STUDIES ON THE ALKYLATION OF QUINOLIN-2(1*H*)-ONE DERIVATIVES

CHIA-LING CHEN[1], I-LI CHEN[2], JIH-JUNG CHEN[2], DAU-CHANG WEI[2], HAN-JIE HSIEH[2], KEN-MING CHANG[3], CHERNG-CHYI TZENG[3] AND TAI-CHI WANG[2]*

[1]Department of Pharmacy, KUO General Hospital, Tainan City 700, Taiwan
[2]Department of Pharmacy, Tajen University, Pingtung 907, Taiwan
[3]Departament of Medicinal and Applied Chemistry, College of Life Science, Kaohsiung Medical University, Kaohsiung 807, Taiwan

ABSTRACT

Alkylation of quinolin-2(1*H*)-one (**1**) and its C(6) and C(7) substituted dervatives (OMe, OBn, and Cl) with 2-bromoacetophenone or chloroacetone under basic condition (K_2CO_3 in DMF) gave a mixture of N_1- and O_2- alkylated products with the former one as a major product. However, alkylation of 8-methoxy-, 8-benzyloxy-, and 8-chloro- quinolin-2(1*H*)-ones under the same reaction conditions gave exclusively O_2-alkylated products.

Keywords: N-Alkylation; O-Alkylation; Quinolin-2(1*H*)-one.

INTRODUCTION

Quinolin-2(1*H*)-one (carbostyril) skeleton is present in a large number of biologically active compounds which exhibit antiplatelet, anti-inflammatory, anti-ulcer, vasodilatory, and phosphodiesterase inhibitory activities[1-12]. Carteolol, for example, has been used clinically as a β-adrenergic blocking agent[8]. Over the past few years, we were particularly interested in the synthesis of α-methylene-γ-butyrolactones bearing heterocycles such as coumarins, flavones, xanthones, quinolines, and quinolin-2(1*H*)-ones and the evaluation of their cardiovascular and cytotoxic activities[9-14]. Among these heterocycles, coumarins exhibited the most potent inhibitory activities on the high-K^+-medium, Ca^{2+}-induced vasoconstriction, and the norepinephrine-induced phasic and tonic vasoconstrictions, while quinolin-2(1*H*)-ones proved to be the most active against platelet aggregation. A number of quinolin-2(1*H*)-one α-methylene-γ-butyrolactones were found to exhibit potent antiproliferative activities[14].

These biologically active quinolin-2(1*H*)-one derivatives were synthesized from their hydroxyl precursors by alkylation and the *Reformatsky*-type condensation. The *Reformatsky*-type condensation is quite straightforward while the alkylation of quinolin-2(1*H*)-one involves a competitive alkylation leading to the mixture of N_1- and O_2- alkylated products. Although it is well known that alkylation of 2-pyridones gave a mixture of both N- and O- alkylated products,[15-17] relatively few systematic studies of this phenomenon have been published. Hopkins *et al*[18] demonstrated that alkylation of 2-pyridone with benzyl chloride and sodium salt in DMF occurred at N_1-position whereas using the silver salt in benzene afforded exclusively the O_2-alkylated product. The Mitsunobu reaction has also been applied to alkylate 2-pyridones to discover the relationship between the ratio of N- and O- alkylation products.[19,20]

The alkylation of C-5 substituted 2-phenyl-4-quinolones was also investigated and showed that the ratio of *N*-alkylation *versus* O-alkylation is highly dependent on the property of C-5 group. Both *N*-alkylation and O-alkylation products were detected for C-5 methoxy derivative while the sole product of N-alkylation was obtained for the C-5 hydroxy derivative. The alkylation of these 2-phenyl-4-quinolones was conducted under several conditions (NaH/THF, NaH/DMF, K_2CO_3/acetone, K_2CO_3/DMF) at different temperatures. The K_2CO_3/DMF system and temperature elevation led to the highest yields but there was no significant influence on the regioselectivity compared to the other systems used.[21] Studies on N-alkylation *versus* O-alkylation in various ambident heterocyclic compounds under phase transfer conditions have also been reported.[22-25] We have obtained a mixture of N_1- and O_2- alkylated products from the alkylation of quinolin-2(1*H*)-one (**1**) with N_1-alkylation as the major product (*Scheme* 1)[10]. Alkylation of 6-acetoxyquinolin-2(1*H*)-one (**2**) gave a mixture of N_1- and O_2- alkylated products with N_1-alkylation as the major product[11]. However, a sole O_2-alkylated product was obtained from the alkylation of 8-acetoxyquinolin-2(1*H*)-one (**9**) with 2-bromoacetophenone and potassium carbonate in DMF[12]. Guo *et. al.* have also reported that the alkylation of 8-hydroxyquinolin-2(1*H*)-one with 3-methoxybenzyl bromide under basic condition to afford a mixture of N_1- and O_2- alkylated products with the former one as a major product[26]. Alkylation of 8-hydroxyquinolin-2(1*H*)-one was similar to **2** but was distincted from **9** prompted us to explore the alkylation of various quinolin-2(1*H*)-one derivatives. The steric and electronic effects of different substituents which influence the N_1- and O_2- alkylation of quinolin-2(1*H*)-ones are described.

RESULTS AND DISCUSSION

Alkylation of quinolin-2(1*H*)-one (**1**) with 2-bromoacetophenone and potassium carbonate in DMF gave a mixture of N_1- and O_2- alkylated products (**13a** and **13b** respectively) with **13a** as a major product (Scheme 1) but not a sole product as our previous report[10]. The structure of **13a** was confirmed by the long-range $^1H,^{13}C$-HETCOR experiment in which N(1)-CH_2 (5.81 ppm) was coupled to C-atoms with resonances of 192.37 (^2J), 162.11 (^3J), 139.55 (^3J), and 48.68 (^1J) ppm corresponding to C(2'), C(2), C(8a), and C(1') respectively. Structure of **13b** was also confirmed by $^1H,^{13}C$-HETCOR experiment in which O(2)-CH_2 (5.76 ppm) was coupled to C-atoms with resonances of 194.49 (^2J), 160.68 (^3J), and 67.48 (^1J) ppm corresponding to C(2'), C(2), and C(1') respectively. It is worth to mention that one-dimensional ^1H-NMR spectra along is not enough to assign the site of alkylation since chemical shifts of N(1)-CH_2 (5.81 ppm) and O(2)-CH_2 (5.76 ppm) are not distinguishable. However, one-dimensional ^{13}C-NMR spectra provide very useful informations in which C(1') showed a upfield shift at 48.68 ppm for N_1-alkylated product **13a** and a downfield shift at 67.48 ppm for O_2-alkylated product **13b**. A view of a single molecule of **13a** and **13b** respectively are given in Figure 1.

