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Synthesis of 3-Hydroxy-4-arylquinolin-2-ones Including Viridicatol via a Darzens Condensation – Friedel-Crafts Alkylation Strategy

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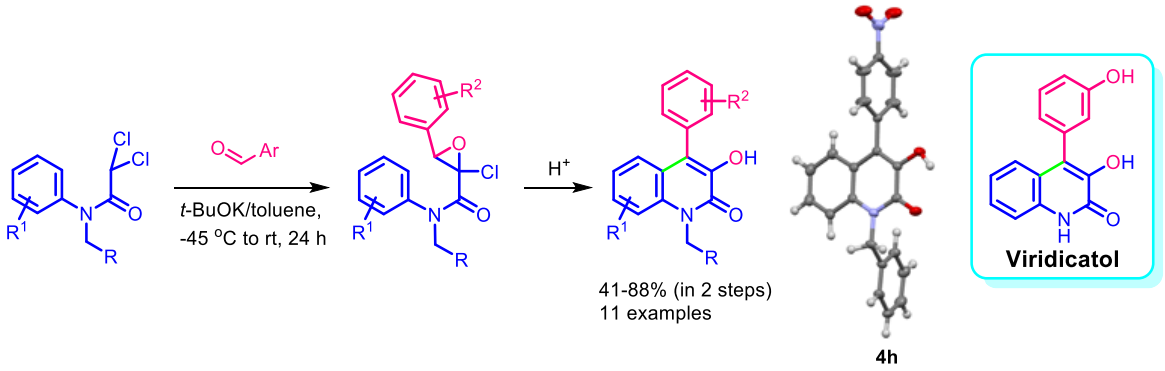
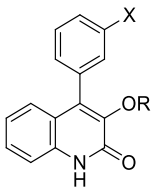
ABSTRACT: The new efficient synthesis of biologically important 3-hydroxy-4-arylquinolin-2-ones through the Darzens condensation (epoxidation) of dichloroacetanilides with aromatic aldehydes followed by one-pot dechlorative epoxide-arene cyclization is described. This methodology has been utilized for the synthesis of naturally occurring viridicatol, a fungal metabolite isolated from penicillium species.



INTRODUCTION

Functionalized 4-arylquinolin-2-ones are a valuable class of biologically active compounds.[1-7] In particular, 3-hydroxy-4-arylquinolin-2-ones, including fungal metabolites viridicatin,[2] viridicatol,[3] and 3-*O*-methylviridicatin,[4] (Fig. 1) have attracted much attention. For example, 3-*O*-methylviridicatin from the fungus *Penicillium puberulum* have been reported by Heguy and co-workers to inhibit the replication of the human immunodeficiency virus (HIV) induced by the tumor necrosis factor (TNF-α) with an IC_{50} of 2.5 μM.[5] Desaubry and co-workers synthesized 3-*O*-methylviridicatin analogues with improved *anti*-TNF-α properties.[6] Furthermore, compounds containing the 3-hydroxyquinolin-2-one skeleton have also been intensively studied as pharmaceutical agents such as the anti-allergy agent TA-270,[7] selective inhibitors of HIV-1 reverse transcriptase,[8] potent D-amino acid oxidase (DAAO)[9] and mitogen-activated protein (MAP) kinase[10] inhibitors, [^{3}H]-glycine binding to rat cortical membranes inhibitors,[11] and maxi-K channel openers with antibacterial activities.[12]

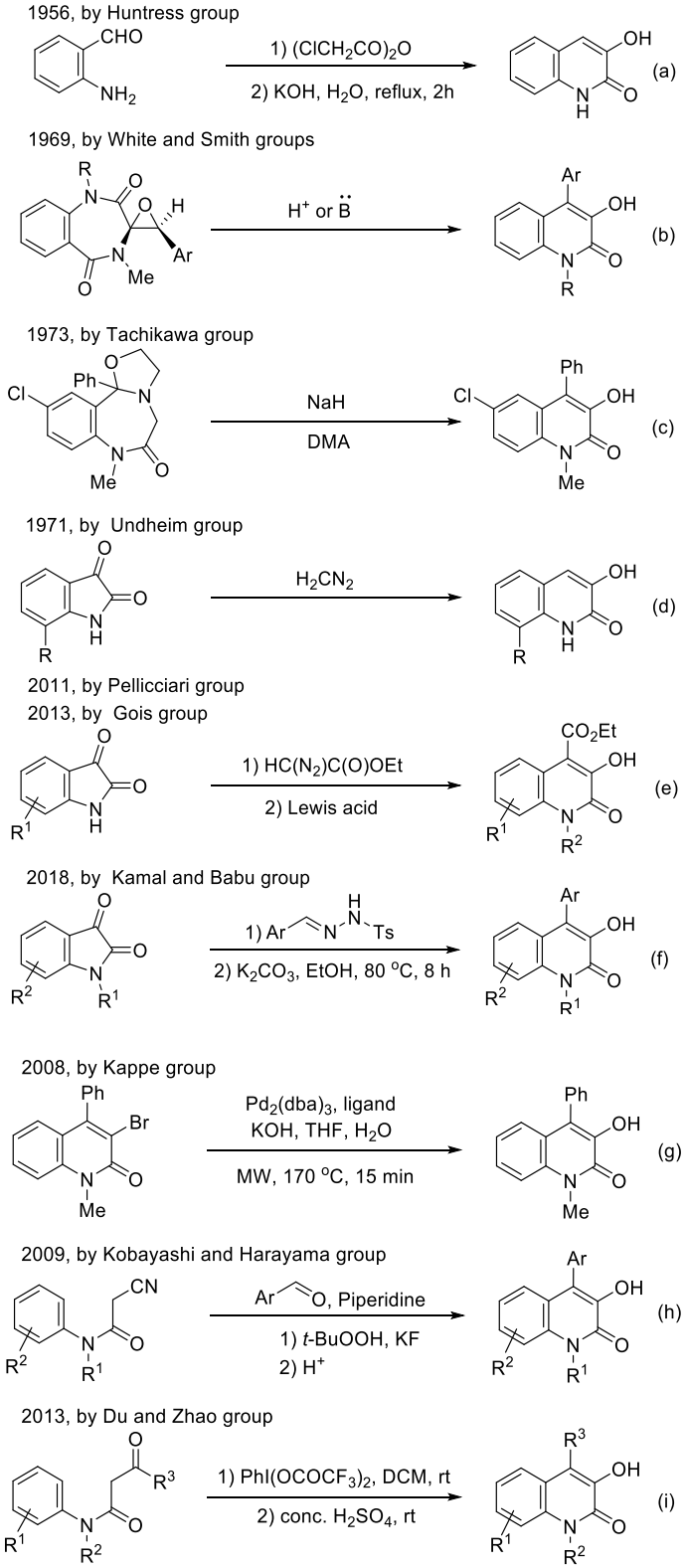


Viridicatin (R = H, X = H)
Viridicatol (R = H, X = OH)
3-*O*-Methylviridicatin (R = Me, X = H)

Figure 1. Representatives of 3-hydroxy-4-arylquinolin-2(1*H*)-ones found in natural products.

However, the synthesis of 3-hydroxy-4-quinolin-2-ones has remained largely unexplored: only a few synthetic strategies have been developed for the construction of the skeleton. The first Friedlander type condensations,[13] was reported by Huntress and co-workers[14] where 2-(*N*-chloroacetamino)benzaldehyde was obtained by the reaction of 2-aminobenzaldehyde with chloroacetic anhydride, which was then converted to 3-hydroxyquinolin-2(1*H*)-one in the presence of a base (Scheme 1a). The transformation of cyclopenin and cyclopenol into viridicatin and viridicatol through a decarboxylation/rearrangement process was realized by White and Smith groups (Scheme 1b).[15] About the rearrangement of benzo[6,7]-1,4-diazepino[5,4-*b*]oxazole derivatives was reported by Tachikawa (Scheme 1c).[16] The condensation process of diazomethane (Scheme 1d)[17] and its derivatives (Scheme 1e)[18] with isatins was realized by Undheim, Pellicciari and Gois groups. Taking into account of the strategy that laid down in the works[17,18] a regioselective ring expansion reaction of isatins with aldehydes promoted by *p*-toluenesulfonylhydrazide has been developed to construct various 3-hydroxy-4-arylquinolin-2(1*H*)-ones, which proceeds via an in situ generated α-aryl/heteroaryldiazomethane was described by Kamal and Babu (Scheme 1f).[19] Kappa and co-workers carried out the Pd-catalyzed coupling reactions (Scheme 1g).[20] An intramolecular annulation reactions of the readily available cyanoacetanilides through a one-pot Knoevenagel condensation/epoxidation of cyanoacetanilides followed by decyanative epoxide-arene cyclization was reported by Kobayashi and Harayama (Scheme 1h).[21] The synthesis from the readily avaible *N*-phenylacetoacetamide derivatives through $PhI(OCOCF_3)_2$-mediated α-hydroxylation and H_2SO_4-promoted intramolecular condensation was demonstrated by Du and Zhao (Scheme 1i).[22] Although the existing methods have their own merits in the preparation of certain 3-hydroxyquinolin-2-one derivatives, the search for a general method that is applicable for the construction of the 3-hydroxyquinolin-2-one ring bearing a variety of substituents would therefore be of significant value.

Scheme 1. Methods for the Synthesis of the 3-Hydroxyquinolin-2-one Skeleton

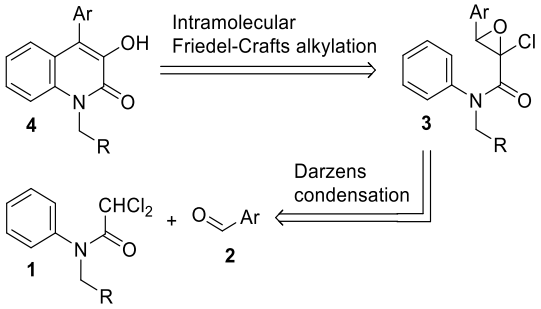


RESULTS AND DISCUSSION

Our strategy for the synthesis of the 3-hydroxy-4-arylquinolin-2-ones is outlined in Scheme 2, where **4** is obtained from **3** via the intramolecular Friedel-Crafts alkylation.[23] In turn, **3** can be prepared from dichloroacetanilides **1** and aromatic aldehydes **2** under the Darzens condensation conditions.[24] We assumed that Cl atom would function not only as an electron-withdrawing group at the condensation step (**1** + **2** → **3**) but also as a leaving group from the epoxide moiety with the intermediate formation of an enolizable ketone group at the cyclization step (**3** → **4**). The salient features of our method are as follows: (1) a variety of dichloroacetanilides **1** and

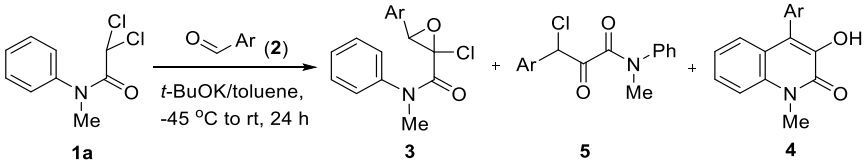
aldehydes **2** are readily available; (2) only two steps are required for the rapid synthesis of **4** with diverse substitution patterns; (3) facile isolation of **4** is accomplished by a simple aqueous workup.

Scheme 2. Strategy for the Synthesis of 3-Hydroxy-4-arylquinolin-2-ones **4**



We first examined the reaction between 2,2-dichloro-*N*-methyl-*N*-phenylacetamide **1a** and aromatic aldehydes having different substituents on the aromatic ring and their various electronic effects (Table 1). It is known, that the nature of substituents in aromatic aldehydes determines the direction of reaction and the structure of the products of Darzens condensation.[24b,25] After a brief survey of reactions under standard Darzens condensation conditions, we found that the desired 2-chloro-3-(3-nitrophenyl)-*N*-methyl-*N*-phenyloxirane-2-carboxamide **3d** was obtained as the sole product in 88% yield when 3-nitrobenzaldehyde **2d** (entry 4) was used. In the case of benzaldehyde **2a** (entry 1) as a carbonyl component for Darzens condensation, the formation of 3-chloro-*N*-methyl-2-oxo-*N*,3-diphenylpropanamide **5a** took place as the main product along with trace amounts of the corresponding oxirane-2-carboxamide **3a** and 3-hydroxy-4-phenylquinolin-2-one **4a**. When 4-chloro- (**2b**) and 4-bromo- (**2c**) benzaldehydes (entries 2, 3) were used as the carbonyl components the reactions proceeded with the formation of 3-(4-chlorophenyl)- (**5b**) and 3-(4-bromophenyl)- (**5c**) 3-chloro-2-oxo-*N*-methyl-*N*-phenylpropionamides as major products with the 3-hydroxyquinolin-2-one derivatives **4b** and **4c** as minor products, respectively.

Table 1. Selection of the Types of Desired Aldehydes **2**



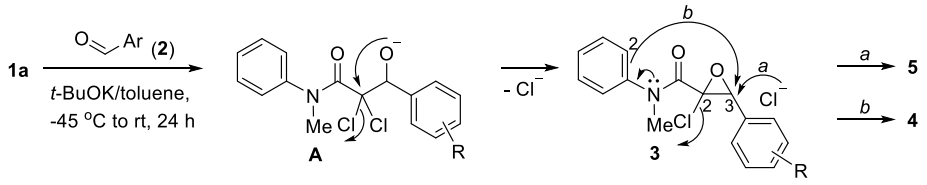
entry	**2** (Ar)	**3** (yield, %)	**5** (yield, %)	**4** (yield, %)
1	**2a** (C_6H_5)	**3a** (traces)[a]	**5a** (86)	**4a** (traces)[a]
2	**2b** (4-ClC_6H_4)	**3b** (0)	**5b** (75)	**4b** (8)
3	**2c** (4-BrC_6H_4)	**3c** (0)	**5c** (80)	**4c** (6)
4	**2d** (3-$O_2NC_6H_4$)	**3d** (88)	**5d** (0)	**4d** (0)

[a] Compounds **3a** and **4a** are detected in NMR ^{1}H spectra of reaction mixtures.
Compounds with underlined numbers were characterized by X-ray diffraction (see SI).

