Tetrahedron 69 (2013) 10826–10835

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Oxidative ring opening of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones into *N*-(α-ketoacyl)anthranilic acids

Stanislav Kafka [a,*], Karel Proisl [a], Věra Kašpárková [a], Damijana Urankar [b], Roman Kimmel [a], Janez Košmrlj [b,*]

[a] Department of Chemistry, Faculty of Technology, Tomas Bata University in Zlin, 762 72 Zlin, Czech Republic
[b] Faculty of Chemistry and Chemical Technology, University of Ljubljana, 1000 Ljubljana, Slovenia

ARTICLE INFO

Article history:
Received 8 August 2013
Received in revised form 14 October 2013
Accepted 28 October 2013
Available online 1 November 2013

Dedicated to Professor Slovenko Polanc on his 65th birthday

Keywords:
N-(α-Ketoacyl)anthranilic acid
Quinolinones
Quinolinediones
Paraperiodic acid
Periodate

ABSTRACT

N-(α-Ketoacyl)anthranilic acids were prepared by oxidative ring opening of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones by using paraperiodic acid (H_5IO_6) or sodium periodate ($NaIO_4$). The optimisation of the reaction conditions is described as well as the utilisation of *N*-(α-ketoacyl)anthranilic acids in the preparation of anthranilic acid hydrochlorides.

1. Introduction

N-(α-Ketoacyl)anthranilic acids, exemplified by *N*-pyruvoylanthranilic acid A in Fig. 1, can serve as valuable precursors for the construction of heterocycles, such as 4*H*-benzo[*d*][1,3]oxazin-4-ones (**B**)[1] and 1*H*-benzo[*e*][1,4]oxazepin-2,5-diones (**C** and **D**).[2] In coordination chemistry, *N*-(α-ketoacyl)anthranilic acid derivatives can serve as multidentate ligands for transition metal ions.[3] *N*-Pyruvoylanthranilic acid (**A**) has been proposed to be an intermediate in the biosynthesis of anthranilic acid.[4]

Despite potential biological and synthetic relevance the synthesis of *N*-(α-ketoacyl)anthranilic acids has remained largely unexplored. Although several methods exist for the preparation of α-ketoamides,[5] to our knowledge, the synthetic procedures to the title compounds are largely limited to amidation of α-ketoacyl chlorides with anthranilic acid.[2,6–9] An exception is the work of Podesva and co-workers[8] who reported in 1968 that oxidative ring opening of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones with paraperiodic acid (H_5IO_6)[10,11] leads to *N*-(α-ketoacyl)anthranilic acids. Unfortunately, this reaction was only demonstrated on two substrates and was not investigated further. Induced by our research interest in the chemistry of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones[12–24] and due to a need for preparing *N*-(α-ketoacyl)anthranilic acids we were prompted to explore the scope of the title reaction. Herein we report the optimisation of the reaction conditions and comparison between paraperiodic acid and sodium periodate ($NaIO_4$) to finally afford the target compounds in good to excellent yields.

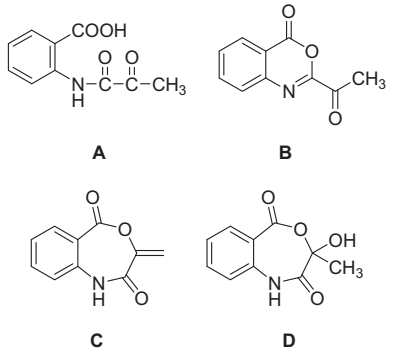


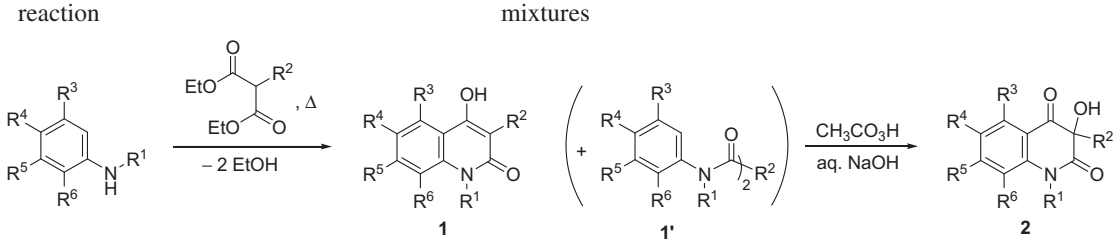
Fig. 1. The structure of *N*-pyruvoylanthranilic acid **A** and its heterocyclic products **B**–**D**.

* Corresponding authors. Fax: +420 57 72 10 172 (S.K.); fax: +386 1 241 9220 (J.K.); e-mail addresses: kafka@ft.utb.cz (S. Kafka), janez.kosmrlj@fkkt.uni-lj.si (J. Košmrlj).

0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.10.092

2. Results and discussion

The starting compounds for this study were prepared by known thermal condensation of the appropriate anilines with substituted malonates to give 4-hydroxyquinolin-2(1*H*)-ones **1**.[12,25,26] In few cases very small amounts of propanediamide side products **1′** were formed, which were easily removed from the reaction mixtures by filtration. Subsequent oxidation of 4-hydroxyquinolin-2(1*H*)-ones **1** into 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones **2** was accomplished with peroxyacetic acid in aqueous alkali following the literature reported methods.[12,16,27] Employing several anilines and 2-substituted diethyl malonates afforded sixteen 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones **2**. The key of substituents is given in Scheme 1 and Table 1.

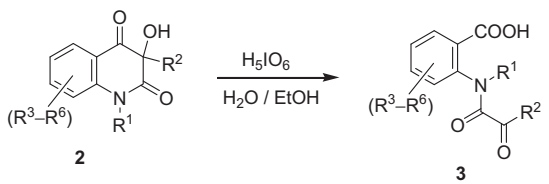


Scheme 1. The preparation of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones **2**. For key of substituents, see Table 1.

Table 1
Key of substituents R^1–R^6

2	R^1	R^2	R^3	R^4	R^5	R^6
a	H	Me	H	H	H	H
b	H	Et	H	H	H	H
c	H	Et	H	OMe	H	H
d	H	Et	H	H	OMe	H
e	H	Et	H	H	H	OMe
f	H	Et	H	Me	H	H
g	H	Et	H	H	H	Me
h	H	Et	Cl	H	H	Me
i	H	Bu	H	H	H	H
j	H	Bu	H	Me	H	Me
k	H	Bu	H	OMe	H	OMe
l	H	Bu	H	H	–(CH)$_4$–	
m	H	Ph	H	H	H	H
n	Me	Et	H	H	H	H
o	Me	Bu	H	H	H	H
p	Me	Ph	H	H	H	H

Having in hand the library of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones **2a**–**p** we focused our attention on the oxidative ring opening as shown in Scheme 2. Initially, the transformation was attempted with 3-ethyl-3-hydroxyquinoline-2,4(1*H*,3*H*)-dione (**2b**). By employing an equimolar amount of paraperiodic acid (H_5IO_6) in wet ethanol at room temperature, the reaction was conducted for 24 h with 2-[(2-oxobutanoyl)amino]benzoic acid (**3b**) isolated in good yield (Table 2, Entry 1). These reaction conditions as well as the outcome were comparable to those reported by Podesva and co-workers[8] for H_5IO_6 oxidation of 6-chloro-3-hydroxy-3-phenylquinoline-2,4(1*H*,3*H*)-dione and its *N*-methyl derivative. Unfortunately, as it is evident by comparing entries 1, 5, 7, 10, 17, 22, 26 and 27 (Table 2) the generalization of this reaction protocol to other analogues **2** turned out to be rather limited requiring prolonged reaction times of as much of several days and affording products **3** in moderate yields. These unacceptably slow conversions of compounds **2** could be attributed to their sparing solubility in water-rich reaction media. Attempts to accelerate the reactions by heating were counterproductive, resulting in complex mixtures of products and consequently low yield of **3** (compare entries 27 with 28). Also unsatisfactory were the results of oxidations conducted in other solvents, such as acetic acid and *N*,*N*-dimethylformamide (compare entry 17 with 19 and 20, and entry 26 with 31).



Scheme 2. Oxidative ring opening of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones **2** with paraperiodic acid (H_5IO_6) into *N*-(α-ketoacyl)anthranilic acids **3**.