Under the same alkylating conditions, quinolin-2(1*H*)-one substituted with an electron-donating group such as methoxy **3**, benzyloxy **4**, or with an electron-withdrawing group such as chloro **5**, at C(6)-position gave a mixture of N_1- and O_2- alkylated products with the N_1- alkylation as the major product as shown in Scheme 1. Therefore, the electronic environment did not affect the type of alkylation. Accordingly, alkylation of C(7)-substituted quinolin-2(1*H*)-ones **6**, **7**, and **8** afforded N_1-alkylated products **18a**, **19a**, and **20a** as major products.

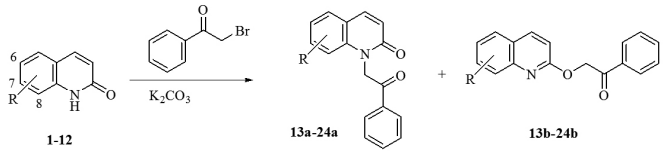
However, this type of alkylation can not be applied to C(8)-substituted quinolin-2(1*H*)-ones. Treatment of 8-methoxyquinolin-2(1*H*)-one (**10**) with 2-bromoacetophenone and potassium carbonate in DMF gave O_2-alkylated product, 8-methoxy-2-(2-oxo-2-phenylethoxy) quinoline (**22b**), as a sole product in a 75% yield. Accordingly, O_2-alkylated products **21b**[12], **23b**, and **24b** were obtained from the alkylation of their respective precursors **9**, **11**, and **12**.

To confirm the application of this type of alkylation, further experiments were carried out by using chloroacetone as an alkylating agent as shown in Scheme 2. Treatment of C(6) and C(7) substituted quinolin-2(1*H*)-ones with chloroacetone and potassium carbonate in DMF gave a mixture of N_1- and O_2-alkylated products with the former one as a major product. The typical peak of ^1H-NMR spectra are not distinguishable, for example, N(1)-CH_2 (5.11 ppm) for **25a** and O(2)-CH_2 (5.04 ppm) for **25b**. However, ^{13}C-NMR spectra provide very useful informations in which C(1') showed a downfield shift at 70.07 ppm for O_2-alkylated product **25b** and a upfield shift at 52.03 ppm for N_1-alkylated product **25a**. Alkylation of C(8)-substituted quinolin-2(1*H*)-ones under the same reaction conditions afforded O_2-alkylated product as a sole product. Therefore, the site of alkylation could be controlled mostly by the steric effect

in which less hindered C(6) and C(7) substituted quinolin-2(1*H*)-ones alkylated at N_1- and O_2- positions with the former one as a major product while C(8) substituted counterparts alkylated exclusively at less hindered O_2-position.

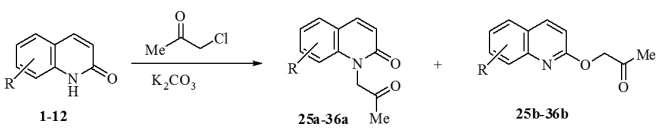
Alkylating agents may also affect the regioselectivity in which the N/O ratio for higher bulky 2-bromoacetophenone is less than that of less bulky chloroacetone due to higher steric hindrance of N-alkylation than that of O-alkylation. For example, the N/O ratio is 2.7 (62/23) for 6-benzyloxy derivative (entry 4, Scheme 1) using 2-bromoacetophenone as an alkylating agent while the N/O ratio is 7.1 (71/10) using chloroacetone (entry 4, Scheme 2) as an alkylating agent.

Scheme 1. Alkylation of quinolin-2(1*H*)-one with 2-bromoacetophenone.



Starting material	R	Products	Yield (%)
1	H	**13a/13b**	66/7
2	6-OAc	**14a/14b**	39/16
3	6-OMe	**15a/15b**	80/7
4	6-OBn	**16a/16b**	62/23
5	6-Cl	**17a/17b**	64/28
6	7-OMe	**18a/18b**	65/12
7	7-OBn	**19a/19b**	79/13
8	7-Cl	**20a/20b**	87/7
9	8-OAc	**21a/21b**	0/74
10	8-OMe	**22a/22b**	0/75
11	8-OBn	**23a/23b**	0/91
12	8-Cl	**24a/24b**	0/94

Scheme 2. Alkylation of quinolin-2(1*H*)-one with chloroacetone.



Starting material	R	Products	Yield (%)
1	H	**25a/25b**	67/10
2	6-OAc	**26a/26b**	75/6
3	6-OMe	**27a/27b**	56/7
4	6-OBn	**28a/28b**	71/10
5	6-Cl	**29a/29b**	85/9
6	7-OMe	**30a/30b**	84/8
7	7-OBn	**31a/31b**	62/8
8	7-Cl	**32a/32b**	76/8
9	8-OAc	**33a/33b**	0/76
10	8-OMe	**34a/34b**	0/67
11	8-OBn	**35a/35b**	0/75
12	8-Cl	**36a/36b**	0/89

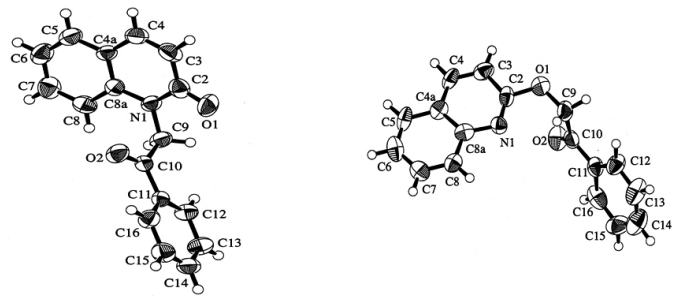


Figure 1. X-Ray crystallographic structures of **13a** and **13b**

CONCLUSIONS

In conclusion, we report herein the selective alkylation of certain substituted quinolin-2(1*H*)-one derivatives. Our results indicated that alkylation of relatively bulky 8-methoxy-, 8-benzyloxy-, and 8-chloro- quinolin-2(1*H*)-ones under classical conditions (2-bromoacetophenone or chloroacetone, DMF, K_2CO_3) gave exclusively O_2-alkylated products. This selectivity can not be applied to C(6) and C(7) substituted quinolin-2(1*H*)-one counterparts in which alkylation occurred at both N_1- and O_2- positions with the former one as a major product. Therefore, alkylation of substituted quinolin-2(1*H*)-ones was controlled by the steric effect but not the electronic effect.

EXPERIMENTAL

TLC: Precoated (0.2 mm) silica gel 60-F_{254} plates from EM Laboratories, Inc.; detection by UV light (254 nm). M.p.: Electrothermal IA9100 digital melting-point apparatus; uncorrected. ^{1}H and ^{13}C-NMR spectra: Varian-Unity-400 spectrometer at 400 and 100 MHz or Varian-Gemini-200 spectrometer at 200 and 50 MHz, chemical shifts *d* in ppm with $SiMe_4$ as an internal standard (= 0 ppm), coupling constants *J* in Hz. Elemental analyses were carried out on a Heraeus CHN-O-Rapid elemental analyzer, and results were within ± 0.4% of calculated values.