The formation of three types of compounds in different ratios during the course of the reaction of 2,2-dichloro-*N*-methyl-*N*-phenylacetamide **1a** with various aromatic aldehydes **2a-d** is due to the degree of the stability of chloroepoxides **3** formed under the standard Darzens condensation. This stability of chloroepoxides **3** depends on the nature of the substituents in the aromatic ring in position 3 of epoxide ring. The presence of a strong electron-withdrawing nitro group (Table

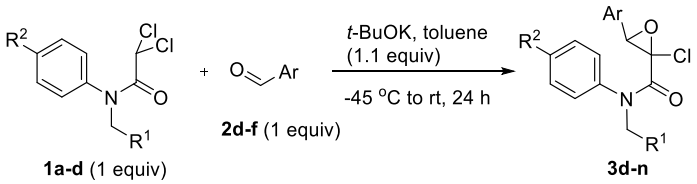
1, entry 4) compensates for the effect of the electron-withdrawing chlorine atom in position 2 of the epoxide ring which increases the stability of the epoxide ring (Scheme 3). In other cases (Table 1, entries 1-3), due to the chlorine atom at position 2 of the epoxide ring, the O-C3 bond is weakened, which makes the C3 atom of the epoxide ring sensitive to nucleophilic attack either by chlorine anion leading to **5**, or by the second carbon atom of an anilide benzene ring with the formation of **4**. With these results, it is evident that to achieve the goal we must use aromatic aldehydes with the strong electron withdrawing groups.

Scheme 3. Proposed Reaction Mechanism for the Darzens Condensaton and the formation of **4** and **5**



With the optimized conditions identified for aromatic aldehydes, we examined the substrate scope of the reaction with respect to the nitrogen (R^1) substituents of dichloroacetanilides **1** (Table 2, entry 1-9). The reaction showed remarkable tolerance to a range of substituents R^1 with markedly different steric and electronic properties in the cases of **1a-c** (R^2 = H). We examined the reactions of the *N*-benzyl and *N*-4-methoxybenzyl derivatives **1b** and **1c** as these can be readily deprotected. Notably, the large-scale reactions can also be conducted easily and inexpensively. For example, the reaction proceeded cleanly and efficiently to afford 7.81 g of **3f** when carried out with 20 mmol (6.48 g) of **1c** (entry 3). To expand the utility of this reaction, we next examined the effect of methyl group in the position 4 of the aromatic ring **1** (entries 10-11). The substituent was found to have no effect on the Darzens condensation, and in these cases the formation of corresponding 3-(3-nitrophenyl)- **(3m)** and 3-(4-cyanophenyl)- **(3n)** 2-chloro-*N*-(4-methoxybenzyl)-*N*-(*p*-tolyl)oxirane-2-carboxamides takes place, respectively, as white light-yellow solids in high yields.

Table 2. Substrate Scope of Dichloroacetanilides **1**

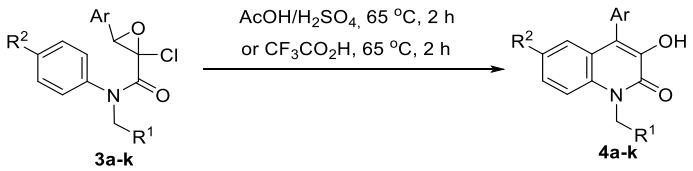


entry	**1**	R^1	R^2	**2**	Ar	product **3**	yield, %
1	**1a**	H	H	**2d**	3-$NO_2C_6H_4$	**3d**	88
2	**1b**	Ph	H	**2d**	3-$NO_2C_6H_4$	**3e**	75
3	**1c**	4-$MeOC_6H_4$	H	**2d**	3-$NO_2C_6H_4$	**3f**	89
4	**1a**	H	H	**2e**	4-$NO_2C_6H_4$	**3g**	71
5	**1b**	Ph	H	**2e**	4-$NO_2C_6H_4$	**3h**	72
6	**1c**	4-$MeOC_6H_4$	H	**2e**	4-$NO_2C_6H_4$	**3i**	87
7	**1a**	H	H	**2f**	4-CNC_6H_4	**3j**	65
8	**1b**	Ph	H	**2f**	4-CNC_6H_4	**3k**	62
9	**1c**	4-$MeOC_6H_4$	H	**2f**	4-CNC_6H_4	**3l**	86
10	**1d**	4-$MeOC_6H_4$	Me	**2d**	3-$NO_2C_6H_4$	**3m**	89
11	**1d**	4-$MeOC_6H_4$	Me	**2f**	4-CNC_6H_4	**3n**	87

Compound with underlined number was characterized by X-ray diffraction (see SI).

The intramolecular Friedel-Crafts alkylation of anilides of arylchloroglycidic acids was carried out according to our strategy (Scheme 2). Cyclization of epoxides **3d-l** took place smoothly to afford the desired quinolinones **4d-l** in 91-99% yields (Table 3). Cyclization of epoxides **3m,n** was complicated by partial isomerization of them to 3-(3-nitrophenyl)- **(5m)** and 3-(4-cyanophenyl)- **(5n)** 3-chloro-2-oxo-*N*-(4-methoxybenzyl)-*N*-(*p*-tolyl)propionamides under the reaction conditions (Fig. 2). Products **4m,n** were isolated by recrystallization from acetone, and products **5m,n** were isolated by evaporating the acetone filtrate followed by flash chromatography on silica gel column using $CHCl_3$ as eluent.

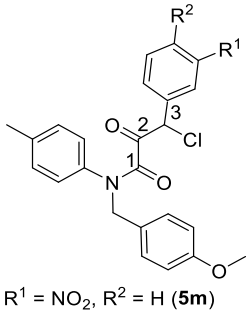
Table 3. Intramolecular Friedel-Crafts Alkylation



entry	R^1	R^2	Ar	**3**	product **4**	yield[a], %
1	H	H	3-$NO_2C_6H_4$	**3d**	**4d**	93 (94)
2	Ph	H	3-$NO_2C_6H_4$	**3e**	**4e**	95 (92)
3	4-$MeOC_6H_4$	H	3-$NO_2C_6H_4$	**3f**	**4f**	99 (91)
4	H	H	4-$NO_2C_6H_4$	**3g**	**4g**	98 (97)
5	Ph	H	4-$NO_2C_6H_4$	**3h**	**4h**	96 (94)
6	4-$MeOC_6H_4$	H	4-$NO_2C_6H_4$	**3i**	**4i**	98 (93)
7	H	H	4-CNC_6H_4	**3j**	**4j**	99 (97)
8	Ph	H	4-CNC_6H_4	**3k**	**4k**	99 (95)
9	4-$MeOC_6H_4$	H	4-CNC_6H_4	**3l**	**4l**	98 (91)
10	4-$MeOC_6H_4$	Me	3-$NO_2C_6H_4$	**3m**	**4m**	46
11	4-$MeOC_6H_4$	Me	4-CNC_6H_4	**3n**	**4n**	48

[a]The products are obtained by two methods.

Compound with underlined number was characterized by X-ray diffraction (see SI).



$R^1 = NO_2$, $R^2 = H$ (**5m**)

$R^1 = H$, $R^2 = CN$ (**5n**)

Figure 2. Representatives of 3-(Aryl)-3-chloro-2-oxo-*N*-(4-methoxybenzyl)-*N*-(*p*-tolyl)propionamides.

The structures of all the compounds (Fig. 3) were established by various 1D/2D NMR correlation methods.[26] First, the proton spin systems of the Ar1 (Q), Ar2 and N-CH_2R moieties were identified by COSY method. The number of NOEs between protons of these fragments allows unequivocally correlate their mutual spatial position and assign exactly protons of Q moiety. Then all corresponding protonated carbons were established by ^{1}H-^{13}C HSQC spectra. And finally, upon ^{1}H-^{15}N HSQC/HMBC connectivities structures of both halves up to C1 and C2 were established in the case of **3** and **5** compounds. Differentiation of **3** *versus* **5** was based on

^{13}C CSs of C1 and C2: while in **5** these carbons resonates in the low field region typical for carbonyl carbons, in **3** the CSs of C2 are at higher fields (77-78 ppm) characteristic for epoxy carbons. GIAO chemical shift calculations[27] strongly supports the above conclusion (see Table 1 in SI).

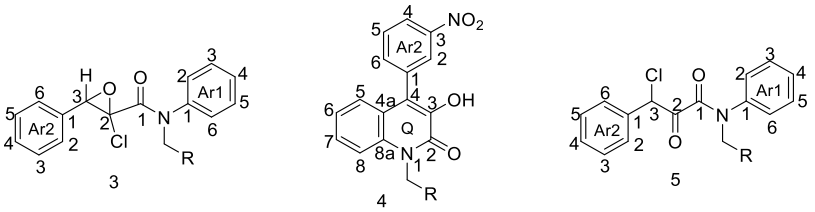
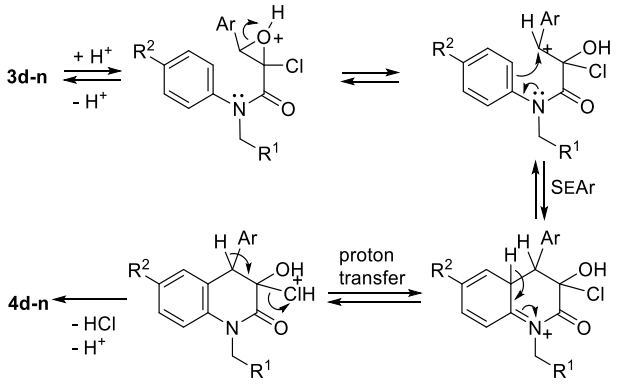


Figure 3. Numbering of Atoms and Designation of Aromatic Fragments in the Structures **3-5**.

The first step of intramolecular Friedel-Crafts alkylation is the protonation of the oxirane oxygen atom of the anilide of arylchloroglycidic acid **3d-n** to a carbocation that undergoes an electrophilic aromatic substitution in the second step. Subsequent proton transfer, elimination of HCl and deprotonation of the carbon atom C4 give rise to the neutral substituted 4-arylquinolinones **4d-n** (Scheme 4).

Scheme 4. Proposed Reaction Mechanism



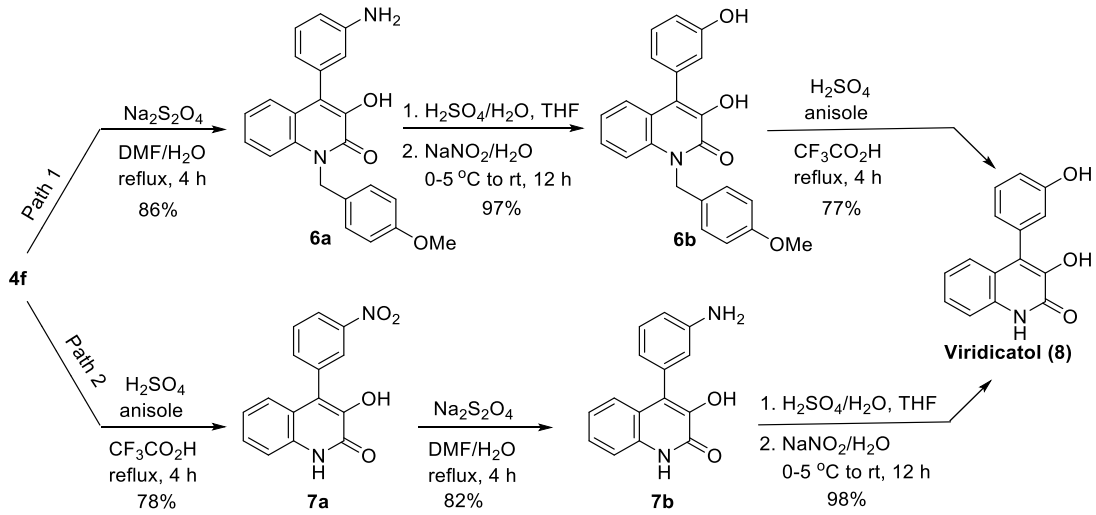
It should be pointed out that the intramolecular cyclization of *N*,3-diaryloxirane-2-carboxamides proceed with the involvement of the acid-catalyzed Meinwald rearrangement in its first stage and the intramolecular Friedel-Crafts alkylation processes in the second stage with the formation of 3-arylquinolin-2(1*H*)-ones,[24b,25,28] but in the present intramolecular cyclization of 2-chloro-*N*,3-diaryloxirane-2-carboxamides **3d-n** the process proceeds directly with the involvement of the intramolecular Friedel-Crafts alkylation with the formation of 4-arylquinolin-2-ones.

Darzens condensation was best performed under mild conditions using *t*-BuOK as the catalyst (equiv amount of *t*-BuOK, toluene, -45 ºC to rt, 24 h), and the intramolecular Friedel-Crafts alkylation proceeded efficiently under optimized conditions (AcOH/H_2SO_4 or CFCOOH, 65 ºC, ~2 h). It was noted that 4-arylquinolin-2-ones **4d-l** in both cases were obtained as solid by simple aqueous workup and did not require the purification, whereas **4n,m** were easily purified by recrystallization from acetone.

Finally, the conversion of the resulting 3-hydroxy-4-(3-nitrophenyl)-*N*-(4-methoxybenzyl)-quinolin-2-one **4f** to quinolinone with a free NH function and OH group in aromatic component was examined (Scheme 5) to obtain viridicatol **8**. Attempts to convert the amino derivative **6b** to viridicatol **8** or the amino derivative **7a** to the hydroxy derivative **7b** using the Bucherer reaction[29] or by heating them with H_3PO_4 at 210 °C,[30] used for similar systems, have not been

successful. We have developed two different sequences of three-step methods for converting **4f** to viridicatol **8**, which in the key stage include the treatment of the amine by an aqueous solution of sodium nitrite in the presence of sulfuric acid. As shown in Scheme 4, there is no principal difference at what stage the protective group is removed, the nitro group is reduced to the amino group and amino group is replaced by the hydroxy group. The total yield in both cases is approximately the same (64 and 63%).