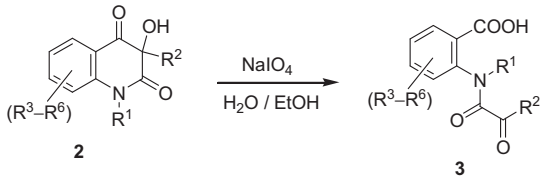
Table 2
Screening for the optimal reaction conditions for the oxidation of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones **2** with paraperiodic acid (H_5IO_6) into *N*-(α-ketoacyl)anthranilic acids **3** shown in Scheme 2 [a]

Entry	**2**	Equiv of H_5IO_6	Solvent (mL/mmol of **2**)	Temperature	Reaction time	**3**, yield[b]
1	**2b**	1.0	30% EtOH (11)	rt	24 h[c]	**3b**, 92,[d] 47
2	**2b**	3.0	60% EtOH (4.8)	rt	9 h	**3b**, 88
3	**2b**	4.0	EtOH (7.7)	rt	24 h	**3b**, 84
4	**2b**	7.9	EtOH (32.5)	rt	24 h	**3b**, 85
5	**2c**	1.3	EtOH (15)	rt	5 days	**3c**, 63
6	**2c**	8.0	EtOH (15)	rt	21 h	**3c**, 73
7	**2d**	1.3	60% EtOH (8.6)	rt	7 days	**3d**, 89,[d] 59
8	**2d**	6.0	EtOH (10)	rt	30 h	**3d**, 81,[e] 70
9	**2d**	8.0	EtOH (10)	rt	7 h	**3d**, 51
10	**2e**	1.3	EtOH (5.9)	rt	3 days	**3e**, 88
11	**2e**	6.0	EtOH (5.0)	rt	24 h	**3e**, 81
12	**2e**	8.0	EtOH (5.5)	rt	22 h	**3e**, 79,[d] 63
13	**2f**	4.0	EtOH (5.4)	rt	27 h	**3f**, 88
14	**2h**	6.5	EtOH (6.5)	rt	24 h	**3h**, 71
15	**2j**	4.0	EtOH (4.9)	rt	11	**3j**, 73
16	**2k**	3.0	EtOH (2.5)	rt	23 h	**3k**, 97,[e] 87
17	**2m**	1.5	EtOH (15)	rt	9 days[c]	**3m**, 46
18	**2m**	8.0	EtOH (40)	rt	5.5 h	**3m**, 95,[e] 84
19	**2m**	1.1	AcOH (20)	rt	5 days	**3m**, 59
20	**2m**	1.1	DMF (3.3)	rt	4 days	**3m**, 38
21	**2n**	6.0	EtOH (15)	rt	2 h	**3n**, 62
22	**2o**	1.5	EtOH (13)	rt	5 days[c]	**3o**, 50[f]
23	**2o**	2.0	EtOH (8.3)	rt	6 h	**3o**, 64
24	**2o**	4.1	EtOH (4.4)	rt	4.5 h	**3o**, 63
25	**2o**	8.0	EtOH (4.8)	rt	4.5 h	**3o**, 65
26	**2p**	1.1	EtOH (11)	rt	3 days	**3p**, 59
27	**2p**	1.3	EtOH (16)	rt	2 days	**3p**, 58
28	**2p**	1.3	EtOH (5.3)	reflux	5.5 h	**3p**, 25[f]
29	**2p**	8.0	EtOH (25)	rt	5 h	**3p**, 92
30	**2p**	8.0	EtOH (12.5)	rt	6 h	**3p**, 75,[e] 63
31	**2p**	2.0	DMF (3.3)	rt	3 days	**3p**, 39[f]

[a] *Reaction conditions*: 1 mmol of **2** in solvent, equiv of H_5IO_6 (aqueous solution, 1.25 mL of water/mmol of H_5IO_6), temperature.
[b] Refers to percent yield of pure product obtained after purification by recrystallization, unless otherwise noted.
[c] The reaction was stopped despite the fact that some starting material remained unconsumed (TLC).
[d] Crude product, isolated by filtration from the reaction mixture, contaminated by small amounts of impurities by TLC.
[e] Crude product, isolated by filtration from the reaction mixture, pure according to TLC and IR analysis.
[f] Isolated by column chromatography.

Finally, we found out that using paraperiodic acid in 3–8 M excess to 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones **2** significantly reduced the reaction times giving products **3** in good to excellent yields (entries 2–4, 6, 8, 9, 11–16, 18, 21, 24, 25, 29, 30). It is also evident from Table 2 that for the optimal performance the amount of paraperiodic acid should not be exceeded as this can cause a serious loss of products **3**, presumably by overoxidation (compare entries 8 with 9 and 11 with 12, for example). Thus, fine tuning of the reaction conditions for optimal results is suggested for each specific substrate **2**.

Periodic acid is known to equilibrate in solution with different species including periodate.[10] Since considerably different reactivity towards organic compounds have been reported for these two species we were prompted to test the oxidation of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones **2** also with sodium periodate ($NaIO_4$) (Scheme 3). As demonstrated in Table 3, this oxidizing agent proved to be equally or in some instances slightly less reactive than H_5IO_6 providing the same products, *N*-(α-ketoacyl) anthranilic acids **3**, in up to 91% yield.



Scheme 3. Oxidative ring opening of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones **2** with sodium periodate ($NaIO_4$) into *N*-(α-ketoacyl)anthranilic acids **3**.

Table 3
Oxidation of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones **2** with sodium periodate ($NaIO_4$) into *N*-(α-ketoacyl)anthranilic acids **3** shown in Scheme 3 [a]

Entry	**2**	Equiv of $NaIO_4$	Solvent (mL/mmol of **2**)	Reaction time	**3**, yield[b]
1	**2a**	3.0	EtOH (4.0)	2 days	**3a**, 90
2	**2b**	8.0	EtOH (7.5)	24 h	**3b**, 79,[c] 44
3	**2c**	8.0	EtOH (25)	3 days[d]	**3c**, 67
4	**2d**	8.0	EtOH (27)	3 days[d]	**3d**, 26
5	**2e**	8.0	EtOH (3.8)	10 h	**3e**, 70
6	**2g**	8.0	EtOH (2.5)	20 h	**3g**, 44
7	**2i**	3.1	EtOH (3.3)	22 h	**3i**, 95,[e] 83
8	**2i**	3.7	EtOH (1.0)	8 h	**3i**, 86,[e] 71
9	**2l**	3.1	EtOH (6.9)	28 h	**3l**, 65
10	**2m**	8.0	EtOH (41)	24 h	**3m**, 91[e]
11	**2o**	8.0	EtOH (25)	4 h	**3o**, 60
12	**2p**	8.0	EtOH (25)	21 h	**3p**, 56,[e] 49

[a] *Reaction conditions*: 1 mmol of **2** in solvent, equiv of $NaIO_4$ (aqueous solution, 1.25 mL/mmol of $NaIO_4$), room temperature.
[b] Refers to percent yield of pure product obtained after purification by recrystallization, unless otherwise noted.
[c] Crude product, isolated by filtration from the reaction mixture, contaminated by small amounts of impurities by TLC.
[d] The reaction was stopped after 3 days despite the fact that some starting material remained unconsumed (TLC).
[e] Crude product, isolated by filtration from the reaction mixture, pure according to TLC and IR analysis.

The fact that sodium periodate ($NaIO_4$) and paraperiodic acid equilibrate in solution and comparable results from Tables 2 and 3 suggests that the same species is operating in the oxidative ring opening of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones **2**.

All compounds under this investigation were fully characterized by standard analytical and spectroscopic techniques. Some compounds were previously described in the literature with limited or no NMR spectroscopic data, which we decided to provide herein. For compounds **2h**, **j** and **3a**, **h**, **i**, **j**, **l**, **p** proton and carbon peak assignments were made on the basis of 2D NMR spectra: $^1H-^1H$ COSY, $^1H-^{13}C$ HSQC, $^1H-^{13}C$ HMBC and $^1H-^{15}N$ HMBC. Characteristic in ^{13}C NMR spectra of *N*-(α-ketoacyl)anthranilic acids **3a**–**m** (R^1=H, R^2=alkyl) are resonances for the carboxyl, amide (NCO) and α-ketoacyl (NC(O)CO) carbon atoms, resonating at 166–169 ppm, 158–161 ppm and 196–201 ppm, respectively. The presence of a methyl group at the amide nitrogen atom (**3n**, **o**) results in downfield shift of amide (NCO) and α-ketoacyl (NC(O)CO) carbon resonances to 166 ppm and 200–201 ppm, respectively. The phenyl group in compounds **3m**, **p** shows a considerable effect to α-ketoacyl (NC(O)CO) carbon atom, shifting its resonance upfield to 187–192 ppm (Fig. 2). In a few instances (**2j** and **3a**, **h**, **i**, **j**), ^{15}N NMR chemical shifts were extracted from 2D $^1H-^{15}N$ HMBC spectra. In comparison to **2j** (δ_N=129 ppm), the nitrogen atom in **3j** is shielded and resonates at 118 ppm. Single crystal analysis confirmed the structures of compounds **1e**,[38] **1p**[28] and **2e**,[29] as reported previously.

