-chloroquinoline), 1-(1-methyl-2-benzimidazole), or 1-(2-benzothiazole)] or substantially lower activities [1-(1-ethoxyethyl)-2-benzimidazole, 2-naphthyl, or phenyl]. The quinoline and chalcone moieties may be connected by either an ethenyl or a methoxy spacer. The acidic moiety at the chalcone B ring may be attached to the 2′-, 3′-, 4′-, or 5′-position, for both the 3- and 4-substituted chalcones. There are no general patterns to specify which substitution positions gave the most potent compounds. The series contains several potent *CysLT*$_1$ receptor antagonists, with K_D values approaching the nanomolar range, as measured by the displacement of [^{3}H]LTD$_4$ from guinea pig lung membranes. Antagonism of LTD$_4$-induced contraction of guinea pig ileum, the inhibition of antigen-induced contraction of guinea pig trachea *in vitro*, and the inhibition of LTD$_4$-induced increase of vascular permeability *in vivo* are determined for chalcones with high *CysLT*$_1$ receptor affinities (K_D values below 0.1 μM). 2′-Hydroxy-4-(2-quinolinylmethoxy)-5′-(5-tetrazolyl)chalcone (**14**, VUF 4819) showed good activity in both *in vitro* and *in vivo* assays and has been selected for further evaluation.

Introduction

Asthma is a chronic inflammation condition of the airways, which affects about 5% of the population of the industrialised areas. Asthmatic reactions, which are characterized by bronchial hyperresponsiveness and reversible airway obstruction, are mediated by a wide range of endogenous chemicals known as inflammatory mediators. During the last two decades leukotrienes have been identified as important bronchoconstrictors, and their pharmacological effects mimic the pathological changes seen in asthma both *in vitro* and *in vivo*.[1−8] Inhaled LTC$_4$ and LTD$_4$ are 1000-fold more potent bronchoconstrictors than histamine. Although the bronchoconstriction induced by LTE$_4$ is less potent, it has a more prolonged effect compared with LTC$_4$ and LTD$_4$.[9] The biological actions of leukotrienes are, at least partly, mediated via activation of high-affinity receptors. There are at least two distinct receptor subtypers for cysteinyl leukotrienes, designated as *CysLT*$_1$ (previously known as LTD$_4$ receptor[10]) and *CysLT*$_2$ (previously LTC$_4$ receptor). *CysLT*$_1$ receptor activation leads to bronchoconstriction, mucus secretion, and increased bronchial hyperresponsiveness characteristic of asthma. Although LTC$_4$, the endogenous ligand for *CysLT*$_2$ receptors, has similar biological effects as LTD$_4$, the functional consequences of selective *CysLT*$_2$ receptor activation remains unclear.[11] This is partly because of the chemical instability of LTC$_4$, which readily converts to LTD$_4$ under most experimental conditions.[12] The unravelling of the biosynthetic pathway and the pathological role of peptidoleukotrienes in human diseases[1,13] has led to the development of leukotriene biosynthesis inhibitors (5-lipoxygenase inhibitors and FLAP inhibitors) and *CysLT*$_1$ receptor antagonists[14] as potential therapeutic agents. Recent studies on these compounds have demonstrated clinical efficacy in human asthma, and both classes of agents are considered as promising candidates for a new generation of potent and selective drugs against asthma.[2,6,15−19]

FPL 55712 (sodium 7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)-2-hydroxypropyl]-4-oxo-8-propyl-4*H*-1-benzopyran-2-carboxylate) was first described in 1973 as what turned out to be the first selective *CysLT*$_1$ receptor antagonist.[20] Until the structure elucidation of the peptidoleukotrienes in 1980,[21] FPL 55712 was the only lead structure. During the past 15 years several potent and selective *CysLT*$_1$ antagonists have been developed (Scheme 1).[14] At first the development of new *CysLT*$_1$ antagonist was mainly inspired by FPL 55712[22] or LTD$_4$ analogues, e.g. probilukast (SK&F 104353).[23−28] Later new leads were discovered, which led to the development of a wide range of compounds such as the indole zafirlukast (ICI 204,219),[29−33] the benzamide pranlukast (ONO-1078),[34,35] the thiazole Ro 24-5913 [(E)-4-[[3-[2-(4-cyclobutyl-2-thiazolyl)ethenyl]phenyl]amino]-2,2-diethyl-4-oxobutanoic acid][36,37] and quinolines such as RG 12553 [5-[7-[[3-(2-quinolinylmethoxy)phenyl]methoxy]-4-oxo-4*H*-1-benzopyran-2-yl]-1*H*-tetrazole][38] and montelukast (MK-476),[39] as highly potent antagonists at the

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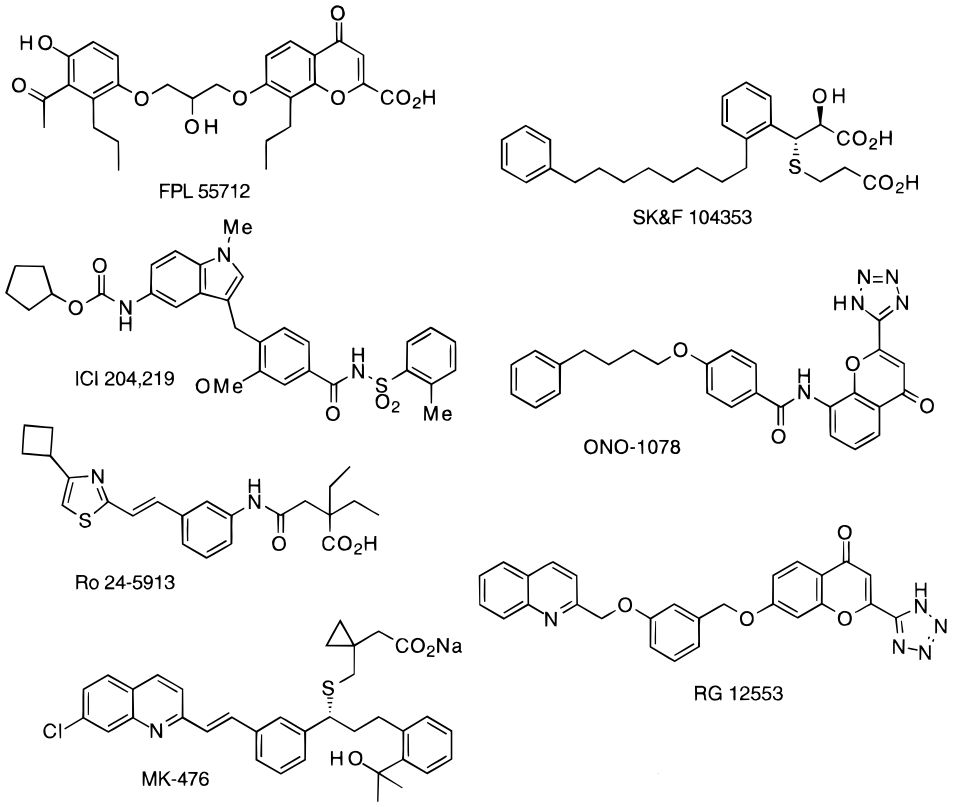
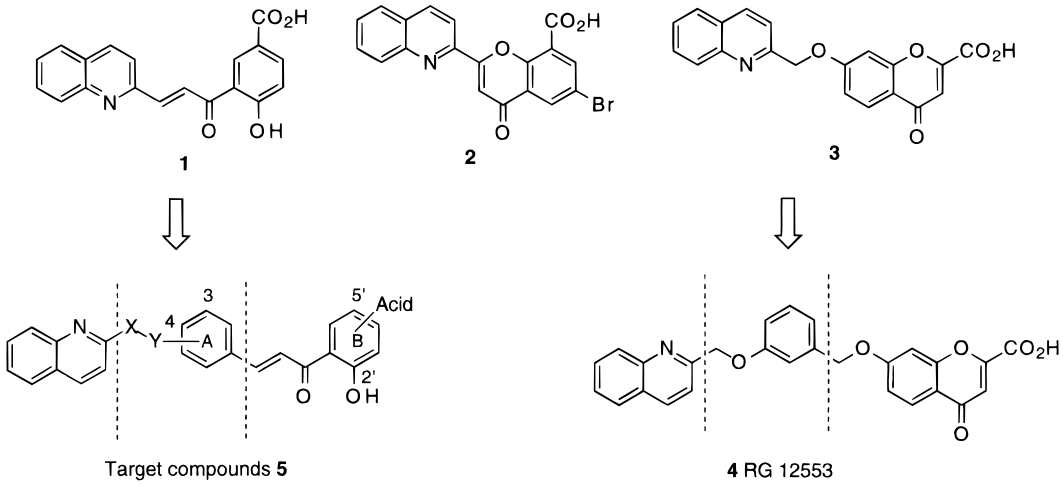
Scheme 1. Potent $CysLT_1$ Receptor Antagonists



Scheme 2. Optimization of Lead Structure **1**



$CysLT_1$ receptor (see Scheme 1 for the structures of these $CysLT_1$ antagonists).

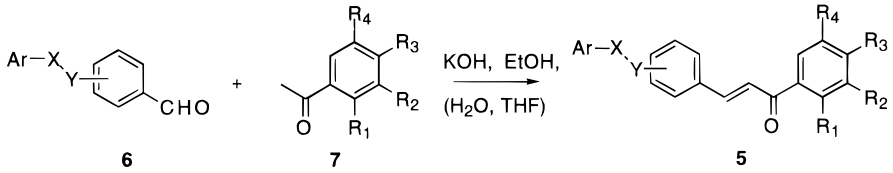
In our search for antiasthmatic drugs we became therefore interested in the development of $CysLT_1$ receptor antagonists.[40,41] Our attempts to find new lead structures for $CysLT_1$ receptor antagonists started with the synthesis of carboxylated flavonoids,[41] compounds which are known for their antianaphylactic properties.[42−46] We found two new lead structures, **1** and **2** (Scheme 2), which showed weak but significant affinities for the $CysLT_1$ receptor having K_D values of $1.11 \pm 0.14 \times 10^{-5}$ and $1.48 \pm 0.28 \times 10^{-5}$ M, respectively.

It is known in the literature that the distance between the quinoline moiety and the acidic function is important for $CysLT_1$ receptor affinity. For example, when the chromone **3** is modified by insertion of a methoxyphenyl spacer, the resulting **4** (RG 12553) is 70000-fold more active than **3**.[38] We started the optimization of **1** with the introduction of a similar spacer, leading to chalcones with general structure **5**. In this paper we describe the synthesis and pharmacology of these carboxylated chalcones as potent $CysLT_1$ receptor antagonists.

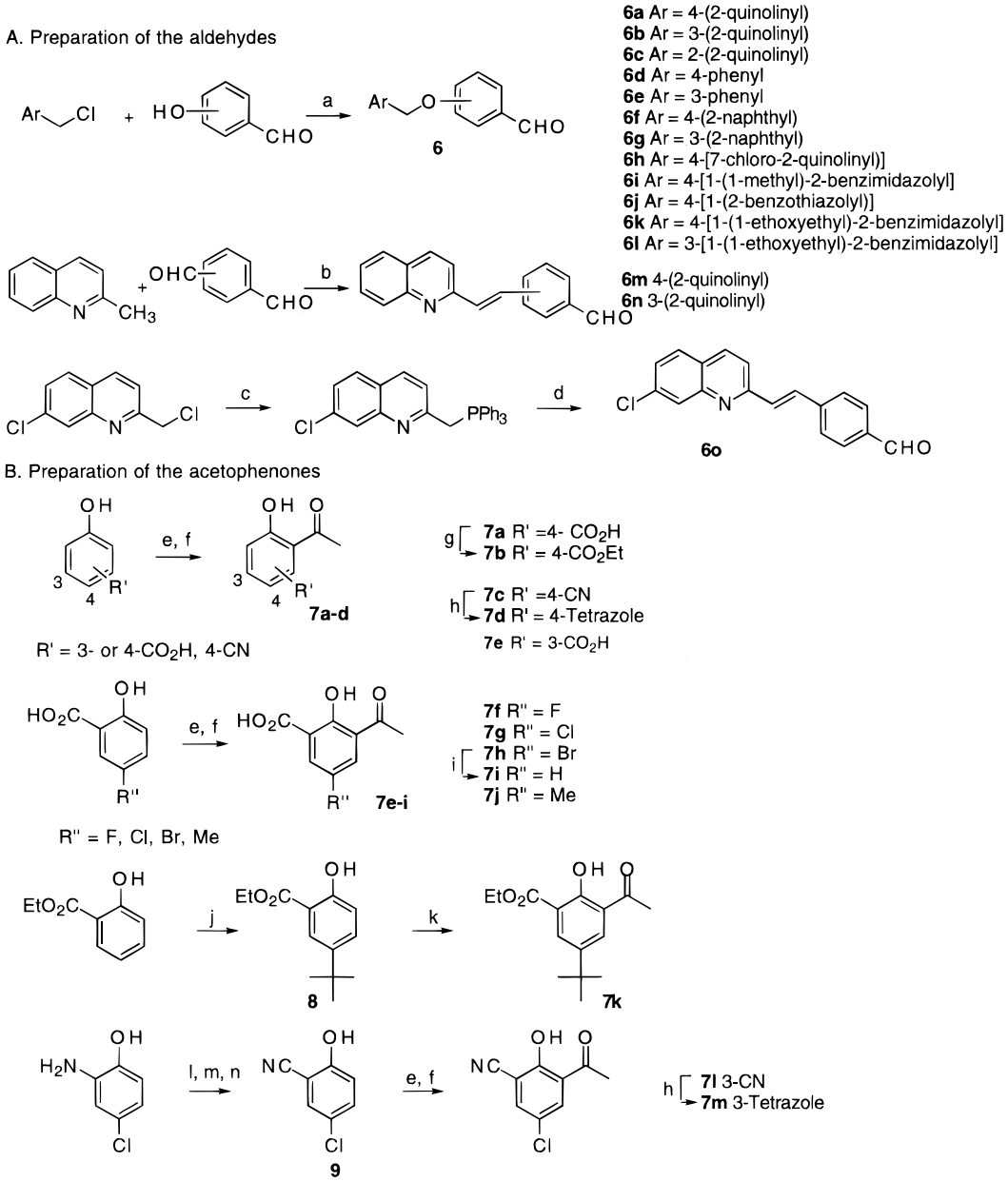
Synthesis

Chalcones **5** were prepared by Claisen−Schmidt condensation of aldehydes **6** with the suitable acetophenones **7** (Scheme 3).[47−49] Reaction of equimolar amounts of the aldehyde and the acetophenone in a mixture of ethanol and water, containing potassium or sodium hydroxide, at room temperature for several days gave the chalcones in variable yields. The chalcones were purified by crystallization or by column chromatography.

Scheme 3. Synthesis of the Chalcones



Scheme 4. Preparation of the Starting Materials[a]

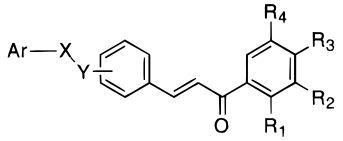


[a] (a) K_2CO_3, DMF, 90 °C; (b) Ac_2O, xylene, reflux; (c) PPh_3, toluene, reflux; (d) 1,4-benzenedicarboxaldehyde, *t*-BuOK, THF; (e) Ac_2O, H_2SO_4; (f) $AlCl_3$, △; (g) ethanol, H_2SO_4; (h) NaN_3, NH_4Cl, DMF, 100 °C; (i) H_2 (15 bar) Pd/C, ethanol. (j) $AlCl_3$, CH_2Cl_2, *t*-BuCl; (k) $AlCl_3$, CH_2Cl_2, AcBr; (l) $NaNO_2$, H_3O^+; (m) KI, H_2O; (n) CuCN, DMF, reflux.

Ether-substituted aldehydes (**6**, X—Y is CH_2O) were prepared by alkylation of the suitable hydroxybenzaldehydes with aryl halides to form the arylmethoxy aldehydes **6a**—**k** (Scheme 4A). Styryl aldehydes (**6**, X—Y is CH═CH) were obtained by condensation of 2-methylquinoline with 1,3- or 1,4-benzenedicarboxaldehyde in refluxing xylene in the presence of acetic anhydride (**6l** and **6m**, Scheme 4A),[50] or by reaction of the Wittig salt of 7-chloro-2-(chloromethyl)quinoline with 1,4-benzenedicarboxaldehyde to give aldehyde **6n**.

Acetophenones **7a**—**c** and **7h**—**i** were prepared according to literature procedures.[41,43,46] The synthetic routes to the acetophenones are shown in Scheme 4B. Synthesis of the acetophenones involves the introduction of the acyl group via a Fries rearrangement or by Friedel—Crafts acylation (**7k**). For the synthesis of **7i**, protection of the para position is necessary to avoid acylation at this position. Compound **7i** was prepared by reductive cleavage of the bromine from **7h**.[41] For the preparation of **7l** the cyano group was first introduced