Scheme 5. The Synthesis of Viridicatol



CONCLUSION

In summary, we have demonstrated a new and efficient approach for the synthesis of biologically active 3-hydroxy-4-arylquinolin-2-ones **4** by fully exploiting the chlorooxirane groups[31] of the anilides of arylchloroglycidic acids **3**. Substrates for the reactions are widely available or can be readily prepared, thus greatly enhancing the synthetic potential of the method. The development of synthetic applications is under investigation and will be reported in due course.

EXPERIMENTAL SECTION

General Information. All NMR experiments were performed with 600, 500 and 400 MHz (600.1, 500.1 and 400.1 MHz for ^{1}H NMR; 150.9, 125.7 and 100.6 MHz for ^{13}C NMR; 60.8 and 50.6 MHz for ^{15}N NMR, respectively) spectrometers equipped with 5 mm diameter gradient inverse broad band probehead and a pulsed gradient unit capable of producing magnetic field pulse gradients in the z-direction of 53.5 G cm^{-1}, and were carried out at 303 K. DPFGROE[32] and TOCSY spectra were obtained using Hermite-shaped pulse for selective excitation. Chemical shifts (δ in ppm) are referenced to the solvents DMSO-d_6 (δ = 2.49 ppm for ^{1}H and 39.5 ppm for ^{13}C NMR) and $CDCl_3$ (δ = 7.24 ppm for ^{1}H and 77.0 ppm for ^{13}C NMR), to external CD_3NO_2 (380.2 ppm) for ^{15}N NMR spectra (conversion factor to NH_3: -380.2 ppm). The quantum chemical calculations were performed using a Gaussian 98w software package.[33] Full geometry optimizations have been carried out within the framework of DFT (B3LYP) method using 6-31G(d) basis sets. Chemical shifts (CSs) were calculated by the GIAO method at the same level of theory.[27] All data were referred to TMS (^{13}C) and NH_3 (^{15}N) chemical shifts, which were calculated under the same conditions.

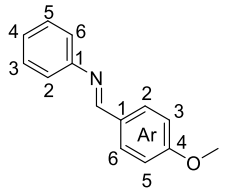
The MALDI mass spectra were recorded on an Ultraflex III TOF/TOF mass spectrometer (Bruker Daltonic GmbH, Bremen, Germany) in the reflection mode with the registration of positively charged ions. Measurement were made in the range m/z 200-1000. The *m*/*z* values of monoisotopic ions are given in the descriptions. Samples were dissolved in DMF or $CHCl_3$ at concentration 4 mg/mL. A solution of the matrix (*p*-nitroaniline, 2.5-dihydroxybenzoic acid) in

acetonitrile at concentration 10 mg/mL was prepared. A calibration mixture of PEG-300 (acetonitrile solution at concentration 1 mg/mL) or crown ethers (methanol solution at concentration 1 mg/mL) were used to obtain high-resolution mass spectra. Samples were deposited by the dried-droplet method. Matrix solution (0.5 mkL), analyte solution (0.5 mkL) and calibration mixture solutions (0.5 mkL) were deposited on the metal target MTP AnchorChip™.

Compounds **1a-d** were prepared by the modification of a literature procedure from dichloroacetylchloride and *N*-methyl-, *N*-benzylanilines or *N*-(4-methoxybenzyl)anilines.[34] *N*-Methyl- and *N*-benzylanilines are commercially available and were used without further purification. *N*-(4-Methoxybenzyl)anilines were prepared in 2 step according to a literature procedure.[20]

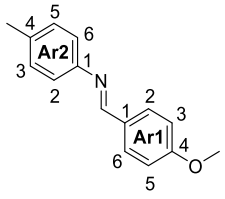
Synthesis of *N*-(4-methoxybenzyl)anilines. *Step 1 (Synthesis of Imines).* To a round-bottom flask, were introduced 4-methoxybenzaldehyde (5.44 g (4.84 mL), 40 mmol) and 60 mL of water. Aniline or *p*-toluidine (40 mmol) was added in one portion and the flask was kept at rt under vigorous stirring for 3 h. The crude precipitate was filtered and dried in air. *Step 2 (Reduction of Imines).* To a stirred solution of the imines (15 mmol) obtained in accordance with the above procedure in MeOH (75 mL) $NaBH_4$ (1.13 g, 30 mmol) was added in portion at 25-32 °C within 10 minutes and the resulting suspension stirred at same temperature for 4 h. The reaction mixture was left overnight at room temperature. The mixture was poured into ice-cold water (200 mL). The precipitate was filtered, washed with water and dried in air.

(4-Methoxybenzyliden)-N-phenylimine.



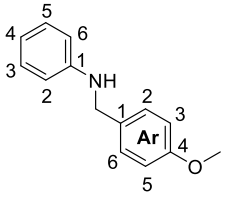
Yield: 7.86 g (93%), light-yellow solid, mp 73-74 °C (45-48 °C;[35] 49.5-50.1 °C;[36] 66-68 °C[37]); IR (KBr): ν_{max} 1603, 1568, 1508, 1248, 1164, 1023, 844, 765, 689 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.89 (s, 3H, OMe), 7.01 (d, J=8.6 Hz, 2H, H2,6-NPh), 7.25 (dd, J=7.3, 7.4 Hz, 1H, H4-NPh); 7.31 (d, J=6.5 Hz, 2H, H3,5-Ar), 7.40 (dd, J=8.4, 7.4 Hz, 2H, H3,5-NPh), 7.98 (d, J=6.3 Hz, 2H, H2,6-Ar), 8.43 (s, 1H, N=CH); Anal. Calcd for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.62; H, 6.18; N, 6.67%.

4-Methoxybenzyliden-N-(4-tolyl)imine.



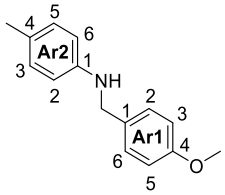
Yield: 8.20 g (91%), white solid, mp 100-101 °C (95-96 °C;[38] 93-94 °C;[39] 83 °C[40]); IR (KBr): ν_{max} 1604, 1569, 1508, 1249, 1166, 1025, 838, 546 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.39 (s, 3H, Me), 3.89 (s, 3H, OMe), 7.00 (d, J=8.9 Hz, 2H, H3,5-Ar_1), 7.18 (d, J=8.2 Hz, 2H, H3,5-Ar_2), J=7.19 (d, J=8.1 Hz, 2H, H2,6-Ar_2), 7.89 (d, J=8.8 Hz, 2H, H2,6-Ar_1), 8.42 (s, 1H, N=CH); Anal. for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.62; H, 6.68; N, 6.38%.

N-(4-methoxybenzyl)aniline.



Yield 3.18 g (99%), white solid, mp 72-73 °C (65-67 °C[41]); IR (KBr): ν_{max} 3419, 1605, 1509, 1250, 753 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.84 (s, 3H, OMe), 4.29 (s, 3H, NCH_2), 6.68 (d, *J*=7.6 Hz, 2H, H2,6-NPh), 6.76 (dd, *J*=7.3, 7.3 Hz, 1H, H4-NPh), 6.92 (d, *J*=8.6 Hz, 2H, H3,5-Ar), 7.22 (ddd, *J*=7.6, 7.4, 0.9 Hz, 2H, H3,5-NPh), 7.33 (d, *J*=8.6 Hz, 2H, H-2,6-Ar). Anal.Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.72; H, 6.98; N, 6.61%.

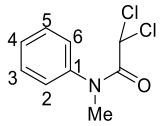
N-(4-methoxybenzyl)-p-toluidine.



Yield 3.34 g (98%), white solid, mp 75-76 °C (82-83 °C[42]); IR (KBr): ν_{max} 3378, 1613, 1510, 1300, 1237, 1179, 1028, 810 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (s, 3H, Me), 3.82 (s, 3H, OMe), 4.25 (s, 3H, NCH_2), 6.62 (d, *J*=8.3 Hz, 2H, H2,6-Ar2), 6.89 (d, *J*=8.6 Hz, 2H, H3,5-Ar1), 7.01 (d, *J*=8.2 Hz, 2H, H3,5-Ar2), 7.31 (d, *J*=8.6 Hz, 2H, H2,6-Ar1); Anal.Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 78.99; H, 7.68; N, 6.31%.

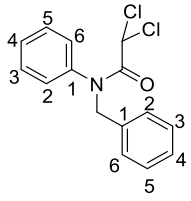
Amidation of 2,2-dichloroacetyl chloride. A solution of 2,2-dichloroacetyl chloride (4.72 g (3.1 mL), 32 mmol) in anhydrous ether (10 mL) was added at 0-5 °C to a stirred mixture of anilines (30 mmol) and Et_3N (3.24 g (4.5 mL), 32 mmol) in ether (150 mL). The reaction mixture was stirred for 2 h without external cooling and then slowly with stirring water (200 mL) was added. The precipitate was filtered, washed with water and dried in air to afford desired amides **1a** and **1b**. Products **1c** and **1d** did not precipitate after treatment of the reaction mixture with water. In this case the organic phase was separated, washed with water (75 mL), dried over Na_2SO_4, filtered, and ether was removed in vacuum to afford the desired amides.

*2,2-Dichloro-N-methyl-N-phenylacetamide (**1a**).*



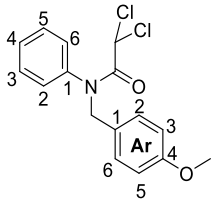
Yield: 5.95 g (91%), white solid, mp 77 °C; IR (KBr): ν_{max} 1687; 1494, 1387, 801, 779, 701, 667, 645, 559 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.36 (s, 3H, NMe), 5.90 (s, 1H, Cl_2CH), 7.30 (dd, *J*=8.1, 1.3 Hz, 2H, H2,6-Ph), 7.43-7.54 (m, 3H, H3,4,5-Ph); Anal. Calcd for $C_9H_9Cl_2NO$: C, 49.57; H, 4.16; Cl, 32.51; N, 6.42. Found: C, 49.52; H, 4.18; Cl, 32.68; N, 6.39%.

*2,2-Dichloro-N-benzyl-N-phenylacetamide (**1b**).*



Yield: 7.85 g (89%), white solid, mp 107-108 °C; IR (KBr): ν_{max} 1677, 1495, 1400, 701 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.93 (s, 2H, NCH_2), 5.86 (s, 1H, Cl_2CH), 7.05-7.45 (m, 10H, 2Ph); Anal. Calcd for $C_{15}H_{13}Cl_2NO$: C, 61.24; H, 4.45; Cl, 24.10; N, 4.76. Found: C, 61.57; H, 4.46; Cl, 24.51; N, 4.42%.

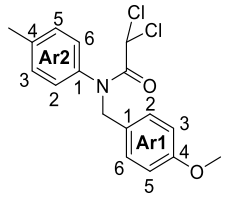
*2,2-Dichloro-N-(4-methoxybenzyl)-N-phenylacetamide (**1c**).*



Yield: 9.43 g (97%), light brown thick oil, crystallizing upon prolonged standing (7 days or more) at room temperature to light brown crystal, mp 58-59 °C; IR: ν_{max} 1683, 1513, 1494, 1404,

1249, 806, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.80 (s, 3H, OMe), 4.85 (s, 2H, NCH_2), 5.82 (s, 1H, Cl_2CH), 6.81 (d, *J*=8.6 Hz, 2H, H3,5-Ar), 7.02 (ddd, *J*=7.8, 5.2, 1.7 Hz, 2H, H2,6-NPh), 7.11 (d, *J*=8.6 Hz, 2H, 2,6-Ar), 7.35-7.45 (m, 3H, H3,4,5-NPh); Anal. Calcd for $C_{16}H_{15}Cl_2NO_2$: C, 59.28; H, 4.66; Cl, 21.87; N, 4.32. Found: C, 59.53; H, 4.58; Cl, 21.53; N, 4.40%.

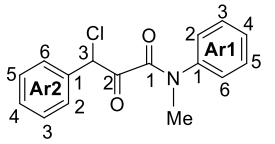
*2,2-Dichloro-N-(4-methoxybenzyl)-N-(4-tolyl)acetamide (**1d**).*



Yield: 9.94 g (98%), light brown thick, IR: ν_{max} 1686, 1613, 1513, 1249, 1177, 1032, 806 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H, Me), 3.80 (s, 3H, OMe), 4.83 (s, 2H, NCH_2), 5.84 (s, 1H, Cl_2CH), 6.81 (d, *J*=8.7 Hz, 2H, H3,5-Ar1), 6.90 (d, *J*=8.0 Hz, 2H, H3,5-Ar_2), 7.11 (d, *J*=8.6 Hz, 2H, 2,6-Ar1), 7.18 (d, *J*=7.9 Hz, 2H, H2,6-Ar2); Anal. Calcd for $C_{17}H_{17}Cl_2NO_2$: C, 60.37; H, 5.07; Cl, 20.96; N, 4.14. Found: C, 60.54; H, 5.36; Cl, 21.03; N, 4.01.