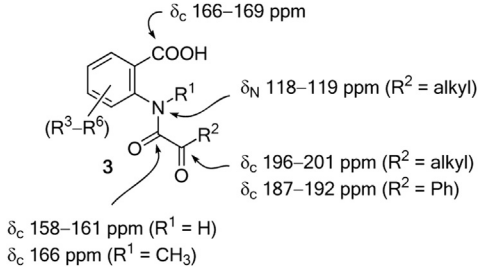
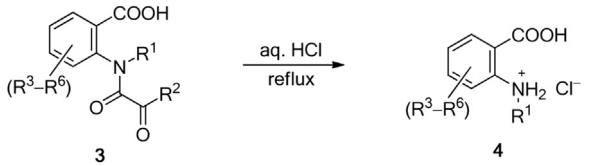


Fig. 2. Selected ^{13}C and ^{15}N chemical shifts for compounds **3**.

An easy access to *N*-(α-ketoacyl)anthranilic acids **3** renders these compounds as attractive precursors for the preparation of various benzo-fused heterocyclic compounds. Additionally, through a simple hydrolytic workup compounds **3** can be converted into the corresponding anthranilic acid derivatives. In this context it is noteworthy that the chemistry reported herein provides a facile entry to highly functionalized anthranilic acids that are inaccessible through other routes. To demonstrate this, selected *N*-(α-ketoacyl)anthranilic acids **3b**–**e**, **n** were hydrolysed with hot aqueous HCl, affording anthranilic acid hydrochlorides **4b**–**e**, **n** in good to excellent yields as shown in Scheme 4 and Table 4.



Scheme 4. Hydrolysis of *N*-(α-ketoacyl)anthranilic acids **3** into anthranilic acid hydrochlorides **4**.

Table 4
Hydrolysis of **3** into anthranilic acid hydrochlorides **4**

Entry	**3**	Reaction time (h)	**4**, yield (%)
1	**3b**	4	**4b**, 85
2	**3c**	6	**4c**, 91
3	**3d**	7	**4d**, 64
4	**3e**	1	**4e**, 68
5	**3n**	2	**4n**, 73

3. Conclusions

We report an easy approach to *N*-(α-ketoacyl)anthranilic acids by paraperiodic acid or sodium periodate mediated ring opening of

3-hydroxyquinoline-2,4(1*H*,3*H*)-diones. The scope of the reaction was investigated and under optimized reaction conditions *N*-(α-ketoacyl)anthranilic acids were obtained in good to excellent isolated yield. These compounds can serve as valuable precursors for the preparation of highly functionalized anthranilic acid derivatives that are inaccessible through other routes.

4. Experimental section

4.1. General

The column chromatography was carried out on Fluka Silica gel 60 (particle size 0.063–0.2 mm, activity acc. Brockmann and Schodder 2–3). Melting points were determined on the microscope hot stage, Kofler, PolyTherm, manufacturer Helmut Hund GmbH, Wetzlar. TLC was carried out on pre-coated TLC sheets ALUGRAM® SIL G/UV$_{254}$ for TLC, MACHEREY-NAGEL. NMR spectra were recorded on a Bruker Avance DPX 300 spectrometer operating at 300 MHz (^{1}H) and 75 MHz (^{13}C), and Bruker Avance III 500 MHz NMR instrument operating at 500 MHz (^{1}H), 126 MHz (^{13}C) and 51 MHz (^{15}N). Proton spectra were referenced to TMS as internal standard. Carbon chemical shifts were determined relative to the ^{13}C signal of DMSO-d_6 (39.5 ppm). ^{15}N chemical shifts were extracted from ^{1}H–^{15}N HMBC spectra determined with respect to external nitromethane and are corrected to external ammonia by addition of 380.5 ppm. Chemical shifts are given on the δ scale (parts per million). Coupling constants (J) are given in Hertz. Multiplicities are indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broadened). Infrared spectra were recorded on Mattson 3000 FTIR Spectrometer or Thermo Scientific Nicolet iS10 FT-IR Spectrometer using samples in potassium bromide disks and only the strongest/structurally most important peaks are listed; absorption bands intensities are indicated as follows: s (strong), m (medium), w (weak) or b (broad). MS (EI) spectra were recorded on a Shimadzu QP-2010 instrument at 70 eV. HRMS spectra were recorded with Agilent 6224 Accurate Mass TOF LC/MS system. Elemental analyses (C, H, N) were performed with FlashEA1112 Automatic Elemental Analyzer (Thermo Fisher Scientific Inc.).

4.2. General procedure for the preparation of 4-hydroxyquinolin-2(1*H*)-ones (1)

A mixture of the appropriate aniline (100 mmol) and substituted diethyl malonate (102 mmol) was heated in a flask equipped with distillation head on a metal bath at 220–230 °C for 1 h and then at 260–270 °C until the distillation of ethanol stopped (3–6 h). With the exception of preparation of **1f**, **l**, **m**, the hot liquid reaction mixture was carefully poured into stirred toluene (50 mL), cooled down to room temperature and the precipitate was collected by filtration. In the case of **1f**, **l**, **m**, the hot reaction mixture solidified and it was cooled down to room temperature. The above precipitate or solidified material was mixed with aqueous sodium hydroxide solution (0.5 M, 250 mL) and toluene (50 mL). The substance that remained undissolved (in the preparation of **1c** and **1m**) was removed by filtration, purified by recrystallization and identified as propanediamide derivatives (**1c**′ and **1m**′, respectively). The layers of the filtrate were separated and the aqueous layer was washed with toluene (2×40 mL). The water layer was treated with decolorizing charcoal, filtered and then acidified with 10% HCl to Congo red. The precipitated hydroxyquinolone **1** was collected by filtration, washed with water, and if necessary, purified by recrystallization.

*4.2.1. 4-Hydroxy-3-methylquinolin-2(1H)-one (**1a**).*[30,31] White powder, yield 13.5 g (77%), mp 274–275 °C (ethanol), mp[30] 268 °C, mp[31] 265–268 °C (butanol). ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.02 (s, 3H), 7.15 (ddd, 1H, J=7.7, 7.7, 1.0 Hz), 7.27 (d, 1H, J=7.7 Hz), 7.44 (ddd, 1H, J=7.7, 7.7, 1.0 Hz), 7.89 (dd, 1H, J=8.1, 1.0 Hz), 10.13 (br s, 1H), 11.36 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 9.4, 106.8, 114.8, 115.4, 121.0, 122.4, 129.6, 137.2, 157.1, 163.8; IR (cm^{-1}): ν 2600–3400 br, 1643 s, 1607 s, 1501 m, 1478 m, 1401 s, 1342 m, 1284 m, 1274 s, 1225 m, 1160 m, 752 m. HRMS (ESI+): m/z calcd for $C_{10}H_{10}NO_2^+$ $[M+H]^+$ 176.0706, found 176.0707.

*4.2.2. 3-Ethyl-4-hydroxyquinolin-2(1H)-one (**1b**).*[32–34] Colourless solid, yield 13.1 g (69%), mp 265–267 °C (ethanol), mp[33] 260–261 °C (ethanol). ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.03 (t, 3H, J=7.4 Hz), 2.59 (q, 2H, J=7.4 Hz), 7.14 (ddd, 1H, J=7.6, 7.6, 1.0 Hz), 7.26 (d, 1H, J=7.6 Hz), 7.44 (ddd, 1H, J=7.6, 7.6, 1.0 Hz), 7.88 (dd, 1H, J=7.6, 1.0 Hz), 10.06 (br s, 1H), 11.31 (br s, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 13.2, 16.4, 113.0, 114.8, 115.4, 120.9, 122.5, 129.6, 137.3, 156.6, 163.4; IR (cm^{-1}): ν 2600–3400 br, 1638 s, 1605 s, 1590 s, 1553 m, 1500 m, 1428 m, 1401 m, 1269 m, 1207 s, 1151 m, 754 m. IR:[34] 1641 cm^{-1}. HRMS (ESI+): m/z calcd for $C_{11}H_{12}NO_2^+$ $[M+H]^+$ 190.0863, found 190.0866.