1-(2-Oxo-2-phenylethyl)quinolin-2(1*H*)-one (13a) and **2-(2-Oxo-2-phenylethoxy)quinoline (13b)**

Quinolin-2(1*H*)-one (1.45 g, 10 mmol), K_2CO_3 (1.38 g, 10 mmol), and dry DMF (50 mL) were stirred at rt for 30 min. To this solution was added 2-bromoacetophenone (1.99 g, 10 mmol) in dry DMF (10 mL) in one portion. The resulting mixture was continued to stir at rt for 24 h (TLC monitoring), and then poured into ice-water (100 mL). The mixture was extracted with CH_2Cl_2 (3×75 mL). The organic layer was combined, washed with H_2O, dried (Na_2SO_4), and then evaporated to give a brown solid which was purified by column chromatography on silica gel (AcOEt/Hexane 1:1). The proper fractions were combined and evaporated to furnish a residual solid which was crystallized from CH_2Cl_2/Et_2O 1:10 to afford **13a** (1.74 g, 66 %) and **13b** (0.17 g, 7 %).

13a: Mp 164-165 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81 (s, 2H, H-C(1')), 6.75 (d, 1H, *J* = 9.6 Hz, H-C(3)), 6.98 (d, 1H, *J* = 9.6 Hz, ArH), 7.19-7.22 (m, 1H, ArH), 7.42-7.67 (m, 5H, ArH), 7.75 (d, 1H, *J* = 9.6 Hz, H-C(4)), 8.08-8.10 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 48.68 (C(1')), 114.02, 120.78, 121.17, 122.26, 128.10, 128.89, 129.02, 130.68, 133.95, 134.87, 139.55, 139.86, 162.11 (C(2)), 192.37 (C(2')). Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.52; H, 5.01; N, 5.35.

13b: Mp 115-116 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.76 (s, 2H, H-C(1')), 7.10 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.32-7.73 (m, 7H, ArH), 8.01-8.08 (m, 3H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$): δ 67.48 (C(1')), 112.75, 124.28, 125.42, 127.24, 127.40, 127.94, 128.75, 129.49, 133.49, 135.08, 139.23, 146.02, 160.68 (C(2)), 194.49 (C(2')). Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.40; H, 5.00; N, 5.31.

6-Methoxy-1-(2-oxo-2-phenylethyl)quinolin-2(1*H*)-one (15a) and **6-Methoxy-2-(2-oxo-2-phenylethoxy)quinoline (15b)**

Prepared from 6-methoxyquinolin-2(1*H*)-one and 2-bromoacetophenone by the same procedure as described for **13a** and **13b**. **15a**: 80 % yield. Mp 196-197 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.83 (s, 3H, MeO), 5.79 (s, 2H, H-C(1')), 6.77 (d, 1H, *J* = 9.6 Hz, H-C(3)), 6.92 (d, 1H, *J* = 9.2 Hz, H-C(8)), 7.02 (d, 1H, *J* = 2.8 Hz, H-C(5)), 7.06 (dd, 1H, *J* = 9.2, 2.8 Hz, H-C(7)), 7.51-

7.54 (m, 2H, ArH), 7.62-7.66 (m, 1H, ArH), 7.69 (d, 1H, *J* = 9.2 Hz, H-C(4)), 8.06-8.09 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 48.84 (C(1¢)), 55.65 (MeO), 110.77, 115.36, 119.33, 121.50, 121.62, 128.10, 128.89, 133.96, 134.00, 134.84, 139.39, 154.79, 161.72 (C(2)), 192.54 (C(2¢)). Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.65; H, 5.15; N, 4.68.

15b: 7 % yield. Mp 94-95 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.88 (s, 3H, MeO), 5.74 (s, 2H, H-C(1¢)), 7.04 (d, 1H, *J* = 2.4 Hz, H-C(5)), 7.08 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.23 (dd, 1H, *J* = 8.8, 2.4 Hz, H-C(7)), 7.50-7.54 (m, 2H, ArH), 7.60-7.62 (m, 1H, ArH), 7.63 (d, 1H, *J* = 8.8 Hz, H-C(8)), 7.95 (d, 1H, *J* = 8.8 Hz, H-C(4)), 8.05-8.07 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.75 (MeO), 67.74 (C(1¢)), 106.33, 113.10, 121.46, 126.23, 128.19, 128.70, 129.01, 133.76, 135.32, 138.57, 141.55, 156.52, 159.63 (C(2)), 194.95 (C(2¢)). Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.78; H, 5.29; N, 4.60.

6-Benzyloxy-1-(2-oxo-2-phenylethyl)quinolin-2(1*H*)-one (16a) and **6-Benzyloxy-2-(2-oxo-2-phenylethoxy)quinoline (16b)**

Prepared from 6-benzyloxyquinolin-2(1*H*)-one and 2-bromoacetophenone by the same procedure as described for **13a** and **13b**. **16a**: 62 % yield. Mp 177-178 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.09 (s, 2H, CH_2O), 5.78 (s, 2H, H-C(1¢)), 6.76 (d, 1H, *J* = 9.2 Hz, H-C(3)), 6.91 (d, 1H, *J* = 9.2 Hz, H-C(8)), 7.10 (d, 1H, *J* = 2.8 Hz, H-C(5)), 7.13 (dd, 1H, *J* = 8.8, 2.8 Hz, H-C(7)), 7.31-7.44 (m, 5H, ArH), 7.51-7.55 (m, 2H, ArH), 7.63-7.68 (m, 2H, ArH), 8.07-8.09 (m, 1H, ArH), 8.08 (d, 1H, *J* = 9.2 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 48.87 (C(1¢)), 70.55 (CH_2O), 112.19, 115.37, 119.98, 121.49, 121.77, 127.42, 128.15, 128.66, 128.92, 133.99, 134.23, 134.84, 136.52, 139.39, 153.91, 161.77 (C(2)), 192.55 (C(2¢)). Anal. Calcd for $C_{24}H_{19}NO_3$: C, 78.03; H, 5.18; N, 3.79. Found: C, 77.68; H, 5.21; N, 3.66.

16b: 23 % yield. Mp 145-146 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.14 (s, 2H, CH_2O), 5.75 (s, 2H, H-C(1¢)), 7.09 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.13 (d, 1H, *J* = 2.8 Hz, H-C(5)), 7.32 (dd, 1H, *J* = 9.2, 2.8 Hz, H-C(7)), 7.34-7.37 (m, 1H, ArH), 7.38-7.43 (m, 2H, ArH), 7.46-7.49 (m, 2H, ArH), 7.51-7.54 (m, 2H, ArH), 7.61-7.63 (m, 1H, ArH), 7.64 (d, 1H, *J* = 9.2 Hz, H-C(8)), 7.95 (d, 1H, *J* = 8.8 Hz, H-C(4)), 8.05-8.08 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 67.83 (C(1¢)), 70.54 (CH_2O), 107.82, 113.16, 121.91, 126.20, 127.78, 128.20, 128.32, 128.74, 128.88, 129.02, 133.77, 135.31, 136.95, 138.66, 141.61, 155.68, 159.71 (C(2)), 194.89 (C(2¢)). Anal. Calcd for $C_{24}H_{19}NO_3$: C, 78.03; H, 5.18; N, 3.79. Found: C, 78.00; H, 5.20; N, 3.78.