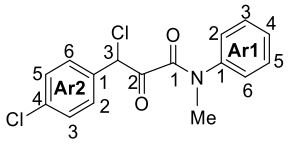
Synthesis of 3-chloro-2-oxo-3-aryl-*N*-methyl-*N*-phenylpropionamides (5a-c). To a stirred solution of 2,2-dichloro-*N*-methyl-*N*-phenylacetamide (**1a)** (3.45 g, 16 mmol) and aldehyde **2a-c** (1.69 g, 16 mmol) in anhydrous toluene (300 mL) under a nitrogen atmosphere *t*-BuOK (2.15 g, 19 mmol) was added in portions at -45 °C within 30 minutes and the resulting suspension stirred at same temperature for 1 h. The reaction mixture was allowed to warm to room temperature for 3 h. The resulting pale-yellow mixture was stirred at this temperature for additional 3 h and left overnight. The reaction mixture was quenched to ice water (300 mL). The organic layer was separated, washed twice with water, brine (2×100 mL), dried over $MgSO_4$ and the solvent was removed in vacuum to give a yellowish viscous liquid, which solidified overnight. In the NMR ^1H spectrum of this mixture along with the main product **5** was detected in small amounts of by-products **3** and **4** (Table 1). By flash chromatography on silica gel column using a mixture of cyclohexane-AcOEt (49/1) as eluent was isolated analytically pure 3-chloro-2-oxo-3-aryl-*N*-methyl-*N*-phenylpropanamides (**5)** and small amounts of 3-hydroxy-4-aryl-*N*-methylquinolin-2-ones (**4)**.

*3-Chloro-2-oxo-3-phenyl-N-methyl-N-phenylpropionamide (**5a**).*



Yield 3.95 g (86%), light-yellow solid, mp 80-81 °C; IR (KBr): ν_{max} 1724, 1642; 1594, 1495, 1097, 730, 722, 696 cm^{-1}; NMR (500 MHz, $CDCl_3$): δ 3.31 (s, 3H, NMe), 6.10 (s, 1H, ClCH), 6.91 (dd, *J*=7.9, 1.7 Hz, 2H, H2,6-Ar1), 7.25-7.32 (m, 5H, H3,4,5-Ar1, H2,6-Ar2), 7.37 (d, *J*=7.3 Hz, 2H, H3,5-Ar2), 7.46 (d, *J*=7.2, 7.2 Hz, 1H, H4-Ar2); $^{13}C\{^1H\}$ NMR (150.9 MHz, $CDCl_3$): δ 189.1 (C2), 164.6 (C1), 140.8 (C1-Ar1), 133.3 (C1-Ar2), 129.33 (C4-Ar2), 129.27 (C3-Ar1), 128.9 (C2-Ar2), 128.8 (C3-Ar2), 128.2 (C4-Ar1), 126.6 (C2-Ar1), 62.6 (C3), 37.1 (NMe); ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 124.4; HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{16}H_{14}ClNO_2Cs$ 419.9762; Found 419.9753.

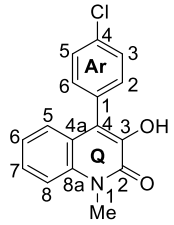
*3-Chloro-2-oxo-3-(4-chlorophenyl)-N-methyl-N-phenylpropionamide (**5b**).*



Yield 5.53 g (75%), light-yellow solid, mp 89-90 °C; IR (KBr): ν_{max} 1725, 1641, 1596, 1495, 1088, 765, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.34 (s, 3H, NMe), 6.01 (s, 1H, ClCH), 7.01 (dd, *J*=7.6, 1.9 Hz, 2H, H2,6-Ar1), 7.18 (d, *J*=8.4 Hz, 2H, H2,6-Ar2), 7.31-7.36 (m, 5H, H3,4,5-

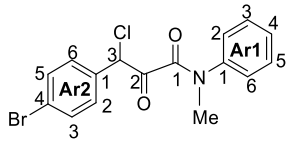
Ar1, H3,5-Ar2); $^{13}C\{^{1}H\}$ NMR (150.9 MHz, $CDCl_3$): δ 189.0 (C2), 164.5 (C1), 140.9 (C1-Ar1), 135.5 (C4-Ar2), 132.0 (C1-Ar2), 130.3 (C2-Ar2), 129.4 (C3-Ar2), 129.1 (C3-Ar1), 128.4 (C4-Ar1), 126.7 (C2-Ar1), 61.5 (C3), 37.2 (NMe); ^{15}N NMR (50.6 MHz, CDCl3): δ 124.6; HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{16}H_{13}Cl_2NO_2Cs$ 453.9372, 455.9345; Found 453.9361, 455.9339.

*3-Hydroxy-4-(4-chlorophenyl)-N-methylquinolin-2-one (**4b**).*



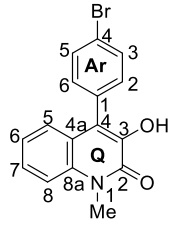
Yield 0.37 g (8%), white solid, mp 242 °C (244-246 °C[22]); IR (KBr): ν_{max} 3247, 1626, 1600, 1270, 754 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ 3.79 (d, *J*=1.2 Hz, 3H, NMe), 7.12 (d, *J*=8.1 Hz, 1H, H5-Q), 7.19 (dd, *J*=8.0, 7.2 Hz, 1H, H6-Q), 7.36 (dd, *J*=8.3, 1.4 Hz, 2H, H2,6-Ar), 7.47 (ddd, *J*=8.5, 7.1, 1.4 Hz, 1H, H7-Q), 7.57 (d, *J*=8.5 Hz, 1H, H8-Q), 7.58 (dd, *J*=8.3, 11.4 Hz, 2H, H3,5-Ar), 9.33 (s, 1H, OH); $^{13}C\{^{1}H\}$ NMR (125.7 MHz, DMSO-d_6): δ 157.9 (C2-Q), 141.8 (C3-Q), 134.3 (C8a-Q), 132.49 (C1-Ar), 132.47 (C4-Ar), 131.8 (C2-Ar), 128.5 (C3-Ar), 126.9 (C7-Q), 124.7 (C5-Q), 122.6 (C6-Q), 121.7 (C4-Q), 121.0 (C4a-Q), 114.8 (C8-Q), 30.0 (NMe); ^{15}N NMR (50.6 MHz, DMSO-d_6): δ 142.3; HRMS (MALDI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{13}ClNO_2$ 286.0629; Found 286.0635.

*3-Chloro-2-oxo-3-(4-bromophenyl)-N-methyl-N-phenylpropionamide (**5c**).*



Yield: 6.72 g (80%), light-yellow solid, mp 81-82 °C; IR (KBr): ν_{max} 1735, 1653; 1593, 1493, 1485, 1070, 780, 700, 508 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.33 (s, 3H, NMe), 5.99 (s, 1H, ClCH), 7.01 (dd, *J*=7.2, 1.3 Hz, 2H, H2,6-Ar1), 7.11 (d, *J*=8.5 Hz, 2H, H2,6-Ar2), 7.30-7.34 (m, 3H, H3,4,5-Ar1), 7.46 (d, *J*=8.5 Hz, 2H, H3,5-Ar2); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 188.9 (C2), 164.4 (C1), 140.8 (C1-Ar1), 132.5 (C1-Ar2), 132.0 (C3-Ar2), 130.4 (C2-Ar2), 129.4 (C3-Ar1), 128.4 (C4-Ar1), 126.6 (C2-Ar1), 123.6 (C4-Ar2), 61.5 (C3), 37.1 (NMe); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{16}H_{13}BrClNO_2Cs$ 497.8867, 499.8846; Found 497.8856, 499.8834.

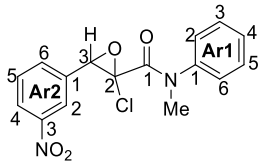
*3-Hydroxy-4-(4-bromophenyl)-N-methylquinolin-2-one (**4c**).*



Yield 0.32 g (6%), white solid, mp 248-250 °C (252-254 °C[20]); IR (KBr): ν_{max} 3240, 1625, 1601, 1270, 754 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ 3.78 (s, 3H, NMe), 7.11 (dd, *J*=8.0, 1.3 Hz, 1H, H5-Q), 7.19 (ddd, *J*=8.0, 7.1, 1.0 Hz, 1H, H6-Q), 7.30 (d, *J*=8.5 Hz, 2H, H2,6-Ar), 7.47 (ddd, *J*=8.5, 7.1, 1.5 Hz, 1H, H7-Q), 7.57 (d, 1H, *J*=8.0 Hz, 1H, H8-Q), 7.71 (d, *J*=8.5 Hz, 2H, H3,5-Ar), 9.34 (s, 1H, OH); $^{13}C\{^{1}H\}$ NMR (125.7 MHz, DMSO-d6): δ 157.9 (C2-Q), 141.8 (C3-Q), 134.3 (C8a-Q), 132.9 (C1-Ar), 132.2 (C2-Ar), 131.4 (C3-Ar), 127.0 (C7-Q), 124.7 (C5-Q), 122.6 (C6-Q), 121.8 (C4-Q), 121.1 (C4a-Q), 121.0 (C4-Ar), 114.8 (C8-Q), 30.0 (NMe); ^{15}N NMR (50.6 MHz, DMSO-d6): δ 141.7; HRMS (MALDI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{13}BrNO_2$ 330.0124, 332.0105; Found 330.0131, 332.0114.

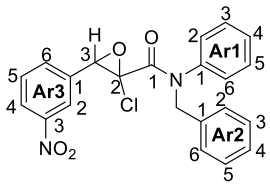
General procedure for the preparation of *N*-substituted 2-chloro-3-aryl-*N*-phenyloxirane-2-carboxamides (3). To a stirred solution of 2,2-dichloroacetamide **1** (20 mmol) and aldehyde **2** (20 mmol) in anhydrous toluene (300 mL) under a nitrogen atmosphere *t*-BuOK (2.45 g, 22 mmol) was added in portions at -45 °C within 30 minutes and the resulting suspension stirred at same temperature for 1 h. The reaction mixture was allowed to reach the room temperature for 5 h. The mixture was stirred at this temperature for additional 3 h and left overnight. The reaction mixture was quenched to ice water (100 mL). The organic layer was separated, washed twice with water, brine (2×100 mL), dried over $MgSO_4$. The organic layer was evaporated under reduced pressure and the oily residue was diluted with dry *i*-PrOH (5 mL) and left at the ambient temperature. During 3-8 h the crystals that precipitated were collected by suction filtration, washed with *i*-PrOH (2×5 mL), dried in air to afford the analytically pure *N*-substituted 2-chloro-3-aryl-*N*-phenyloxirane-2-carboxamides (**3**).

*2-Chloro-3-(3-nitrophenyl)-N-methyl-N-phenyloxirane-2-carboxamide (**3d**).*



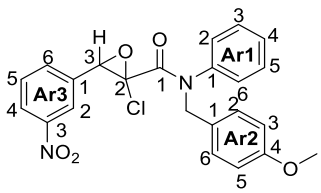
Yield: 5.86 g (88%), yellow solid, mp 146-148 °C; IR (KBr): ν_{max} 1726, 1655, 1532, 1352, 699 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 3.39 (s, 3H, NMe), 4.18 (s, 1H, H3), 7.31 (d, *J*=7.7 Hz, 1H, H6-Ar2), 7.39 (d, *J*=4.3 Hz, 2H, H2,6-Ar1), 7.46 (dd, *J*=7.9, 8.0 Hz, 1H, H5-Ar2), 7.50 (c, 1H, H2-Ar2), 7.52-7.57 (m, 3H, H3,4,5-Ar2), 8.14 (d, *J*=8.2 Hz, 1H, H4-Ar3); $^{13}C\{^1H\}$ NMR (150.9 MHz, $CDCl_3$): δ 162.9 (C1), 147.8 (C3-Ar2), 141.5 (C1-Ar1), 133.2 (C1-Ar2), 132.7 (C6-Ar2), 130.0 (C3-Ar1), 128.98 (C4-Ar1), 128.95 (C5-Ar2), 127.5 (C2-Ar1), 123.8 (C4-Ar2), 122.0 (C2-Ar2), 77.3 (C2), 63.0 (C3), 38.2 (NMe); ^{15}N NMR (60.8 MHz, $CDCl_3$): δ 368 (NO_2), 122 (N1); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{16}H_{13}ClN_2O_4Cs$ 464.9613; Found 464.9632.

*2-Chloro-3-(3-nitrophenyl)-N-benzyl-N-phenyloxirane-2-carboxamide (**3e**).*



Yield: 6.13 g (75%), light-yellow solid, mp 124-126 °C; IR (KBr): ν_{max} 1672, 1531, 1352, 702 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 4.22 (s, 1H, H3), 4.86, 5.06 (AB, *J*=14.3 Hz, 2H, CH_2), 7.17 (d, *J*=7.6 Hz, 2H, H2,6-Ar1), 7.23 (dd, *J*=7.6, 2.4 Hz, 2H, H2,6-Ar2), 7.28-7.35 (m, 4H, H3,4,5-Ar2, H6-Ar3), 7.43-7.52 (m, 5H, H3,4,5-Ar1, H2,5-Ar3), 8.14 (d, *J*=8.2 Hz, 1H, H4-Ar3); $^{13}C\{^1H\}$ NMR (150.9 MHz, $CDCl_3$): δ 162.9 (C1), 147.8 (C3-Ar3), 139.7 (C1-Ar1), 135.8 (C2-Ar2), 133.2 (C1-Ar3), 132.7 (C6-Ar3), 129.7 (C3-Ar1), 129.2 (C5-Ar3), 128.94 (C4-Ar1), 128.90 (C2-Ar2), 128.8 (C2-Ar1), 128.6 (C3-Ar2), 127.9 (C4-Ar2), 123.8 (C4-Ar3), 122.0 (C2-Ar3), 77.6 (C2), 63.1 (C3), 54.0 (CH_2); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{22}H_{17}ClN_2O_4Cs$ 540.9926; Found 540.9909.