*4.2.3. 3-Ethyl-4-hydroxy-6-methoxyquinolin-2(1H)-one (**1c**).*[32,35] Yellowish solid, yield 14.0 g (64%), mp 220–224 °C (ethanol), mp[35] 172 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.04 (t, 3H, J=7.3 Hz), 2.60 (q, 2H, J=7.3 Hz), 3.80 (s, 3H), 7.10 (dd, 1H, J=8.9, 2.5 Hz), 7.22 (d, 1H, J=8.9 Hz), 7.39 (d, 1H, J=2.5 Hz), 9.98 (br s, 1H), 11.20 (br s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 13.2, 16.4, 55.4, 104.3, 113.5, 115.8, 116.2, 118.6, 131.8, 153.8, 156.2, 162.9; IR (cm^{-1}): ν 2700–3500b, 1648 s, 1623 s, 1556 m, 1511 s, 1466 m, 1446 m, 1422 m, 1380 m, 1330 m, 1288 m, 1271 m, 1243 m, 1222 s, 1179 m, 1147 m, 1118 m; MS (EI) m/z (%): 220 ($[M+1]^+$, 13), 219 ($[M]^+$, 95), 218 (35), 204 (100), 106 (23), 55 (26); Anal. Calcd for $C_{12}H_{13}NO_3$ (219.24): C, 65.74; H, 5.98; N, 6.39%. Found: C, 65.50; H, 5.93; N, 6.41%.

*4.2.4. 3-Ethyl-4-hydroxy-7-methoxyquinolin-2(1H)-one (**1d**).*[32,36] White solid, yield 14.9 g (68%), mp 262–266 °C (ethanol), mp[36] 260–261 °C (methanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.03 (t, 3H, J=7.4 Hz), 2.56 (q, 2H, J=7.4 Hz), 3.80 (s, 3H), 6.77 (d, 1H, J=8.5 Hz), 6.79 (s, 1H), 7.80 (d, 1H, J=8.5 Hz), 9.92 (br s, 1H), 11.15 (br s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 13.3, 16.2, 55.2, 97.7, 109.4, 109.5, 110.5, 124.0, 139.0, 156.9, 160.5, 163.8; IR (cm^{-1}): ν 2700–3300, 2971 m, 1624 s, 1595 s, 1556 s, 1437 s, 1425 s, 1272s, 1222 s, 1153 m, 1112 m, 1031 m, 882, 856 m, 833 m; MS (EI) m/z (%):220 ($[M+1]^+$, 7), 219 ($[M]^+$, 50), 204 (100), 191 (22); Anal. Calcd for $C_{12}H_{13}NO_3$ (219.24): C, 65.74; H, 5.98; N, 6.39%. Found: C, 65.69; H, 6.22; N, 6.22%.

*4.2.5. 3-Ethyl-4-hydroxy-8-methoxyquinolin-2(1H)-one (**1e**).*[32,34,37] White solid, yield 13.6 g (62%), mp 225–227 °C (ethanol), mp[34] 226–227 °C, mp[37] 225–226 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.02 (t, 3H, J=7.3 Hz), 2.58 (q, 2H, J=7.3 Hz), 3.89 (s, 3H), 7.08–7.13 (m, 2H), 7.48 (dd, 1H, J=4.6, 4.6 Hz), 10.04 (br s, 1H), 10.11 (br s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 13.1, 16.4, 56.0, 110.3, 113.4, 114.3, 115.9, 120.8, 127.3, 145.4, 156.7, 162.7; IR (cm^{-1}): ν 2700–3400 br, 1635 s, 1604 s, 1571 s, 1492 m, 1393 m, 1333 m, 1302 m, 1267 m, 1254 m, 1223 m, 1155 m, 1089 s, 771 m,724 m; IR:[34] 1640 cm^{-1}. MS (EI) m/z (%): 220 ($[M+1]^+$, 5), 219 ($[M]^+$, 34), 218 (23), 204 (31), 149 (28), 71 (27), 69 (28), 57 (100), 55 (35), 43 (30), 41 (34). X-ray structure is reported.[38]

*4.2.6. 3-Ethyl-4-hydroxy-6-methylquinolin-2(1H)-one (**1f**).* White solid, yield 12.0 g (59%), mp 261–264 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.02 (t, J=7.4 Hz, 3H), 2.35 (s, 3H), 2.58 (q, 2H, J=7.4 Hz), 7.16 (d, 1H, J=8.2 Hz), 7.26 (dd, 1H, J=8.2, 1.6 Hz), 7.68 (s, 1H), 9.96 (br s, 1H), 11.22 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 13.2, 16.3, 20.6, 112.9, 114.6, 115.2, 122.0, 129.6, 130.7, 135.2, 156.3, 163.2; IR (cm^{-1}):

ν 3131 m, 2976 m, 1640 s, 1622 s, 1558 s, 1513 m, 1433 m, 1416 m, 1332 m, 1233 m, 1207 m, 1149 m, 1116 m, 855 w, 814 w; HRMS (ESI+): *m/z* calcd for $C_{12}H_{14}NO_2^+$ ($[M+H]^+$): 204.1019, found 204.1022. Anal. Calcd for $C_{12}H_{13}NO_2$ (203.24): C, 70.92; H, 6.45; N, 6.89%. Found: C, 70.75; H, 6.43; N, 6.79%.

4.2.7. 3-Ethyl-4-hydroxy-8-methylquinolin-2(1H)-one (***1g***).[39] Yellow solid, yield 12.2 g (60%), mp 228–229 °C (acetic acid), mp[39] 217.5–220 °C (acetic acid). ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.04 (t, 3H, *J*=7.4 Hz), 2.41 (s, 3H), 2.61 (q, 2H, *J*=7.4 Hz), 7.06 (dd, 1H, *J*=7.7, 7.7 Hz), 7.30 (d, 1H, *J*=7.7 Hz), 7.77 (d, 1H, *J*=7.7 Hz), 10.04 (br s, 1H), 10.47 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 13.2, 16.4, 17.4, 112.7, 115.5, 120.5, 120.6, 122.9, 130.9, 135.7, 157.0, 163.7; IR (cm^{-1}): ν 3395 m, 2966 m, 2934 m, 1636 s, 1601 s, 1565 s, 1488 m, 1396 m, 1334 m, 1292 m, 1238 s, 1210 s, 1151 s, 766 m; HRMS (ESI+): *m/z* calcd for $C_{12}H_{14}NO_2^+$ $[M+H]^+$ 204.1019, found 204.1024.

4.2.8. 5-Chloro-3-ethyl-4-hydroxy-8-methylquinolin-2(1H)-one (***1h***). White solid, yield 11.6 g (49%), mp 235–238 °C (ethanol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ 1.02 (t, 3H, *J*=7.3 Hz), 2.38 (s, 3H), 2.60 (q, 2H, *J*=7.3 Hz), 7.10 (d, 1H, *J*=8.0 Hz), 7.23 (d, 1H, *J*=8.0 Hz), 9.98 (br s, 1H), 10.41 (br s, 1H); ^{13}C NMR (DMSO-d_6, 126 MHz) δ 12.8, 16.2, 17.4, 112.4, 114.3, 122.5, 124.2, 127.0, 130.7, 137.8, 157.2, 162.4; IR (cm^{-1}): ν 3471 m, 3166 w, 2959 w, 2870 w, 1647 s, 1459 w, 1338 w, 1324 w, 1210 w, 1147 m, 822 w, 628 w; HRMS (ESI+): *m/z* calcd for $C_{12}H_{13}ClNO_2^+$ $[M+H]^+$ 238.0629, found 238.0630. Anal. Calcd for $C_{12}H_{12}ClNO_2$ (237.68): C, 60.64; H, 5.09; N, 5.89%. Found: C, 60.53; H, 5.05; N, 5.92%.