6-Chloro-1-(2-oxo-2-phenylethyl)quinolin-2(1*H*)-one (17a) and **6-Chloro-2-(2-oxo-2-phenylethoxy)quinoline (17b)**

Prepared from 6-chloroquinolin-2(1*H*)-one and 2-bromoacetophenone by the same procedure as described for **13a** and **13b**. **17a**: 64 % yield. Mp 213-214 ºC. ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.78 (s, 2H, H-C(1¢)), 6.78 (d, 1H, *J* = 9.5 Hz, H-C(3)), 6.91 (d, 1H, *J* = 9.0 Hz, H-C(8)), 7.38 (dd, 1H, *J* = 9.0, 2.4 Hz, H-C(7)), 7.50-7.57 (m, 2H, ArH), 7.56 (d, 1H, *J* = 2.4 Hz, H-C(5)), 7.63-7.67 (m, 1H, ArH), 7.87 (d, 1H, *J* = 9.5 Hz, H-C(4)), 8.05-8.10 (m, 2H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$): δ 48.82 (C(1¢)), 115.57, 121,79, 122.54, 127.78, 128.09, 128.16, 129.00, 130.65, 134.19, 134.69, 138.16, 138.72, 161.86 (C(2)), 192.07 (C(2¢)). Anal. Calcd for $C_{17}H_{12}NO_2Cl$: C, 68.58; H, 4.06; N, 4.70. Found: C, 68.47; H, 4.07; N, 4.77.

17b: 28 % yield. Mp 123-124 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.76 (s, 2H, H-C(1¢)), 7.13 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.49 (dd, 1H, *J* = 8.8, 2.4 Hz, H-C(7)), 7.51-7.55 (m, 2H, ArH), 7.61-7.66 (m, 2H, ArH), 7.69 (d, 1H, *J* = 2.4 Hz, H-C(5)), 7.96 (d, 1H, *J* = 8.8 Hz, H-C(8)), 8.05 (d, 1H, *J* = 8.8 Hz, H-C(4)), 8.04-8.06 (m, 1H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 67.80 (C(1¢)), 114.06, 126.27, 126.54, 128.16, 129.01, 129.07, 129.94, 130.42, 133.89, 135.15, 138.56, 144.69, 160.14 (C(2)), 194.45 (C(2¢)). Anal. Calcd for $C_{17}H_{12}NO_2Cl$: C, 68.58; H, 4.06; N, 4.70. Found: C, 68.45; H, 4.08; N, 4.73.

7-Methoxy-1-(2-oxo-2-phenylethyl)quinolin-2(1*H*)-one (18a) and **7-Methoxy-2-(2-oxo-2-phenylethoxy)quinoline (18b)**

Prepared from 7-methoxyquinolin-2(1*H*)-one and 2-bromoacetophenone by the same procedure as described for **13a** and **13b**. **18a**: 65 % yield. Mp 171-172 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.78 (s, 3H, MeO), 5.76 (s, 2H, H-C(1¢)), 6.44 (d, 1H, *J* = 2.4 Hz, H-C(8)), 6.60 (d, 1H, *J* = 9.2 Hz, H-C(3)), 6.80 (dd, 1H, *J* = 8.8, 2.4 Hz, H-C(6)), 7.49 (d, 1H, *J* = 8.8 Hz, H-C(5)), 7.51-7.55 (m, 2H, ArH), 7.63-7.65 (m, 1H, ArH), 7.68 (d, 1H, *J* = 9.6 Hz, H-C(4)), 8.07-8.10 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 49.14 (C(1¢)), 55.74 (MeO), 99.42, 109.60, 115.34, 118.24, 128.38, 129.18, 130.69, 134.25, 135.14, 139.98, 141.45, 162.08, 162.77 (C(2)), 192.95 (C(2¢)). Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.70; H, 5.17; N, 4.78.

18b: 12 % yield. Mp 137-138 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.87 (s, 3H, MeO), 5.77 (s, 2H, H-C(1¢)), 6.96 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.01 (dd, 1H, *J* = 8.8, 2.4 Hz, H-C(6)), 7.07 (d, 1H, *J* = 2.4 Hz, H-C(8)), 7.50-7.55 (m, 2H, ArH), 7.59 (d, 1H, *J* = 9.2 Hz, H-C(5)), 7.61-7.65 (m, 1H, ArH), 7.96 (d, 1H, *J* = 8.8 Hz, H-C(4)), 8.06-8.09 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.64 (MeO), 67.78 (C(1¢)), 106.76, 110.24, 116.69, 120.47, 128.22, 128.66, 129.00, 133.77, 135.27, 139.16, 148.05, 161.20, 161.51 (C(2)), 194.75(C(2¢)). Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.47; H, 5.24; N, 4.39.

7-Benzyloxy-1-(2-oxo-2-phenylethyl)quinolin-2(1*H*)-one (19a) and **7-Benzyloxy-2-(2-oxo-2-phenylethoxy)quinoline (19b)**

Prepared from 7-benzyloxyquinolin-2(1*H*)-one and 2-bromoacetophenone by the same procedure as described for **13a** and **13b**. **19a**: 79 % yield. Mp 185-186 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.99 (s, 2H, CH_2O), 5.66 (s, 2H, H-C(1¢)), 6.45 (d, 1H, *J* = 2.4 Hz, H-C(8)), 6.57 (d, 1H, *J* = 9.6 Hz, H-C(3)), 6.83 (dd, 1H, *J* = 8.8, 2.4 Hz, H-C(6)), 7.25-7.28 (m, 5H, ArH), 7.45 (d, 1H, *J* = 8.8 Hz, H-C(5)), 7.48-7.51 (m, 2H, ArH), 7.60-7.65 (m, 2H, ArH), 8.01 (d, 1H, *J* = 9.6 Hz, H-C(4)), 8.02 -8.03 (m, 1H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 49.19 (C(1¢)), 70.65 (CH_2O), 100.38, 110.55, 115.48, 118.30, 127.68, 128.41, 128.50, 128.94, 129.17, 130.67, 134.29, 135.07, 136.28, 139.98, 141.38, 161.21, 162.77 (C(2)), 192.65 (C(2¢)). Anal. Calcd for $C_{24}H_{19}NO_3$: C, 78.03; H, 5.18; N, 3.79. Found: C, 78.00; H, 5.21; N, 3.79.