Table 1. Carboxylated Chalcones and Their *CysLT*$_1$ Receptor Affinities



compd	Ar	XY	pos XY	R_1	R_2	R_3	R_4	K_D (nM),[a] (% inhibn at 10^{-5} M)
1								11100 ± 1400
10	2-quinolinyl	CH_2O	4	OH	H	H	CO_2H	450 ± 27
11	2-quinolinyl	CH_2O	4	OH	H	H	CO_2Et	(16%)
12	2-quinolinyl	CH_2O	4	OH	Cl	H	CO_2H	1700 ± 710
13	2-quinolinyl	CH_2O	4	OH	H	H	CN	4310 ± 770
14	2-quinolinyl	CH_2O	4	OH	H	H	CN_4H	14 ± 6
15	2-quinolinyl	CH_2O	3	OH	H	H	CO_2H	609 ± 88
16	2-quinolinyl	CH_2O	3	OH	H	H	CN	(38%)
17	2-quinolinyl	CH_2O	3	OH	H	H	CN_4H	209 ± 79
18	2-quinolinyl	CH_2O	2	OH	H	H	CO_2H	(18%)
19	phenyl	CH_2O	4	OH	H	H	CO_2H	(23%)
20	phenyl	CH_2O	3	OH	H	H	CO_2H	33500 ± 6700
21	phenyl	CH_2O	2	OH	H	H	CO_2H	(0%)
22	2-naphthyl	CH_2O	3	OH	H	H	CN_4H	19200 ± 3500
23	2-naphthyl	CH_2O	4	OH	H	H	CN_4H	(4%)
24	1-[(1-methyl)-2-benzimidazolyl]	CH_2O	4	OH	H	H	CN_4H	32 ± 11
25	1-[(1-ethoxyethyl)-2-benzimidazolyl]	CH_2O	4	OH	H	H	CN_4H	527 ± 32
26	1-[(1-ethoxyethyl)-2-benzimidazolyl]	CH_2O	3	OH	H	H	CN_4H	8850 ± 640
27	1-[(1-ethoxyethyl)-2-benzimidazolyl]	CH_2O	4	OH	H	CO_2H	H	62400 ± 5900
28	1-[(1-ethoxyethyl)-2-benzimidazolyl]	CH_2O	3	OH	CO_2H	H	Cl	10500 ± 4000
29	1-(2-thiazolyl)	CH_2O	4	OH	H	H	CN_4H	233 ± 67
30	2-(7-chloroquinoline)	CH_2O	4	OH	H	H	CN_4H	196 ± 38
31	2-(7-chloroquinoline)	C═C	4	OH	H	H	CN_4H	239 ± 30
32	2-quinolinyl	CH_2O	4	OH	CO_2H	H	H	307 ± 125
33	2-quinolinyl	CH_2O	4	OH	CO_2H	H	F	396 ± 82
34	2-quinolinyl	CH_2O	4	OH	CO_2H	H	Cl	732 ± 56
35	2-quinolinyl	CH_2O	4	OH	CO_2H	H	Br	2100 ± 800
36	2-quinolinyl	CH_2O	3	OH	CO_2H	H	H	415 ± 165
37	2-quinolinyl	CH_2O	3	OH	CO_2H	H	Cl	104 ± 18
38	2-quinolinyl	CH_2O	3	OH	CO_2H	H	Br	205 ± 51
39	2-quinolinyl	CH_2O	4	OH	H	CO_2H	H	1210 ± 280
40	2-quinolinyl	CH_2O	3	OH	H	CO_2H	H	928 ± 67
41	2-quinolinyl	CH_2O	4	H	H	CN	H	(9%)
42	2-quinolinyl	CH_2O	3	H	H	CN	H	(7%)
43	2-quinolinyl	CH_2O	4	CO_2H	H	H	H	143 ± 52
44	2-quinolinyl	CH_2O	3	CO_2H	H	H	H	31 ± 4
45	2-quinolinyl	C═C	4	OH	CO_2H	H	H	200 ± 52
46	2-quinolinyl	C═C	4	OH	H	H	CO_2H	585 ± 130
47	2-quinolinyl	C═C	3	OH	H	H	CN	346 ± 98
48	2-quinolinyl	C═C	3	OH	H	H	CN_4H	21 ± 5
49	2-quinolinyl	C═C	3	OH	CO_2H	H	H	26 ± 4
50	2-quinolinyl	C═C	3	OH	CO_2H	H	F	140 ± 26
51	2-quinolinyl	C═C	3	OH	CO_2H	H	Cl	6.6 ± 3.0
52	2-quinolinyl	C═C	3	OH	CO_2H	H	Br	207 ± 26
53	2-quinolinyl	C═C	3	OH	CO_2H	H	Me	105 ± 18
54	2-quinolinyl	C═C	3	OH	CO_2H	H	*t*-Bu	208 ± 39
55	2-quinolinyl	C═C	3	OH	CN	H	Cl	449 ± 91
56	2-quinolinyl	C═C	3	OH	CN_4H	H	Cl	828 ± 360
57	2-quinolinyl	C═C	3	OH	H	H	OCH_2CO_2H	175 ± 130
58	2-quinolinyl	C═C	3	OH	H	H	OCH_2CN_4H	45 ± 15
59	2-quinolinyl	C═C	3	OH	H	OCH_2CO_2H		204 ± 72
60	2-quinolinyl	CH_2O	4	OMe	H	H	CO_2H	188 ± 142
61	2-quinolinyl	CH_2O	4	OMe	H	H	CO_2Me	357 ± 27
62	2-quinolinyl	CH_2O	4	O-*n*-Bu	H	H	CO_2H	(42%)
63	2-quinolinyl	CH_2O	3	O-*n*-Bu	H	H	CO_2H	300 ± 16
ONO-1078								1
FPL 55712								1122

[a] The affinity data are obtained from binding assays in guinea pig lung membranes *vs* [^{3}H]LTD$_4$. K_D values are presented as means ± SD of three determinations. [b] Percent inhibition is determined as the quotient of the maximum binding minus the counting at the highest drug concentration and the maximum binding times 100.

by a Sandmeyer reaction of 2-amino-4-chlorophenol to give **9**. Subsequent acetylation and Fries rearrangement gave acetophenone **7l** in good yield.

Results and Discussion

The chalcones listed in Table 1 were tested by a binding assay of guinea pig lung membranes against [^{3}H]LTD$_4$ to determine their *CysLT*$_1$ receptor affinities. As expected, the insertion of a methoxyphenyl spacer into lead structure **1** resulted in compound **10** with 24-fold increase of *CysLT*$_1$ receptor affinity. Comparison of **10**, **15**, and **18** revealed that the relative position of substitution at this methoxyphenyl ring was important for the receptor affinity. Both para and meta substitution of the quinoline moiety to the chalcone A ring are allowed, but substitution of the heterocycle at the ortho

position leads to an almost complete loss of activity. The much lower affinities of **11**, **13**, and **16** indicate that the presence of an acidic substituent at the chalcone B -ring is important, although nitrile, **13**, **47**, and **55** have micromolar *CysLT*$_1$ affinities.

Analogous to the findings of other groups,[38,51,52] the quinoline moiety was found to play a crucial role in the *CysLT*$_1$ antagonistic activity of the carboxylated chalcones. Replacement of the quinoline by phenyl (**19**, **20**, and **21**) or naphthyl (**22** and **23**) reduced the activity at least 100-fold, indicating that the quinoline nitrogen plays a crucial role in binding to the receptor. Substitution of the quinoline for several other nitrogen-containing heterocyclic systems (**24**−**31**) does not yield compounds with improved activities (compare **24**, **25**, **29**, and **30** with reference compound **14**), with the 1-(1-(ethoxyethyl)-2-benzimidazolyl) derivative **25** having the lowest activity. The loss of activity may be either due to steric bulk or electronic factors. Changing the ether connecting the heterocycle with the chalcone moiety to an ethenyl bridge does not affect the affinities significantly, but in the case of **36** and **49** the ethenyl-connected **49** is significantly more active than the ether-linked analogue **36**.

Although the presence of a negatively charged moiety at the chalcone B ring seems to be important, no general conclusion about the nature or position of this moiety can be drawn. Carboxylic acids can be substituted at the 2′- (**43** and **44**), 3′- (**32** and **36**) 4′- (**39** and **40**), or 5′-position (**10** and **15**) in both the 3- and 4-substituted chalcones without major changes in activity. Introduction of a two-atom spacer between the acidic moiety and the chalcone B ring (**57**, **58**, and **59**) also does not largely change the affinity. Replacement of the carboxylic acid by tetrazoles can yield either more (compare **10** and **14**), equally (**15** and **17**), or less active compounds (**51** and **56**), possibly due to different orientations toward the interaction site at the receptor. Also the nonacidic nitriles and esters (**11** and **61**) show an unambiguous behavior.

Introduction of additional substituents on the chalcone B ring only slightly affects the receptor affinities. Within the series **49**−**54** the introduction of a fluorine, bromine, methyl, or *tert*-butyl at the 5′-position results in a 10-fold decrease of activity, while the chlorine analogue **51** has the affinity in the same range as the unsubstituted chalcone **49**. Although minor variations among these compounds are observed, no general trend was found. Disruption of the carbonyl-2′-hydroxy hydrogen bond by methylation of the 2′-hydroxyl group (**60**) does not significantly affect the *CysLT*$_1$ receptor affinity. Although affinity of the *n*-butyloxy analogue **62** has decreased substantially, probably due to the steric bulk, the 2′-(*n*-butyloxy)-3-substituted analogue **63** has submicromolar affinity to the *CysLT*$_1$ receptor, indicating a different alignment of this compound at the receptor.

Compounds with *CysLT*$_1$ receptor affinities under 0.1 μM were selected for further pharmacological evaluation of their functional activities. Compounds **14**, **24**, **48**, **49**, **51**, and **58** were tested for the inhibition of LTD$_4$-induced contraction of guinea pig ileum; the IC$_{50}$ values of these compounds are displayed in Table 2. The selected chalcones displayed antagonistic activities, with IC$_{50}$ values ranging from 360 to 23 nM. Compounds **14**, **49**, **58**, and **24** were also tested for their inhibitory effect on the antigen-induced contraction of guinea pig trachea *in vitro*.[53] Only **14** displayed significant activity in this assay, the other compounds were essentially inactive (Table 2), possibly due to a poor solubility. In Figure 1 the activity of **14** in the antigen-induced contraction assay is compared to FPL 55712, and ONO-1078. Compound **14** is more active than FPL 55712, but less active than ONO-1078 in this model, which closely resembles the asthmatic situation. The potency of compound **14**, FPL 55712 and ONO-1078 in inhibiting antigen-induced contraction of guinea pig trachea thus correlates with their *CysLT*$_1$ receptor affinities. Finally compounds **14**, **49**, and **51** were also tested for their *in vivo* activity in the inhibition of LTD$_4$-induced increase of vascular permeability in guinea pigs. Again only **14** showed good activity in this assay, **14** exhibited 72% inhibition of the LTD$_4$-induced vascular permeability increase. Compounds **49** and **51** showed no significant inhibition of the vascular permeability increase when administered at the dose of 10 mg/kg ip; this may be due to pharmacokinetic causes.

Table 2. Functional Tests of Selected Chalcones

compd	K_D (nM)[a]	IC$_{50}$ (nM)[b]	% inhibition of antigen-induced contraction[c]	% inhibition of LTD$_4$-induced increase of vascular permeability[d]
14	14 ± 6	240	52	72
48	21 ± 5	46		
49	26 ± 4	52	0	<10
51	6.6 ± 3	360		<10
58	45 ± 15	23	0	
24	32 ± 11	190	6	
FPL 55712	1122		38	
ONO-1078	1		80	100 (1 μM ip)

[a] The affinity data are obtained from binding assays in guinea pig lung membranes *vs* [^{3}H]LTD$_4$. The data are means of three determinations. [b] Inhibition of LTD$_4$-induced contraction of guinea pig ileum. [c] Inhibition of ovalbumin-induced contraction (10 ng/mL) of guinea pig trachea at the drug concentration of 10 μM. [d] Decreased permeability of Evan's blue dye (50 mg/kg) after injection of 10 ng/site of LTD$_4$, at a drug concentration of 10 mg/kg ip.

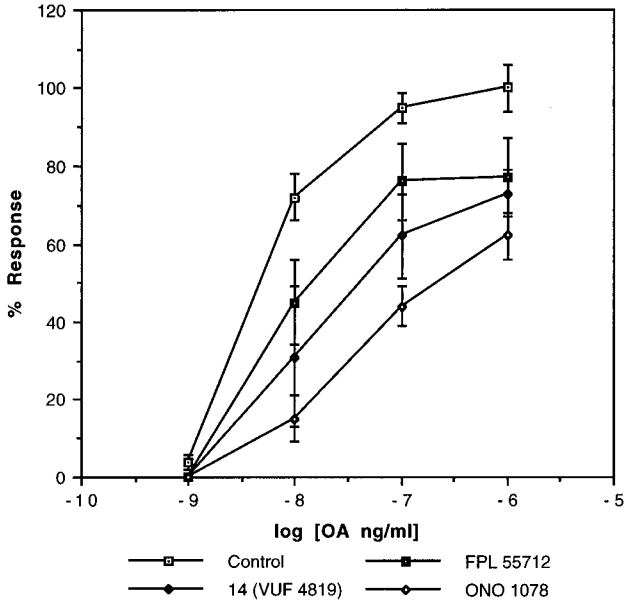


Figure 1. Inhibition of ovalbumin-induced contraction of guinea pig trachea by compound **14** as compared to FPL 55712 and ONO-1078 at drug concentrations of 10^{-5} M.

Conclusions

Starting from our lead structure **1** we have developed a new series of quinoline-substituted carboxylated chalcones with $CysLT_1$ antagonistic activities showing about 800 times higher affinity for this receptor. Several chalcones (Table 1) possess affinities for the $CysLT_1$ receptor approaching the nanomolar range. More extensive pharmacological testing of a selected number of chalcones has shown the ligands to be potent $CysLT_1$ antagonists with IC_{50} values as low as 23 nM in the LTD_4-induced contraction of guinea pig ileum, comparable to their receptor affinities.

Structure−activity relationship studies indicate a preference for the presence of a negatively charged (acidic) moiety at the chalcone B ring, although in some cases nitrile or ester analogues also exhibit moderate activity. The quinoline moiety may be substituted at either the 3- or the 4-position, replacement of this heterocycle by other aromatic groups results in compounds with either comparable activities [2-(7-chloroquinoline), 1-(1-methyl-2-benzimidazole) or 1-(2-benzothiazole)] or lower activities (e.g. 1-(1-(ethoxyethyl)-2-benzimidazole), 2-naphthyl, or phenyl). The quinoline and chalcone moieties may be connected either by an ethenyl or an methoxy spacer. Regarding the positions of the acidic moieties, there were no patterns to specify which substitution patterns gave the most potent compounds. The sometimes unpredictable behavior of carboxylated chalcones in their binding capacity suggest that they may have different alignments in their mode of binding to the $CysLT_1$ receptor.

Pharmacological testing of selected chalcones in *in vitro* and *in vivo* assays led to the selection of **14** (VUF 4819) for further development. This compound exhibits, in contrast to **49**, **51**, and **58**, activity in all assays described and has an attractive pharmacological profile. The lack of activity of **58**, **51**, and **49** in the *in vivo* or *in vitro* functional assays might be caused by a poor absorption or other pharmacokinetic properties.

Experimental Section

A. Pharmacology. 1. Radioligand Displacement Studies with [^{3}H]LTD_4. The method is very similar to that described previously.[40] Briefly, a mixture of total volume of 0.3 mL containing 0.2 nM [^{3}H]LTD_4, guinea pig lung membrane proteins (±170 μg/mL), and the testing compound in a 10 mM piperazine-*N*,*N*′-bis(2-ethanesulfonic acid) buffer (pH 7.5) was incubated at 22 °C for 30 min. The piperazine-*N*,*N*′-bis(2-ethanesulfonic acid) buffer contains 10 mM $CaCl_2$, 10 mM $MgCl_2$, 50 mM NaCl, 2 mM cysteine, and 2 mM glycine. The reaction was terminated by the addition of 5 mL of ice-cold Tris-HCl/NaCl buffer (10 mM/100 mM, pH 7.5). The mixture was immediately filtered under vacuum (Whatman GF/C filters), and the filters were washed once with 20 mL of ice-cold buffer. The retained radioactivity was determined by a liquid scintillation counter. In the saturation experiment, 2 μM LTD_4 was used to define the nonspecific binding. A single, saturable binding site with B_{max} = 988 fmol/mg protein was found from the saturation experiment. The K_D of [^{3}H]LTD_4 was found to be 2.16×10^{-10} M, and no cooperativity was detected when the data were analyzed by Hill plots (slope = 0.99).

2. *In Vitro* Inhibition of LTD_4-Induced Contraction of Guinea Pig Ileum. The method is similar to that described previously.[40] Male guinea pigs were killed by a sharp blow to the head, and ileum sections (2 cm) were removed immediately. Each segment was tied to a holder and attached to a transducer by means of a thread, leaving the lumen open. The ilea were then transferred to 20 mL organ baths maintained at 29 °C and continuously aerated with 95% O_2 and 5% CO_2 and washed with Tyrode's solution containing atropine (10^{-6} M) and pyrilamine (10^{-6} M). The contraction of ileum was measured isotonically (resting tension was 1.0 g). The test compounds were dissolved in dimethyl sulfoxide and after 30 min of preincubation of the test compounds at different concentrations (10^{-5} to 3×0.10^{-9} M), the contraction induced by 10^{-8} M LTD_4 was obtained. Indomethacin (10^{-6} M) was added in the organ baths 10 min before the administration of LTD_4. IC_{50} values were calculated from the percent inhibition at the different drug concentrations.

3. *In Vivo* Inhibition of LTD_4-Induced Vascular Permeability Increase in Guinea Pigs. The assay is based on that described previously.[40] Male Hartley guinea pigs (about 300 g) were deprived of food for 24 h but allowed free access to water. The test compound was suspended or dissolved in 0.5% carboxymethylcellulose or saline and was given by intraperitoneal injection. One hour later, Evans blue dye was injected intravenously at the dose of 50 mg/kg, and immediately LTD_4 was injected intradermally to the backs of the animals at the dose of 50 ng/site. Thirty minutes later the dorsal skin was removed, Evans blue dye was extracted, and the concentration of dye was determined. The result was represented as inhibitory percent to control.

4. *In Vitro* Inhibition of Antigen-Induced Contraction of Guinea Pig Trachea. The assay is based on that described previously.[53] Male Hartley guinea pigs (450−500 g) are sensitesed by ip injection of 2 mg of ovalbumin (OA) in 200 μL of saline (0.9% NaCl). The procedure was performed at least 2 weeks before the experiments. The sensitized animals were sacrificed by a sharp blow to the head and trachea were isolated, carefully trimmed of excess fatty and connective tissue, and cut into strips of equal width (one full cartilage ring, ∼2 mm). The preparation was performed under 50 mM Na^+/K^+ phosphate buffer. Each preparation was placed in a 20 mL water-jacketed organ bath containing Krebs buffer which was maintained at 37 °C and constantly aerated with 95% O_2−5% CO_2. The Krebs buffer contained, besides the usual composites, 3 μM indomethacin. The tissues were placed under 0.5 g of passive tension and equilibrated for 60 min, during which they were washed every 15 min with fresh indomethacin-containing Krebs solution. Before the challenge with ovalbumin, the tissues were incubated with or without the testing drug for 30 min. Tissues were contracted with a single concentration of ovalbumin (5 ng/mL) for an indicated time (20−60 min). After this period, carbachol (10 μM) was added to the preparations, and the antigen-induced response, which was recorded continuously, was expressed as a percentage of this reference carbachol contraction. Only one OA-induced contraction was generated per preparation.

B. Chemistry. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC 200 (^{1}H NMR: 200.1 MHz, ^{13}C NMR 50.29 MHz) or a Bruker 400 MSL spectrometer (^{1}H NMR 400.1 MHz, ^{13}C NMR 100.63 MHz). ^{1}H NMR chemical shifts (δ) are reported in ppm relative to $CHCl_3$ (δ = 7.25 ppm) or DMSO-d_5 (δ = 2.5 ppm); ^{13}C NMR chemical shifts (δ) are reported in ppm relative to $CHCl_3$ (δ = 77.0 ppm) or DMSO-d_5 (δ = 39.5 ppm). Coupling constants are given in hertz. 2D-NMR (H−H and C−H) COSY techniques were frequently used to support interpretation of 1D spectra. The multiplicity of the carbon signals was determined by DEPT or APT spectra, or by a combination of a normal decoupled carbon spectrum in combined with a CH correlation. The symbols used are (p) for primary, (s) for secondary, (t) for tertiary, and (q) for quaternary carbon signals. The spectra were measured at room temperature at 200 MHz, unless stated otherwise.

FAB (-HRMS) measurements were performed on a Finnigan MAT 90 spectrometer equipped with a WATV Cs ion gun, operated at a beam current of approximately 2 μA at 25 kV. High-resolution mass spectra were recorded on a Finnigan MAT-90. Melting points were measured on a Mettler FP-5 + FP-52 apparatus equiped with a microscope and are uncorrected.

Starting materials were commercially available; acetophenones **7a**,[46] **7b**,[46] **7c**,[43] **7h**,[41] **7i**,[41] ONO-1078,[35] and FPL 55712[54] were prepared according to literature procedures. All chalcones had elemental analysis within 0.4% of theoretical value unless otherwise indicated. However, compounds having an

elemental analyses slightly outside of this range were found to be pure by both spectroscopic and chromatographic criteria.