4.2.9. 3-Butyl-4-hydroxyquinolin-2(1H)-one (***1i***).[20] White solid (microscopic crystals), yield 14.1 g (65%), mp 195–201, 54%, mp 201–204 °C (ethanol), mp[20] 199–200 °C (ethanol). For ^{1}H and ^{13}C NMR spectra see Ref. 20. IR (cm^{-1}): ν 2700–3400 br, 2954 m, 1639 s, 1604 s, 1590 s, 1557 m, 1503 m, 1480 m, 1469 m, 1426 m, 1404 m, 1273 m, 1197 s, 1154 s, 761 s; Anal. Calcd for $C_{13}H_{15}NO_2$ (217.26): C, 71.87; H, 6.96; N, 6.45%. Found: C, 71.67; H, 6.04; N, 6.39%.

4.2.10. 3-Butyl-4-hydroxy-6,8-dimethylquinolin-2(1H)-one (***1j***). Colourless shiny crystals, yield 14.7 g (60%), mp 225–228 °C (ethanol). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.90 (t, 3H, *J*=7.3 Hz), 1.30–1.45 (m, 4H), 2.31 (s, 3H), 2.37 (s, 3H), 2.56–2.60 (m, 2H), 7.12 (s, 1H), 7.56 (s, 1H), 9.88 (br s, 1H), 10.40 (br s, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 14.1, 17.2, 20.6, 22.3, 22.8, 30.5, 111.4, 115.4, 120.0, 122.8, 129.4, 132.2, 133.7, 157.1, 163.7; IR (cm^{-1}): ν 3382 s, 2931 m, 2849 m, 1645 s, 1618 s, 1381 m, 1329 m, 1257 m, 1238 s, 1168 s, 1134 s, 1103 m, 1069 m, 871 m, 493 m; HRMS (ESI−): *m/z* calcd for $C_{15}H_{18}NO_2^-$ $[M-H]^-$ 244.1343, found 244.1338; calcd for $C_{15}H_{19}NO_2$ (245.32): C, 73.44; H, 7.81; N, 5.71%. Found: C, 73.51; H, 6.52; N, 5.11%.

4.2.11. 3-Butyl-4-hydroxy-6,8-dimethoxyquinolin-2(1H)-one (***1k***). Colourless crystals, yield 15.3 g (55%), mp 240–244 °C (ethanol). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.90 (t, 3H, *J*=7.3 Hz), 1.29–1.46 (m, 4H), 2.54–2.59 (m, 2H), 3.80 (s, 3H), 3.87 (s, 3H), 6.74 (d, 1H, *J*=2.4 Hz), 6.98 (d, 1H, *J*=2.4 Hz), 9.96 (br s, 1H), 10.12 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 14.1, 22.3, 23.0, 30.4, 55.4, 56.1, 95.2, 100.8, 112.8, 115.7, 122.2, 146.6, 154.0, 156.7, 162.5; IR (cm^{-1}): ν 3374 s, 2954 m, 2929 m, 1661 m, 1613 s, 1583 m, 1504 s, 1327 m, 1257 s, 1228 m, 1206 s, 1162 s, 1093 s, 1056 m; HRMS (ESI+): *m/z* calcd for $C_{15}H_{20}NO_4^+$ $[M+H]^+$ 278.1387, found 278.1386. Anal. Calcd for $C_{15}H_{19}NO_4$ (277.32): C, 64.97; H, 6.91; N, 5.05%. Found: C, 65.02; H, 6.94; N, 5.04%.

4.2.12. 3-Butyl-4-hydroxybenzo[h]quinolin-2(1H)-one (***1l***). General procedure was followed for the preparation of this compound with one exception; the temperature of the metal bath was kept at 180 °C throughout the condensation. White crystals, yield 24.9 g (93%), mp 309–313 °C (ethanol). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.93 (t, 3H, *J*=7.2 Hz), 1.35–1.44 (m, 2H), 1.46–1.53 (m, 2H), 2.65–2.70 (m, 2H), 7.58–7.67 (m, 3H), 7.96 (d, 1H, *J*=7.4 Hz), 7.99 (d, 1H, *J*=8.9 Hz), 8.90 (d, 1H, *J*=8.0 Hz), 10.19 (br s, 1H), 11.82 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 14.1, 22.3, 22.9, 30.4, 111.2, 111.8, 120.0, 121.3, 121.4, 122.3, 126.2, 127.4, 128.3, 133.5, 134.0, 157.9, 164.0; IR (cm^{-1}): ν 1763 s, 1618 m, 1601 m, 1196 s, 1067 m, 779 m; MS (EI) *m/z* (%): 268 ($[M+1]^+$, 5), 267 (M^+, 24), 238 (17), 226 (16), 225 (100), 224 (33), 115 (16), 55 (18); HRMS (ESI−): *m/z* calcd for $C_{17}H_{16}NO_2^-$ $[M-H]^-$ 266.1187, found 266.1187. Anal. Calcd for $C_{17}H_{17}NO_2$ (267.32): C, 76.38; H, 6.41; N, 5.24%. Found: C, 76.29; H, 6.49; N, 5.07%.

4.2.13. 4-Hydroxy-3-phenylquinolin-2(1H)-one (***1m***).[32,40] White solid, yield 20.9 g (88%), mp 334–338 °C (acetic acid), mp[40] 325–327 °C (DMF). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.16–7.21 (m, 1H), 7.28–7.33 (m, 2H), 7.37–7.43 (m, 4H), 7.49–7.53 (m, 1H), 7.96 (dd, 1H, *J*=8.1, 1.0 Hz), 10.10 (br s, 1H), 11.49 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 112.6, 114.9, 115.4, 121.1, 123.1, 126.9, 127.7, 130.6, 131.2, 133.4, 138.0, 157.3, 162.7; IR (cm^{-1}): ν 2700–3330 br, 1645 s, 1610 s, 1588 s, 1499 m, 1408 m, 1365 m, 1289 m, 1244 m, 1226 m, 757 m, 696 m, 557 m; HRMS (ESI+): *m/z* calcd for $C_{15}H_{12}NO_2^+$ $[M+H]^+$ 238.0863, found 238.0866.

4.2.14. 3-Ethyl-4-hydroxy-1-methylquinolin-2(1H)-one (***1n***).[41] White solid, yield 18.1 g (89%), mp 188–191 °C, mp[41] 184–185 °C (ethanol). ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.03 (t, 3H, *J*=7.4 Hz), 2.63 (q, 2H, *J*=7.4 Hz), 3.59 (s, 3H), 7.22–7.27 (m, 1H), 7.46 (br d, 1H, *J*=8.3 Hz), 7.55–7.60 (m, 1H), 7.99 (dd, 1H, *J*=8.0, 1.4 Hz), 10.09 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 13.2, 17.2, 29.1, 112.6, 114.2, 116.3, 121.2, 123.0, 130.1, 138.2, 155.4, 162.6; IR (cm^{-1}): ν 2700–3400 br, 2964 w, 1641 s, 1607 s, 1584 s, 1571 s, 1392 m, 1219 s, 1205 s, 1165 s, 1126 m, 750 s; HRMS (ESI+): *m/z* calcd for $C_{12}H_{14}NO_2^+$ $[M+H]^+$ 204.1019, found 204.1020.

4.2.15. 3-Butyl-4-hydroxy-1-methylquinolin-2(1H)-one (***1o***). Colourless crystals, yield 16.4 g (71%), mp 145–149 °C (ethanol), mp[42] 141 °C. For NMR data, see Ref. 20. IR (cm^{-1}): ν 2800–3400 br, 2954 w, 1632 m, 1604 s, 1582 s, 1466 w, 1342 w, 1192 s, 1165 m, 1157 m, 1083 w, 747 m, 471 w.