19b: 13 % yield. Mp 146-147 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.12 (s, 2H, CH_2O), 5.77 (s, 2H, H-C(1¢)), 6.97 (d, 1H, *J* = 9.6 Hz, H-C(3)), 7.10 (dd, 1H, *J* = 8.8, 2.4 Hz, H-C(6)), 7.17 (d, 1H, *J* = 2.4 Hz, H-C(8)), 7.32-7.42 (m, 3H, ArH), 7.44-7.47 (m, 2H, ArH), 7.51-7.55 (m, 2H, ArH), 7.61-7.66 (m, 2H, ArH), 7.97 (d, 1H, *J* = 8.8 Hz, H-C(5)), 8.06-8.09 (m, 1H, ArH), 8.07 (d, 1H, *J* = 9.6 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 67.83 (C(1¢)), 70.29 (CH_2O), 107.91, 110.38, 117.04, 120.62, 127.88, 128.23, 128.33, 128.75, 128.86, 128.93, 129.01, 133.78, 135.30, 136.80, 139.19, 160.35, 161.51 (C(2)), 194.75 (C(2¢)). Anal. Calcd for $C_{24}H_{19}NO_3$: C, 78.03; H, 5.18; N, 3.79. Found: C, 78.40; H, 5.26; N, 3.71.

7-Chloro-1-(2-oxo-2-phenylethyl)quinolin-2(1*H*)-one (20a) and **7-Chloro-2-(2-oxo-2-phenylethoxy)quinoline (20b)**

Prepared from 7-chloroquinolin-2(1*H*)-one and 2-bromoacetophenone by the same procedure as described for **13a** and **13b**. **20a**: 87 % yield. Mp 180-181 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.76 (s, 2H, H-C(1¢)), 6.75 (d, 1H, *J* = 9.2 Hz, H-C(3)), 6.97 (d, 1H, *J* = 2.0 Hz, H-C(8)), 7.19 (dd, 1H, *J* = 8.4, 2.0 Hz, H-C(6)), 7.52 (d, 1H, *J* = 8.4 Hz, H-C(5)), 7.55-7.59 (m, 2H, ArH), 7.66-7.71 (m, 1H, ArH), 7.72 (d, 1H, *J* = 9.2 Hz, H-C(4)), 8.09-8.12 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 49.05 (C(1¢)), 114.37, 119.51, 121.49, 123.10, 128.46, 129.27, 130.34, 134.48, 134.87, 137.21, 139.57, 140.71, 162.15 (C(2)), 192.04 (C(2¢)). Anal. Calcd for $C_{17}H_{12}NO_2Cl{\cdot}0.2H_2O$: C, 67.76; H, 4.14; N, 4.65. Found: C, 67.92; H, 4.02; N, 4.66.

20b: 7 % yield. Mp 106-107 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.76 (s, 2H, H-C(1¢)), 7.10 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.32 (dd, 1H, *J* = 8.4, 2.0 Hz, H-C(6)), 7.51-7.55 (m, 2H, ArH), 7.62-7.66 (m, 1H, ArH), 7.64 (d, 1H, *J* = 8.4 Hz, H-C(5)), 7.70 (d, 1H, *J* = 2.4 Hz, H-C(8)), 8.01 (d, 1H, *J* = 8.8 Hz, H-C(4)), 8.03-8.06 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 67.94 (C(1¢)), 113.26, 123.99, 125.46, 126.65, 128.16, 128.79, 129.10, 133.94, 135.07, 135.65, 139.29, 146.75, 161.66 (C(2)), 194.31 (C(2¢)). Anal. Calcd for $C_{17}H_{12}NO_2Cl$: C, 68.58; H, 4.06; N, 4.70. Found: C, 68.22; H, 4.05; N, 4.64.

8-Methoxy-2-(2-oxo-2-phenylethoxy)quinoline (22b)

Prepared from 8-methoxyquinolin-2(1*H*)-one and 2-bromoacetophenone by the same procedure as described for **13a** and **13b**. 75 % yield. Mp 161-162 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.88 (s, 3H, MeO), 5.80 (s, 2H, H-C(1¢)), 6.99-7.01 (m, 1H, ArH), 7.14 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.27-7.34 (m, 2H, ArH), 7.49-7.54 (m, 2H, ArH), 7.59-7.63 (m, 1H, ArH), 8.03 (d, 1H, *J* = 8.8 Hz, H-C(4)), 8.07-8.10 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.17 (MeO), 67.53 (C(1¢)), 109.54, 113.16, 119.66, 124.34, 126.55, 128.13, 128.65, 133.37, 135.46, 137.48, 139.42, 154.14, 160.16 (C(2)), 194.94 (C(2¢)). Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.64; H, 5.19; N, 4.80.

8-Benzyloxy-2-(2-oxo-2-phenylethoxy)quinoline (23b)

Prepared from 8-benzyloxyquinolin-2(1*H*)-one and 2-bromoacetophenone by the same procedure as described for **13a** and **13b**. 91 % yield. Mp 132-133 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.16 (s, 2H, CH_2O), 5.86 (s, 2H, H-C(1¢)), 7.07 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.15-7.28 (m, 5H, ArH), 7.33-7.37 (m, 3H, ArH), 7.44-7.48 (m, 2H, ArH), 7.59-7.62 (m, 1H, ArH), 8.02-8.06 (m, 2H, ArH), 8.05 (d, 1H, *J* = 8.8 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 67.81 (C(1¢)), 71.38 (CH_2O), 112.83, 113.26, 120.62, 124.48, 126.94, 127.16, 127.72, 128.15, 128.53, 128.71, 129.02, 133.71, 135.27, 137.61, 139.65, 153.42, 160.31 (C(2)), 194.62 (C(2¢)). Anal. Calcd for $C_{24}H_{19}NO_3$: C, 78.03; H, 5.18; N, 3.79. Found: C, 78.01; H, 5.17; N, 3.61.

8-Chloro-2-(2-oxo-2-phenylethoxy)quinoline (24b)

Prepared from 8-chloroquinolin-2(1*H*)-one and 2-bromoacetophenone by the same procedure as described for **13a** and **13b**. 94 % yield. Mp 183-184 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.80 (s, 2H, H-C(1¢)), 7.16 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.24-7.28 (m, 1H, ArH), 7.49-7.53 (m, 2H, ArH), 7.59-7.67 (m, 3H, ArH), 8.04-8.07 (m, 2H, ArH), 8.05 (d, 1H, *J* = 8.8 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 67.73 (C(1¢)), 113.54, 124.25, 126.33, 126.58, 127.99, 128.74, 129.74, 131.44, 133.50, 135.28, 139.69, 142.38, 161.01 (C(2)), 194.45 (C(2¢)). Anal. Calcd for $C_{17}H_{12}NO_2Cl$: C, 68.58; H, 4.06; N, 4.70. Found: C, 68.42; H, 4.11; N, 4.81.