4-(2-Quinolinylmethoxy)benzaldehyde (6a). A mixture of 6.42 g (30 mmol) of 2-(chloromethyl)quinoline hydrochloride, 3.66 g (30 mmol) of 4-hydroxybenzaldehyde, and 9.11 g (66 mmol) of anhydrous potassium carbonate in 50 mL of DMF was heated overnight at 90 °C. The solvent was removed *in vacuo*, and the remaining mixture was extracted with ethyl acetate. The combined organic layers were washed with 1 N NaOH and brine and dried over Na_2SO_4. Removal of the solvent yielded the pure product: mp 81.0−82.1 °C;, yield 91%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.41 (s, 2H, CH_2O), 7.10 (d, 2H, ^3J = 8.7 Hz, H3, H5), 7.47−7.51 (m, 1H, H6-quinoline), 7.58 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.67−7.71 (m, 1H, H7-quinoline), 7.74−7.79 (m, 1H, H5-quinoline), 7.79 (d, 2H, ^3J = 8.7 Hz, H2, H6), 8.07 (d, 1H, ^3J = 8.3 Hz, H8-quinoline), 8.15 (d, 1H, ^3J = 8.5 Hz, H4-quinoline), 9.86 (s, 1H, ArCHO).

3-(2-Quinolinylmethoxy)benzaldehyde (6b). The compound was prepared in a similar way as described for 4-(2-quinolinylmethoxy)benzaldehyde except using 3-hydroxybenzaldehyde and heating for 6 h: yield 61%; mp 55.1−57.1 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.35 (s, 2H, CH_2O), 7.20 (m, 1H, H4), 7.36−7.47 (m, 3H, H5-quinoline, H6-quinoline, H5), 7.64−7.69 (m, 1H, H7-quinoline), 7.72−7.76 (m, 1H, H6), 8.01 (d, 1H, ^3J = 8.3 Hz, H8-quinoline), 8.11 (d, 1H, ^3J = 8.5 Hz, H4-quinoline), 9.87 (s, 1H, ArCHO).

2-(2-Quinolinylmethoxy)benzaldehyde (6c). The compound was prepared in a similar way as described for 4-(2-quinolinylmethoxy)benzaldehyde, except using 2-hydroxybenzaldehyde, the product was obtained as a brown oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.48 (s, 2H, CH_2O), 7.06 (d 1H, ^3J = 8.4 Hz, H3), 7.45−7.58 (m, 2H, H5, H6-quinoline), 7.66 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.69−7.88 (m, 4H, H5-quinoline, H7-quinoline, H4, H6), 8.20 (d, 1H, ^3J = 8.5 Hz, H4-quinoline), 8.30 (d, 1H, ^3J = 8.3 Hz, H8-quinoline), 10.64 (s, 1H, ArCHO).

4-(Benzyloxy)benzaldehyde (6d). Analogous to the preparation of 4-(2-quinolinylmethoxy)benzaldehyde using benzyl bromide as the alkylating agent: yield 86%; mp 70.0−71.8 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.14 (s, 2H, CH_2O), 7.05 (d, 2H, ^3J = 8.8 Hz, H3, H5), 7.33−7.45 (m, 5H, Ph), 7.83 (d, 2H, ^3J = 8.8 Hz, H2, H6), 9.87 (s, 1H, CHO).

3-(Benzyloxy)benzaldehyde (6e). Analogous to the preparation of 4-(2-quinolinylmethoxy)benzaldehyde using benzyl bromide as the alkylating agent: yield: 75%; mp 50.8−52.2 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.11 (s, 2H, CH_2O), 7.21−7.47 (m, 10H, Ar-H), 9.96 (s, 1H, CHO).

4-(2-Naphthylmethoxy)benzaldehyde (6f). Analogous to the preparation of 4-(2-quinolinylmethoxy)benzaldehyde using 2-(chloromethyl)naphthalene as the alkylating agent: yield 9.85 g (37.6 mmol, 59%) of the product as a white powder; mp 106−108 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.31 (s, 2H, CH_2O), 7.12 (d, 2H, ^3J = 8.8 Hz, H3, H5), 7.42−7.58 (m, 3H, Ar-H), 7.76−7.92 (m, 6H, Ar-H), 9.89 (s, 1H, CHO). Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.48; H, 5.42.

3-(2-Naphthylmethoxy)benzaldehyde (6g). Analogous to the preparation of 3-(2-quinolinylmethoxy)benzaldehyde using 2-chloromethylnaphthalene as the alkylating agent: yield 17.01 g (46.7 mmol, 47%); mp 107−110 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.29 (s, 2H, CH_2O), 7.22−7.32 (m, 1H, Ar-H), 7.41−7.59 (m, 6H, Ar-H), 7.80−7.92 (m, 4H, Ar-H), 9.98 (s, 1H, CHO). Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found C, 82.43; H, 5.40.

4-[[2-(7-Chloroquinolinyl)]methoxy]benzaldehyde (6h). Analogous to the preparation of 4-(2-quinolinylmethoxy)-benzaldehyde using 7-chloro-2-(chloromethyl)quinoline as the alkylating agent. The crude product was obtained as an oil and purified by column chromatography using $CHCl_3$−methanol (10:1). The pure product was obtained as pale yellow needles: yield 64%; mp 130−133 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.44 (s, 2H, CH_2O), 7.13 (d, 2H, ^3J = 8.8 Hz, H3, H5), 7.52 (dd, 1H, ^3J = 8.5 Hz, ^4J = 2.0 Hz, H6-quinoline), 7.64 (d, 1H, ^3J = 8.3 Hz, H3-quinoline), 7.73 (d, 1H, ^3J = 8.3 Hz, H5-quinoline), 7.84 (d, 1H, ^3J = 8.8 Hz, H2, H6), 8.09 (d, 1H, ^4J = 2.0 Hz, H8-quinoline), 8.19 (d, 1H, ^3J = 8.3 Hz, H4-quinoline), 9.89 (s, 1H, CHO).

4-[(1-Methyl-2-1*H*-benzimidazolyl)methoxy]benzaldehyde (6i). Analogous to the preparation of 4-(2-quinolinylmethoxy)benzaldehyde using 2-(chloromethyl)-1-methyl-1*H*-benzimidazole as the alkylating agent: yield 3.97 g (14.9 mmol, 50%); mp 140−142 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.48 (s, 2H, CH_2O), 7.14−7.42 (m, 5H, Ar-H), 7.71−7.90 (m, 3H, Ar-H), 7.71−7.90 (m, 3H, Ar-H), 9.88 (s, 1H, CHO). Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.11; H, 5.26; N, 10.59.

4-(2-1*H*-Benzothiazolylmethoxy)benzaldehyde (6j). Analogous to the preparation of 4-(2-quinolinylmethoxy)-benzaldehyde using 2-(chloromethyl)1*H*-benzothiazole as the alkylating agent: yield 3.03 g (11.3 mmol, 38%); mp 135−137 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.57 (s, 2H, CH_2O), 7.16 (d, 2H, ^3J = 8.8 Hz, H3, H5), 7.35−7.57 (m, 2H, H5-benzothiazole, H6-benzothiazole), 7.87 (d, 2H, ^3J = 8.8 Hz, H2, H6), 7.91 (d, 1H, ^3J = 8.3 Hz, H4-benzothiazole), 8.06 (d, 1H, ^3J = 8.8 Hz, H7-benzothiazole), 9.90 (s, 1H, CHO). Anal. Calcd for $C_{15}H_{11}NO_2S$: C, 66.90; H, 4.12; N, 5.20; S, 11.91. Found: C, 66.72; H, 4.13; N, 5.22; S, 11.95.

4-[[1-(Ethoxyethyl)-2-1*H*-benzimidazolyl]methoxy]benzaldehyde (6k). Analogous to the preparation of 4-(2-quinolinylmethoxy)benzaldehyde using 2-(chloromethyl)-1-(ethoxyethyl)-1*H*-benzimidazole as the alkylating agent: yield 4.56 g (14.1 mmol, 70%); mp 96−97 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.10 (t, ^3J = 6.8 Hz, OCH_2CH_3), 3.29 (q, 2H, ^3J = 6.8 Hz, OCH_2CH_3), 3.75 (t, 2H, ^3J = 5.4 Hz, NCH_2CH_2O), 4.49 (t, 2H, ^3J = 5.4 Hz, NCH_2CH_2O), 5.57 (s, 2H, CH_2O), 7.14−7.47 (m, 5H, Ar-H),7.74−7.89 (m, 3H, Ar-H), 9.89 (s, 1H, CHO). Anal. ($C_{19}H_{20}N_2O_3$) C, H, N.

3-[[1-(Ethoxyethyl)-2-1*H*-benzimidazolyl]methoxy]benzaldehyde (6l). To a solution of 6.71 g (28 mmol) of 2-(chloromethyl)-1-(ethoxyethyl)benzimidazole, 3.43 g (28.1 mmol) of 3-hydroxybenzaldehyde, and 0.97 g (3 mmol) of tetra-*n*-butylammonium bromide in 70 mL of DMF was added 4.27 g (31 mmol) of potassium carbonate. The reaction mixture was stirred at room temperature for 7 days and poured into water. The precipitate was collected by filtration, washed with water, and dried. Recrystallization from acetone−*n*-hexane gave 7.49 g (23 mmol, 82%) of **6l** as yellow prisms: mp 98−100 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.10 (t, ^3J = 6.8 Hz, OCH_2CH_3), 3.39 (q, 2H, ^3J = 6.8 Hz, OCH_2CH_3), 3.76 (t, 2H, ^3J = 5.4 Hz, NCH_2CH_2O), 4.49 (t, 2H, ^3J = 5.4 Hz, NCH_2CH_2O), 5.52 (s, 2H, $ArCH_2O$), 7.23−7.53 (m, 6H, Ar-H), 7.58 (d, 1H, ^4J = 1.0 Hz, Ar-H), 7.74−7.83 (m, 1H, Ar-H), 9.98 (s, 1H, CHO). Anal. Calcd for $C_{19}H_{20}N_2O_3$: C, 70.35; H, 6.22; N, 8.64. Found: C, 70.32; H, 6.18; N, 8.67.

4-[2-(2-Quinolinyl)ethenyl]benzaldehyde (6m). A solution of 30 g (0.22 mol) of 1,4-benzenedicarboxaldehyde, 21 g (0.15 mol) of 2-methyl quinoline, and 41.5 mL, (0.40 mol) of acetic anhydride in 160 mL of xylene was refluxed for 7 h. After the solution was cooled to room temperature, 200 mL of petroleum ether (40−60 °C) was added and the precipitate (the bis adduct) was filtered. The mother liquor was concentrated *in vacuo*, and the crude product was recrystallized from ethanol twice, yielding 13.6 g of product: mp 111.9−113.0 °C; yield 35%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.46−7.51 (m, 2H, Ar-H), 7.54−7.80 (m, 6H, Ar-H, H-olefin), 7.87−7.91 (m, 2H, Ar-H), 8.08 (d, 1H, ^3J = 8.4 Hz, Ar-H), 8.14 (d, 1H, ^3J = 8.6 Hz, H4-quinoline), 10.00 (s, 1H, CHO).

3-[2-(2-Quinolinyl)ethenyl]benzaldehyde (6n). This compound was prepared in a similar way as 4-[2-(2-quinolinyl)-ethenyl]benzaldehyde. After the mixture was cooled down, the solvent was evaporated, and the crude product was dissolved in ethyl acetate and washed with 1 N NaOH, water, and brine. Drying over Na_2SO_4 and removal of the solvent gave the crude product as a brown oil. The oil was dissolved in hot ethanol and cooled down. The first precipitate (the bis adduct) was removed and washed with ethanol. Two crystallizations from ethanol gave 18.6 g of the pure product: yield 48%; mp 78.6−80.8 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.42−7.89 (m, 9H, Ar-H, H-olefin), 8.05−8.16 (m, 3H, Ar-H), 10.04 (s, 1H, CHO).

4-[2-(7-Chloro-2-quinolinyl)ethenyl]benzaldehyde (6o). Step 1. [(7-Chloro-2-quinolinyl)methyl]triphenylphosphonium Chloride. To a solution of 7-chloro-2-(chloromethyl)quinoline (4.81 g, 22.7 mmol) in toluene (100 mL) was added triphenylphosphine (7.74 g, 29.51 mmol). The mixture was

refluxed for 24 h and evaporated. Precipitates were collected and washed with ether to give a gray powder of the product, which was used for the next step without further purification: yield 8.54 g (18.0 mmol, 79%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.09 (d, 2H, $^2J_{PH}$ = 14.4 Hz, CH_2P), 7.43 (dd, 1H, ^3J = 8.6 Hz, ^4J = 2.0 Hz, H6-quinoline), 7.49 (d, 1H, ^4J = 2.0 Hz, H8-quinoline), 7.57−7.65 (m, 7 H, H_{meta}-phenyl, H5-quinoline), 7.68−7.77 (m, 3H, H_{para}-phenyl), 7.88−7.97 (m, 6H, H_{ortho}-phenyl), 8.05 (d, 1H, ^3J = 8.6 Hz, H3-quinoline), 8.25 (d, 1H, ^3J = 8.5 Hz, H4-quinoline).

Step 2. 4-[2-(7-Chloro-2-quinolinyl)ethenyl]benzaldehyde. To a suspension of [(7-chloro-2-quinolinyl)methyl]-triphenylphosphonium chloride (3.97 g, 8.37 mmol) in THF (100 mL) was added a solution of 939 mg (8.37 mmol) of *t*-BuOK in 50 mL of THF under a N_2 atmosphere. The mixture was stirred at room temperature for 4 h, and a solution of 996 mg (8.37 mmol) of 1,4-benzenedicarboxaldehyde in 50 mL of THF was added. The reaction mixture was then stirred for 2 h and then stirred for another hour after the addition of 50 mL of water. Then 150 mL of water was added, and the product was extracted with chloroform. The combinded organic layers were dried over anhydrous Na_2SO_4, filtered over a short column of silica gel, and evaporated to give 1.71 g (5.82 mmol, 70%) of the product as yellow needles: mp 178−180 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.47 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.0 Hz, H6-quinoline), 7.49 (d, 1H, ^3J = 15.9 Hz, H-olefin), 7.64 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.73 (d, 1H, ^3J = 8.5 Hz, H5-quinoline), 7.78 (d, 2H, ^3J = 8.3 Hz, Ar-H), 7.78 (d, 1H, ^3J = 15.9 Hz, H-olefin), 7.92 (d, 2H, J = 8.3 Hz, Ar-H), 8.10 (d, 1H, ^4J = 2.0 Hz, H8-quinoline), 8.14 (d, 1H, ^3J = 8.8 Hz, H4-quinoline), 10.03 (s, 1H, CHO). Anal. Calcd for $C_{18}H_{12}NOCl$: C, 73.60; H, 4.12; N, 4.77; Cl, 12.07. Found: C, 73.49; H, 4.18; N, 4,84; Cl, 12.12.

2-Hydroxy-5-(5-tetrazolyl)acetophenone (7d). A mixture of 5-cyano-2-hydroxyacetophenone (2.0 g, 12.4 mmol), sodium azide (4.1 g, 62 mmol), and ammonium chloride (3.35 g, 62 mmol) in 35 mL of DMF was heated at 100 °C for 3 days. The reaction mixture was poured out in water and acidified to pH = 5. The product was extracted with ethyl acetate and dried, and the solvent was removed *in vacuo*. The crude product was crystallized from ethanol to yield 1.42 g of pure product: yield 56%; mp 181.8−184.9 °C; ^{1}H NMR (DMSO) δ 2.69 (s, 3H, $COCH_3$), 7.20 (d, 1H, ^3J = 8.7 Hz, H3), 8.14 (dd, 1H, ^3J = 8.7 Hz, ^4J = 1.7 Hz, H4), 8.52 (d, 1H, ^4J = 1.7 Hz, H6), 12.07 (br s, 1H, ArOH).

4-Acetyl-3-hydroxybenzoic Acid (7e). Step 1. 3-Acetoxybenzoic Acid. To a solution of 3-hydroxybenzoic acid (10.07 g, 73 mmol) in acetic anhydride (10 mL) was added 0.2 mL of concentrated sulfuric acid. The mixture was stirred at 60 °C for 1 h. After the mixture was allowed to stand at room temperature overnight, the precipitate was collected, washed with benzene, and dried. Recrystallization from acetone−hexane yielded 8.92 g (50 mmol, 68%) of the product as colorless prisms: mp 121−123 °C; ^{1}H NMR ($CDCl_3$) δ 2.34 (s, 3H, OCOCH_3), 7.36 (dd, 1H, ^3J = 7.8 Hz, ^4J = 2.0 Hz, ^4J = 1.5 Hz, H4), 7.50 (t, 1H, ^3J = 7.8 Hz, H5), 7.83 (t, 1H, ^4J = 2.0 Hz, H2), 8.00 (dt, 1H, ^3J = 7.8 Hz, ^4J = 1.6 Hz, H6); MS *m/z* 180 (M^+). Anal. Calcd for $C_9H_8O_4 \cdot 0.05H_2O$: C, 59.70; H, 4.51. Found: C, 59.69; H, 4.52.

Step 2. 4-Acetyl-3-hydroxybenzoic Acid (7e). A mixture of 3-(acetyloxy)benzoic acid (46.16 g, 0.26 mol) and $AlCl_3$ (136.2 g, 1.02 mol) was heated to 160 °C for 3 h. After the mixture was cooled down to room temperature, 1 N HCl and ice was added, and the product was extracted with ethyl acetate. The organic layers were washed with brine and dried over anhydrous $MgSO_4$, and the solvent was evaporated. Recrystallization from ethanol gave 8.33 g (46 mmol, 18%) of the product as a yellow powder: mp 204−205 °C; ^{1}H NMR ($CDCl_3$): δ 2.70 (s, 3H, COCH_3), 7.52 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.0 Hz, H6), 7.54 (d, 1H, ^4J = 2.0 Hz, H2), 7.87 (d, 1H, ^3J = 8.8 Hz, H5), 12.07 (s, 1H, ArOH). Anal. Calcd for $C_9H_8O_4$: C, 60.00; H, 4.48. Found: C, 59.90; H, 4.42.

3-Carboxy-5-fluoro-2-hydroxyacetophenone (7f). This compound was prepared in a similar way as 5-bromo-3-carboxy-2-hydroxyacetophenone: yield 35%; mp 156.8−159.2 °C; ^{1}H NMR (200 MHz, DMSO) δ 2.61 (s, 3H, $COCH_3$), 7.66−7.79 (m, 2H, H3, H5), 11.88 (br s, 2H, ArOH, $ArCO_2H$); ^{13}C NMR (DMSO) δ 30.63 (p), 115.96 (q, J_{CF} = 6.6 Hz), 120.80 (t, J_{CF} = 24.3 Hz), 121.54 (t, J_{CF} = 24.0 Hz), 126.57 (q, J_{CF} = 5.5 Hz), 153.34 (q, J_{CF} = 153.34 Hz), 157.17 (q), 170.22 (q), 197.40 (q).

3-Carboxy-5-chloro-2-hydroxyacetophenone (7g). This compound was prepared in a similar way as 5-bromo-3-carboxy-2-hydroxyacetophenone: yield 45%; mp 173.7−175.8 °C; ^{1}H NMR (200 MHz, DMSO) δ 2.60 (s, 3H, $COCH_3$), 7.84 (d, 1H, ^4J = 2.7 Hz, H6), 7.92 (d, 1H, ^4J = 2.7 Hz, H4), 12.28 (br s, 2H, ArOH, $ArCO_2H$); ^{13}C NMR (50 MHz, DMSO) δ 30.62 (p), 116.38 (q), 122.16 (q), 126.90 (q), 133.60 (t), 134.35 (t), 159.37 (q), 170.11 (q), 196.76 (q).