4.2.16. 4-Hydroxy-1-methyl-3-phenylquinolin-2(1H)-one (***1p***).[43] White solid, yield 23.4 g (93%), mp 227–230 °C, mp[43] 226 °C (ethanol). ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.61 (s, 3H), 7.27–7.31 (m, 1H), 7.30–7.37 (m, 3H), 7.39–7.43 (m, 2H), 7.52 (br d, 1H, *J*=8.3 Hz), 7.63–7.67 (m, 1H), 8.05 (dd, 1H, *J*=8.0, 1.4 Hz), 10.07 (br s, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 29.5, 112.3, 114.4, 116.3, 121.4, 123.6, 127.0, 127.8, 131.0, 131.2, 133.7, 139.0, 156.2, 162.0; IR (cm^{-1}): ν 2750–3250 br, 3060 w, 2953 w, 1629 s, 1612 s, 1594 s, 1581 s, 1572 s, 1328 m, 1251 m, 755 m, 693 m, 511 w; MS (EI) *m/z* (%): 252 ($[M+1]^+$, 16), 251 ($[M]^+$, 96), 250 (100), 134 (45), 125 (11), 116 (12), 91 (10), 77 (27). HRMS (ESI+): *m/z* calcd for $C_{16}H_{14}NO_2^+$ $[M+H]^+$ 252.1019, found 252.1022. X-ray structure is reported.[28]

4.2.17. 2-Ethyl-N,N′-bis(4-methoxyphenyl)propanediamide (***1c′***). White solid, yield 1.37 g (4%), mp 237–241 °C (ethanol–benzene). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.92 (t, 3H, *J*=7.4 Hz) 1.91 (dq, 2H, *J*=7.4, 7.4 Hz), 3.33 (t, 1H, *J*=7.4 Hz), 3.72 (s, 6H), 6.86–6.91 (m, 4H), 7.50–7.54 (m, 4H), 9.80 (br s, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 12.0, 23.1, 55.2, 56.2, 113.8, 120.9, 132.0, 155.3, 167.5; IR (cm^{-1}): ν 3279 m, 2968 w, 2836 w, 1673 s, 1601 m, 1539 m, 1512 s, 1412 m, 1249 m, 1236 m, 1166 m, 1029 m, 824 m; MS (EI) *m/z* (%): 343 ($[M+1]^+$, 10), 342 (M^+, 47), 193 (38), 178 (63), 149 (20), 124 (13), 123 (100), 122 (42), 108 (40), 55 (10);

HRMS (ESI+): *m*/*z* calcd for $C_{19}H_{23}N_2O_4^+$ $[M+H]^+$ 343.1652, found 343.1650.

*4.2.18. N,N′,2-Triphenylpropanediamide (**1m′**).*[44] White solid, yield 1.65 g (5%), mp 198–202 °C (ethanol), mp[44] 201–202 °C (ethanol). ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.88 (s, 1H), 7.04–7.08 (m, 2H), 7.28–7.34 (m, 5H), 7.36–7.40 (m, 2H), 7.44–7.48 (m, 2H), 7.59–7.63 (m, 4H), 10.25 (br s, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 59.9, 119.3, 123.6, 127.4, 128.2, 128.8, 129.0, 135.5, 138.9, 166.6; IR (cm^{-1}): ν 3313 m, 1672 s, 1647 m, 1618 m, 1605 s, 1551 s, 1497 s, 1443 s, 1334 m, 763 m, 749 m, 718 m, 697 m; HRMS (ESI+): *m*/*z* calcd for $C_{21}H_{19}N_2O_2^+$ $[M+H]^+$ 331.1441, found 331.1441.

4.3. General procedure for the preparation of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones (2)

To a solution of the appropriate 4-hydroxyquinolin-2(1*H*)-one (**1**, 20 mmol) in aqueous sodium hydroxide solution (0.5 M, 20 mL), peroxyacetic acid (32–36 wt. % in dilute acetic acid, 20 mL, 100 mmol) was added dropwise under stirring during 30 min. The precipitate was collected by filtration and washed with small portions of 5% aqueous potassium carbonate solution until the filter cake is free of potentially unreacted starting material **1** (until the filtrate is not clear solution upon acidification with conc. hydrochloric acid). Then the solid was washed with water (3×30 mL), air dried and recrystallized from the appropriate solvent. Analytical and spectral data of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones **2** are given below.

*4.3.1. 3-Hydroxy-3-methylquinoline-2,4(1H,3H)-dione (**2a**).*[45] White solid, yield 2.94 g (77%), mp 212–216 °C (ethanol), mp[45] 201 °C (ethanol–water). ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.40 (s, 3H), 5.81 (s, 1H), 7.09 (d, 1H, *J*=8.0 Hz), 7.10–7.14 (m, 1H), 7.60 (ddd, 1H, *J*=7.7, 7.7, 1.5 Hz), 7.75 (dd, 1H, *J*=7.7, 1.3 Hz), 10.76 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 26.2, 78.0, 116.2, 118.4, 122.5, 127.0, 136.0, 141.5, 173.3, 196.2; IR (cm^{-1}): ν 1709 s, 1671 s, 1614 s, 1598 m, 1487 m, 1455 m, 1441 m, 1405 m, 1243 m, 1190 m, 753 m; HRMS (ESI+): *m*/*z* calcd for $C_{10}H_{10}NO_3^+$ $[M+H]^+$ 192.0655, found 192.0658.

*4.3.2. 3-Ethyl-3-hydroxyquinoline-2,4(1H,3H)-dione (**2b**).*[27] White solid, yield 3.73 g (91%), mp 174–176 °C (benzene–ethanol), mp[27] 170–172 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.78 (t, 3H, *J*=7.4 Hz), 1.66–1.82 (m, 2H), 5.65 (s, 1H), 7.07 (d, 1H, *J*=8.0 Hz), 7.09–7.13 (m, 1H), 7.59 (ddd, 1H, *J*=7.7, 7.7, 1.5 Hz), 7.72 (dd, 1H, *J*=7.7, 1.4 Hz), 10.76 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 7.4, 32.8, 82.0, 116.2, 119.1, 122.5, 126.7, 135.9, 141.4, 172.9, 196.0; IR (cm^{-1}): ν 3457 m, 1709 s, 1667 s, 1617 m, 1487 m, 1365 m, 1185 m, 774 m, 753 m; MS (EI) *m*/*z* (%): 97(22), 83(25), 74(26), 72(73), 71(22), 69(32), 59(100), 55(48); HRMS (ESI+): *m*/*z* calcd for $C_{11}H_{12}NO_3^+$ $[M+H]^+$ 206.0812, found 206.0816. Anal. Calcd for $C_{11}H_{11}NO_3$ (205.21): C, 64.23; H, 5.40; N, 6.83%. Found: C, 64.08; H, 5.37; N, 6.65%.

*4.3.3. 3-Ethyl-3-hydroxy-6-methoxyquinoline-2,4(1H,3H)-dione (**2c**).*[35] Yellow solid, yield 4.29 (89%), mp 186–193 °C (ethanol), mp[35] 198 °C (water–DMF). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.78 (t, 3H, *J*=7.5 Hz), 1.65–1.82 (m, 2H), 3.78 (s, 3H), 5.62 (br s, 1H), 7.02 (d, 1H, *J*=8.8 Hz), 7.18 (d, 1H, *J*=3.0 Hz), 7.22 (dd, 1H, *J*=8.8 Hz, 3.0 Hz), 10.58 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 7.4, 32.9, 55.5, 81.8, 108.4, 117.8, 119.6, 123.8, 135.4, 154.6, 172.5, 196.1; IR (cm^{-1}): ν 3414 m, 3200–2800 br, 3072 m, 1709 s, 1669 s, 1625 m, 1502 s, 1431 m, 1282 s, 1212 m, 1182 m, 1160 m, 848 m; MS (EI) *m*/*z* (%): 236 ($[M+1]^+$, 9), 235 (M^+, 63), 220 (20), 123 (20), 122 (47), 109 (29), 106 (28), 79 (26), 57 (21), 52 (26); HRMS (ESI+): *m*/*z* calcd for $C_{12}H_{14}NO_4^+$ $[M+H]^+$ 236.0917, found 236.0916; Anal. Calcd for $C_{12}H_{13}NO_4 \cdot {}^1/_3\ H_2O$ (241.24): C, 59.76; H, 5.71; N, 5.81%. Found: C, 59.82; H, 5.78; N, 5.52%.