1-(2-Oxopropyl)quinolin-2(1*H*)-one (25a) and **2-(2-Oxopropoxy) quinoline (25b)**

Prepared from quinolin-2(1*H*)-one and chloroacetone by the same procedure as described for **13a** and **13b**. **25a**: 67 % yield. Mp 108-109 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.24 (s, 3H, Me), 5.11 (s, 2H, H-C(1¢)), 6.73 (d, 1H, *J* = 9.6 Hz, H-C(3)), 7.00-7.24 (m, 2H, ArH), 7.51-7.58 (m, 2H, ArH), 7.74 (d, 1H, *J* = 9.6 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.06 (Me), 52.03 (C(1¢)), 113.69, 120.69, 121.20, 122.51, 129.12, 130.90, 139.30, 139.95, 161.89 (C(2)), 202.49 (C(2¢)). Anal. Calcd for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.66; H, 5.51; N, 6.94.

25b: 10 % yield. Oily. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.27 (s, 3H, Me), 5.04 (s, 2H, H-C(1¢)), 7.03 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.39-7.61 (m, 2H, ArH), 7.71-7.79 (m, 2H, ArH), 8.04 (d, 1H, *J* = 9.0 Hz, H-C(4)). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.45 (Me), 70.07 (C(1¢)), 112.54, 124.44, 125.40, 127.29, 127.42, 129.64, 139.35, 146.00, 160.61 (C(2)), 204.89 (C(2¢)). Anal. Calcd for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.33; H, 5.71; N, 6.83.

6-Methoxy-1-(2-oxopropyl)quinolin-2(1*H*)-one (27a) and **6-Methoxy-2-(2-oxopropoxy)quinoline (27b)**

Prepared from 6-methoxyquinolin-2(1*H*)-one and chloroacetone by the same procedure as described for **13a** and **13b**. **27a**: 56 % yield. Mp 171-172 ºC. ^{1}H NMR (400 NHz, $CDCl_3$): δ 2.22 (3H, s, Me), 3.85 (s, 3H, MeO), 5.09 (s, 2H, H-C(1¢)), 6.74 (d, 1H, *J* = 9.6 Hz, H-C(3)), 6.94 (d, 1H, *J* = 9.2 Hz, H-C(8)), 7.03 (d, 1H, *J* = 2.8 Hz, H-C(5)), 7.13 (dd, 1H, *J* = 9.2, 2.8 Hz, H-C(7)), 7.68 (d, 1H, *J* = 9.6 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.11 (Me), 52.24 (C(1¢)), 55.74 (MeO), 111.02, 115.05, 119.48, 121.50, 121.82, 133.82, 139.48, 155.00, 161.53 (C(2)), 202.78 (C(2¢)). Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.64; H, 5.75; N, 6.03.

27b: 7 % yield. Mp 78-79 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.25 (s, 3H, Me), 3.89 (s, 3H, MeO), 5.00 (s, 2H, H-C(1¢)), 7.00 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.05 (d, 1H, *J* = 2.8 Hz, H-C(5)), 7.27 (dd, 1H, *J* = 9.2, 2.8 Hz, H-C(7)), 7.68 (d, 1H, *J* = 9.2 Hz, H-C(8)), 7.95 (d, 1H, *J* = 8.8 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.42 (Me), 55.51 (MeO), 70.08 (C(1¢)), 106.15, 112.61, 121.31, 125.97, 128.48, 138.36, 141.29, 156.37, 159.29 (C(2)), 205.07 (C(2¢)). Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.50; H, 5.66; N, 6.06.

6-Benzyloxy-1-(2-oxopropyl)quinolin-2(1*H*)-one (28a) and **6-Benzyloxy-2-(2-oxopropoxy)quinoline (28b)**

Prepared from 6-benzyloxyquinolin-2(1*H*)-one and chloroacetone by the same procedure as described for **13a** and **13b**. **28a**: 71 % yield. Mp 184-185 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.22 (s, 3H, Me), 5.09 (s, 2H, CH_2O), 5.10 (*s*, 2H, H-C(1¢)), 6.73 (d, 1H, *J* = 9.2 Hz, H-C(3)), 6.94 (d, 1H, *J* = 9.2 Hz, H-C(8)), 7.10 (d, 1H, *J* = 2.8 Hz, H-C(5)), 7.20 (dd, 1H, *J* = 9.2, 2.8 Hz, H-C(7)), 7.33-7.45 (m, 5H, ArH), 7.66 (1H, d, *J* = 9.6 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.39 (Me), 52.44 (C(1¢)), 70.80 (CH_2O), 112.54, 115.30, 120.37, 121.70, 122.02, 127.71, 128.45, 128.95, 134.16, 136.67, 139.75, 154.31, 161.77 (C(2)), 202.98 (C(2¢)). Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 74.16; H, 5.57; N, 4.52.

28b: 10 % yield. Mp 115-116 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (s, 3H, Me), 5.01 (s, 2H, CH_2O), 5.15 (s, 2H, H-C(1¢)), 7.01 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.14 (d, 1H, *J* = 2.8 Hz, H-C(5)), 7.33-7.43 (m, 3H, ArH), 7.36 (dd, 1H, *J* = 9.2, 2.8 Hz, H-C(7)), 7.47-7.48 (m, 2H, ArH), 7.70 (d, 1H, *J* = 9.2 Hz, H-C(8)), 7.94 (d, 1H, *J* = 8.8 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.72 (Me), 70.28 (C(1¢)), 70.56 (CH_2O), 107.83, 112.93, 114.14, 121.99, 126.20, 127.77, 128.34, 128.89, 136.94, 138.64, 141.74, 155.74, 159.63 (C(2)), 205.45 (C(2¢)). Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 74.44; H, 5.60; N, 4.55.

6-Chloro-1-(2-oxopropyl)quinolin-2(1*H*)-one (29a) and **6-Chloro-2-(2-oxopropoxy)quinoline (29b)**

Prepared from 6-chloroquinolin-2(1*H*)-one and chloroacetone by the same procedure as described for **13a** and **13b**. **29a**: 85 % yield. Mp 178-179 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.27 (s, 3H, Me), 5.10 (s, 2H, H-C(1¢)), 6.76 (d, 1H, *J* = 9.6 Hz, H-C(3)), 6.92 (d, 1H, *J* = 9.2 Hz, H-C(8)), 7.44 (dd, 1H, *J* = 9.2, 2.0 Hz, H-C(7)), 7.56 (d, 1H, *J* = 2.0 Hz, H-C(5)), 7.65 (d, 1H, *J* = 9.6 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.22 (Me), 52.07 (C(1¢)), 115.24, 121.71, 122.53, 128.01, 128.21, 130.83, 137.90, 138.80, 161.48 (C(2)), 201.79 (C(2¢)). Anal. Calcd for $C_{12}H_{10}NO_2Cl$: C, 61.16; H, 4.28; N, 5.94. Found: C, 61.13; H, 4.32; N, 6.01.

29b: 9 % yield. Mp 108-109 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (s, 3H, Me), 5.03 (s, 2H, H-C(1¢)), 7.06 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.54 (dd, 1H, *J* = 8.8, 2.0 Hz, H-C(7)), 7.69 (d, 1H, *J* = 8.8 Hz, H-C(8)), 7.70 (d, 1H, *J* = 2.8 Hz, H-C(5)), 7.95 (d, 1H, *J* = 8.8 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.42 (Me), 70.14 (C(1¢)), 113.64, 126.04, 126.25, 128.81, 129.91, 130.35, 138.42, 144.46, 160.84 (C(2)), 204.39 (C(2¢)). Anal. Calcd for $C_{12}H_{10}NO_2Cl$: C, 61.16; H, 4.28; N, 5.94. Found: C, 61.18; H, 4.37; N, 5.93.