3-Carboxy-2-hydroxy-5-methylacetophenone (7j). This compound was prepared in a similar way as 5-bromo-3-carboxy-2-hydroxyacetophenone: yield 82%; mp 122.2−125.8 °C; ^{1}H NMR (200 MHz, DMSO) δ 2.32 (s, 3H, $ArCH_3$), 2.67 (s, 3H, $COCH_3$), 7.77 (d, 1H, ^4J = 2.3 Hz, H3/5), 8.05 (d, 1H, ^4J = 2.3 Hz, H3/5), 9.25 (br s, 1H, CO_2H), 13.45 (br s, 1H, ArOH); ^{13}C NMR (50 MHz, DMSO) δ 19.34 (p), 30.62 (p), 114.31 (q), 125.04 (q), 127.13 (q), 135.15 (t), 135.78 (t), 158.93 (q), 171.19 (q), 198.11 (q).

5-*tert*-Butyl-3-(ethoxycarbonyl)-2-hydroxyacetophenone (7k). Ethyl salicylate (10 g, 60 mmol) was dissolved in 50 mL of dichloromethane. To this solution was added anhydrous aluminum chloride (11.75 g, 88 mmol), followed by the dropwise addition of *tert*-butyl chloride (5.60 g, 60 mmol). After the mixture was stirred 3 h at room temperature, 14.8 g (120 mmol) of acetyl bromide was slowly added. The reaction mixture was stirred overnight and poured onto ice containing 3 M HCl. The product was extracted with ethyl acetate, and removal of the solvent yielded the crude product which was purified by column chromatography (ethyl acetate/petroleum ether (40−60 °C) 1:20): yield 45% (7.20 g); mp 63.5−65.3 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.24 (s, 9H, $C(CH_3)_3$), 1.36 (t, 3H, ^3J = 7.1 Hz, $CO_2CH_2CH_3$), 2.62 (s, 3H, $COCH_3$), 4.36 (q, 2H, ^3J = 7.1 Hz, $CO_2CH_2CH_3$), 7.93 (d, 1H, ^4J = 2.7 Hz, H4), 7.98 (d, 1H, ^4J = 2.7 Hz, H6); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.06 (p), 30.65 (p), 34.02 (q), 61.53 (s), 114.51 (q), 125.05 (q), 132.14 (t), 133.16 (t), 141.13 (q), 159.62 (q), 169.16 (q), 200.02 (q).

3-Cyano-5-chloro-2-hydroxyacetophenone (7l). 2-Amino-4-chlorophenol (50 g, 0.35 mol) was dissolved in 500 mL of 2.5 N HCl. The solution was cooled to 0 °C, and 25.25 g (0.37 mol) of $NaNO_2$ in 50 mL of water was slowly added. After 30 min of stirring, the reaction mixture was positive toward starch/KI, and a cooled solution of 70 g (0.42 mol) of KI in 100 mL of water was slowly added. The reaction mixture was allowed to warm to room temperature overnight and extracted with ethyl acetate. Removal of the solvent gave 89.7 g (0.35 mol, 99%) of 4-chloro-2-iodophenol as a purple solid. This compound (85 g, 0.33 mol) was dissolved in 150 mL of DMF together with 32.5 g (0.36 mol) of CuCN. After the mixture was refluxed for 2 h, the DMF was removed *in vacuo* and the product was dissolved in ethyl acetate and washed with water. Insoluble salts were removed by filtration. Removal of the solvent yielded 40.4 g (0.26 mol) of 5-chloro-2-hydroxybenzonitrile (**9**), which was used in the next step without further purification: yield 80%; mp 150.3−152.6 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.02 (d, 1H, ^3J = 9.0 Hz, H3), 7.53 (dd, 1H, ^3J = 9.0 Hz, ^4J = 2.7 Hz, H4), 7.75 (d, 1H, ^4J = 2.7 Hz, H6), 11.41 (br s, 1H, ArOH); ^{13}C NMR (50 MHz, $CDCl_3$) δ 100.09 (q), 115.46 (q), 117.60 (t), 122.41 (q), 131.80 (t), 134.27 (t), 158.99 (q).

To a suspention of 39.25 g (0.25 mol) of 5-chloro-2-hydroxybenzonitrile (**9**) in 40 mL of acetic anhydride was added 0.5 mL of concentrated sulfuric acid. The reaction mixture was heated at 60 °C for 10 min, water was added, and the product was extracted with ethyl acetate. The organic layers were washed with 1 N NaOH and brine, dried over Na_2SO_4, and concentrated *in vacuo*. 2-(Acetyloxy)-5-chlorobenzonitrile was obtained as a brown solid (45 g, 92%) and directly used in the next step: ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.29 (s, 3H, ArO-$COCH_3$), 7.14 (d, 1H, ^3J = 8.8 Hz, H3), 7.47 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.5 Hz, H4), 7.54 (d, 1H, ^4J = 2.5 Hz, H6); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.47 (p), 108.26 (q), 113.71 (q), 131.47 (q), 132.41 (t), 134.11 (t), 150.71 (q), 167.87 (q).

A stirred mixture of (acetyloxy)-5-chlorobenzonitrile (44 g, 0.23 mol) and 99 g (0.75 mol) of aluminum chloride was heated at 160 °C for 3 h. After being cooled to room temperature, the solidified reaction mixture was powdered in a mortar and poured into ice containing 100 mL of concentrated HCl. The slurry was extracted with ethyl acetate (3 × 350 mL), washed with 1 N HCl (3 × 200 mL) and brine (400 ml), and dried over Na_2SO_4. The solvent was evaporated, and traces of side products were removed by washing with dichloromethane. 3-Cyano-5-chloro-2-hydroxyacetophenone (16.5 g) was obtained as a brown solid: yield 38%; mp 137.9−139.8 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.72 (s, 3H, $COCH_3$), 8.21 (d, 1H, ^4J = 2.5 Hz, H4/6), 8.32 (d, 1H, ^4J = 2.5 Hz, H4/6), 12.77 (br s, 1H, ArOH); ^{13}C NMR (50 MHz, $CDCl_3$) δ 27.11 (p), 102.54 (q), 114.07 (q), 121.40 (q), 122.75 (q), 135.91 (t), 138.52 (t), 160.95 (q), 204.08 (q).

5-Chloro-2-hydroxy-3-(5-tetrazolyl)acetophenone (7m). This compound was prepared from 3-cyano-5-chloro-2-hydroxyacetophenone analogous to the preparation of 2-hydroxy-5-(5-tetrazolyl)acetophenone: yield 5%; mp °C; ^{1}H NMR (200 MHz, DMSO) δ 2.76 (s, 3H, $COCH_3$), 8.26 (s, 2H, H4, H6); ^{13}C NMR (50 MHz, DMSO) δ 27.40 (p), 114.63 (q), 121.48 (q), 122.98 (q), 133.57 (t), 134.44 (t), 156.71 (q), 205.04 (q).

3-Acetyl-5-chloro-4-hydroxybenzoic Acid (7n). Step 1. 4-Acetoxy-3-chlorobenzoic Acid. To a solution of 3-chloro-4-hydroxybenzoic acid hemihydrate (10.16 g, 56 mmol) in 20 mL of acetic anhydride was added 0.5 mL of concentrated H_2SO_4. The reaction mixture was stirred at 100 °C for 3 h and allowed to stand at room temperature overnight. 4-Acetoxy-3-chlorobenzoic acid was collected as colorless leaflets, which were washed with benzene: yield 8.95 g (41.7 mmol, 75%); mp 149−151 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.40 (s, 3H, $OCOCH_3$), 7.27 (d, 1H, ^3J = 8.8 Hz, H5), 8.05 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.0 Hz, H6), 8.21 (d, 1H, ^4J = 2.0 Hz, H2); MS *m*/*z* 216 (M^+ for ^{37}Cl), 214 (M^+ for ^{35}Cl). Anal. Calcd for $C_9H_7ClO_4$: C, 50.37; H, 3.29; Cl, 16.25. Found: C, 50.29; H, 3.23; Cl, 16.54.

Step 2. 3-Acetyl-5-chloro-4-hydroxybenzoic Acid (7n). A mixture of 4-acetoxy-3-chlorobenzoic acid (8.95 g, 41.7 mmol) and $AlCl_3$ (22.23 g, 167 mmol) were heated to 180 °C for 3 h. After addition of ice and 1 N HCl, the reaction mixture was extracted with ethyl acetate. The combined organic layers were washed with water and dried over $MgSO_4$, and the solvent was evaporated. The residual oil was crystallized from ethyl acetate to give 2.97 g (13.8 mmol) of the product as a yellow powder: yield 33%; mp 238−241 °C dec; ^{1}H NMR (200 MHz, CD_3OD) δ 2.73 (s, 3H, $COCH_3$), 8.17 (d, 1H, ^4J = 2.0 Hz, H2/6), 8.48 (d, 1H, ^4J = 2.0 Hz, H2/6); MS *m*/*z* 216 (M^+ for ^{37}Cl), 214 (M^+ for ^{35}Cl). Anal. Calcd for $C_9H_7ClO_4$: C, 50.37; H, 3.29; Cl, 16.52. Found: C, 50.34; H, 3.22; N, 0.01; Cl, 16.37.

Methyl 3-Acetyl-4-methoxybenzoate (7o). To a solution of 3-acetyl-4-hydroxybenzoic acid (3.60 g, 20 mmol) and methyl iodide (5.68 g, 40 mmol) in 60 mL of DMF was added 11.06 g (80 mmol) of K_2CO_3. The reaction mixture was stirred at room temperature for 2 h, and the DMF was evaporated. After addition of water the product was extracted with chloroform. The combined organic layers were dried over $MgSO_4$, and the solvent was evaporated. The residual oil was crystallized from acetone−hexane to give 1.42 g (6.8 mmol, 34%) of the product as a brown powder. Another 1.05 g was recovered from the filtrate: total yield 59%; mp 83−85 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.62 (s, 3H, $COCH_3$), 3.90 (s, 3H, CO_2CH_3), 3.98 (s, 3H, OCH_3), 7.02 (d, 1H, ^4J = 8.8 Hz, H5), 8.16 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.0 Hz, H6), 8.40 (d, 1H, ^4J = 2.0 Hz, H2).

***n*-Butyl 3-Acetyl-4-*n*-butoxybenzoate (7p).** A mixture of 3-acetyl-4-hydroxybenzoic acid (3.92 g, 21.8 mmol), *n*-butyl iodide (8.81 g, 47.9 mmol), and potassium carbonate (13.24 g, 95.8 mmol) in 70 mL of DMF was stirred at room temperature for 16 h. The solvent was evaporated. Water was added to the residue, and the product was extracted with chloroform. The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, and evaporated. The residual oil was purified by column chromatography using ethyl acetate/hexane (1:4) as eluent. Evaporation of the solvent yielded 5.32 g (18.2 mmol) of the product as a colorless oil. Recrystallization from hexane yielded the product as colorless prisms: yield 84%; mp 39−40 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.97 (t, 3H, ^3J = 6.8 Hz, $O(CH_2)_3CH_3$), 1.01 (t, 3H, ^3J = 6.8 Hz, $(CH_2)_3CH_3$), 1.96−1.35 (m, 8 H, 2 $OCH_2(CH_2)_2CH_3$), 2.64 (s, 3H, $COCH_3$), 4.13 (t, 2H, ^3J = 6.8 Hz, $OCH_2(CH_2)_2CH_3$), 4.30 (t, 2H, ^3J = 6.8 Hz, $CO_2CH_2(CH_2)_2CH_3$), 6.99 (d, 1H, ^3J = 8.8 Hz, H5), 8.13 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.5 Hz, H6), 8.39 (d, 1H, ^4J = 2.5 Hz, H2). Anal. ($C_{17}H_{24}O_4$) C, H.

General Procedure for Chalcone Synthesis. Chalcones were prepared according to this procedure, unless stated otherwise. Equimolar amounts (10 mmol) of the desired benzaldehyde and the suitable acetophenone were dissolved in 50 mL of ethanol, and 25 mL of 25% KOH in water was added. If excessive precipitate was formed, more solvent was added to facilitate the stirring. In case of the 2-[ethenyl(2-quinolinyl)]benzaldehydes, THF was added to improve the solubility. The reaction mixture was stirred at room temperature for 1 week and poured onto ice. Acidification with 3 N HCl (pH 3−5) gave a yellow precipitate which was filtered and washed with water. The crude products were purified by column chromatography and/or recrystallization from suitable (mixtures of) solvents.

5′-Carboxy-2′-hydroxy-4-(2-quinolinylmethoxy)chalcone (10): recrystallization from DMF/ethanol; yield 30%; mp 242.7−246.7 °C; ^{1}H NMR (400 MHz, DMSO) δ 5.47 (s, 2H, CH_2O), 7.10 (d, 1H, ^3J = 8.7 Hz, H3′), 7.16 (d, 2H, ^3J = 8.8 Hz, H3, H5), 7.61−7.65 (m, 1H, H6-quinoline), 7.69 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.77 (d, 1H, ^3J = 15.6 Hz, Hα), 7.77−7.82 (m, 1H, H7-quinoline), 7.81 (d, 1H, ^3J = 15.6 Hz, Hβ), 7.88 (d, 2H, ^3J = 8.8 Hz, H2, H6), 8.00 (d, 1H, ^3J = 8.2 Hz, H5-quinoline), 8.03−8.05 (m, 2H, H4′, H8-quinoline), 8.43 (d, 1H, ^3J = 8.5 Hz, H4-quinoline), 8.55 (d, 1H, ^4J = 2.1 Hz, H6′); ^{13}C NMR (50 MHz, DMSO) δ 70.69 (s), 115.15 (t), 117.64 (t), 119.40 (t), 120.09 (t), 121.51 (q), 121.56 (q), 126.48 (t), 126.99 (q), 127.26 (q), 127.77 (t), 128.25 (t), 129.76 (t), 131.05 (t), 132.05 (t), 135.77 (t), 137.01 (t), 144.68 (t), 146.63 (q), 156.86 (q), 160.33 (q), 163.93 (q), 166.30 (q), 192.50 (q); MS *m*/*z* 425 (M^+). Anal. Calcd for $C_{26}H_{19}NO_5 \cdot 0.3$DMF: C, 72.22; H, 4.75; N, 4.07. Found: C, 72.21; H, 4.69; N, 3.51.

5′-(Carboxyethyl)-2′-hydroxy-4-(2-quinolinylmethoxy)chalcone (11). A mixture of 4-(2-quinolinylmethoxy)benzaldehyde (2 mmol) and 5-(ethoxycarbonyl)-2-hydroxyacetophenone (2 mmol) was stirred in 25 mL of a 7% solution of KOH in ethanol at room temperature for 1 week. The reaction mixture was poured onto ice and acidified with 3 N HCl. The crude product was collected by filtration and purified by recrystallization from ethyl acetate: yield 55%; mp 167.7−168.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (t, 3H, ^3J = 7.1 Hz, $CO_2CH_2CH_3$), 4.41 (q, 2H, ^3J = 7.1 Hz, $CO_2CH_2CH_3$), 5.46 (s, 2H, CH_2O), 7.04 (d, 1H, J = 8.7 Hz, H3′), 7.11 (d, 2H, ^3J = 8.7 Hz, H3, H5), 7.56−7.59 (m, 1H, H6-quinoline), 7.60 (d, 1H, ^3J = 15.3 Hz, Hα), 7.66−7.68 (m, 1H, H7-quinoline), 7.67 (d, 2H, ^3J = 8.7 Hz, H2, H6), 7.74−7.78 (m, 1H, H5-quinoline), 7.84 (d, 1H, ^3J = 8.1 Hz, H8-quinoline), 7.94 (d, 1H, ^3J = 15.3 Hz, Hβ), 8.10 (d, 1H, ^3J = 8.4 Hz, H3-quinoline), 8.15 (dd, 1H, ^3J = 8.7 Hz, ^4J = 2.0 Hz, H4′), 8.22 (d, 1H, ^3J = 8.5 Hz, H4-quinoline), 8.65 (d, 1H, ^4J = 2.0 Hz, H6′), 13.44 (s, 1H, ArOH); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.25 (p), 60.93 (s), 71.26 (s), 115.35 (t), 117.02 (t), 118.47 (t), 118.85 (t), 119.30 (q), 120.97 (q), 126.54 (t), 127.42 (q), 127.57 (t), 128.78 (t), 129.78 (t), 130.76 (t), 131.83 (t), 136.61 (t), 137.01 (t), 146.05 (t), 147.39 (q), 156.87 (q), 160.88 (q), 165.52 (q), 166.97 (q), 193.20 (q); HRMS *m*/*e* (M^+) calcd for $C_{28}H_{23}NO_5$ 453.1576, found 453.1570 ± 0.0006. Anal. ($C_{28}H_{23}NO_5 \cdot {}^1/_6H_2O$) C, H, N.

4′-Carboxy-3′-chloro-2′-hydroxy-4-(2-quinolinylmethoxy)chalcone (12): recrystallization from DMF/ethanol; yield 14%; mp 243−245 °C; ^{1}H NMR (200 MHz, DMSO) δ 5.48 (s, 2H, CH_2O), 7.19 (d, 2H, ^3J = 8.8 Hz, H3, H5), 7.52−8.10 (m, 9H, Hα, Hβ, H2, H6, H3-quinoline, H5-quinoline, H6-quinoline, H7-quinoline, H8-quinoline), 8.17 (d, 1H, ^4J = 2.0 Hz, H4′), 8.44 (d, 1H, ^3J = 8.8 Hz, H4-quinoline), 8.72 (d, 1H, ^4J = 2.0 Hz, H6′), 14.02 (br s, 1H, ArOH); MS *m*/*z* 461 (M^+ for ^{37}Cl), 459 (M^+ for ^{35}Cl). Anal. ($C_{26}H_{18}ClNO_5 \cdot 0.3H_2O$) C, H, N, Cl.

5′-Cyano-2′-hydroxy-4-(2-quinolinylmethoxy)chalcone (13): recrystallization from DMF; yield 88%; mp 192.6−193.8 °C; ^{1}H NMR (400 MHz, DMSO) δ 5.47 (s, 2H, CH_2O), 7.14 (d, 1H, ^3J = 8.7 Hz, H3′), 7.19 (d, 2H, ^3J = 8.8 Hz, H3,

H5), 7.61−7.65 (m, 1H, H6-quinoline), 7.69 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.78−7.84 (m, 1H, H7-quinoline)7.82 (d, 1H, ^3J = 15.5 Hz, Hα), 7.90 (d, 1H, ^3J = 15.5 Hz, Hβ), 7.92 (d, 2H, ^3J = 8.8 Hz, H2, H6), 7.92−7.94 (m, 1H, H4′), 8.00−8.04 (m, 2H, H5-quinoline, H8-quinoline), 8.41 (d, 1H, ^3J = 8.5 Hz, H4-quinoline), 8.71 (d, 1H, ^4J = 2.0 Hz, H6′), 13.07 (br s, 1H, ArOH); ^{13}C NMR (50 MHz, DMSO) δ 70.78 (s), 101.36 (q), 115.16 (t), 118.43 (q), 118.98 (q), 119.26 (t), 119.41 (t), 121.86 (t), 126.46 (t), 126.98 (t), 127.21 (t), 127.75 (t), 128.31 (t), 129.73 (t), 131.26 (t), 135.49 (q), 136.91 (t), 138.10 (q), 145.62 (t), 146.72 (q), 156.85 (q), 160.58 (q), 164.31 (q), 192.00 (q). HRMS *m*/*e* (M^+) calcd for $C_{26}H_{18}N_2O_3$ 406.1317, found 406.1315 ± 0.0005. Anal. ($C_{26}H_{18}N_2O_3$) C, H, N.