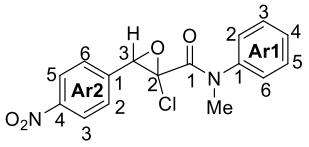
*2-Chloro-3-(3-nitrophenyl)-N-(4-methoxybenzyl)-N-phenyloxirane-2-carboxamide (**3f**).*



Yield: 7.81 g (89%), tan solid, mp 106-107 °C; IR (KBr): ν_{max} 1671, 1528, 1515, 1350, 1254, 703 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 3.80 (s, 3H, OMe), 4.21 (s, 1H, H3), 4.80, 4.99 (AB, *J*=14.1 Hz, 2H, CH_2), 6.82 (d, *J*=8.7 Hz, 2H, H3,5-Ar2), 7.14 (d, *J*=8.8 Hz, 2H, H2,6-Ar2), 7.15 (d, *J*=9.7 Hz, 2H, H2,6-Ar1), 7.30 (d, *J*=7.6 Hz, 1H, H6-Ar3), 7.43-7.52 (m, 5H, H3,4,5-Ar1,

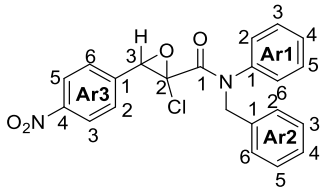
H2,5-Ar3), 8.14 (d, *J*=8.2 Hz, H4-Ar3); $^{13}C\{^{1}H\}$ NMR (150.9 MHz, $CDCl_3$): δ 162.7 (C1), 159.3 (C4-Ar2), 147.7 (C3-Ar3), 139.6 (C1-Ar1), 133.2 (C1-Ar3), 132.6 (C2-Ar2), 130.3 (C2-Ar2), 129.6 (C3-Ar1), 129.1 (C5-Ar3), 128.9 (C2-Ar1+C4-Ar1), 127.9 (C1-Ar2), 123.7 (C4-Ar3), 121.9 (C2-Ar3), 113.9 (C3-Ar2), 77.6 (C2), 63.0 (C3), 55.1 (OMe), 53.4 (CH_2); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{23}H_{19}ClN_2O_5Cs$ 571.0031; Found 571.0046.

*2-Chloro-3-(4-nitrophenyl)-N-methyl-N-phenyloxirane-2-carboxamide (**3g**).*



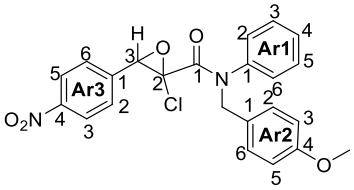
Yield: 4.72 g (71%), tan solid, mp 141-143 °C; IR (KBr): ν_{max} 1671, 1520, 1346, 956, 705 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.39 (s, 3H, NMe), 4.20 (s, 1H, H3), 7.03 (d, *J*=8.4 Hz, 2H, H2,6-Ar2), 7.39 (d, *J*=7.4 Hz, 2H, H2,6-Ar1), 7.46-7.56 (m, 3H, H3,4,5-Ar1), 8.11 (d, *J*=8.4 Hz, 2H, H3,5-Ar2); $^{13}C\{^{1}H\}$ NMR (150.9 MHz, $CDCl_3$): δ 162.8 (C1), 148.2 (C4-Ar2), 141.7 (C1-Ar1), 138.1 (C1-Ar2), 130.0 (C3-Ar1), 128.7 (C4-Ar1), 127.9 (C2-Ar2), 127.6 (C2-Ar1), 123.0 (C3-Ar2), 77.4 (C2), 63.0 (C3), 38.3 (NMe); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{16}H_{13}ClN_2O_4Cs$ 464.9613; Found 464.9630.

*2-Chloro-3-(4-nitrophenyl)-N-benzyl-N-phenyloxirane-2-carboxamide (**3h**).*



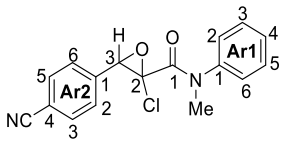
Yield: 5.89 g (72%), light-yellow solid, mp 123-124 °C; IR (KBr): ν_{max} 1669, 1521, 1348, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.27 (s, 1H, H3), 4.87, 5.06 (AB, *J*=14.2 Hz, 2H, CH_2), 7.01 (d, *J*=8.7 Hz, 2H, H2,6-Ar3), 7.19 (dd, *J*=7.9, 2.3 Hz, 2H, H2,6-Ar1), 7.22 (dd, *J*=7.6, 2.8 Hz, 2H, H2,6-Ar2), 7.26-7.32 (m, 3H, H3,4,5-Ar2), 7.41-7.47 (m, 3H, H3,4,5-Ar1), 8.09 (d, *J*=8.7 Hz, 2H, H3,5-Ar3); $^{13}C\{^{1}H\}$ NMR (125.7 MHz, $CDCl_3$): δ 162.8 (C1), 148.1 (C4-Ar3), 139.7 (C1-Ar1), 138.0 (C1-Ar3), 135.8 (C1-Ar2), 129.6 (C3-Ar1), 128.8 (C2-Ar2+C2-Ar1+C4-Ar1), 128.6 (C3-Ar2), 127.9 (C4-Ar2), 127.8 (C2-Ar3), 123.0 (C3-Ar3), 77.6 (C2), 63.0 (C3), 54.0 (CH_2); ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 137 (N1); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{22}H_{17}ClN_2O_4Cs$ 540.9926; Found 540.9947.

*2-Chloro-3-(4-nitrophenyl)-N-(4-methoxybenzyl)-N-phenyloxirane-2-carboxamide (**3i**).*



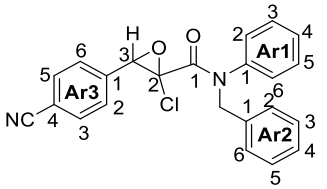
Yield: 7.63 g (87%), white solid, mp 114-115 °C; IR (KBr): ν_{max} 1672, 1523, 1349, 1251, 700 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.80 (s, 3H, OMe), 4.23 (s, 1H, H3), 4.81, 4.97 (AB, *J*=14.2 Hz, 2H, CH_2), 6.82 (d, *J*=8.4 Hz, 2H, H3,5-Ar2), 7.00 (d, *J*=8.3 Hz, 2H, H2,6-Ar3), 7.13 (d, *J*=8.5 Hz, 2H, H2,6-Ar2), 7.16 (d, *J*=7.3 Hz, 2H, H2,6-Ar1), 7.42-7.47 (m, 3H, H3,4,5-Ar1), 8.09 (d, *J*=8.3 Hz, 2H, H3,5-Ar3); $^{13}C\{^{1}H\}$ NMR (150.9 MHz, $CDCl_3$): δ 162.7 (C1), 159.3 (C4-Ar2), 148.2 (C4-Ar3), 139.7 (C1-Ar1), 138.1 (C1-Ar3), 130.3 (C2-Ar2), 129.6 (C3-Ar1), 129.0 (C2-Ar1), 128.8 (C4-Ar1), 127.9 (C1-Ar2), 127.8 (C2-Ar3), 123.0 (C3-Ar3), 113.9 (C3-Ar2), 77.7 (C2), 63.1 (C3), 55.2 (OMe), 53.5 (CH_2); ^{15}N NMR (60.8 MHz, $CDCl_3$): δ 368 (NO_2), 138 (N1); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{23}H_{19}ClN_2O_5Cs$ 571.0031; Found 571.0046.

*2-Chloro-3-(4-cyanophenyl)-N-methyl-N-phenyloxirane-2-carboxamide (**3j**).*



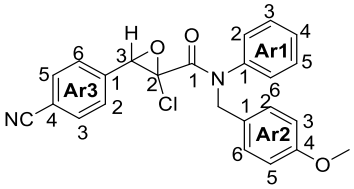
Yield: 4.07 g (65%), white solid, mp 152-153 °C; IR (KBr): ν_{max} 2227, 1669, 1265, 675, 598 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 3.37 (s, 3H, NMe), 4.15 (s, 1H, H3), 6.95 (d, *J*=7.9 Hz, 2H, H2,6-Ar2), 7.37 (d, *J*=7.4 Hz, 2H, H2,6-Ar1), 7.47 (dd, *J*=6.9, 6.9 Hz, 1H, H4-Ar1), 7.50 (dd, *J*=7.4, 6.9 Hz, 2H, H3,5-Ar1), 7.53 (d, *J*=7.8 Hz, 2H, H3,5-Ar2); $^{13}C\{^1H\}$ NMR (150.9 MHz, $CDCl_3$): δ 162.8 (C1), 141.6 (C1-Ar1), 136.1 (C1-Ar2), 131.5 (C3-Ar2), 129.9 (C3-Ar1), 128.5 (C4-Ar1), 127.6 (C2-Ar2), 127.5 (C2-Ar1), 118.2 (CN), 112.7 (C4-Ar2), 77.4 (C2), 63.1 (C3), 38.2 (NMe); ^{15}N NMR (60.8 MHz, $CDCl_3$): δ 122 (N1). HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{17}H_{13}ClN_2O_2Cs$ 444.9715; Found 444.9728.

*2-chloro-3-(4-cyanophenyl)- N-benzyl-N-phenyloxirane-2-carboxamide (**3k**).*



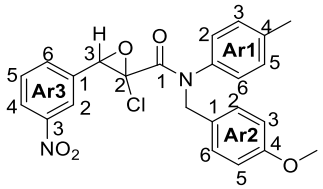
Yield: 4.82 g (62%), white solid, mp 124-125 °C; IR (KBr): ν_{max} 2229, 1668, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 4.21 (s, 1H, H3), 4.87, 5.04 (AB, *J*=14.2 Hz, 2H, CH_2), 6.97 (d, *J*=8.0 Hz, 2H, H2,6-Ar3), 7.17 (dd, *J*=7.6, 3.8 Hz, 2H, H2,6-Ar1), 7.22 (dd, *J*=7.2, 3.0 Hz, 2H, H2,6-Ar2), 7.28-7.35 (m, 3H, H3,4,5-Ar2), 7.40-7.45 (m, 3H, H3,4,5-Ar1), 7.54 (d, *J*=8.0 Hz, 2H, H3,5-Ar3); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 162.9 (C1), 139.8 (C1-Ar1), 136.2 (C1-Ar3), 135.8 (C1-Ar2), 131.6 (C3-Ar3), 129.6 (C3-Ar1), 128.9 (C2-Ar1+C2-Ar2), 128.8 (C4-Ar1), 128.6 (C3-Ar2), 127.9 (C4-Ar2), 127.6 (C2-Ar3), 118.2 (CN), 112.8 (C4-Ar3), 77.8 (C2), 63.2 (C3), 54.1 (CH_2); ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 137 (N1); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{23}H_{17}ClN_2O_2Cs$ 521.0028; Found 521.0049.

*2-Chloro-3-(4-cyanophenyl)-N-(4-methoxybenzyl)-N-phenyloxirane-2-carboxamide (**3l**).*



Yield: 6.03 g (72%), white solid, mp 123-124 °C; IR (KBr): ν_{max} 2231, 1670, 1513, 1251, 579 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.81 (s, 3H, OMe), 4.18 (s, 1H, H3), 4.82, 4.97 (AB, *J*=14.0 Hz, 2H, CH_2), 6.83 (d, *J*=8.7 Hz, 2H, H3,5-Ar2), 6.96 (d, *J*=8.4 Hz, 2H, H2,6-Ar3), 7.10-7.16 (m, 4H, H2,6-Ar1, H2,6-Ar2), 7.40-7.46 (m, 3H, H3,4,5-Ar1), 7.54 (d, *J*=8.3 Hz, 2H, H3,5-Ar3); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 162.8 (C1), 159.3 (C4-Ar2), 139.7 (C1-Ar1), 136.3 (C1-Ar3), 131.6 (C3-Ar3), 130.4 (C2-Ar2), 129.6 (C3-Ar1), 129.0 (C2-Ar1), 128.8 (C4-Ar1), 128.2 (C1-Ar2), 127.6 (C2-Ar3), 118.2 (CN), 114.0 (C3-Ar2), 112.8 (C4-Ar3), 77.8 (C2), 63.2 (C3), 55.2 (OMe), 53.6 (CH_2); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{24}H_{19}ClN_2O_3Cs$ 551.0133; Found 551.0156.

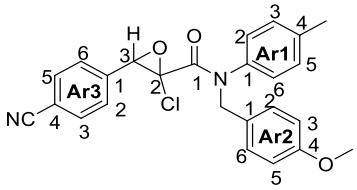
*2-Chloro-3-(3-nitrophenyl)-N-(4-methoxybenzyl)-N-(4-tolyl)oxirane-2-carboxamide (**3m**).*



Yield: 7.70 g (85%), light-yellow solid, mp 134-135 °C; IR (KBr): ν_{max} 1672, 1528, 1513, 1348, 1252 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 2.44 (s, 3H, Me), 3.79 (s, 3H, OMe), 4.19 (s, 1H,

H3), 4.75, 4.96 (AB, *J*=14.1 Hz, 2H, CH_2), 6.82 (d, *J*=8.6 Hz, 2H, H3,5-Ar2), 7.01 (d, *J*=8.1 Hz, 2H, H2,6-Ar1), 7.13 (d, *J*=8.6 Hz, 2H, H2,6-Ar2), 7.25 (d, *J*=8.0 Hz, 2H, H3,5-Ar1), 7.35 (d, *J*=7.8 Hz, 1H, H6-Ar3), 7.42 (s, 1H, H2-Ar3), 7.45 (dd, *J*=8.0, 7.9 Hz, 1H, H5-Ar3), 8.13 (d, *J*=8.1, 1H, H4-Ar3); $^{13}C\{^1H\}$ NMR (150.9 MHz, $CDCl_3$): δ 162.8 (C1), 159.2 (C4-Ar2), 147.7 (C3-Ar3), 139.5 (C4-Ar1), 136.9 (C1-Ar1), 133.3 (C1-Ar3), 132.7 (C6-Ar3), 130.4 (C2-Ar2), 130.3 (C3-Ar1), 128.9 (C5-Ar3), 128.6 (C2-Ar1), 128.1 (C1-Ar2), 123.7 (C4-Ar3), 121.9 (C2-Ar3), 113.9 (C3-Ar2), 77.6 (C2), 63.1 (C3), 55.2 (OMe), 53.4 (CH_2), 21.1 (Me); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{24}H_{21}ClN_2O_5Cs$ 585.0188; Found 585.0170.