7-Methoxy-1-(2-oxopropyl)quinolin-2(1*H*)-one (30a) and **7-Methoxy-2-(2-oxopropoxy)quinoline (30b)**

Prepared from 7-methoxyquinolin-2(1*H*)-one and chloroacetone by the same procedure as described for **13a** and **13b**. **30a**: 84 % yield. Mp 113-114 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.20 (s, 3H, Me), 3.84 (s, 3H, MeO), 5.05 (s, 2H, H-C(1¢)), 6.44 (d, 1H, *J* = 2.0 Hz, H-C(8)), 6.56 (d, 1H, *J* = 9.6 Hz, H-C(3)), 6.81 (dd, 1H, *J* = 8.8, 2.0 Hz, H-C(6)), 7.48 (d, 1H, *J* = 8.8 Hz, H-C(5)), 7.66 (d, 1H, *J* = 9.6 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.30 (Me), 52.50 (C(1¢)), 55.83 (MeO), 98.87, 110.02, 115.15, 118.16, 130.79, 140.07, 141.20, 162.29, 162.51 (C(2)), 203.19 (C(2¢)). Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.44; H, 5.68; N, 6.00.

30b: 8 % yield. Mp 96-97 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (s, 3H, Me), 3.92 (s, 3H, MeO), 5.01 (s, 2H, H-C(1¢)), 6.89 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.04 (dd, 1H, *J* = 8.8, 2.4 Hz, H-C(6)), 7.13 (d, 1H, *J* = 2.4 Hz, H-C(8)), 7.60 (d, 1H, *J* = 8.8 Hz, H-C(5)), 7.96 (d, 1H, *J* = 8.4 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.68 (Me), 55.71 (MeO), 70.40 (C(1¢)), 106.77, 109.98, 116.90, 120.44, 128.66, 139.25, 148.06, 161.33, 161.44 (C(2)), 205.58 (C(2¢)). Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.20; H, 5.88; N, 5.93.

7-Benzyloxy-1-(2-oxopropyl)quinolin-2(1*H*)-one (31a) and **7-Benzyloxy-2-(2-oxopropoxy)quinoline (31b)**

Prepared from 7-benzyloxyquinolin-2(1*H*)-one and chloroacetone by the same procedure as described for **13a** and **13b**. **31a**: 62 % yield. Mp 103-104 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.17 (s, 3H, Me), 5.02 (s, 2H, CH_2O), 5.12 (s, 2H, H-C(1¢)), 6.51 (d, 1H, *J* = 2.4 Hz, H-C(8)), 6.58 (d, 1H, *J* = 9.6 Hz, H-C(3)), 6.89 (dd, 1H, *J* = 8.8, 2.4 Hz, H-C(6)), 7.35-7.44 (m, 5H, ArH), 7.49 (d, 1H, *J* = 8.8 Hz, H-C(5)), 7.66 (d, 1H, *J* = 9.6 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.31 (Me), 52.49 (C(1¢)), 70.68 (CH_2O), 99.95, 110.81, 115.32, 118.30, 127.78, 128.61, 129.02, 130.79, 136.21, 140.05, 141.14, 161.35, 162.50 (C(2)), 202.99 (C(2¢)). Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 74.27; H, 5.59; N, 4.54.

31b: 8 % yield. Mp 133-134 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (s, 3H, Me), 5.01 (s, 2H, CH_2O), 5.18 (s, 2H, H-C(1¢)), 6.90 (d, 1H, *J* = 8.4 Hz, H-C(3)), 7.13 (dd, 1H, *J* = 8.8, 2.4 Hz, H-C(6)), 7.24 (d, 1H, *J* = 2.4 Hz, H-C(8)), 7.34-7.38 (m, 1H, ArH), 7.40-7.44 (m, 2H, ArH), 7.48-7.51 (m, 2H, ArH), 7.63 (d, 1H, *J* = 8.8 Hz, H-C(5)), 7.97 (d,1H, *J* = 8.4 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.72 (Me), 70.39 (C(1¢)), 70.47 (CH_2O), 107.90, 110.12, 117.25, 120.59, 127.90, 128.38, 128.76, 128.89, 136.75, 139.29, 147.96, 160.48, 161.43 (C(2)), 205.54 (C(2¢)). Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 74.24; H, 5.57; N, 4.53.

7-Chloro-1-(2-oxopropyl)quinolin-2(1*H*)-one (32a) and **7-Chloro-2-(2-oxopropoxy)quinoline (32b)**

Prepared from 7-chloroquinolin-2(1*H*)-one and chloroacetone by the same procedure as described for **13a** and **13b**. **32a**: 76 % yield. Mp 158-159 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.31 (s, 3H, Me), 5.23 (s, 2H, H-C(1¢)), 6.65 (d, 1H, *J* = 9.2 Hz, H-C(3)), 7.31 (dd, 1H, *J* = 8.4, 1.6 Hz, H-C(6)), 7.51 (d, 1H, *J* = 1.6 Hz, H-C(8)), 7.77 (d, 1H, *J* = 8.4 Hz, H-C(5)), 7.98 (d, 1H, *J* = 9.6 Hz, H-C(4)). ^{13}C NMR (100 MHz, DMSO-d_6): δ 28.10 (Me), 52.34 (C(1¢)), 115.06, 119.51, 121.46, 122.98, 131.22, 136.41, 140.27, 141.09, 161.56 (C(2)), 202.86 (C(2¢)). Anal. Calcd for $C_{12}H_{10}NO_2Cl$: C, 61.16; H, 4.28; N, 5.94. Found: C, 61.09; H, 4.25; N, 5.96.

32b: 8 % yield. Mp 93-94 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.27 (s, 3H, Me), 5.04 (s, 2H, H-C(1¢)), 7.03 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.35 (dd, 1H, *J* = 8.4, 2.0 Hz, H-C(6)), 7.65 (d, 1H, *J* = 8.4 Hz, H-C(5)), 7.79 (d, 1H, *J* = 1.6 Hz, H-C(8)), 8.12 (d, 1H, *J* = 8.8 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.67 (Me), 70.62 (C(1¢)), 113.02, 123.95, 125.69, 126.51, 128.84, 135.94, 139.55, 146.51, 161.53 (C(2)), 204.19 (C(2¢)). Anal. Calcd for $C_{12}H_{10}NO_2Cl$: C, 61.16; H, 4.28; N, 5.94. Found: C, 61.19; H, 4.28; N, 5.93.