2′-Hydroxy-4-(2-quinolinylmethoxy)-5′-(5-tetrazolyl)-chalcone (14): column chromatography using ethyl acetate/petroleum ether (40−60)/acetic acid (10:10:1), recrystallization from DMF; yield 68%; mp 232.7−233.3 °C; ^{1}H NMR (400 MHz, DMSO) δ 5.48 (s, 2H, CH_2O), 7.20 (d, 2H, ^3J = 8.3 Hz, H3, H5), 7.21 (d, 1H, ^3J = 8.2 Hz, H3′), 7.61−7.65 (m, 1H, H6-quinoline), 7.69 (d, 1H, ^3J = 8.4 Hz, H3-quinoline), 7.78−7.82 (m, 1H, H7-quinoline), 7.84 (s, 2H, Hα, Hβ), 7.88 (d, 2H, ^3J = 8.3 Hz, H2, H6), 8.00−8.04 (m, 2H, H5-quinoline, H8-quinoline), 8.15 (d, 1H, ^3J = 8.8 Hz, H4′), 8.43 (d, 1H, ^3J = 8.4 Hz, H4-quinoline), 8.64 (s, 1H, H6′), 12.00 (s, 1H, ArOH); ^{13}C NMR (50 MHz, DMSO) δ 70.66 (s), 115.16 (q), 115.22 (t), 118.67 (t), 119.42 (t), 119.74 (t), 121.93 (q), 126.53 (t), 126.99 (q), 127.24 (q), 127.78 (t), 128.15 (t), 129.25 (t), 129.84 (t), 130.97 (t), 133.57 (t), 137.13 (t), 144.90 (t), 146.51 (q), 156.80 (q), 160.43 (q), 162.63 (q), 192.35 (q); MS *m*/*z* 450 (MH^+). Anal. ($C_{26}H_{19}N_5O_3.1.0H_2O$) C, H, N.

5′-Carboxy-2′-hydroxy-3-(2-quinolinylmethoxy)chalcone (15): recrystallization from DMF/ethanol; yield 10%; mp 190.6−192.4 °C; ^{1}H NMR (400 MHz, DMSO) δ 5.46 (s, 2H, CH_2O), 7.04 (d, 1H, ^3J = 8.7 Hz, H3′), 7.19 (d, 1H, ^3J = 8.4 Hz, H4), 7.19−7.23 (m, 1H, H5), 7.38−7.42 (m, 1H, H6-quinoline), 7.46−7.48 (s, 1H, H2), 7.73 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.75 (d, 1H, ^3J = 15.7 Hz, Hα), 7.77−7.80 (m, 1H, H7-quinoline), 7.96 (d, 1H, ^3J = 15.7 Hz, Hβ), 8.00 (d, 1H, ^3J = 8.5 Hz, H5-quinoline), 8.02−8.06 (m, 2H, H8-quinoline, H4′), 8.44 (d, 1H, ^3J = 8.5 Hz, H4-quinoline), 8.53 (d, 1H, ^4J = 2.0 Hz, H6′); ^{13}C NMR (50 MHz, DMSO) δ 68.21 (s), 114.69 (t), 117.35 (t), 117.59 (t), 120.06 (t), 121.54 (q), 122.12 (q), 122.34 (t), 123.69 (t), 124.42 (t), 127.30 (q), 127.90 (t), 128.34 (t), 130.05 (t), 132.09 (t), 135.72 (t), 135.82 (q), 141.57 (t), 142.16 (q), 143.87 (t), 155.96 (q), 157.89 (q), 163.45 (q), 166.30 (q), 192.41 (q); MS *m*/*z* 425 (M^+). Anal. Calcd for $C_{26}H_{19}NO_5$·1.5AcOH: C, 67.58; H, 4.89; N, 2.72. Found: C, 67.08; H, 4.43; N, 2.75.

5′-Cyano-2′-hydroxy-3-(2-quinolinylmethoxy)chalcone (16): recrystallization from DMF; yield 19%; mp 210.4−211.9 °C; ^{1}H NMR (400 MHz, DMSO) δ 5.42 (s, 2H, CH_2O), 7.16 (d, 1H, ^3J = 8.7 Hz, H3′), 7.21−7.23 (m, 1H, H4), 7.40−7.44 (m, 1H, H5), 7.50−7.52 (m, 1H, H6), 7.61−7.65 (m, 1H, H6-quinoline), 7.71−7.82 (m, 4H, H2, Hα, H3-quinoline, H7-quinoline), 7.94−8.04 (m, 4H, Hβ, H5-quinoline, H8-quinoline, H4′), 8.44 (d, 1H, ^3J = 8.5 Hz, H4-quinoline), 8.68 (s, 1H, H6′), 12.90 (s, 1H, ArOH); ^{13}C NMR (50 MHz, DMSO) δ 70.78 (s), 101.61 (q), 114.81 (t), 117.54 (t), 118.42 (q), 118.91 (t), 119.48 (t), 122.18 (q), 122.33 (t), 122.47 (t), 126.46 (t), 127.00 (q), 127.79 (t), 128.34 (t), 129.74 (t), 129.97 (t), 135.57 (t), 136.90 (t), 138.29 (t), 145.35 (t), 146.75 (q), 157.10 (q), 158.39 (q), 163.90 (q), 174.54 (q), 192.16 (q). Anal. ($C_{26}H_{18}N_2O_3$) C, H, N.

2′-Hydroxy-3-(2-quinolinylmethoxy)-5′-(5-tetrazolyl)-chalcone (17): column chromatography ethyl acetate/petroleum ether (40−60)/acetic acid (10:10:1); crystallized from DMF/ethanol; yield 25%; mp 228.4−229.9 °C; ^{1}H NMR (400 MHz, DMSO) δ 5.45 (s, 2H, CH_2O), 7.20−7.24 (m, 1H, H5), 7.22 (d, 1H, ^3J = 8.6 Hz, H3′), 7.42−7.46 (m, 1H, H6-quinoline), 7.46−7.48 (m, 1H, H4), 7.59−7,63 (m, 1H, H7-quinoline), 7,-64 (s, 1H, H2), 7.72 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.75−7.78 (m, 1H, H6), 7.80 (d, 1H, ^3J = 15.7 Hz, Hα), 7.94 (d, 1H, ^3J = 15.7 Hz, Hβ), 7.99 (d, 1H, ^3J = 7.1 Hz, H5-quinoline), 8.02 (d, 1H, ^3J = 8.5 Hz, H8-quinoline), 8.16 (dd, 1H, ^3J = 8.6 Hz, ^4J = 1.8 Hz, H4′), 8.43 (d, 1H, ^3J = 8.5 Hz, H4-quinoline), 8.61 (d, 1H, ^4J = 1.8 Hz, H6′), 12.32 (s, 1H, ArOH); ^{13}C NMR (50 MHz, DMSO) δ 70.75 (s), 114.75 (t), 115.02 (q), 117.31 (t), 118.63 (t), 119.45 (t), 121.91 (t), 122.51 (q), 123.14 (t), 126.44 (t), 126.99 (q), 127.77 (t), 128.32 (t), 129.35 (t), 129.71 (t), 130.01 (t), 133.57 (t), 135.71 (q), 136.91 (t), 144.40 (t), 146.73 (q), 157.10 (q), 158.39 (q), 162.20 (q), 192.36 (q), 223.66 (q). Anal. ($C_{26}H_{19}N_5O_3$·1.4H_2O) C, H, N.

5′-Carboxy-2′-hydroxy-2-(2-quinolinylmethoxy)chalcone (18): column chromatography ethyl acetate/petroleum ether (40−60)/acetic acid (10:10:1), crystallized from DMF/ethanol; yield 26%; mp 168.9−169.1 °C; ^{1}H NMR (200 MHz, $CDCl_3$, droplet DMSO) δ 5.25 (s, 2H, CH_2O), 6.76 (d, 1H, ^3J = 8.7 Hz, H3′), 6.79−6.82 (m, 2H, H3, H5), 7.10−7.14 (m, 1H, H6-quinoline), 7.27−7.31 (m, 1H, H7-quinoline), 7.44 (d, 1H, ^3J = 8.6 Hz, H3-quinoline), 7.45−7.65 (m, 4H, H4, H6, Hα, H5-quinoline), 7.79 (d, 1H, ^3J = 9.0 Hz, H8-quinoline), 7.89 (dd, 1H, ^3J = 8.7 Hz, ^4J = 1.7 Hz, H4′), 7.99 (d, 1H, ^3J = 8.6 Hz, H4-quinoline), 8.18 (d, 1H, ^3J = 15.5 Hz, Hβ), 8.44 (d, 1H, ^4J = 1.7 Hz, H6′), 13.08 (s, 1H, ArOH); ^{13}C NMR (50 MHz, DMSO): δ 71.07 (s), 113.02 (t), 117.49 (t), 119.09 (t), 121.09 (t), 121.49 (q), 122.32 (q), 122.87 (q), 123.34 (t), 126.46 (t), 126.97 (q), 127.75 (t), 128.33 (t), 128.78 (t), 129.72 (t), 131.92 (t), 132.43 (t), 135.48 (t), 137.01 (t), 138.95 (t), 146.69 (q), 156.86 (q), 156.96 (q), 163.26 (q), 166.27 (q), 192.75 (q); MS *m*/*z* 425 (M^+). Anal. ($C_{26}H_{19}NO_5$·0.8AcOH) C, H, N.

4-(Benzyloxy)-5′-carboxy-2′-hydroxychalcone (19): recrystallization from ethanol: yield 70%; mp 212.1−215.3 °C; ^{1}H NMR (200 MHz, DMSO) δ 5.18 (s, 2H, OCH_2Ph), 7.10 (d, 3H, ^3J = 8.6 Hz, H3′, H3, H5), 7.31−7.49 (m, 5H, Ph), 7.81 (s, 2H, Hα, Hβ), 7.87 (d, 2H, ^3J = 8.6 Hz, H2, H6), 8.05 (dd, 1H, ^3J = 8.6 Hz, ^4J = 1.8 Hz, H4′), 8.57 (d, 1H, ^4J = 1.8 Hz, H6′), 12.81 (br s, 1H, ArOH), 12.92 (br s, 1H, ArCOOH); ^{13}C NMR (50 MHz, DMSO) δ 69.20 (s), 115.07 (t), 117.65 (t), 119.75 (t), 121.44 (q), 121.54 (q), 126.98 (q), 127.57 (t), 127.74 (t), 128.24 (t), 131.02 (t), 132.05 (t), 135.81 (q), 136.37 (t), 144.88 (t), 160.58 (q), 164.04 (q), 166.33 (q), 192.55 (q); HRMS *m*/*e* (M^+) calcd for $C_{23}H_{18}O_5$ 374.1154, found 374.1156 ± 0.0006.

3-(Benzyloxy)-5′-carboxy-2′-hydroxychalcone (20): recrystallization from ethanol; yield 52%; mp 103.4−104.9 °C; ^{1}H NMR (200 MHz, DMSO) δ 5.16 (s, 2H, PhCH_2O), 6.72−7.80 (m, 1H, H5), 7.05−7.08 (m, 1H, H4), 7.32−7.59 (m, 8H, *Ph*CH_2O, Hα, H2, H3′), 7.73 (d, 1H, ^3J = 7.4 Hz, H6), 7.88 (d, 1H, ^3J = 16.2 Hz, Hβ), 7.94−7.98 (m, 2H, H4′, H6′); ^{13}C NMR (50 MHz, DMSO) δ 69.02 (s), 113.91 (t), 115.64 (t), 115.88 (t), 116.72 (t), 119.02 (q), 120.82 (t), 126.51 (q), 127.09 (t), 127.59 (t), 128.21 (t), 129.81 (t), 133.83 (t), 134.56 (t), 136.19 (q), 136.68 (q), 140.87 (t), 158.44 (q), 163.84 (q), 171.06 (q), 190.51 (q); HRMS *m*/*e* (M^+) calcd for $C_{23}H_{18}O_5$ 372.0998, found 372.0997 ± 0.0006. Anal. ($C_{23}H_{18}O_5$·0.4KCl) C, H.

2-(Benzyloxy)-5′-carboxy-2′-hydroxychalcone (21): recrystallization from ethanol: yield 25%; mp 172.1−175.5 °C; ^{1}H NMR (200 MHz, DMSO) δ 5.23 (s, 2H, PhCH_2O), 7.01−7.12 (m, 2H, H3, H5), 7.16−7.53 (m, 7H, H4, H6, Ph), 7.86 (d, 1H, ^3J = 15.8 Hz, Hα), 7.94−8.03 (m, 1H, H4′), 8.11 (d, 1H, ^3J = 15.8 Hz, Hβ), 8.45 (d, 1H, ^4J = 1.9 Hz, H6′); ^{13}C NMR (50 MHz, DMSO) δ 69.55 (s), 112.97 (t), 117.54 (t), 120.82 (t), 121.51 (q), 122.03 (q), 122.74 (q), 122.82 (t), 127.36 (t), 127.75 (t), 128.32 (t), 128.84 (t), 131.88 (t), 132.42 (t), 135.59 (t), 136.40 (q), 139.24 (t), 157.21 (q), 163.46 (q), 166.31 (q), 192.81 (q); HRMS *m*/*e* (M^+) calcd for $C_{23}H_{18}O_5$ 374.1154, found 374.1153 ± 0.0006.

2′-Hydroxy-3-(2-naphthylmethoxy)-5′-(5-tetrazolyl)-chalcone (22): recrystallization from DMF/ethanol; yield 53%; mp 217−218 °C; ^{1}H NMR (200 MHz, DMSO) δ 5.36 (s, 2H, CH_2O), 7.15−7.25 (m, 2H, H3′, H4), 7.37−7.66 (m, 6H, H-arom), 7.76−8.05 (m, 6H, Hα, Hβ, H-arom), 8.17 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.0 Hz, H4′), 8.63 (d, 1H, ^4J = 2.0 Hz, H6′), 12.37 (br s, 1H, ArOH); MS *m*/*z* 448 (M^+). Anal. ($C_{27}H_{20}N_4O_3$) C, H, N.

2′-Hydroxy-4-(2-naphthylmethoxy)-5′-(5-tetrazolyl)-chalcone (23): recrystallization from DMF/ethanol; yield 44%; mp 256−258 °C; ^{1}H NMR (200 MHz, DMSO) δ 5.40 (s, 2H, CH_2O), 7.20 (d, 2H, ^3J = 8.8 Hz, H3, H5), 7.22 (d, 1H, ^3J = 8.8 Hz, H3′), 7.40−7.67 (m, 3H, Ar-H), 7.86−8.03 (m, 8H, Hα, Hβ, 6Ar-H), 8.16 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.0 Hz, H4′), 8.67 (d, 1H, ^4J = 2.0 Hz, H6′), 12.66 (s, 1H, ArOH); MS *m*/*z* 448 (M^+). Anal. ($C_{27}H_{20}N_4O_3$·$^1/_3H_2O$) C, H, N.

2′-Hydroxy-4-[(1-methyl-2-1*H*-benzimidazolyl)methoxy]-5′-(5-tetrazolyl)chalcone (24): recrystallization from DMF/

ethanol; yield 61%; mp 248−250 °C; ^{1}H NMR (400 MHz, DMSO) δ 3.98 (s, 3H, NCH_3), 5.70 (s, 2H, CH_2O), 7.23 (d, 1H, ^3J = 8.7 Hz, H3′), 7.29 (d, 2H, ^3J = 8.6 Hz, H3, H5), 7.41−7.48 (m, 2H, H5-benzimidazole, H6-benzimidazole), 7.77 (d, 1H, ^3J = 7.9 Hz, H4/7 benzimidazole), 7.81 (d, 1H, ^3J = 8.0 Hz, H4/7 benzimidazole), 7.87 (d, 1H, ^3J = 15.5 Hz, Hα), 7.95−8.00 (m, 1H, Hβ), 8.01 (d, 2H, ^3J = 8.8 Hz, H2, H6), 8.20 (dd, 1H, ^3J = 8.6 Hz, ^4J = 1.5 Hz, H4′), 8.85 (d, 1H, ^4J = 1.5 Hz, H6′), 12.70 (s, 1H, ArOH); MS *m*/*z* 452 (M^+). Anal. ($C_{25}H_{20}N_6O_3 \cdot 1.3H_2O$) C, H, N.

4-[(1-Ethoxyethyl)-2-1*H*-benzimidazolyl)methoxy]-2′-hydroxy-5′-(5-tetrazolyl)chalcone (25): recrystallization from DMF/ethanol; yield 42%; mp 234−236 °C; ^{1}H NMR (200 MHz, DMSO) δ 1.01 (t, 3H, ^3J = 6.8 Hz, OCH_2CH_3), 3.42 (q, 2H, ^3J = 6.8 Hz, OCH_2CH_3), 3.74−3.90 (m, 2H, NCH_2CH_2O), 4.69−4.84 (m, 2H, NCH_2CH_2O), 5.84 (s, 2H, CH_2O), 7.24 (d, 2H, ^3J = 8.7 Hz, H3, H5), 7.31 (d, 1H, ^3J = 8.8 Hz, H3′), 7.45−7.67 (m, 2H, H6-benzimidazole, H5-benzimidazole), 7.78−8.35 (m, 7H, Hα, Hβ, H2, H6, H4-benzimidazole, H7-benzimidazole), 9.08 (d, 1H, ^4J = 2.0 Hz, H6′), 12.91 (s, 1H, ArOH). Anal. ($C_{28}H_{26}N_6O_4 \cdot DMF \cdot HCl \cdot 0.3H_2O$) C, H, N, Cl.

3-[(1-Ethoxyethyl)-2-1*H*-benzimidazolyl)methoxy]-2′-hydroxy-5′-(5-tetrazolyl)chalcone (26): recrystallization from DMF/ethanol; yield 67%; mp 234−236 °C; ^{1}H NMR (200 MHz, DMSO) δ 0.98 (t, 3H, ^3J = 7.3 Hz, OCH_2CH_3), 3.43 (q, 2H, ^3J = 7.3 Hz, OCH_2CH_3), 3.86 (t, 2H, J = 4.9 Hz, NCH_2CH_2O), 4.86 (t, 2H, ^3J = 4.9 Hz, NCH_2CH_2O), 5.96 (s, 2H, CH_2O), 7.26 (d, 1H, ^3J = 8.7 Hz, H3′), 7.28−7.33 (m, 1H, H4), 7.45−7.67 (m, 4H, Ar-H), 7.80−8.08 (m, 4H, Hα, Ar-H), 8.29 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.4 Hz, H4′), 8.37 (d, 1H, ^3J = 15.6 Hz, Hβ), 9.20 (d, 1H, ^4J = 2.0 Hz, H6′), 12.78 (s, 1H, ArOH). Anal. ($C_{28}H_{26}N_6O_4 \cdot HCl \cdot {}^2/_3EtOH$) C, H, N, Cl.