*4.3.4. 3-Ethyl-3-hydroxy-7-methoxyquinoline-2,4(1H,3H)-dione (**2d**).* White solid, yield 83%, mp 162–164 °C (benzene). ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.78 (t, 3H, *J*=7.4 Hz), 1.63–1.84 (m, 2H), 3.83 (s, 3H), 5.57 (s, 1H), 6.58 (d, 1H, *J*=2.3 Hz), 6.70 (dd, 1H, *J*=8.7, 2.3 Hz), 7.70 (d, 1H, *J*=8.7 Hz), 10.67 (br s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 7.4, 33.2, 55.7, 81.2, 100.0, 109.7, 112.6, 129.0, 143.6, 165.1, 173.1, 194.2; IR (cm^{-1}): ν 3258 s, 3067 m, 1713 s, 1668 s, 1612 s, 1589 s, 1482 m, 1461 m, 1409 m, 1349 m, 1274 s, 1207 s, 1173 s, 1119 s, 1108 m; Anal. Calcd for $C_{12}H_{13}NO_4 \cdot 1/6C_6H_6$: C, 62.90; H, 5.68; N, 5.64%. Found: C, 63.01; H, 5.73; N, 5.60%. The presence and quantity of residual benzene in the sample is confirmed by ^{1}H and ^{13}C NMR resonances at δ 7.37 ppm and 128.3 ppm, respectively.

*4.3.5. 3-Ethyl-3-hydroxy-8-methoxyquinoline-2,4(1H,3H)-dione (**2e**).*[29] Yellow crystals, yield 83%, mp 70–72 °C (benzene). ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.78 (t, 3H, *J*=7.4 Hz), 1.61–1.86 (m, 2H), 3.87 (s, 3H), 5.63 (s, 1H), 7.09 (dd, 1H, *J*=7.9, 7.9 Hz), 7.29 (d, 1H, *J*=7.9 Hz), 7.31 (d, 1H, *J*=7.9 Hz), 9.85 (br s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 7.3, 32.9, 56.2, 82.2, 117.1, 117.7, 119.5, 122.6, 131.0, 146.3, 172.4, 196.0; IR (cm^{-1}): ν 3579 m, 3486 m, 1710 s, 1667 s, 1615 m, 1591 m, 1508 m, 1384 m, 1266 s, 1203 m, 1187 m, 1018 m, 1004 m. Anal. Calcd for $C_{12}H_{13}NO_4 \cdot H_2O$: C, 56.91; H, 5.97; N, 5.53%. Found: C, 56.90; H, 5.88; N, 5.57%. The presence of H_2O in a 1:1 ratio relative to **2e** was confirmed by single crystal structure analysis.[29]

*4.3.6. 3-Ethyl-3-hydroxy-6-methylquinoline-2,4(1H,3H)-dione (**2f**).* White solid, yield 91%, mp 198–205 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.78 (t, 3H, *J*=7.4 Hz), 1.65–1.81 (m, 1H), 2.25 (s, 3H), 5.62 (s, 1H), 6.98 (d, 1H, *J*=8.2 Hz), 7.41 (dd, 1H, *J*=8.2, 1.7 Hz), 7.52 (d, 1H, *J*=1.7 Hz), 10.67 (br s, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 7.3, 20.0, 32.9, 81.9, 116.1, 118.9, 126.3, 131.7, 136.7, 139.1, 172.7, 196.1; IR (cm^{-1}): ν 3588 w, 3449 w, 3191 w, 2914 w, 1712 s, 1670 s, 1618 m, 1504 m, 1421 w, 1200 w, 1159 w, 849 w, 540 w; HRMS (ESI−): *m*/*z* calcd for $C_{12}H_{12}NO_3^-$ ($[M-H]^-$) 218.0823, found 218.0827.

*4.3.7. 3-Ethyl-3-hydroxy-8-methylquinoline-2,4(1H,3H)-dione (**2g**).* Yellow solid, yield 66%, mp 164 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.78 (t, 3H, *J*=7.2 Hz), 1.64–1.81 (m, 1H), 2.31 (s, 3H), 5.66 (br s, 1H), 7.04 (dd, 1H, *J*=7.6, 7.6 Hz), 7.45 (d, 1H, *J*=7.6 Hz), 7.58 (d, 1H, *J*=7.6 Hz), 9.94 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 7.3, 17.2, 32.8, 82.0, 119.5, 122.3, 124.4, 124.6, 137.0, 139.3, 173.1, 196.2; IR (cm^{-1}): ν 3585 m, 3472 m, 3294 m, 1706 s, 1668 s, 1598 m, 1469 m, 1374 m, 1194 m; HRMS (ESI+): *m*/*z* calcd for $C_{12}H_{14}NO_3^+$ $[M+H]^+$ 220.0968, found 220.0974.

*4.3.8. 5-Chloro-3-ethyl-3-hydroxy-8-methylquinoline-2,4(1H,3H)-dione (**2h**).* Colourless solid, yield 4.16 g (82%), mp 158–166 °C (cyclohexane). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.80 (t, 3H, *J*=7.2 Hz, CH_3CH_2), 1.76 (q, 2H, *J*=7.2 Hz, CH_2), 2.28 (s, 3H, CH_3–C8), 5.76 (br s, 1H, OH), 7.11 (d, 1H, *J*=8.1 Hz, H6), 7.38 (d, 1H, *J*=8.1 Hz, H7), 9.99 (br s, 1H, NH); ^{13}C NMR (126 MHz, DMSO-d_6) 7.8 (CH_3CH_2), 17.3 (CH_3–C8), 32.2 (CH_2), 83.2 (C3), 117.8 (C4a), 124.2 (C8), 124.7 (C6), 129.5 (C5), 136.2 (C7), 140.3 (C8a), 172.0 (C2), 194.9 (C4); IR (cm^{-1}): ν 3438 m, 3294 m, 1717 s, 1682 s, 1587 s, 1499 m, 1458 m, 1389 m, 1375 m, 1272 m, 1250 m, 1187 s, 1064 m, 1053 m, 813 m; HRMS (ESI+): *m*/*z* calcd for $C_{12}H_{13}ClNO_3^+$ $[M+H]^+$ 254.0578, found 254.0578.

*4.3.9. 3-Butyl-3-hydroxyquinoline-2,4(1H,3H)-dione (**2i**).* Yield[24] 3.73 g (80%), mp[24] 146–149 °C (benzene). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.77 (t, 3H, *J*=7.0 Hz), 1.12–1.28 (m, 4H), 1.62–1.78 (m, 4H), 5.67 (br s, 1H), 7.08 (d, 1H, *J*=8.0 Hz), 7.09–7.13 (m, 1H), 7.59

(ddd, 1H, J=7.6, 7.6, 1.8 Hz), 7.72 (dd, 1H, J=7.6, 1.8 Hz), 10.79 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 13.8, 22.0, 24.7, 39.3, 81.7, 116.2, 119.0, 122.5, 126.7, 135.9, 141.4, 172.9, 196.1; IR (cm^{-1}): ν 3476 m, 3192 w, 2950 m, 2866 m, 1705 s, 1666 s, 1617 m, 1595 m, 1486 m, 1382 m, 1091 m, 755 m; HRMS (ESI+): m/z calcd for $C_{13}H_{16}NO_3^+$ $[M+H]^+$ 234.1125, found 234.1126.

*4.3.10. 3-Butyl-3-hydroxy-6,8-dimethylquinoline-2,4(1H,3H)-dione (**2j**).* Colourless microcrystals, yield 4.93 g (87%), mp 175–184 °C (cyclohexane). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.76 (t, 3H, J=7.5 Hz, CH_3CH_2), 1.10–1.29 (m, 4H, $CH_2CH_2CH_3$), 1.61–1.75 (m, 2H, CH_2–C3), 2.25 (s, 3H, CH_3–C6), 2.27 (s, 3H, CH_3–C8), 5.63 (s, 1H, OH), 7.27 (s, 1H, H7), 7.38 (s, 1H, H5), 9.86 (br s, 1H, NH); ^{13}C NMR (126 MHz, DMSO-d_6) δ 13.7 (CH_3CH_2), 17.1 (CH_3–C8), 19.8 (CH_3–C6), 21.9 (CH_2CH_3), 24.6 (CH_2CH_2–C3), 39.3 (CH_2–C3), 81.7 (C3), 119.3, 124.1 (C5), 124.5, 131.4, 137.0, 137.9 (C7), 173.1 (C2), 196.3 (C4); ^{15}N NMR (DMSO-d_6, 51 MHz): 129; IR (cm^{-1}): ν 3455 m, 3231 m, 2954 m, 2932 m, 1704 s, 1662 s, 1615 m, 1491 s, 1378 s, 1283 m, 1236 m, 1220 m, 1158 m, 1068 m, 791 w; HRMS (ESI+): m/z Calcd for $C_{15}H_{20}NO_3^+$ $[M+H]^+$ 262.1438, found 262.1437; Anal. Calcd for $C_{17}H_{17}NO_3$ (283.32): C, 72.07; H, 6.05; N, 4.94%. Found: C, 72.16; H, 6.13; N, 5.11%.