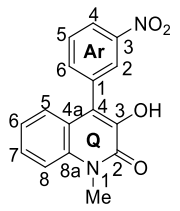
*2-Chloro-3-(4-cianophenyl)-N-(4-methoxybenzyl)-N-(4-tolyl)oxirane-2-carboxamide (**3n**).*



Yield: 7.53 g (87%), light-yellow solid, mp 139 °C; IR (KBr): ν_{max} 2227, 1668, 1611, 1512, 1247, 1026, 956, 849, 578 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.43 (s, 3H, Me), 3.81 (s, 3H, OMe), 4.17 (s, 1H, H3), 4.78, 4.93 (AB, *J*=14.0 Hz, 2H, CH_2), 6.83 (d, *J*=8.7 Hz, 2H, H3,5-Ar2), 6.97 (d, *J*=8.3 Hz, 2H, H2,6-Ar3), 7.01 (d, *J*=8.2 Hz, 2H, H2,6-Ar1), 7.13 (d, *J*=8.6 Hz, 2H, H2,6-Ar2), 7.21 (d, *J*=8.1 Hz, 2H, H3,5-Ar1), 7.54 (d, *J*=8.4 Hz, 2H, H3,5-Ar3); $^{13}C\{^1H\}$ NMR (150.9 MHz, $CDCl_3$): δ 188.9 (C2), 164.0 (C1), 159.3 (C4-Ar2), 138.9 (C1-Ar3), 138.9 (C4-Ar1), 136.2 (C1-Ar1), 132.4 (C3-Ar3), 130.2 (C2-Ar2), 129.9 (C3-Ar1), 129.6 (C2-Ar3), 127.9 (C2-Ar1), 127.7 (C1-Ar2), 118.1 (CN), 113.9 (C3-Ar2), 113.2 (C4-Ar3), 61.3 (C3), 55.2 (OMe), 52.8 (CH2), 21.1 (Me); HRMS (MALDI-TOF) *m/z*: Calcd for $[M + Cs]^+$ $C_{25}H_{21}ClN_2O_3Cs$ 565.0290; Found 565.0294.

General procedure for the preparation of 3-hydroxy-4-arylquinolin-2-ones (4). *Method A:* A suspension of oxirane-2-carboxamide **3d-n** (5 mmol) in a mixture of acetic (10 mL) and sulfuric (0.5 mL) acids was transferred to the solution by heating at 60 to 65 °C for 30 min. The resulting solution was heated at this temperature with stirring for 2 h or until a precipitation took place. The sediment precipitated after cooling the reaction mixture or during the process was filtered, washed with water (3×10 mL), dried in air to afford the analytically pure 3-hydroxy-4-arylquinolin-2-one **4d-l**. The compounds **4m,n** required additional purification. The crude product was washed with acetone (2×3 mL). The collected by filtration and dried in air compound corresponded to analytically pure 3-hydroxy-4-arylquinolin-2-one **4m,n**. Products **5m,n** were isolated by evaporating the acetone filtrate followed by flash chromatography on silica gel column using $CHCl_3$ as eluent. *Method B:* A solution of oxirane-2-carboxamide **3d-l** (5 mmol) in trifluoroacetic acid (10 mL) was heated at 60 to 65 ° C with stirring for 2 hour. The sediment that precipitated upon the addition of water (30 mL) was filtered, washed with water, and dried in air to afford the analytically pure 3-hydroxy-4-arylquinolin-2-one **4d-l**.

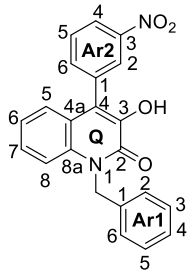
*3-Hydroxy-4-(3-nitrophenyl)-N-methylquinolin-2-one (**4d**).*



Yield: 1.38 g (93%) (1.39 g (94%)), white solid, mp 274-276 °C; IR (KBr): ν_{max} 3269, 1602, 1525, 1346, 1283, 1268, 765 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 3.93 (s, 3H, NMe), 7.25 (dd, *J*=8.0, 7.0 Hz, 1H, H6-Q), 7.29 (dd, *J*= 8.0, 1.2 Hz, 1H, H5-Q), 7.48 (d, *J*=8.4 Hz, 1H, H8-Q), 7.52 (ddd, *J*=8.3, 7.0, 1.4 Hz, 1H, H7-Q), 7.73 (ddd, *J*=7.9, 7.7, 1.7 Hz, 1H, H5-Ar), 7.80 (d, *J*=7.7 Hz, 1H, H6-Ar), 8.34 (s, 1H, H2-Ar), 8.35 (d, *J*=8.0 Hz, 1H, H4-Ar); $^{13}C\{^1H\}$ NMR

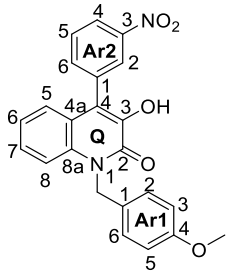
(150.9 MHz, $CDCl_3$): δ 158.8 (C2), 148.6 (C3-Ar), 141.4 (C3), 136.4 (C6-Ar), 134.8 (C1-Ar), 134.5 (C8a), 129.6 (C5-Ar), 127.8 (C7), 125.4 (C5), 125.3 (C2-Ar), 123.5 (C6), 123.2 (C4-Ar), 121.1 (C4a), 120.5 (C4), 114.6 (C8), 30.6 (NMe); HRMS (MALDI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{13}N_2O_4$ 297.0870; Found 297.0863.

*3-Hydroxy-4-(3-nitrophenyl)-N-benzylquinolin-2-one (**4e**).*



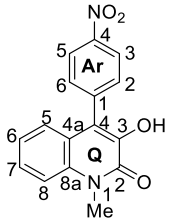
Yield: 1.77 g (95%) (1.71 g (92%)), tan solid, mp 230-232 °C; IR (KBr): ν_{max} 3236, 1625, 1601, 1528, 1346, 1265, 737 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.73 (s, 2H, CH_2), 7.20 (dd, *J*=7.5, 7.4 Hz, 1H, H6-Q), 7.28-7.33 (m, 3H, H5-Q, H2,6-Ar1), 7.34-7.44 (m, 5H, H7,8-Q, H3,4,5-Ar1), 7.76 (dd, *J*=7.9, 7.7 Hz, 1H, H5-Ar2), 7.84 (d, *J*=7.6 Hz, 1H, H6-Ar2), 8.37 (d, *J*=8.0 Hz, 1H, H4-Ar2), 8.39 (s, 1H, H2-Ar2); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 159.1 (C2-Q), 148.5 (C3-Ar2), 141.3 (C3-Q), 136.4 (C6-Ar2), 135.4 (C1-Ar1), 134.8 (C1-Ar2), 133.9 (C8a-Q), 129.7 (C5-Ar2), 129.0 (C3-Ar1), 127.8 (C7-Q), 127.7 (C4-Ar1), 126.6 (C2-Ar1), 125.5 (C5-Q), 125.3 (C2-Ar2), 123.5 (C6-Q), 123.3 (C4-Ar2), 121.3 (C4-Q), 121.1 (C4a-Q), 115.5 (C8-Q), 47.3 (CH_2); HRMS (MALDI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{22}H_{17}N_2O_4$ 373.1183; Found 373.1196.

*3-Hydroxy-4-(3-nitrophenyl)-N-(4-methoxybenzyl)quinolin-2-one (**4f**).*



Yield: 1.99 g (99%) (1.83 g (91%)), white solid, mp 162-165 °C; IR (KBr): ν_{max} 3269, 1617, 1601, 1530, 1513, 1349, 1246, 744 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.81 (s, 3H, OMe), 5.66 (s, 2H, CH_2), 6.90 (d, *J*=8.5 Hz, 2H, H3,5-Ar1), 7.20 (dd, *J*=7.7, 7.2 Hz, 1H, H6-Q), 7.26 (d, *J*=8.5 Hz, 2H, H2,6-Ar1), 7.29 (d, *J*=7.8 Hz, 1H, H5-Q), 7.40 (dd, *J*=8.1, 7.3 Hz, 1H, H7-Q), 7.47 (d, *J*=8.3 Hz, 1H, H8-Q), 7.75 (dd, *J*=7.9, 7.7 Hz, 1H, H5-Ar2), 7.83 (d, *J*=7.6 Hz, 1H, H6-Ar2), 8.36 (d, *J*=8.0, 1H, H4-Ar2), 8.38 (s, 1H, H2-Ar2); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 159.1 (C2-Q), 159.0 (C4-Ar1), 148.5 (C3-Ar2), 141.3 (C3-Q), 136.4 (C6-Ar2), 134.8 (C1-Ar2), 133.9 (C8a-Q), 129.7 (C5-Ar2), 128.1 (C2-Ar1), 127.8 (C7-Q), 127.5 (C1-Ar1), 125.4 (C5-Q), 125.3 (C2-Ar2), 123.5 (C6-Q), 123.3 (C4-Ar2), 121.4 (C4a-Q), 121.1 (C4-Q), 115.5 (C8-Q), 114.4 (C3-Ar1), 55.3 (OMe), 46.7 (CH_2); ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 153 (N1), 369 (NO_2);); HRMS (MALDI-TOF) *m/z*: Calcd for $[M + Cs]^+$ $C_{23}H_{18}N_2O_5Cs$ 535.0265; Found 535.0283.

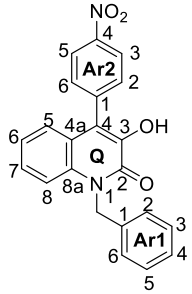
*3-Hydroxy-4-(4-nitrophenyl)-N-methylquinolin-2-one (**4g**).*



Yield: 1.45 g (98%) (1.44 g (97%)), white solid, mp 284-285 °C (276-278 °C[22]); IR (KBr): ν_{max} 3256, 1626, 1600, 1513, 1347, 1267, 753 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.94 (s, 3H,

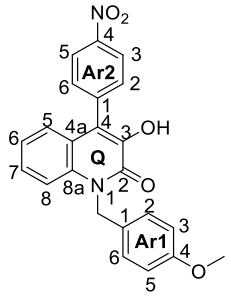
NMe), 7.24-7.33 (m, 2H, H5,6-Q), 7.50 (d, *J*=8.3 Hz, 1H, H8-Q), 7.54 (ddd, *J*=8.4, 6.8, 1.6 Hz, 1H, H7-Q), 7.65 (d, *J*=8.8 Hz, 2H, H2,6-Ar), 8.41 (d, *J*=8.8 Hz, 2H, H3,5-Ar); $^{13}C\{^{1}H\}$ NMR (125.7 MHz, $CDCl_3$): δ 158.8 (C2-Q), 147.8 (C4-Ar), 141.1 (C3-Q), 140.0 (C1-Ar), 134.4 (C8a-Q), 131.3 (C2-Ar), 127.9 (C7-Q), 125.5 (C5-Q), 123.8 (C3-Ar), 123.6 (C6-Q), 121.2 (C4-Q), 121.0 (C4a-Q), 114.6 (C8-Q), 30.7 (NMe); ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 141 (N1), 369 (NO_2); HRMS (MALDI-TOF) *m/z*: Calcd for $[M + H]^+$ $C_{16}H_{13}N_2O_4$ 297.0870; Found 297.0862.

*3-Hydroxy-4-(4-nitrophenyl)-N-benzylquinolin-2-one (**4h**).*



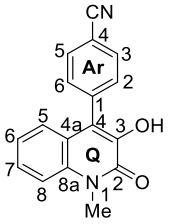
Yield: 1.79 g (96%) (1.75 g (94%)), light-yellow solid, mp 265-267 °C (258-260 °C[22]); IR (KBr): ν_{max} 3281, 1620, 1599, 1516, 1349, 1258, 754 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.72 (s, 2H, CH_2), 7.19 (dd, *J*=8.1, 6.8 Hz, 1H, H6-Q), 7.28-7.38 (m, 4H, H5-Q, H2,4,6-Ar1), 7.35-7.40 (m, 4H, H3,5-Ar1, H7,8-Q), 7.69 (d, *J*=8.8 Hz, 2H, H2,6-Ar2), 8.43 (d, *J*=8.8 Hz, 2H, H3,5-Ar2); $^{13}C\{^{1}H\}$ NMR (150.9 MHz, $CDCl_3$): δ 159.1 (C2), 147.8 (C4-Ar2), 141.0 (C3), 140.0 (C1-Ar2), 135.4 (C1-Ar1), 133.9 (C8a), 131.3 (C6-Ar2), 129.0 (C3-Ar1), 127.9 (C7), 127.8 (C4-Ar1), 126.7 (C2-Ar1), 125.6 (C5), 123.9 (C5-Ar2), 123.5 (C6), 121.5 (C4), 121.2 (C4a), 115.5 (C8), 47.3 (CH_2); HRMS (MALDI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{22}H_{17}N_2O_4$ 373.1183; Found 373.1195.

*3-Hydroxy-4-(4-nitrophenyl)-N-(4-methoxybenzyl)quinolin-2-one (**4i**).*



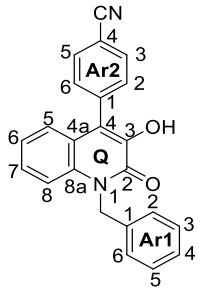
Yield: 1.97 g (98%) (1.87 (93%)), tan solid, mp 267-269 °C; IR (KBr): ν_{max} 3284, 1621, 1601, 1514, 1350, 1249, 751 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.80 (s, 3H, OMe), 5.65 (s, 2H, CH_2), 6.90 (d, *J*=8.6 Hz, 2H, H3,5-Ar1), 7.19 (dd, *J*=7.6, 7.5 Hz, 1H, H6-Q), 7.26 (d, *J*=8.7 Hz, 2H, H2,6-Ar1), 7.28 (d, 1H, *J*=7.4 Hz, H5-Q), 7.39 (dd, *J*=8.2, 7.4 Hz, 1H, H7-Q), 7.46 (d, *J*=8.3 Hz, 1H, H8-Q), 7.68 (d, *J*=8.5 Hz, 2H, H2,6-Ar2), 8.42 (d, *J*=8.5 Hz, 2H, H3,5-Ar2); $^{13}C\{^{1}H\}$ NMR (150.9 MHz, $CDCl_3$): δ 159.2 (C4-Ar1), 159.0 (C2), 147.8 (C4-Ar2), 141.1 (C3), 140.0 (C1-Ar2), 133.9 (C8a), 131.3 (C6-Ar2), 128.2 (C2-Ar1), 127.8 (C7), 127.5 (C1-Ar1), 125.5 (C5), 123.9 (C5-Ar2), 123.5 (C6), 121.3 (C4), 121.2 (C4a), 115.5 (C8), 114.4 (C3-Ar1), 55.3 (OMe), 46.8 (CH_2); HRMS (MALDI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{23}H_{19}N_2O_5$ 403.1288; Found 403.1298.