4′-Carboxy-4-[(1-ethoxyethyl)-2-1*H*-benzimidazolyl]-2′-hydroxychalcone (27): recrystallization from DMF/ethanol; yield 38%; mp 222−225 °C; ^{1}H NMR (200 MHz, DMSO) δ 1.01 (t, 3H, ^3J = 7.0 Hz, OCH_2CH_3), 3.37 (q, 2H, ^3J = 7.0 Hz, OCH_2CH_3), 3.71 (t, 2H, ^3J = 4.9 Hz, NCH_2CH_2O), 4.50−4.54 (m, 2H, NCH_2CH_2O), 5.55 (s, 2H, CH2O), 7.20−7.26 (m, 2H, H5-benzimidazole, H6-benzimidazole), 7.22 (d, 2H, ^3J = 8.6 Hz, H3, H5), 7.47−7.50 (m, 2H, H3′, H5′), 7.65−7.70 (m, 2H, H4-benzimidazole, H7-benzimidazole), 7.80 (s, 2H, Hα, Hβ), 7.89 (d, 2H, ^3J = 8.6 Hz, H2, H6), 8.17 (d, 1H, ^3J = 8.7 Hz, H6′), 12.15 (s, 1H, ArOH), 13.34 (br s, 1H, $ArCO_2H$); MS *m*/*z* 486 (M^+). Anal. ($C_{28}H_{26}N_2O_5$) C, H, N.

3′-Carboxy-5′-chloro-3-[(1-ethoxyethyl)-2-1*H*-benzimidazolyl]-2′-hydroxychalcone (28): recrystallization from DMF/ethanol; yield 42%; mp 206−208 °C; ^{1}H NMR (200 MHz, DMSO) δ 1.00 (t, 3H, ^3J = 7.3 Hz, OCH_2CH_3), 3.39 (q, 2H, ^3J = 7.3 Hz, OCH_2CH_3), 3.75 (t, 2H, ^3J = 5.4 Hz, NCH_2CH_2O), 4.59 (t, 2H, ^3J = 4.9 Hz, NCH_2CH_2O), 5.60 (s, 2H, CH_2O), 7.16−7.20 (m, 1H, H4), 7.30−7.48 (m, 4H, Ar-H), 7.53−7.81 (m, 5H, Hα, Hβ, Ar-H), 7.83 (d, 1H, ^4J = 2.9 Hz, H4′/6′), 7.93 (d, 1H, ^4J = 2.5 Hz, H4′/6′); MS *m*/*z* 522 (M^+ for ^{37}Cl), 520 (M^+ for ^{35}Cl). Anal. ($C_{28}H_{25}ClN_2O_6$) C, H, N, Cl.

4-(2-1*H*-Benzothiazolylmethoxy)-2′-hydroxy-5′-(5-tetrazolyl)chalcone (29): recrystallization from DMF/ethanol; yield 18%; mp 244−247 °C; ^{1}H NMR (200 MHz, DMSO) δ 5.74 (s, 2H, CH_2O), 7.24 (d, 1H, ^3J = 8.8 Hz, H3′), 7.25 (d, 2H, ^3J = 8.7 Hz, H3, H5), 7.45−7.61 (m, 2H, H5-benzothiazole, H6-benzothiazole), 7.87 (s, 2H, Hα, Hβ), 7.92 (d, 2H, ^3J = 8.7 Hz, H2, H6), 8.05 (d, 1H, ^3J = 7.2 Hz, H4-benzothiazole), 8.14−8.20 (m, 2H, H4′, H7-benzothiazole), 8.66 (d, 1H, ^4J = 2.1 Hz, H6′), 12.57 (s, 1H, ArOH); MS *m*/*z* 455 (M^+). Anal. Calcd for $C_{24}H_{17}N_5O_3S$: C, 63.28; H, 3.76; N, 15.38; S, 7.04. Found: C, 62.53; H, 4.28; N, 14.75; S, 9.08.

4-[(7-Chloro-2-quinolinyl)methoxy]-2′-hydroxy-5′-(5-tetrazolyl)chalcone (30). To a solution of 2-hydroxy-5-(5-tetrazolyl)acetophenone (231 mg, 1.13 mmol) and 4-[(7-chloro-2-quinolinyl)methoxy]benzaldehyde (300 mg, 1.01 mmol) in 2 mL of ethanol and 1 mL of water was added KOH (56.5 mg, 1.01 mmol). The mixture was refluxed for 2 days and evaporated. A mixed solvent of chloroform and methanol (10:1 v/v) and 2 N HCl was added to the residue. The aqueous layer was separated and extracted with a mixture of chloroform and methanol (4:1 v/v). The combined organic layers were evaporated, and the product was obtained as a crystalline solid: recrystallization from DMF/ethanol gave 149 mg (0.31 mmol) of the product as yellow needles: yield 23%; mp 173−177 °C; ^{1}H NMR (400 MHz, DMSO) δ 5.49 (s, 2H, CH_2O), 7.19 (d, 2H, ^3J = 8.6 Hz, H3, H5), 7.22 (d, 1H, ^3J = 8.8 Hz, H3′), 7.68 (dd, 1H, ^3J = 8.7 Hz, ^4J = 1.7 Hz, H6-quinoline), 7.75 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.84 (d, 1H, ^3J = 15.4 Hz, Hα), 7.95 (d, 2H, ^3J = 8.5 Hz, H2, H6), 7.97 (d, 1H, ^3J = 15.5 Hz, Hβ), 8.07−8.09 (m, 2H, H5-quinoline, H8-quinoline), 8.19 (dd, 1H, ^3J = 8.7 Hz, ^4J = 1.7 Hz, H4′), 8.51 (d, 1H, ^3J = 8.5 Hz, H4-quinoline), 8.84 (d, 1H, ^4J = 1.7 Hz, H6′), 12.72 (s, 1H, ArOH).

4-[2-(7-Chloro-2-quinolinyl)ethenyl]-2′-hydroxy-5′-(5-tetrazolyl)chalcone (31): obtained as a brown powder after recrystallization from DMF/ether; yield 8%; mp 262−265 °C; ^{1}H NMR (400 MHz, DMSO) δ 7.24 (d, 1H, ^3J = 8.7 Hz, H3′), 7.66−7.70 (m, 3H, H6-quinoline, Hα, H3-quinoline), 7.86−7.91 (m, 3H, H3, H5, H-olefin), 8.02−8.16 (m, 6H, H2, H6, 2H-olefin, H5-quinoline, H8-quinoline), 8.22 (dd, 1H, ^3J = 8.7 Hz, ^4J = 1.7 Hz, H4′), 8.56 (d, 1H, ^3J = 8.6 Hz, H4-quinoline), 8.86 (d, 1H, ^4J = 1.7 Hz, H6′), 12.59 (s, 1H, ArOH).

3′-Carboxy-2′-hydroxy-4-(2-quinolinylmethoxy)chalcone (32): column chromatography ethyl acetate/petroleum ether (40−60)/acetic acid (10:10:1); recrystallization from DMF/ethanol; yield 38%; mp 232.9−235.3 °C; ^{1}H NMR (400 MHz, DMSO) δ 5.44 (s, 2H, CH_2O), 6.78 (t, 1H, ^3J = 7.6 Hz, H5′), 7.14 (d, 2H, ^3J = 8.6 Hz, H3, H5), 7.57 (d, 1H, ^3J = 15.8 Hz, Hα),7.60−7.64 (m, 1H, H6-quinoline), 7.67−7.81 (m, 5H, H7-quinoline, H3-quinoline, H2, H6, H4′/6′), 7.73 (d, 1H, ^3J = 15.8 Hz, Hβ), 7.93−7.95 (m, 1H, H4′/6′), 7.99 (d, 1H, ^3J = 8.2 Hz, H5-quinoline), 8.03 (d, 1H, ^3J = 8.5 Hz, H8-quinoline), 8.42 (d, 1H, ^3J = 8.5 Hz, H4-quinoline); ^{13}C NMR (50 MHz, DMSO) δ 70.96 (s), 115.43 (t), 116.23 (t), 118.86 (q), 119.66 (t), 124.76 (t), 126.73 (t), 126.88 (q), 127.26 (q), 127.28 (q), 128.03 (t), 128.60 (t), 130.00 (t), 130.35 (t), 134.21 (t), 134.59 (t), 137.20 (t), 141.39 (t), 147.00 (q), 157.27 (q), 159.97 (q), 164.02 (q), 170.91 (q), 190.84 (q); MS *m*/*z* 425 (M^+). Anal. ($C_{26}H_{19}NO_5 \cdot 1.1H_2O$) C, H, N.

3′-Carboxy-5′-fluoro-2′-hydroxy-4-(2-quinolinylmethoxy)chalcone (33): column chromatography ethyl acetate/petroleum ether (40−60)/acetic acid (10:10:1); recrystallization from DMF/ethanol; yield 40%; mp 219.5−220.3 °C; ^{1}H NMR (400 MHz, DMSO) δ 5.46 (s, 2H, CH_2O), 7.15 (d, 2H, ^3J = 8.4 Hz, H3, H5), 7.55 (d, 1H, ^3J = 15.7 Hz, Hα), 7.64 (d, 1H, ^3J = 15.7 Hz, Hβ), 7.63−7.66 (m, 1H, H6-quinoline), 7.69 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.75−7.82 (m, 5H, H2, H6, H4′, H6′, H7-quinoline), 8.01 (d, 1H, ^3J = 8.2 Hz, H5-quinoline), 8.04 (d, 1H, ^3J = 8.5 Hz, H8-quinoline), 8.45 (d, 1H, ^3J = 8.5 Hz, H4-quinoline); ^{13}C NMR (50 MHz, DMSO) δ 70.53 (s), 115.17 (t), 116.38 (q, $^3J_{CF}$ = 6.6 Hz), 119.42 (t), 119.90 (t, $^2J_{CF}$ = 24.0 Hz), 121.42 (t, $^2J_{CF}$ = 24.1 Hz), 122.67 (t), 126.56 (t), 127.00 (q), 127.28 (q), 127.55 (q, $^3J_{CF}$ = 5.9 Hz), 127.80 (t), 128.02 (t), 129.90 (t), 130.67 (t), 137.27 (t), 144.11 (t), 146.36 (q), 153.44 (q, $^1J_{CF}$ = 236.9 Hz), 156.70 (q), 156.81 (q), 160.17 (q), 169.66 (q), 190.02 (q); MS *m*/*z* 443 (M^+). Anal. ($C_{26}H_{18}FNO_5 \cdot 1.3HCl$) C, H, N.

3′-Carboxy-5′-chloro-2′-hydroxy-4-(2-quinolinylmethoxy)chalcone (34): recrystallization from THF/ethanol; yield 19%; mp 222.1−222.5 °C; ^{1}H NMR (400 MHz, 335 K, DMSO) δ 5.45 (s, 2H, CH_2O), 7.15 (d, 2H, ^3J = 8.4 Hz, H3, H5), 7.56 (d, 1H, ^3J = 15.7 Hz, Hα), 7.60−7.64 (m, 2H, Hβ, H6-quinoline), 7.68 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.73 (d, 1H, ^3J = 8.4 Hz, H2, H6), 7.77−7.81 (m, 1H, H7-quinoline), 7.85 (br s, 1H, H4′ or H6′), 7.91(br s, 1H, H4′ or H6′), 7.98 (d, 1H, ^3J = 7.9 Hz, H5-quinoline), 8.03 (d, 1H, ^3J = 8.4 Hz, H8-quinoline), 8.41 (d, 1H, ^3J = 8.5 Hz, H4-quinoline); ^{13}C NMR (50 MHz, DMSO) δ 70.83 (s), 115.42 (t), 117.93 (q), 119.67 (t), 121.95 (q), 123.08 (t), 126.80 (t), 127.26 (q), 127.58 (q), 128,06 (t), 128,36 (t) 128.39 (q), 130.12 (t), 130.91 (t), 133.24 (t), 134.16 (t), 137.45 (t), 144.20 (t), 146.72 (q), 157.10 (q), 159.82 (q), 160.41 (q), 169.76 (q), 190.15 (q). Anal. ($C_{26}H_{18}ClNO_5 \cdot 1.3H_2O$) C, H, N.

5′-Bromo-3′-carboxy-2′-hydroxy-4-(2-quinolinylmethoxy)chalcone (35): column chromatography ethyl acetate/petroleum ether (40−60)/acetic acid (10:10:1); recrystallization from DMF/ethanol; yield 59%; mp 233.7−234.2 °C; ^{1}H NMR (200 MHz, DMSO) δ 5.43 (s, 2H, CH_2O), 7.13 (d, 2H, ^3J = 8.6 Hz, H3, H5), 7.60−7.64 (m, 3H, Hα, Hβ, H6-quinoline), 7.68 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.77 (d, 2H, ^3J = 8.6 Hz, H2, H6), 7.76−7.80 (m, 1H, H7-quinoline), 7.98−8.04 (m, 4H,

H4′, H6′, H5-quinoline, H8-quinoline), 8.43 (d, 1H, ^3J = 8.5 Hz, H4-quinoline); ^{13}C NMR (50 MHz, DMSO) δ 70.93 (s), 106.30 (q), 115.41 (t), 119.63 (t),. 121.97 (q), 124.40 (t), 126.70 (t), 127.24 (q), 127.97 (q), 128.02 (t), 128.56 (t), 128.86 (q), 129.98 (t), 130.41 (t), 135.51 (t), 136.10 (t), 137.20 (t), 141.84 (t), 146.95 (q), 157.22 (q), 160.04 (q), 164.16 (q), 169.34 (q), 189.33 (q); MS *m*/*z* 504 (M^+). Anal. ($C_{26}H_{18}BrNO_5 \cdot 0.5H_2O$) C, H, N.

3′-Carboxy-2′-hydroxy-3-(2-quinolinylmethoxy)chalcone (36): recrystallization from DMF; yield 46%; mp 176.9−178.1 °C; ^{1}H NMR (400 MHz, DMSO) δ 5.44 (s, 2H, CH_2O), 7.06 (t, 1H, ^3J = 7.7 Hz, H5′), 7.15−7.18 (m, 1H, H4), 7.37−7.38 (m, 2H, H5, H6), 7.55 (s, 1H, H2), 7.60−7.62 (m, 1H, H6-quinoline), 7.64−7.67 (m, 2H, Hα, Hβ), 7.72 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.76−7.80 (m, 1H, H7-quinoline) 7.92−7.94 (m, 1H, H4′/6′), 7.95−8.02 (m, 3H, H4′/6′, H5-quinoline, H8-quinoline), 8.43 (d, 1H, ^3J = 8.5 Hz, H4-quinoline); ^{13}C NMR (50 MHz, DMSO) δ 70.64 (s), 114.05 (t), 114.86 (q), 117.38 (t), 118.77 (t), 119.50 (t), 121.90 (t), 125.78 (t), 126.48 (t), 126.70 (q), 126.99 (q), 127.79 (t), 128.18 (t), 129.78 (t), 129.96 (t), 134.50 (t), 135.60 (t), 135.83 (q), 137.04 (t), 143.03 (t), 146.57 (q), 157.15 (q), 158.33 (q), 160.32 (q), 171.03 (q), 191.12 (q). Anal. ($C_{26}H_{19}NO_5 \cdot 0.4H_2O$) C, H, N.

3′-Carboxy-5′-chloro-2′-hydroxy-3-(2-quinolinylmethoxy)chalcone (37): recrystallization from DMF/ethanol; yield 57%; mp 175−177 °C; ^{1}H NMR (200 MHz, DMSO) δ 5.46 (s, 2H, CH_2O), 7.15−7.20 (m, 1H, H4′), 7.40 (d, 2H, ^3J = 5.4 Hz, Ar-H), 7.53−8.07 (m, 10H, Hα, Hβ, Ar-H), 8.46 (d, 1H, ^3J = 8.3 Hz, H4-quinoline); MS *m*/*z* 461 (M^+ for ^{37}Cl), 459 (M^+ for ^{37}Cl). Anal. ($C_{26}H_{18}ClNO_5$) C, H, N, Cl.

5′-Bromo-3′-carboxy-2′-hydroxy-3-(2-quinolinylmethoxy)chalcone (38): recrystallization from DMF; yield 29%; mp 185.1−186.0 °C; ^{1}H NMR (400 MHz, DMSO) δ 5.45 (s, 2H, CH_2O), 7.17−7.18 (m, 1H, H4), 7.36−7.39 (m, 2H, H5, H6), 7.56 (s, 1H, H2), 7.62 (d, 1H, ^3J = 15.6 Hz, Hα), 7.61−7.64 (m, 1H, H6-quinoline), 7.66 (d, 1H, ^3J = 15.7 Hz, Hβ), 7.73 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.78−7.82 (m, 1H, H7-quinoline), 8.00 (d, 1H, ^4J = 2.2 Hz, H4′/6′), 8.02−8.05 (m, 2H, H5-quinoline, H8-quinoline), 8.06 (d, 1H, ^4J = 2.2 Hz, H4′/6′), 8.45 (d, 1H, ^3J = 8.5 Hz, H4-quinoline); ^{13}C NMR (50 MHz, DMSO) δ 70.50 (s), 109.30 (q), 114.27 (t), 117.35 (t), 117.42 (q), 119.47 (t), 121.84 (t), 125.49 (t), 126.72 (t), 126.99 (q), 127.79 (t), 127.96 (t), 128.73 (q), 129.87 (t), 129.93 (t), 135.73 (q), 135.89 (t), 136.97 (t), 137.27 (t), 143.78 (t), 146.32 (q), 157.04 (q), 158.28 (q), 159.55 (q), 169.72 (q), 189.86 (q). Anal. ($C_{26}H_{18}BrNO_3 \cdot HCl$) C, H, N, Br.

4′-Carboxy-2′-hydroxy-4-(2-quinolinylmethoxy)chalcone (39): recrystallization from DMF/ethanol; yield 29%; mp 228−231 °C; ^{1}H NMR (200 MHz, DMSO) δ 5.47 (s, 2H, CH_2O), 7.18 (d, 2H, ^3J = 8.8 Hz, H3, H5), 7.45−7.48 (m, 2H, H3′, H5′), 7.63−7.67 (m, 1H, H6-quinoline), 7.70 (d, 1H, ^3J = 8.8 Hz, H3-quinoline), 7.76−7.80 (m, 1H, H7-quinoline), 7.81 (s, 2H, Hα, Hβ), 7.88 (d, 2H, ^3J = 8.8 Hz, H2, H6), 7.99−8.06 (m, 2H, H5-quinoline, H8-quinoline), 8.16 (d, 1H, ^3J = 8.8 Hz, H6′), 8.44 (d, 1H, ^3J = 8.4 Hz, H4-quinoline); MS *m*/*z* 425 (M^+). Anal. ($C_{26}H_{19}NO_5 \cdot 0.5H_2O$) C, H, N.