8-Methoxy-2-(2-oxopropoxy)quinoline (34b)

Prepared from 8-methoxyquinolin-2(1*H*)-one and chloroacetone by the same procedure as described for **13a** and **13b**. 67 % yield. Mp 55-56 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.33 (s, 3H, Me), 4.01 (s, 3H, MeO), 5.09 (s, 2H, H-C(1¢)), 7.03-7.05 (m, 1H, ArH), 7.07 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.31-7.34 (m, 2H, ArH), 8.02 (d, 1H, *J* = 8.8 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.84 (Me), 56.20 (MeO), 69.95 (C(1¢)), 109.38, 112.88, 119.60, 124.44,

126.51, 137.40, 139.50, 154.17, 159.96 (C(2)), 204.66 (C(2¢)). Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.51; H, 5.73; N, 5.90.

8-Benzyloxy-2-(2-oxopropoxy)quinoline (35b)

Prepared from 8-benzyloxyquinolin-2(1*H*)-one and chloroacetone by the same procedure as described for **13a** and **13b**. 75 % yield. Mp 56-57 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.15 (s, 3H, Me), 5.00 (s, 2H, CH_2O), 5.24 (s, 2H, H-C(1¢)), 7.06 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.09-7.11 (m, 1H, ArH), 7.25-7.42 (m, 5H, ArH), 7.52-7.54 (m, 2H, ArH), 8.02 (d, 1H, *J* = 8.8 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.52 (Me), 69.84 (C(1¢)), 71.07 (CH_2O), 111.76, 112.72, 120.08, 124.31, 126.60, 127.49, 127.86, 128.45, 137.20, 137.83, 139.39, 153.27, 159.81 (C(2)), 204.48 (C(2¢)). Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 74.27; H, 5.71; N, 4.38.

8-Chloro-2-(2-oxopropoxy)quinoline (36b)

Prepared from 8-chloroquinolin-2(1*H*)-one and chloroacetone by the same procedure as described for **13a** and **13b**. 89 % yield. Mp 99-100 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.33 (s, 3H, Me), 5.09 (s, 2H, H-C(1¢)), 7.10 (d, 1H, *J* = 8.8 Hz, H-C(3)), 7.30 (dd, 1H, *J* = 7.6, 7.6 Hz, H-C(6)), 7.64 (dd, 1H, *J* = 8.0, 1.2 Hz, H-C(7)), 7.72 (dd, 1H, *J* = 7.6, 1.2 Hz, H-C(5)), 8.05 (d, 1H, *J* = 8.8 Hz, H-C(4)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.72 (Me), 70.16 (C(1¢)), 113.35, 124.35, 126.37, 126.58, 129.86, 131.44, 139.75, 142.33, 160.89 (C(2)), 203.87 (C(2¢)). Anal. Calcd for $C_{12}H_{10}NO_2Cl$: C, 61.16; H, 4.28; N, 5.94. Found: C, 61.17; H, 4.23; N, 5.98.

REFERENCES

1. M. Tominaga, H. Tone, K. Nakagawa, K. Takada, Y. Hoshino, K. Watanabe, *Chem. Pharm. Bull.* **29**, 2166, (1981).
2. T. Nishi, K. Yamamoto, T. Shimizu, T. Kanbe, Y. Kimura, K. Nakagawa, *Chem. Pharm. Bull*. **31**, 798, (1983).
3. P. Cheng, Q. Zhang, Y.B. Ma, Z.Y. Jiang, X.M. Zhang, F.X. Zhang, J.J. Chen, *Bioorg. Med. Chem. Lett.* **18**, 3787, (2008).
4. C.D. Beadle, J. Boot, N.P. Camp, N. Dezutter, J. Findlay, L. Hayhurst, J.J. Masters, R. Penariol, M.W. Walter, *Bioorg. Med. Chem. Lett.* **15**, 4432, (2005).
5. J.T. Kuethe, A. Wong, C. Qu, J. Smitrovich, I.W. Davies, D.L. Hughes, *J. Org. Chem*. **70**, 2555, (2005).
6. P. Hewawasam, W. Fan, D.A. Cook, K.S. Newberry, C.G. Boissard, V.K. Gribkoff, J. Starrett, N.J. Lodge, *Bioorg. Med. Chem. Lett.* **14**, 4479, (2004).
7. T. Fujioka, S. Teramoto, T. Mori, T. Hosokawa, T. Sumida, M. Tominaga, Y. Yabuuchi, *J. Med. Chem*. **35**, 3607, (1992).
8. B.J. Lipworth, A. Grove, *Br. J. Clin. Pharm*. **43**, 9, (1997).
9. C.C. Tzeng, T.C. Wang, Y.L. Chen, C.J. Wang, Y.L. Chang, C.M. Teng, *Helv. Chim. Acta.* **80**, 1161, (1007).
10. I.L. Chen, Y.L. Chen, T.C. Wang, C.C. Tzeng, *Heterocycles* **60**, 131, (2003).
11. T.C. Wang, Y.L. Chen, C.C. Tzeng, S.S. Liou, W.F. Tzeng, Y.L. Chang, C.M. Teng, *Helv. Chim. Acta.* **81**, 1038, (1998).
12. S.S. Liou, Y.L. Zhao, Y.L. Chang, C.M. Teng, C.C. Tzeng, *Chem. Pharm. Bull.* **45**, 1777, (1997).
13. Y.L. Chen, T.C. Wang, K.C. Fang, N.C. Chang, C.C. Tzeng, *Heterocycles* **50**, 453, (1999).
14. C.C. Tzeng, K.H. Lee, T.C. Wang, C.H. Han, Y.L. Chen, *Pharmaceut. Res*. **17**, 715, (2000).
15. T. Sato, K. Yoshimatsu, J. Otera, *Synlett* 845, (1995).
16. H. Liu, S.-B. Ko, H. Josien, D. P. Curran, *Tetrahedron Lett*. **36**, 8917, (1995).
17. Y. L. Janin, C. Huel, G. Flad, S. Thirot, *Eur. J. Org. Chem*. 1763, (2002).
18. G. Hopkins, J.P. Jonak, H.J. Minnemeyer, H. Tieckelmann, *J. Org. Chem*. **32**, 4040, (1967).
19. D. L. Comins, G. Jianhua, *Tetrahedron Lett*. **35**, 2819, (1994).
20. M. C. Torhan, N. P. Peet, J. D. Williams, *Tetrahedron Letters* **54**, 3926, (2013)
21. M. Hadjeri, A.-M. Mariotte, A. Boumendjel, *Chem. Pharm. Bull*. **49** (10) 1352, (2001).
22. P. Depreux, G. Bethegnies, *Synth. Commun*. **23**(8), 1189 (1993).
23. M. Hedayatullah, *J. Heterocycl. Chem*. **18**, 339 (1981).
24. T. Yamada, M. Ohki, *Synthesis* 631 (1981).
25. C. G. Dave, K. J. Patel, *J. Heterocycl Chem*., **51**, 943 (2014).
26. Z.X. Guo, A.N. Cammidge, A. McKillop, D.C. Horwell, *Tetrahedron Lett.* **40**, 6999, (1999).