*3-Hydroxy-4-(4-cianophenyl)-N-methylquinolin-2-one (**4j**).*



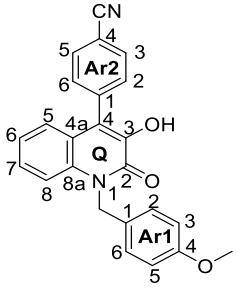
Yield: 1.37 g (99%) (1.34 g (97%)), tan solid, mp 240-242 °C; IR (KBr): ν_{max} 3240, 2226, 1628, 1600, 1265, 754 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.93 (s, 3H, NMe), 7.24 (dd, *J*=7.6, 6.9 Hz, 1H, H6-Q), 7.28 (d, *J*=7.6 Hz, 1H, H5-Q), 7.47 (d, *J*=8.2 Hz, 1H, H8-Q), 7.52 (dd, *J*=8.2, 7.0 Hz, 1H, H7-Q), 7.58 (d, *J*=7.8 Hz, 2H, H2,6-Ar), 7.84 (d, *J*=7.7 Hz, 2H, H3,5-Ar); ^{13}C{^{1}H} NMR (125.7 MHz, $CDCl_3$): δ 158.8 (C2-Q), 141.1 (C3-Q), 138.1 (C1-Ar), 134.5 (C8a-Q), 132.4 (C3-Ar), 131.0 (C2-Ar), 127.8 (C7-Q), 125.5 (C5-Q), 123.4 (C6-Q), 121.2 (C4a-Q), 121.0 (C4-Q), 118.6 (CN), 114.5 (C8-Q), 112.2 (C4-Ar), 30.6 (NMe); ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 140.3 (N1); HRMS (MALDI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{13}N_2O_2$ 277.0972; Found 277.0981.

*3-Hydroxy-4-(4-cianophenyl)-N-benzylquinolin-2-one (**4k**).*



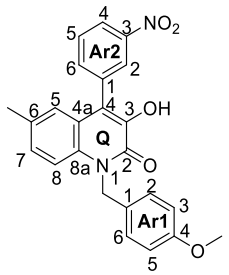
Yield: 1.74 g (99%) (1.67 (95%)), white solid, mp 210-211 °C; IR (KBr): ν_{max} 3307, 2225, 1708, 1620, 1601, 1259, 754 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.72 (s, 2H, CH_2), 7.19 (dd, *J*=8.0, 6.8 Hz, 1H, H6-Q), 7.27-7.33 (m, 4H, H5-Q, H2,4,6-Ar1), 7.34-7.43 (m, 4H, H7,8-Q, 3,5-Ar1), 7.62 (d, *J*=8.3 Hz, 2H, H2,6-Ar2), 7.86 (d, *J*=8.3 Hz, 2H, H3,5-Ar2); ^{13}C{^{1}H} NMR (125.7 MHz, $CDCl_3$): δ 159.1 (C2-Q), 141.0 (C3-Q), 138.1 (C1-Ar2), 135.4 (C1-Ar1), 133.9 (C8a-Q), 132.4 (C3-Ar2), 131.0 (C2-Ar2), 130.0 (C3-Ar1), 127.8 (C7-Q), 127.7 (C4-Ar1), 126.6 (C2-Ar1), 125.6 (C5-Q), 123.5 (C6-Q), 122.0 (C4-Q), 121.3 (C4a-Q), 118.6 (CN), 115.4 (C8-Q), 112.2 (C4-Ar2), 47.3 (CH_2); ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 151 (N1). HRMS (MALDI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{23}H_{17}N_2O_2$ 353.1285; Found 353.1299.

*3-Hydroxy-4-(4-cianophenyl)-N-(4-methoxybenzyl)quinolin-2-one (**4l**).*



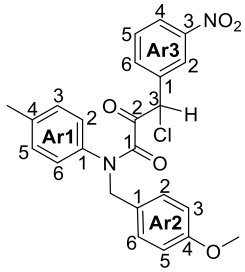
Yield: 1.87 g (98%) (1.74 g (91%)), tan solid, mp 241-243 °C; IR (KBr): ν_{max} 3188, 2230, 1707, 1609, 1594, 1514, 1279, 1248, 762, 748 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.80 (s, 3H, OMe), 5.65 (s, 2H, CH_2), 6.89 (d, *J*=8.7 Hz, 2H, H3,5-Ar1), 7.19 (dd, *J*=7.9, 7.1 Hz, 1H, H6-Q), 7.26 (d, *J*=8.6 Hz, 2H, H2,6-Ar1), 7.27 (d, *J*=7.2 Hz, 1H, H5-Q), 7.39 (ddd, *J*=7.9, 7.1, 1.4 Hz, 1H, H7-Q), 7.46 (d, *J*=8.0 Hz, 1H, H8-Q), 7.61 (d, *J*=8.5 Hz, 2H, H2,6-Ar2), 7.85 (d, *J*=8.5 Hz, 2H, H3,5-Ar2); ^{13}C{^{1}H} NMR (125.7 MHz, $CDCl_3$): δ 159.2 (C4-Ar1), 159.1 (C2-Q), 141.0 (C3-Q), 138.1 (C4-Ar1), 133.9 (C8a-Q), 132.4 (C3-Ar2), 131.0 (C2-Ar2), 128.2 (C2-Ar1), 127.7 (C7-Q), 127.5 (C1-Ar1), 125.6 (C5-Q), 123.4 (C6-Q), 121.7 (C4-Q), 121.3 (C4a-Q), 118.6 (CN), 115.4 (C8-Q), 114.4 (C3-Ar1), 112.3 (C4-Ar2), 55.3 (OMe), 46.7 (CH_2); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{24}H_{18}N_2O_3Cs$ 515.0366; Found 515.0380.

*3-Hydroxy-4-(3-nitrophenyl)-6-methyl-N-(4-methoxybenzyl)quinolin-2-one (**4m**).*



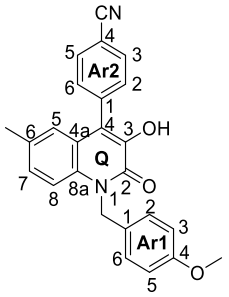
Yield: 0.94 g (45%), white solid, mp 245-247 °C; IR (KBr): ν_{max} 3251, 1613, 1529, 1513, 1349, 1248, 804 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.30 (s, 3H, Me), 3.81 (s, 3H, OMe), 5.64 (s, 2H, CH_2), 6.89 (d, *J*=8.7 Hz, 2H, H3,5-Ar1), 7.03 (s, 1H, H5-Q), 7.20 (d, *J*=8.7 Hz, 1H, H7-Q), 7.25 (d, *J*=8.7 Hz, 2H, H2,6-Ar1), 7.35 (d, *J*=8.6 Hz, 1H, H8-Q), 7.76 (dd, *J*=8.8, 7.7 Hz, 1H, H5-Ar2), 7.82 (d, *J*=7.7 Hz, 1H, H6-Ar2), 8.36 (s, 1H, H2-Ar2), 8.37 (d, *J*=8.6 Hz, 1H, H4-Ar2); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 159.1 (C4-Ar1), 158.8 (C2-Q), 148.6 (C3-Ar2), 141.3 (C3-Q), 136.4 (C6-Ar2), 134.9 (C1-Ar2), 133.1 (C6-Q), 131.9 (C8a-Q), 129.7 (C5-Ar2), 129.0 (C7-Q), 128.1 (C2-Ar1), 127.6 (C1-Ar1), 125.3 (C2-Ar2), 125.2 (C5-Q), 123.2 (C4-Ar2), 121.3 (C4a-Q), 120.9 (C4-Q), 115.4 (C8-Q), 114.4 (C3-Ar1), 55.3 (OMe), 46.7 (CH_2), 20.9 (C6-Me); ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 153 (N1), 367 (NO_2); HRMS (MALDI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{24}H_{21}N_2O_5$ 417.1445; Found 417.1451.

*3-Chloro-2-oxo-3-(3-nitrophenyl)-N-(4-tolyl)-N-(3-methoxybenzyl)propionamide (**5m**).*



Yield: 0.52 g (23%), yellow thick oil; IR: ν_{max} 1728, 1651, 1513, 1352, 1250, 833 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.33 (s, 3H, Me), 3.81 (s, 3H, OMe), 4.84 (d, *J*=11.4 Hz, 2H, NCH_2), 6.04 (s, 1H, H3), 6.74 (d, *J*=8.0 Hz, 2H, H2,6-Ar1), 6.80 (d, *J*=8.4 Hz, 2H, H3,5-Ar2), 7.06 (d, *J*=7.9 Hz, 2H, H3,5-Ar1), 7.09 (d, *J*=8.5 Hz, 2H, H2,6-Ar2), 7.53 (dd, *J*=8.0, 7.9 Hz, 1H, H5-Ar3), 7.63 (d, *J*=7.8 Hz, 1H, H6-Ar3), 8.06 (s, 1H, H2-Ar3), 8.21 (d, *J*=8.1 Hz, 1H, H4-Ar3); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 189.1 (C2), 164.1 (C1), 159.3 (C4-Ar2), 148.3 (C3-Ar3), 139.0 (C4-Ar1), 136.1 (C1-Ar3), 136.0 (C1-Ar1), 134.9 (C6-Ar3), 130.2 (C2-Ar2), 129.9 (C3-Ar1), 129.7 (C5-Ar3), 128.0 (C2-Ar1), 127.7 (C1-Ar2), 124.1 (C4-Ar3), 123.9 (C2-Ar3), 113.9 (C3-Ar2), 60.9 (C3), 55.2 (OMe), 52.7 (CH_2), 21.1 (Me); ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 140.9 (N1), 367.4 (NO_2); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{24}H_{21}ClN_2O_5Cs$ 585.0188; Found 585.0181.

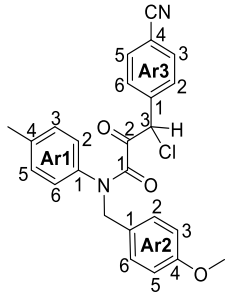
*3-Hydroxy-4-(4-cianophenyl)-6-methyl-N-(4-methoxybenzyl)quinolin-2-one (**4n**).*



Yield: 0.95 g (48%), white solid, mp 277-279 °C; IR (KBr): ν_{max} 3290, 2228, 1609, 1513, 1245, 1036 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.29 (s, 3H, Me), 3.79 (s, 3H, OMe), 5.62 (s, 2H, CH_2), 6.88 (d, *J*=8.7 Hz, 2H, H3,5-Ar1), 7.01 (s, 1H, H5-Q), 7.19 (d, *J*=8.4 Hz, 1H, H7-Q), 7.24 (d, *J*=8.6 Hz, 2H, H2,6-Ar1), 7.33 (d, *J*=8.4 Hz, 1H, H8-Q), 7.59 (d, *J*=8.3 Hz, 2H, H2,6-Ar2),

7.85 (d, *J*=8.2 Hz, 2H, H3,5-Ar2); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 159.1 (C4-Ar1), 158.8 (C2-Q), 141.0 (C3-Q), 138.2 (C1-Ar2), 133.1 (C6-Q), 132.4 (C3-Ar2), 131.9 (C8a-Q), 131.0 (C2-Ar2), 128.9 (C7-Q), 128.1 (C2-Ar1), 127.7 (C1-Ar1), 125.3 (C5-Q), 121.4 (C4-Q), 121.2 (C4a-Q), 118.7 (CN), 115.3 (C8-Q), 114.4 (C3-Ar1), 112.2 (C4-Ar2), 55.3 (OMe), 46.7 (CH2), 20.9 (C6-Me); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{25}H_{20}N_2O_3Cs$ 529.0523; Found 529.0507.

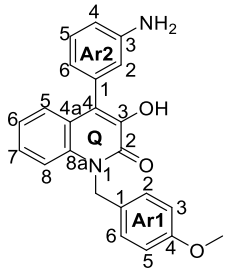
*3-Chloro-2-oxo-3-(4-cianophenyl)-N-(4-tolyl)-N-(3-methoxybenzyl)propionamide (**5n**).*



Yield: 0.58 g (27%), yellow thick oil; IR: ν_{max} 2231, 1732, 1651, 1513, 1249 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): 2.34 (s, 3H, Me), 3.81 (s, 3H, OMe), 4.83 (d, *J*=4.2 Hz, 2H, NCH_2), 5.98 (s, 1H, H3), 6.72 (d, *J*=8.2 Hz, 2H, H2,6-Ar1), 6.81 (d, *J*=8.7 Hz, 2H, H3,5-Ar2), 7.05 (d, *J*=8.1 Hz, 2H, H3,5-Ar1), 7.08 (d, *J*=8.7 Hz, 2H, H2,6-Ar2), 7.39 (d, *J*=8.5 Hz, 2H, H2,6-Ar3), 7.62 (d, *J*=8.4 Hz, 2H, H3,5-Ar3); $^{13}C\{^{1}H\}$ NMR (150.9 MHz, $CDCl_3$): δ 188.9 (C2), 164.0 (C1), 159.3 (C4-Ar2), 138.9 (C1-Ar3), 138.9 (C4-Ar1), 136.2 (C1-Ar1), 132.4 (C3-Ar3), 130.2 (C2-Ar2), 129.9 (C3-Ar1), 129.6 (C2-Ar3), 127.9 (C2-Ar1), 127.7 (C1-Ar2), 118.1 (CN), 113.9 (C3-Ar2), 113.2 (C4-Ar3), 61.3 (C3), 55.2 (OMe), 52.8 (CH2), 21.1 (Me); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{25}H_{21}ClN_2O_3Cs$ 565.0290; Found 565.0277.