4′-Carboxy-2′-hydroxy-3-(2-quinolinylmethoxy)chalcone (40): recrystallization from DMF/ethanol; yield 14%; mp 233−234 °C; ^{1}H NMR (200 MHz, DMSO) δ 5.47 (s, 2H, CH_2O), 7.18−7.22 (m, 1H, H4), 7.40 (t, 1H, ^3J = 7.6 Hz, H5), 7.44−7.52 (m, 2H, H3′, H5′), 7.59−7.63 (m, 1H, H6-quinoline), 7.63−7.83 (m, 3H, Hα, Hβ, H7-quinoline), 7.73 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.91−8.06 (m, 4H, H2, H6, H5-quinoline, H8-quinoline), 8.15 (d, 1H, ^3J = 8.8 Hz, H6′), 8.45 (d, 1H, ^3J = 8.5 Hz, H4-quinoline), 11.96 (s, 1H, ArOH), 13.35 (br s, 1H, $ArCO_2H$); MS *m*/*z* 425 (M^+). Anal. ($C_{26}H_{19}NO_5 \cdot 0.2DMF$) C, H, N.

4′-Cyano-4-(2-quinolinylmethoxy)chalcone (41): recrystallization from DMF; yield 54%; mp 172−175 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.47 (s, 2H, CH_2O), 7.18 (d, 2H, ^3J = 8.8 Hz, H3, H5), 7.59−7.63 (m, 1H, H6-quinoline), 7.69 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.67−7.84 (m, 3H, H7-quinoline, Hα, Hβ), 7.92 (d, 2H, ^3J = 8,8 Hz, H2, H6), 7.99−8.14 (m, 3H, Ar-H), 8.39 (d, 1H, ^3J = 9.6 Hz, Ar-H), 8.43 (d, 1H, H4-quinoline), 8.67 (s, 1H, H2′); MS *m*/*z* 390 (M^+). Anal. ($C_{26}H_{18}N_2O_2$) C, H, N.

4′-Cyano-3-(2-quinolinylmethoxy)chalcone (42): recrystallization from DMF; yield 30%; mp 175−177 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.47 (s, 2H, CH_2O), 7.18−7.23 (m, 1H, H4), 7.41 (t, 1H, ^3J = 7.6 Hz, H5), 7.45−7.50 (m, 1H, H6-quinoline), 7.52−7.59 (m, 1H, H7-quinoline), 7.63−7.82 (m, 4H, Ar-H, Hα, Hβ), 8.00−8.17 (m, 4H, Ar-H), 8.41 (d, 1H, ^3J = 6.9 Hz, Ar-H), 8.45 (d, 1H, ^3J = 8.5 Hz, H4-quinoline), 8.70 (s, 1H, H2′); MS *m*/*z* 390 (M^+). Anal. ($C_{26}H_{18}N_2O_2$) C, H, N.

2′-Carboxy-4-(2-quinolinylmethoxy)chalcone (43): recrystallization from DMF/ethanol; yield 83%; mp 238.240 °C; ^{1}H NMR (200 MHz, DMSO) δ 5.55 (s, 2H, CH_2O), 7.05 (d, 1H, ^3J = 16.3 Hz, Hα), 7.13 (d, 2H, ^3J = 8.9 Hz, H3, H5), 7.17 (d, 1H, ^3J = 16.0 Hz, Hβ), 7.47−7.49 (m, 1H, H3′), 7.57−7,60 (m, 1H, H6-quinoline), 7.60−7.95 (m, 4H, H4′, H5′, H6′, H7-quinoline), 7.69 (d, 2H, ^3J = 8.6 Hz, H2, H6), 7.81 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 8.10−8.19 (m, 2H, H5-quinoline, H8-quinoline), 8.66 (d, 1H, ^3J = 8.5 Hz, H4-quinoline); MS *m*/*z* 409 (M^+). Anal. ($C_{26}H_{19}NO_4 \cdot HCl \cdot 0.25DMF$) C, H, N, Cl.

2′-Carboxy-3-(2-quinolinylmethoxy)chalcone (44): recrystallization from DMF/ethanol; yield 28%; mp 131−134 °C; ^{1}H NMR (200 MHz, DMSO) δ 5.54 (s, 2H, CH_2O), 7.13−7.17 (m, 1H, H4), 7.22−7.24 (m, 1H, Hα, Hβ), 7.33−7.37 (m, 2H, H5, H3′), 7.40−7.51 (m, 2H, H4′, H5′), 7.60−7.64 (m, 1H, H6-quinoline), 7.67−7.69 (m, 1H, H6′), 7.67−7.71 (m, 1H, H7-quinoline), 7.84 (d, 1H, ^3J = 8.6 Hz, H3-quinoline), 7.91−7.94 (m, 2H, H2, H6), 8.10−8.19 (m, 2H, H5-quinoline, H8-quinoline), 8.66 (d, 1H, ^3J = 8.5 Hz, H4-quinoline); MS *m*/*z* 409 (M^+). Anal. ($C_{26}H_{19}NO_4 \cdot 0.8H_2O$) C, H, N.

3′-Carboxy-2′-hydroxy-4-[2-(2-quinolinyl)ethenyl]chalcone (45): recrystallization from DMF; yield 53%; mp 267.1−269.2 °C; ^{1}H NMR (400 MHz, 348 K, DMSO) δ 7.04 (t, 1H, ^3J = 7.7 Hz, H5′), 7.56 (d, 1H, ^3J = 16.2 Hz, Hα), 7.55−7.59 (m, 1H, H6-quinoline), 7.66 (d, 1H, ^3J = 15.7 Hz, Ph*CH*=CH-quinoline), 7.72 (d, 1H, ^3J = 15.7 Hz, PhCH=*CH*-quinoline), 7.75 (m, 1H, H7-quinoline), 7.82 (s, 4H, H2, H3, H5, H6), 7.85−7.89 (m, 2H, Hβ, H3-quinoline), 7.93−7.96 (m, 2H, H5-quinoline, H8-quinoline), 8.01−8.04 (m, 2H, H4′, H6′), 8.36 (d, 1H, ^3J = 8.6 Hz, H4-quinoline); ^{13}C NMR (100 MHz, 348 K, DMSO) δ 115.40 (q), 118.20 (t), 119.66 (t), 125.72 (t), 125.92 (t), 126.59 (q), 126.77 (q), 127.35 (t), 125.40 (t), 128.11 (t), 128.76 (t), 129.47 (t), 129.54 (t), 133.21 (t), 134.17 (t), 134.59 (q), 135.02 (t), 136.30 (t), 138.13 (q), 142.10 (t), 147.09 (q), 154.90 (q), 160.47 (q), 170.46 (q), 248.00 (q); MS *m*/*z* 421 (M^+). Anal. ($C_{27}H_{19}NO_4 \cdot 0.2DMF$) C, H, N.

5′-Carboxy-2′-hydroxy-4-[2-(2-quinolinyl)ethenyl]chalcone (46): recrystallization from DMF; yield 26%; mp 257.7−260.0 °C; ^{1}H NMR (400 MHz, DMSO) δ 7.11 (d, 1H, ^3J = 8.6 Hz, H3′), 7.56−7.64 (m, 2H, H6-quinoline, Hα), 7.75−7.79 (m, 1H, H7-quinoline), 7.80−7.84 (m, 3H, Ar*CH*=*CH*Ar, H3-quinoline), 7.89−8.99 (m, 6H, H2, H3, H5, H6, H5-quinoline, Hβ) 8.04 (d, 1H, ^3J = 8.4 Hz, H8-quinoline), 8.06 (dd, 1H, ^3J = 8.6 Hz, ^4J = 2.1 Hz, H4′), 8.39 (d, 1H, ^3J = 8.6 Hz, H4-quinoline), 8.57 (d, 1H, ^4J = 2.1 Hz, H6′), 12.61 (s, 1H, ArOH), 12.93 (br s, 1H, $ArCO_2H$); ^{13}C NMR (50 MHz, DMSO) δ 117.91 (t), 120.09 (t), 121.88 (q), 121.94 (q), 122.93 (t), 126.53 (t), 127.14 (q), 127.87 (t), 127.89 (t), 128.27 (t), 129.81 (t), 130.18 (t), 130.25 (t), 132.47 (t), 133.80 (t), 134.74 (q), 136.19 (t), 137.05 (t), 138.71 (q), 144.17 (t), 147.14 (q), 155.18 (q), 164.10 (q), 166.58 (q), 192.70 (q); MS *m*/*z* 421 (M^+). Anal. ($C_{27}H_{19}NO_4 \cdot 0.3DMF$) C, H, N.

5′-Cyano-2′-hydroxy-3-[2-(2-quinolinyl)ethenyl]chalcone (47): recrystallization from DMF; yield 38%; mp 221.6−222.3 °C; ^{1}H NMR (400 MHz, DMSO) δ 7.20 (d, 1H, ^3J = 8.6 Hz, H3′), 7.59 (t, 1H, ^3J = 7.6 Hz, H5), 7.61−7.65 (m, 1H, H6-quinoline), 7.73 (d, 1H, ^3J = 16.2 Hz, Hα), 7.85−7.97 (m, 5H, H3-quinoline, H7-quinoline, Hβ, H-olefin, H4′), 8.06−8.14 (m, 5H, H-olefin, H4, H6, H5-quinoline, H8-quinoline), 8.31 (s, 1H, H2), 5.58−5.61 (m, 1H, H4-quinoline), 8.69 (s, 1H, H6′), 12.84 (s, 1H, ArOH); ^{13}C NMR (50 MHz, DMSO) δ 101.61 (q), 104.17 (q), 117.96 (q), 118.45 (q), 118.93 (t), 119.54 (t), 119.67 (t), 120.74 (t), 122.96 (q), 122.81 (t), 126.95 (q), 127.76 (t), 127.95 (t), 128.01 (t), 129.25 (t), 129.49 (t), 129.95 (t), 130.93 (t), 131.33 (t), 134.83 (q), 135.54 (t), 136.44 (q), 138.24 (t), 138.76 (t), 144.92 (t), 163.79 (q), 192.08 (q). Anal. ($C_{27}H_{18}N_2O_2 \cdot 1.5HCl$) C, H, N.

2′-Hydroxy-3-[2-(2-quinolinyl)ethenyl]-5′-(5-tetrazolyl)-chalcone (48): column chromatography using ethyl acetate/

petroleum ether (40−60)/acetic acid (10:10:1); recrystallisation from methanol; yield 5%; mp 226.0−228.2 °C; ^{1}H NMR (400 MHz, 300 K, DMSO) δ 7.24 (d, 1H, ^3J = 8.7 Hz, H3′), 7.54−7.59 (m, 2H, H5, H6-quinoline), 7.66 (d, 1H, ^3J = 16.4 Hz, Hα), 7.75−7.79 (m, 1H, H7-quinoline), 7.85−7.91 (m, 3H, H4, H6, H3-quinoline), 7.89 (d, 1H, ^3J = 15.7 Hz, Ph*CH*=CH-quinoline), 7.90 (d, 1H, ^3J = 16.4 Hz, Hβ), 7.96 (d, 1H, ^3J = 7.7 Hz, H5-quinoline), 8.00 (d, 1H, ^3J = 8.5 Hz, H8-quinoline), 8.05 (d, 1H, ^3J = 15.6 Hz, PhCH=*CH*-quinoline), 8.17 (dd, 1H, ^3J = 8.7 Hz, ^4J = 2.1 Hz, H4′), 8.30 (s, 1H, H2), 8.38 (d, 1H, ^3J = 8.5 Hz, H4-quinoline), 8.66 (d, 1H, ^4J = 2.1 Hz, H6′), 12.39 (br s, 1H, ArOH); ^{13}C NMR (50 MHz, DMSO) δ 115.73 (q), 118.81 (t), 119.99 (t), 122.83 (q), 123.57 (t), 126.34 (t), 127.00 (q), 127.48 (t), 127.86 (t), 128.66 (t), 129.31 (t), 129.52 (t), 129.60 (t), 129.80 (t), 129.86 (t), 129.95 (t), 133.33 (t), 133.81 (t), 135.04 (q), 136.64 (t), 137.02 (q), 144.53 (t), 147.65 (q), 154.97 (q), 155.55 (q), 162.28 (q), 192.74 (q); MS *m*/*z* 445 (M^+). Anal. Calcd for $C_{27}H_{19}N_5O_2$·0.6HCl: C, 69.39; H, 4.23; N, 14.98. Found: C, 69.17; H, 4.27; N, 14.22.

3′-Carboxy-2′-hydroxy-3-[2-(2-quinolinyl)ethenyl]chalcone (49): column chromatography using ethyl acetate/petroleum ether (40−60)/acetic acid (10:10:1); recrystallization from DMF; yield 33%; mp 237.2−240.2 °C; ^{1}H NMR (400 MHz, 300 K, DMSO) δ 7.07 (t, 1H, ^3J = 7.7 Hz, H5′), 7.52 (t, 1H, ^3J = 7.7 Hz, H5), 7.57−7.61 (m, 1H, H6-quinoline), 7.63 (d, 1H, ^3J = 16.4 Hz, Hα), 7.70 (d, 1H, ^3J = 15.9 Hz, Ph*CH*=CH-quinoline), 7.75−7.81 (m, 3H, H4, H6, H7-quinoline), 7.81 (d, 1H, ^3J = 15.9 Hz, PhCH=*CH*-quinoline), 7.90 (d, 1H, ^3J = 16.2 Hz, Hβ), 7.91 (d, 1H, ^3J = 8.6 Hz, H3-quinoline), 7.96 (dd, 1H, ^3J = 7.7 Hz, ^4J = 1.8 Hz, H4′/6′), 7.97 (d, 1H, ^3J = 8.2 Hz, H5-quinoline), 8.01 (d, 1H, ^3J = 8.3 Hz, H8-quinoline), 8.04 (dd, 1H, ^3J = 7.7 Hz, ^4J = 1.8 Hz, H4′/6′), 8.20 (s, 1H, H2), 8.40 (d, 1H, ^3J = 8.6 Hz, H4-quinoline); ^{13}C NMR (100 MHz, 300 K, DMSO) δ 115.38 (q), 118.72 (t, C5′), 119.94 (t, C3-quinoline), 126.20 (t, C-olefin), 126.36 (t, C6-quinoline), 126.89 (q), 127.04 (q), 127.23 (t, C2), 127.82 (t, C5-quinoline), 128.28 (t, C8-quinoline), 129.05 (t, C4/6), 129.24 (t, C-olefin), 129.39 (t, C4/6), 129.50 (t, C5), 130.02 (t), C7-quinoline), 133.74 (t, C-olefin), 134.65 (t, C4′/6′), 135.14 (q), 135.60 (t, C4′/6′), 136.88 (q), 136.92 (t, C4-quinoline), 142.99 (t, C-olefin), 147.19 (q), 155.29 (q), 160.76 (q), 171.09 (q), 191.38 (q). Anal. ($C_{27}H_{19}NO_4$) C, H, N.

3′-Carboxy-5′-fluoro-2′-hydroxy-3-[2-(2-quinolinyl)ethenyl]chalcone (50): recrystallization from DMF; yield 50%; mp 275.7−277.1 °C; ^{1}H NMR (400 MHz, 335 K, DMSO) δ 7.53 (t, 1H, ^3J = 7.7 Hz, H5), 7.60 (d, 1H, ^3J = 16.5 Hz, Hα), 7.58−7.62 (m, 1H, H6-quinoline), 7.71 (d, 1H, ^3J = 15.7 Hz, H-olefin), 7.76−7.91 (m, 5H, H-olefin, H4, H6, H7-quinoline), 7.80 (d, 1H, ^3J = 16.5 Hz, Hβ), 7.89−7.93 (m, 2H, H4′, H6′), 7.97 (d, 1H, ^3J = 8.1 Hz, H5-quinoline), 8.03 (d, 1H, ^3J = 8.3 Hz, H8-quinoline), 8.16 (s, 1H, H2), 8.42 (d, 1H, ^3J = 8.5 Hz, H4-quinoline); ^{13}C NMR (100 MHz, 335 K, DMSO) δ 116.68 (q, $^3J_{CF}$ = 8.5 Hz), 119.63 (t, C3-quinoline), 119.81 (t, $^2J_{CF}$ = 24.5 Hz, C4′/6′), 121.13 (t, $^2J_{CF}$ = 24.4 Hz, C4′/6′), 125.81 (t), 126.18 (t), 126.83 (q), 127.11 (t), 127.54 (t), 127.64 (t), 128.22 (q), 128.62 (t), 128.75 (t), 129.12 (t), 129.22 (t), 129.90 (t), 134.00 (t), 134.93 (q), 136.69 (q), 136.99 (t), 143.33 (t), 146.48 (q), 153.40 (q, $^1J_{CF}$ = 239.2 Hz), 154 86 (q), 156.89 (q), 169.52 (q), 190.01 (q); MS *m*/*z* 439 (M^+). Anal. ($C_{27}H_{18}FNO_4$·0.3H_2O) C, H, N, F.

3′-Carboxy-5′-chloro-2′-hydroxy-3-[2-(2-quinolinyl)ethenyl)]chalcone (51): recrystallization from DMF; yield 48%; mp 278.5−280.9 °C; ^{1}H NMR (400 MHz, 335 K, DMSO) δ 7.52 (t, 1H, ^3J = 7.7 Hz, H5), 7.59 (d, 1H, ^3J = 16.2 Hz, Hα), 7.59−7.63 (m, 1H, H6-quinoline), 7.70 (d, 1H, ^3J = 15.9 Hz, Ph*CH*=CH-quinoline), 7.76 (d, 1H, ^3J = 15.9 Hz, PhCH=*CH*-quinoline), 7.76 (d, 1H, ^3J = 8.0 Hz, H4 or H6), 7.79−7.83 (m, 1H, H7-quinoline), 7.81 (d, 1H, ^3J = 8.3 Hz, H4 or H6), 7.89 (d, 1H, ^4J = 2.8 Hz, H4′ or H6′), 7.94 (d, 1H, ^3J = 16.7 Hz, Hβ), 7.95 (d, 1H, ^4J = 2.8 Hz, H4′ or H6′), 7.96 (d, 1H, ^3J = 8.6 Hz, H3-quinoline), 7.99 (d, 1H, ^3J = 7.5 Hz, H5-quinoline), 8.04 (d, 1H, ^3J = 8.3 Hz, H8-quinoline), 8.14 (s, 1H, H2), 8.46 (d, 1H, ^3J = 8.6 Hz, H4-quinoline); ^{13}C NMR (100 MHz, 335 K, DMSO) δ 117.63 (q), 119.62 (t, C3-quinoline), 121.72 (q), 125.99 (t, C-olefin), 126.38 (t, C6-quinoline), 126.85 (q), 127.13 (t, C8-quinoline), 127.20 (t, C2), 127.63 (t, C5-quinoline), 128.03 (t, Cα), 128.36 (q), 128.88 (t, C4 or C6), 129.15 (t, C4 or C6), 129.26 (t, C5), 130.22 (t, C7-quinoline), 132.92 (t, C4′ or C6′), 133.80 (t, C4′ or C6′), 134.66 (t, Cβ), 134.98 (q), 136.59 (q), 137.55 (t, C4-quinoline), 143.23 (t, C-olefin), 145.67 (q), 154.68 (q), 159.51 (q), 169.41 (q), 189.90 (q); MS *m*/*z* 455 (M^+ for ^{35}-Cl). Anal. ($C_{27}H_{18}ClNO_4$) C, H, N, Cl.

5′-Bromo-3′-carboxy-2′-hydroxy-3-[2-(2-quinolinyl)ethenyl)]chalcone (52): recrystallization from DMF; yield 34%; mp 264.1−266.0 °C; ^{1}H NMR (400 MHz, 335 K, DMSO) δ 7.53 (t, 1H, ^3J = 7.8 Hz, H5), 7.59 (d, 1H, ^3J = 16.4 Hz, Hα), 7.58−7.62 (m, 1H, H6-quinoline), 7.69 (d, 1H, ^3J = 15.9 Hz, Ph*CH*=CH-quinoline), 7.75−7.82 (m, 3H, H4, H6, H7-quinoline), 7.77 (d, 1H, ^3J = 16.4 Hz, Hβ), 7.92 (d, 1H, ^3J = 16 Hz, PhCH=*CH*-quinoline), 7.93 (d, 1H, ^3J = 8.5 Hz, H3-quinoline), 7.97−7.99 (m, 1H, H5-quinoline), 7.98 (d, 1H, ^4J = 2.7 Hz, H4′ or H6′), 8.03 (d, 1H, ^3J = 8.5 Hz, H8-quinoline), 8.07 (d, 1H, ^4J = 2.7 Hz, H4′ or H6′), 8.14 (s, 1H, H2), 8.43 (d, 1H, ^3J = 8.5 Hz, H4-quinoline); ^{13}C NMR (100 MHz, 328 K, DMSO) δ 108.63 (q), 118.28 (q), 119.63 (t), 126.06 (t), 126.26 (t), 126.84 (q), 127.16 (t), 127.44 (t), 127.58 (t), 128.38 (t), 128.77 (t), 128.82 (q), 129.08 (t), 129.23 (t), 130.03 (t), 134.29 (t), 135.00 (q), 135.78 (t), 136.50 (t), 136.65 (q), 137.22 (t), 143.09 (t), 146.24 (q), 154.80 (q), 160.21 (q), 169.29 (q), 189.80 (q); MS *m*/*z* 499 (M^+ for ^{79}Br). Anal. Calcd for $C_{27}H_{18}NO_4$: C, 64.81; H, 3.63; N, 2.80; Br, 15.97. Found: C, 64.55; H, 3.60; N, 2.93; Br, 15.49.

3′-Carboxy-2′-hydroxy-5′-methyl-3-[2-(2-quinolinyl)-ethenyl]chalcone (53): recrystallization from DMF; yield 69%; mp 163.2−163.7 °C; ^{1}H NMR (400 MHz, 335 K, DMSO) δ 2.67 (s, 3H, ArCH_3), 7.72 (t, 1H, ^3J = 7.7 Hz, H5), 7.82−8.02 (m, 8H, H6-quinoline, H3-quinoline, Hα, Hβ, 2H-olefin, H4, H6), 8.06−8.09 (m, 1H, H7-quinoline), 8.06−8.09 (m, 1H, H7-quinoline), 8.15−8.31 (m, 4H, H4′, H6′, H5-quinoline, H2), 8.83 (d, 1H, ^3J = 8.6 Hz, H4-quinoline); ^{13}C NMR (50 MHz, DMSO) δ 19.37 (p), 119.35 (t), 124.21 (t), 124.56 (t), 126.00 (t), 126.22 (q), 126.77 (q), 127.37 (t), 127.51 (t), 127.58 (q), 128.02 (t), 129.21 (t), 129.42 (t), 129.69 (t), 131.76 (t), 134.55 (t), 134.96 (q), 135.79 (t), 137.83 (t), 140.37 (t), 142.29 (t), 15;3.39 (q), 153.48 (q), 158.17 (q), 158.18 (q), 170.89 (q), 190.76 (q); MS *m*/*z* 435 (M^+). Anal. Calcd for $C_{28}H_{21}NO_4$·0.8HCl: C, 72.38; H, 4.73; N, 3.01. Found: C, 72.78; H, 4.94; N, 3.57.

5′-*tert*-Butyl-3′-carboxy-2′-hydroxy-3-[2-(2-quinolinyl)-ethenyl)]chalcone (54): column chromatography using ethyl acetate/petroleum ether (40−60)/acetic acid (10:10:1); recrystallization from methanol; ^{1}H NMR (400 MHz, 335 K, DMSO) δ 1.29 (s, 9H, C(CH_3)$_3$), 7.50 (t, 1H, *J* = 7.5 Hz, H5), 7.53−7.60 (m, 1H, H6-quinoline), 7.55 (d, 1H, *J* = 16.4 Hz, Hα), 7.62 (d, 1H, *J* = 16.0 Hz, H-olefin), 7.66−7.68 (d, 1H, H3-quinoline), 7.71 (d, 1H, *J* = 2.9 Hz, H4′ *o*ρ H6′), 7.73−7.79 (m, 2H, H7-quinoline, H4 or H6), 7.86−7.95 (m, 3H, H4 or H6, H5-quinoline, Hβ), 8.01 (br s, 1H, H2), 8.01−8.03 (m, 1H, H8-quinoline), 8.05 (d, 1H, *J* = 2.9 Hz, H4′ or H6′), 8.08 (d, 1H, *J* = 16.0 Hz, H-olefin), 8.34 (d, 1H, *J* = 8.4 Hz, H4-quinoline), 11.55 (s, 1H, ArOH); ^{13}C NMR (50 MHz, DMSO) δ 31.08 (p), 33.37 (q), 119.75 (t), 120.24 (q), 121.59 (t), 125.57 (q), 126.05 (t), 126.84 (q), 127.08 (t), 127.59 (t), 127.98 (t), 128.29 (t), 128.39 (t), 128.45 (t), 128.67 (t), 129.30 (t), 129.48 (t), 129.65 (t), 131.59 (t), 133.32 (t), 135.64 (q), 136.33 (t), 136.73 (q), 139.53 (t), 147.40 (q), 155.28 (q), 163.19 (q), 171.05 (q), 190.50 (q); MS *m*/*z* 477 (M^+). Anal. ($C_{31}H_{27}NO_4$·0.9HCl) C, H, N.

5′-Chloro-3′-cyano-2′-hydroxy-3-[2-(2-quinolinyl)ethenyl]chalcone (55): recrystallization from DMF; yield 29%; mp 231.6−233.3 °C; ^{1}H NMR (400 MHz, DMSO) δ 7.54−7.59 (m, 2H, H5, H6-quinoline), 7.66 (d, 1H, ^3J = 16.3 Hz, Hα), 7.75−7.78 (m, 1H, H7-quinoline), 7.85−8.02 (m, 7H, H3-quinoline, H5-quinoline, H8-quinoline, Hβ, H-olefin, H4, H6), 8.20 (d, 1H, ^3J = 15.5 Hz, H-olefin), 8.23 (d, 1H, ^4J = 2.0 Hz, H4′/H6′), 8.37−8.39 (m, 2H, H2, H4-quinoline), 8.78 (d, 1H, ^4J = 2.0 Hz, H4′/6′); ^{13}C NMR (50 MHz, DMSO) δ 102.88 (q), 114.37 (q), 119.79 (t), 120.88 (t), 122.06 (q), 122.80 (q), 126.13 (t), 126.89 (q), 127.52 (t), 127.43 (t), 129.33 (t), 9.73 (t), 130.01 (t), 130.18 (t), 133.05 (t), 134.53 (q), 135.09 (t), 136.45 (t), 136.88 (q), 138.66 (t), 146.75 (t), 147.42 (q), 155.18 (q), 162.44 (q), 192.35 (q). Anal. ($C_{27}H_{17}ClN_2O_2$·0.3H_2O) C, H, N, Cl.

5′-Chloro-2′-hydroxy-3-[-2-(2-quinolinyl)ethenyl)]-3′-(5-tetrazolyl)chalcone (56): column chromatography using dichloromethane/methanol (10:1); yield 10%; mp >300 °C; ^{1}H NMR (400 MHz, room temperature DMSO) δ 7.51−7.58 (m, 2H, H5, H6-quinoline), 7.63 (d, 1H, ^3J = 16.4 Hz, Hå), 7.74−

7.77 (m, 1H, H7-quinoline), 7.76−7.91 (m, 7H, H3-quinoline, Hβ, 2H-olefin, H4, H6, H4′/6′), 7.94 (d, 1H, ^3J = 7.4 Hz, H5-quinoline), 8.00 (d, 1H, ^3J = 8.4 Hz, H8-quinoline), 8.20 (d, 1H, ^4J = 2.8 Hz, H4′/6′), 8.24 (s, 1H, H2), 8.36 (d, 1H, ^3J = 8.6 Hz, H4-quinoline); ^{13}C NMR (50 MHz, DMSO) δ 117.52 (q), 119.78 (t), 122.550 (q), 125.17 (t), 126.08 (t), 126.86 (q), 127.27 (t), 127.62 t), 128.44 (t), 129.03 (t), 129.17 (t), 129.33 (t), 129.46 (t), 129.68 (t), 129.91 (t), 133.17 (t), 134.89 (q), 136.38 (t), 136.84 (q), 143.60 (t), 143.64 (t), 147.41 (q), 154.93 (q), 155.02 (q), 155.25 (q), 191.05 (q); MS *m*/*z* 479 (M^+). Anal. Calcd for $C_{27}H_{18}ClN_5O_2 \cdot 1.6H_2O$: C, 63.74; H, 4.20; N, 13.77; Cl, 6.97. Found: C, 63.73; H, 3.83; N, 12.83; Cl, 6.37.

5′-(Carboxymethoxy)-2′-hydroxy-3-[2-(2-quinolinyl)-ethenyl]chalcone (57): recrystallization from DMF; yield 38%; mp 220.0−220.9 °C; ^{1}H NMR (400 MHz, 335 K, DMSO) δ (s, 2H, O*CH*$_2$CO$_2$H), 6.79 (d, 1H, ^3J = 9.0 Hz, H3′), 7.23 (dd, 1H, ^3J = 9.0 Hz, ^4J = 2.9 Hz, H4′), 7.60 (t, 1H, ^3J = 7.7 Hz, H5), 7.68 (d, 1H, H = 2.9 Hz, H6′), 7.69−7.73 (m, 1H, H6-quinoline), 7.76 (d,1H, ^3J = 16.4 Hz, Hα), 7.84−7.93 (m, 4H, Hβ, H-olefin, H4/6, H7-quinoline), 8.03 (d, 1H, ^3J = 15.6 Hz, H-olefin), 8.09−8.15 (m, 3H, H4/6, H5-quinoline, H8-quinoline), 8.22 (d, 1H, ^3J = 8.6 Hz, H3-quinoline), 8.24 (br s, 1H, H2), 8.67 (d, 1H, ^3J = 8.6 Hz, H4-quinoline), 11.90 (s, 1H, ArOH); ^{13}C NMR (100 MHz, 335 K, DMSO) δ 65.49 (s), 115.05 (t), 118.67 (t), 119.73 (t), 121.15 (q), 122.93 (t), 123.37 (t), 124.04 (t), 127.23 (q), 127.24 (q), 128.39 (t), 128.65 (t), 128.80 (t), 129.89 (t), 129.95 (t), 130.66 (t), 133.09 (t), 133.13 (t), 135.40 (q), 135.91 (q), 142.54 (t), 143.87 (t), 150.31 (q), 153.22 (q), 156.72 (q), 170.38 (q), 192.94 (q); MS *m*/*z* 451 (M^+). Anal. ($C_{28}H_{21}NO_5 \cdot$HCl) C, H, N.

2′-Hydroxy-3-[2-(2-quinolinyl)ethenyl]-5′-(5-tetrazolyl-)methoxychalcone (58): column chromatography using dichloromethane/methanol (10:1); recrystallization from DMF/ethanol; yield 54%; mp >300 °C; ^{1}H NMR (200 MHz, DMSO) δ 5.27 (s, 2H, CH$_2$O), 6.95 (d, 1H, ^3J = 9.0 Hz, H3′), 7.33 (dd, 1H, ^3J = 9.0 Hz, ^4J = 2.9 Hz, H4′), 7.56−7.61 (m, 2H, H6-quinoline, H5), 7.74 (d, 1H, ^3J = 16.2 Hz, Hα), 7.74−7.78 (m, 1H, H7-quinoline), 7.81−8.03 (m, 7H, Hβ, H4, H6, H-olefin, H5-quinoline, H8-quinoline, H3-quinoline), 8.07 (d, 1H, ^3J = 8.5 Hz, H4-quinoline), 8.45 (br s, 1H, H2), 12.09 (s, 1H, ArOH); ^{13}C NMR (50 MHz, DMSO) δ 62.76 (s), 114.93 (t), 118.44 (t), 120.23 (t), 120.27 (t), 122.29 (t), 124.92 (t), 126.29 (t), 127.12 (q), 127.42 (t), 127.86 (t), 128.69 (t), 129.56 (t), 129.71 (t), 129.80 (t), 129.89 (t), 129.91 (t), 133.41 (t), 135.08 (q), 136.61 (t), 137.11 (q), 144.63 (t), 147.66 (q), 151.10 (q), 155.53 (q), 156.10 (q), 157.37 (q), 193.41 (q). Anal. Calcd for $C_{28}H_{21}N_5O_3 \cdot 4H_2O$: C, 61.44; H, 5.34; N, 12.79. Found: C, 61.90; H, 4.68; N, 12.66.

4′-(Carboxymethoxy)-2′-hydroxy-3-[2-(2-quinolinyl)-ethenyl]chalcone (59): column chromatography using dichloromethane/methanol (10:1); recrystallization from DMF; yield 43%; mp >300 °C; ^{1}H NMR (200 MHz, DMSO) δ 4.22 (s, 2H, O*CH*$_2$CO$_2$H), 6.31 (d, 1H, ^4J = 2.4 Hz, H3′), 6.50 (dd, 1H, ^3J = 9.1 Hz, ^4J = 2.4 Hz, H5′), 7.50−7.65 (m, 3H, H6-quinoline, H5, H-olefin), 7.79−8.04 (m, 8H, H4, H6, H-olefin, Hα, H3-quinoline, H5-quinoline, H7-quinoline, H8-quinoline), 8.10 (d, 1H, ^3J = 15.5 Hz, H-olefin, 8.30 (d, 1H, ^3J = 9.1 Hz, H6′), 8.38−8.42 (m, 2H, H2, H4-quinoline), 13.49 (s, 1H, ArOH); ^{13}C NMR (50 MHz, DMSO) δ 68.11 (s), 101.26 (t), 108.06 (t), 113.01 (q), 119.86 (t), 121.68 (t), 126.08 (t), 127.76 (t), 126.87 (q), 127.63 (t), 128.43 (t), 129.25 (t), 129.39 (t), 129.40 (t), 129.54 (t), 129.71 (t), 132.08 (t), 1433.24 (t), 135.01 (q), 136.41 (t), 136.78 (q), 143.19 (t), 147.44 (q), 155.27 (q), 165.47 (q), 166.21 (q), 168.40 (q), 191.27 (q). Anal. Calcd for $C_{28}H_{21}NO_5 \cdot$HCl: C, 68.93; H, 4.54; N, 2.87. Found: C, 68.36; H, 4.22; N, 2.91.

5′-Carboxy-2′-methoxy-4-(2-quinolinylmethoxy)]chalcone (60): recrystallization from methanol; yield 15%; mp 224−226 °C; ^{1}H NMR (200 MHz, DMSO) δ 3.94 (s, 3H, OCH$_3$), 5.64 (s, 2H, CH$_2$O), 7.18 (d, 2H, ^3J = 8.7 Hz, H3, H5), 7.30 (d, 1H, ^3J = 8.8 Hz, H3′), 7.31 (d, 1H, ^3J = 15.9 Hz, Hβ), 7.76 (d, 2H, ^3J = 8.7 Hz, H2, H6), 7.78−7.82 (m, 1H, H6-quinoline), 7.88−7.92 (m, 1H, H7-quinoline), 7.90 (d, 1H, ^3J = 8.6 Hz, H3-quinoline), 8.01 (d, 1H, ^4J = 2.2 Hz, H6′), 8.11 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.2 Hz, H4′), 8.18 (d, 1H, ^3J = 8.1 Hz, H5-quinoline), 8.27 (d, 1H, ^3J = 8.5 Hz, H8-quinoline), 8.77 Hd, 1H, ^3J = 8.6 Hz, H4-quinoline); MS *m*/*z* 439 (M^+). Anal. ($C_{27}H_{21}NO_5 \cdot$0.95HCl) C, H, N, Cl.

5′-(Carboxymethyl)-2′-methoxy-4-(2-quinolinylmethoxy)chalcone (61): yield 57%; mp 134−136 °C; ^{1}H NMR (200 MHz, DMSO) δ 3.92 (s, 3H, OCH$_3$), 5.54 (s, 2H, CH$_2$O), 7.16−7.20 (m, 1H, H4), 7.30 (d, 1H, ^3J = 8.8 Hz, H3′), 7.34−7.55 (m, 5H, Hα, Hβ, Ar-H), 7.69−7.74 (m, 1H, Ar-H), 7.83 (d, 1H, ^3J = 8.8 Hz, H4′), 7.84−7.93 (m, 1H, Ar-H), 8.03 (d, 1H, ^4J = 2.4 Hz, Ar-H), 8.05−8.18 (m, 3H, Ar-H), 8.63 (d, 1H, J = 8.3 Hz, H4-quinoline). Anal. ($C_{27}H_{22}ClNO_5$) C, H, N.

2′-(*n*-Butyloxy)-5′-carboxy-4-(2-quinolinylmethoxy)-chalcone (62): yield 58%; mp 232−235 °C; ^{1}H NMR (200 MHz, DMSO) δ 0.76 (t, 3H, ^3J = 7.3 Hz, O(CH$_2$)$_3$*CH*$_3$), 1.36 (m, 2H, O(CH$_2$)$_2$*CH*$_2$CH$_3$), 1.54−1.58 (m, 2H, OCH$_2$*CH*$_2$CH$_2$CH$_3$), 4.16 (t, 2H, ^3J = 5.9 Hz, O*CH*$_2$CH$_2$CH$_2$CH$_3$), 5.57 (s, 2H, CH$_2$O), 7.17 (d, 2H, ^3J = 8.8 Hz, H3, H5), 7.27 (d, 1H, ^3J = 8.8 Hz, H3′), 7.36 (d, 1H, ^3J = 16.1 Hz, Hα), 7.53 (d, 1H, ^3J = 16.1 Hz, Hβ), 7.63−8.22 (m, 9H, Ar-H), 8.65 (d, 1H, ^3J = 8.8 Hz, H4-quinoline); MS *m*/*z* 481 (M^+). Anal. ($C_{30}H_{27}NO_5 \cdot$HCl) C, H, N, Cl.

2′-(*n*-Butyloxy)-5′-carboxy-3-(2-quinolinylmethoxy)-chalcone (63): yield 54%; mp 170−173 °C; ^{1}H NMR (200 MHz, DMSO) δ 0.74 (t, 3H, ^3J = 7.1 Hz, O(CH$_2$)$_3$*CH*$_3$), 1.34 (m, 2H, O(CH$_2$)$_2$*CH*$_2$CH$_3$), 1.56−1.76 (m, 2H, OCH$_2$*CH*$_2$CH$_2$CH$_3$), 4.14 (t, 2H, ^3J = 6.3 Hz, O*CH*$_2$CH$_2$CH$_2$CH$_3$), 5.43 (s, 2H, CH$_2$O), 7.07−7.85 (m, 10H, Hα, Hβ, Ar-H), 7.98−8.05 (m, 4H, Ar-H), 8.43 (d, 1H, ^3J = 8.8 Hz, H4-quinoline); MS *m*/*z* 481 (M^+). Anal. ($C_{30}H_{27}NO_5$) C, H, N.

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