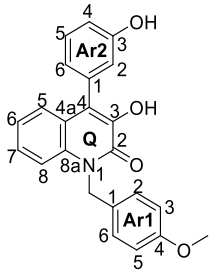
Syntheses of viridicatol 8 from 3-hydroxy-4-(3-nitrophenyl)-*N*-(4-methoxybenzyl)quinolin-2-one (4f). *Method A: Step 1 (Reduction of **4f**).* To a stirred solution of **4f** (0.80 g, 2.0 mmol) in DMF (120 mL) was added a solution of $Na_2S_2O_4$ (1.39 g, 8 mmol) in H_2O (120 mL). The mixture was heated at reflux for 4 h. After cooling, diluted with water (500 mL) and kept at room temperature for 10 h was formed precipitate, which filtered off, washed with water and dried in air to afford of the analytically pure **6a**. *Step 2 (Diazotization of **6a**, followed by the elimination of nitrogen).* To a stirred solution of **6a** (0.56 g, 1.5 mmol) in THF (50 mL) was added diluted with water (1:1) H_2SO_4 (0.5 mL, ~4.5 mmol), followed by a 2.5 M aqueous solution of $NaNO_2$ (0.6 mL, ~6 mmol) was added at 0-5 °C and the resulting mixture stirred at this temperature for 1 h. At the end of this period, a small amount of urea (~6 mg) was added to the reaction mixture for the decomposition of the excess of nitrous acid, after which the stirring was continued at room temperature for 5 h. The reaction mixture was kept at room temperature for a further 6 h, and water (100 mL) was added. The precipitate was filtered, washed with water, dried in air. The resulting a tan solid corresponded to compound **6b** and was used in the next step without purification. *Step 3 (Removal of PMB (p-metoxybenzyl) group).* The compound of **6a** (0.49 g, 1.3 mmol) was heated at reflux in a mixture of trifluoroacetic acid (15 mL), anisole (15 mL) and conc. H_2SO_4 (0.2 mL) for 4 h. The reaction mixture was kept at room temperature for a further 8 h and stirred with ice-cold water/n-hexane (150 mL/150 mL) mixture for 15 min. The resulting precipitate was filtered, washed with water and hexane and dried in air to afford of the analytically pure **8**. *Method B: Step 1 (Removal of PMB group).* The conversion of **4f** (0.80 g, 2.0 mmol) in **7a** was carried out analogously to the procedure described in *Step 3* of *Method A* for **6b**. *Step 2.* The reduction of **7a** (0.42 g, 1.5 mmol) was carried out analogously to the procedure described in *Step 1* of *Method A* for **4f**. *Step 3.* The process diazotization of **7b** (0.28 g, 1.0 mmol) was carried out analogously to the procedure described in Step 2 of *Method A* for **6a**.

*3-Hydroxy-4-(3-aminophenyl)-N-(4-methoxybenzyl)quinolin-2-one (**6a**).*



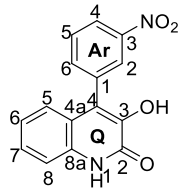
Yield 0.64 g (86%), light violet solid, mp 220-221 °C; IR (KBr): ν_{max} 3366, 1616, 1600, 1513, 1461, 1248, 751 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 3.72 (s, 3H, OMe), 5.15 (s, 2H, NH_2), 5.59 (s, 2H, NCH_2), 6.45 (d, *J*=7.7 Hz, 1H, H6-Ar2), 6.54 (dd, *J*=1.9, 1.8 Hz, 1H, H2-Ar2), 6.63 (d, *J*=7.9 Hz, 1H, H4-Ar2), 6.91 (d, *J*=8.8 Hz, 2H, H3,5-Ar1), 7.14 (dd, *J*=7.5, 7.3 Hz, 1H, H6-Q), 7.15 (dd, *J*=7.9, 7.7 Hz, 1H, H5-Ar2), 7.22 (d, *J*=7.4 Hz, 1H, H5-Q), 7.23 (d, *J*=8.8 Hz, 2H, H2,6-Ar1), 7.32 (dd, *J*=8.3, 7.5, 1H, H7-Q), 7.45 (d, *J*=8.4 Hz, 1H, H8-Q), 9.13 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (125.7 MHz, DMSO-d_6): δ 158.6 (C2-Q), 158.4 (C4-Ar1), 148.6 (C3-Ar2), 141.3 (C3-Q), 134.2 (C1-Ar2), 133.3 (C8a-Q), 128.8 (C5-Ar2), 128.5 (C1-Ar1), 128.0 (C2-Ar1), 126.6 (C7-Q), 125.5 (C5-Q), 124.4 (C4-Q), 122.3 (C6-Q), 122.0 (C4a-Q), 117.1 (C6-Ar2), 115.2 (C2-Ar2), 115.1 (C8-Q), 114.1 (C3-Ar1), 113.2 (C4-Ar2), 55.0 (OMe), 45.0 (CH_2); ^{15}N NMR (50.6 MHz, DMSO-d_6): δ 153 (N1), 60 (NH_2); HRMS (MALDI-TOF) *m/z*: $[M + Cs]^+$ Calcd for $C_{23}H_{20}N_2O_3Cs$ 505.0523; Found 505.0533.

*3-Hydroxy-4-(3-hydroxyphenyl)-N-(4-methoxybenzyl)quinolin-2-one (**6b**).*



Yield 0.54 g (97%), tan solid, mp 242-143 °C (238-242 °C[20]); IR (KBr): ν_{max} 3277, 1614, 1598, 1515, 1253, 1031, 1017, 749 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 3.72 (s, 3H, OMe), 5.60 (s, 2H, NCH_2), 6.75 (s, 1H, H2-Ar2), 6.76 (ddd, *J*=7.8, 2.1, 1.1 Hz, 1H, H6-Ar2), 6.86 (ddd, *J*=8.2, 2.3, 1.0 Hz, 1H, H4-Ar2), 6.91 (d, *J*=8.8 Hz, 2H, H3,5-Ar1), 7.13 (ddd, *J*=8.0, 7.1, 0.8 Hz, 1H, H6-Q), 7.19 (dd, *J*=8.1, 1.5 Hz, 1H, H5-Q), 7.25 (d, *J*=8.8 Hz, 2H, H2,6-Ar1), 7.32 (dd, *J*=8.1, 7.9 Hz, 1H, H5-Ar2), 7.33 (ddd, *J*=8.5, 7.0, 1.5, 1H, H7-Q), 7.47 (d, *J*=8.4 Hz, 1H, H8-Q), 9.26 (s, 1H, OH-Q), 9.54 (s, 1H, OH-Ar2); $^{13}C\{^1H\}$ NMR (125.7 MHz, DMSO-d_6): δ 158.4 (C2-Q), 158.4 (C4-Ar1), 157.3 (C3-Ar2), 141.3 (C3-Q), 134.8 (C1-Ar2), 133.4 (C8a-Q), 129.4 (C5-Ar2), 128.4 (C1-Ar1), 128.1 (C2-Ar1), 126.7 (C7-Q), 125.3 (C5-Q), 123.7 (C4-Q), 122.4 (C6-Q), 121.7 (C4a-Q), 120.4 (C6-Ar2), 116.7 (C2-Ar2), 115.1 (C8-Q), 114.7 (C4-Ar2), 114.1 (C3-Ar1), 55.0 (OMe), 45.0 (CH_2); ^{15}N NMR (50.6 MHz, DMSO-d_6): δ 153.1; HRMS (MALDI-TOF), *m/z*: $[M + H]^+$ Calcd for $C_{23}H_{20}NO_4$ 374.1387; Found 374.1388.

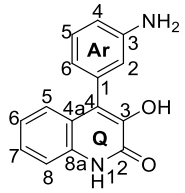
*3-Hydroxy-4-(3-nitrophenyl)-N-(4-methoxybenzyl)quinolin-2-one (**7a**).*



Yield 0.44 g (78%), tan solid, mp 272-274 °C; IR (KBr): ν_{max} 3308, 1669, 1575, 1530, 1504, 1347, 1293 cm^{-1}; ^1H NMR (500 MHz, DMSO-d6): δ 7.05 (d, *J*=8.0 Hz, 1H, H5-Q), 7.11 (dd, *J*=8.1, 6.4, 1.9 Hz, 1H, H6-Q), 7.34-7.41 (m, 2H, H7,8-Q), 7.82-7.85 (m, 2H, H5,6-Ar), 8.18 (dd, *J*=1.5, 1.2 Hz, 1H, H2-Ar), 8.32 (ddd, *J*=6.1, 3.6, 2.9 Hz, 1H, H4-Ar), 9.59 (s, 1H, OH), 12.29 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (100.6 MHz, DMSO-d6): δ 158.0 (C2-Q), 148.0 (C3-Ar), 143.0 (C3-

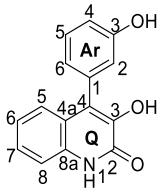
Q), 136.9 (C6-Ar), 135.4 (C1-Ar), 133.2 (C8a-Q), 130.1 (C5-Ar), 126.7 (C7-Q), 124.7 (C2-Ar), 123.8 (C5-Q), 122.7 (C4-Ar), 122.4 (C6-Q), 121.6 (C4-Q), 120.2 (C4a-Q), 115.4 (C8-Q); ^{15}N NMR (50.6 MHz, DMSO-d6): δ 148 (N1), 371 (NO_2); HRMS (MALDI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{11}N_2O_4$ 283.0713; Found 283.0711.

*3-Hydroxy-4-(3-aminophenyl)-N-(4-methoxybenzyl)quinolin-2-one (**7b**).*



Yield 0.31 g (82%), tan solid, mp 277 °C; IR (KBr): ν_{max} 3318, 1654, 1574, 1290, 1227, 752 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ 5.13 (s, 2H, NH_2), 6.43 (d, *J*=7.4 Hz, 1H, H6-Ar), 6.52 (s, 1H, H2-Ar1), 6.62 (d, *J*=8.0 Hz, 1H, H4-Ar), 7.08 (ddd, *J*=7.2, 7.1, 1.9 Hz, 1H, H6-Q), 7.14 (dd, *J*=8.0, 7.5 Hz, 1H, H5-Ar), 7.14 (d, *J*=7.3 Hz, 1H, H5-Q), 7.28-7.35 (m, 2H, H7,8-Q), 8.97 (s, 1H, OH), 12.14 (s, 1H, NH); ^{13}C{^{1}H} NMR (125.7 MHz, DMSO-d_6): δ 159.1 (C2-Q), 148.6 (C3-Ar), 142.0 (C3-Q), 134.2 (C1-Ar), 133.0 (C8a-Q), 128.7 (C5-Ar), 126.3 (C7-Q), 124.8 (C4-Q), 124.7 (C5-Q), 121.9 (C6-Q), 121.1 (C4a-Q), 117.1 (C6-Ar), 115.2 (C2-Ar), 115.1 (C8-Q), 113.2 (C4-Ar); ^{15}N NMR (50.6 MHz, DMSO-d_6): δ 147 (N1), 60 (NH_2); HRMS (MALDI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{13}N_2O_2$ 253.0972; Found 253.0965; $[M + Na]^+$ Calcd for $C_{15}H_{12}N_2O_2Na$ 275.0791; Found 275.0782; $[M + Cs]^+$ Calcd for $C_{15}H_{12}N_2O_2Cs$ 384.9948; Found 384.9961.

*3-Hydroxy-4-(3-aminophenyl)-N-(4-methoxybenzyl)quinolin-2-one (**8**).*



Viridicatol

Yield 0.25 (*Method A) and* 0.25 (*Method B*) g (77 and 98%)**,** tan solid, mp 268-270 °C (268-271 °C[20], 238-240 °C[22]); IR (KBr): ν_{max} 3240, 1652, 1592, 1395, 1283, 1246 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ 6.72 (d, *J*=1.2 Hz, 1H, H2-Ar), 6.73 (d, *J*=7.5 Hz, 1H, H6-Ar), 6.83 (dd, *J*=8.3, 1.5 Hz, 1H, H4-Ar), 7.06-7.13 (m, 2H, H5,6-Q), 7.28-7.37 (m, 3H, H5-Ar, H7,8-Q), 9.10 (s, 1H, OH-Q), 9.53 (s, 1H, OH-Ar), 12.18 (s, 1H, NH); ^{13}C{^{1}H} NMR (125.7 MHz, DMSO-d_6): δ 158.3 (C2-Q), 157.3 (C3-Q), 142.2 (C3-Ar), 134.9 (C1-Ar), 133.1 (C8a-Q), 129.4 (C5-Ar), 126.4 (C7-Q), 124.5 (C5-Q), 124.1 (C4-Q), 122.1 (C6-Q), 120.9 (C4a-Q), 120.4 (C6-Ar), 116.7 (C2-Ar1), 115.2 (C8-Q), 114.6s (C4-Ar); ^{15}N NMR (50.6 MHz, DMSO-d_6): δ 147.3; HRMS (MALDI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{12}NO_3$ 254.0812; Found 254.0820; $[M + Cs]^+$ Calcd for $C_{15}H_{11}NO_3Cs$ 385.9788; Found 385.9798.

ASSOCIATED CONTENT

Supporting information

Experimental procedures and compound characterization data including 1D and 2D NMR spectra for most of compounds, 1D and 2D NMR spectra for most of compounds, computational details for **3a**, **5a**, X-ray crystal data (CIF) for **3e**, **4h**, **5a**, **5b** and **5c**. This material is available free of charge via the Internet at **http://pubs.acs.org**

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Notes

The authors declare no competing financial interest.

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