*4.3.11. 3-Butyl-3-hydroxy-6,8-dimethoxyquinoline-2,4(1H,3H)-dione (**2k**).* Pale yellow crystals, yield 3.34 g (57%), mp 119–121 °C (cyclohexane). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.77 (t, 3H, J=7.0 Hz), 1.11–1.28 (m, 4H), 1.60–1.75 (m, 2H), 3.78 (s, 3H), 3.85 (s, 3H), 5.64 (br s, 1H), 6.77 (d, 1H, J=2.6 Hz), 6.89 (d, 1H, J=2.6 Hz), 9.76 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) 13.8, 22.0, 24.7, 55.5, 56.3, 82.0, 98.8, 106.3, 119.4, 125.5, 147.6, 155.0, 172.3, 196.1 (one resonance not observed); IR (cm^{-1}): ν 3486 m, 3213 m, 2960 m, 2934 m, 1709 s, 1668 s, 1618 m, 1505 s, 1455 m, 1370 m, 1205 m, 1155 m, 841 w; HRMS (ESI+): m/z calcd for $C_{15}H_{20}NO_5^+$ $[M+H]^+$ 294.1336, found 278.1338.

*4.3.12. 3-Butyl-3-hydroxybenzo[h]quinoline-2,4(1H,3H)-dione (**2l**).* Pale yellow solid, yield 4.59 (81%), mp 117–121 °C (benzene). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.76 (t, 3H, J=7.2 Hz), 1.11–1.36 (m, 4H), 1.71–1.86 (m, 2H), 5.79 (s, 1H), 7.62–7.68 (m, 2H), 7.71–7.79 (m, 2H), 7.99 (d, 1H, J=8.3 Hz), 8.65 (d, 1H, J=8.3 Hz), 11.00 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 13.8, 22.0, 24.8, 81.9, 114.4, 121.6, 121.9, 122.7, 123.6, 126.8, 128.6, 129.6, 136.8, 139.7, 174.5, 196.2 (one signal not observed); IR (cm^{-1}): 3489 w, 3294 w, 2955 w, 2928 w, 1705 s, 1666 s, 1626 m, 1578 m, 1389 m, 820 w, 797 w, 765 w; MS (EI) m/z (%): 284 ($[M+1]^+$, 8), 283 (M^+, 41), 240 (38), 199 (100), 198 (50), 170 (13), 142 (14), 140 (17), 115 (45), 114 (16), 57 (22), 41 (19). HRMS (ESI+): m/z calcd for $C_{17}H_{18}NO_3^+$ $[M+H]^+$ 284.1281, found 284.1279. Anal. Calcd for $C_{17}H_{17}NO_3$ (283.32): C, 72.07; H, 6.05; N, 4.94%. Found: C, 71.96; H, 6.06; N, 4.81%.

*4.3.13. 3-Hydroxy-3-phenylquinoline-2,4(1H,3H)-dione (**2m**).*[46,24] White solid, yield 3.80 g (75%), mp 245–250 °C (ethanol), mp[46] 224–226 °C (ethanol). ^{1}H NMR (500 MHz, DMSO-d_6) δ 6.41 (br s, 1H), 7.08–7.15 (m, 2H), 7.27–7.35 (m, 3H), 7.36–7.39 (m, 2H), 7.61 (ddd, 1H, J=7.8, 7.8, 1.3 Hz), 7.68 (dd, 1H, J=7.8, 1.3 Hz), 11.11 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 82.5, 116.4, 119.0, 122.9, 125.4, 127.2, 128.6, 128.7, 136.4, 138.4, 141.4, 171.6, 194.2; IR (cm^{-1}): ν 3441 s, 3250 m, 1732 s, 1708 s, 1675 s, 1613 m, 1482 m, 1368 m, 1169 m, 760 m, 739 m, 696 m; HRMS (ESI+): m/z calcd for $C_{15}H_{12}NO_3^+$ $[M+H]^+$ 254.0812, found 254.0813.

*4.3.14. 3-Ethyl-3-hydroxy-1-methylquinoline-2,4(1H,3H)-dione (**2n**).*[45] White solid, yield 3.16 g (72%), mp 121–126 °C (ethyl acetate), mp[45] 146 °C (xylene–cyclohexane). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.75 (t, 3H, J=7.4 Hz), 1.64–1.80 (m, 2H), 3.38 (s, 3H), 5.73 (br s, 1H), 7.20–7.24 (m, 1H), 7.36 (d, 1H, J=8.4 Hz), 7.69–7.74 (m, 1H), 7.80 (dd, 1H, J=7.7, 1.6 Hz); ^{13}C NMR (126 MHz, DMSO-d_6) δ 7.5, 29.8, 33.2, 82.4, 115.6, 120.4, 123.0, 126.8, 136.0, 142.6, 172.4, 195.3; IR (cm^{-1}): ν 3379 m, 2990 w, 2940 w, 1711 s, 1680 s, 1605 s, 1473 s, 1359 m, 1102 m, 707 w, 755 w, 666 w, 530 w; HRMS (ESI+): m/z calcd for $C_{12}H_{14}NO_3^+$ $[M+H]^+$ 220.0968, found 220.0969.

*4.3.15. 3-Butyl-3-hydroxy-1-methylquinoline-2,4(1H,3H)-dione (**2o**).*[24] White solid, yield 4.20 g (85%), mp 104–108 °C (cyclohexane), mp[24] 104–108 °C (cyclohexane). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.74 (t, 3H, J=7.0 Hz), 1.08–1.28 (m, 4H), 1.61–1.75 (m, 2H), 3.37 (s, 3H), 5.73 (br s, 1H), 7.22 (dd, 1H, J=7.4, 7.4 Hz), 7.35 (d, 1H, J=8.4 Hz), 7.72 (ddd, 1H, J=8.2, 8.2, 1.7 Hz), 7.80 (dd, 1H, J=7.7, 1.6 Hz); ^{13}C NMR (126 MHz, DMSO-d_6) δ 13.7, 21.9, 24.8, 29.8, 39.6, 82.1, 115.6, 120.4, 123.0, 126.9, 136.0, 142.5, 172.4, 195.4; IR (cm^{-1}): ν 3471 m, 2944 m, 1702 s, 1661 s, 1603 s, 1475 s, 1346 m, 1324 m, 1296 m, 1189 m, 1106 m, 1081 s, 1028 m, 1020 m, 769 m.

*4.3.16. 3-Hydroxy-1-methyl-3-phenylquinoline-2,4(1H,3H)-dione (**2p**).*[24,27] White solid, yield 4.81 g (90%), mp 159–162 °C (ethanol), mp[27] 160–162 °C (ethanol–water). For yield,[24] mp[24] and IR spectrum[27] see literature. ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.49 (s, 3H), 6.49 (br s, 1H), 7.18 (dd, 1H, J=7.3, 7.3 Hz), 7.25–7.31 (m, 5H), 7.40 (d, 1H, J=7.3 Hz), 7.68–7.50 (m, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 30.0, 83.0, 116.0, 120.5, 123.3, 125.6, 127.3, 128.7, 136.3, 138.5, 142.4, 171.0, 193.4 (one signal not observed); IR (cm^{-1}): ν 3615 w, 3422 w, 1709 s, 1668 s, 1602 m, 1474 s, 1359 s, 1297 m, 1099 m, 1015 m, 759 m, 744 m, 700 m; MS (EI) m/z (%): 268 ($[M+1]^+$, 5), 267 ($[M]^+$, 26), 162 (65), 146 (11), 105 (100), 91 (12), 77 (43), 51 (12). Anal. Calcd for $C_{16}H_{13}NO_3$ (267.28): C, 71.90; H, 4.90; N, 5.24%. Found: C, 71.71; H, 4.86; N, 5.00%.

4.4. Oxidation of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones 2 with paraperiodic acid into *N*-(α-ketoacyl)anthranilic acids 3

An aqueous solution of H_5IO_6 (1.25 mL of water per 1 mmol of H_5IO_6, Table 2) was added to the stirred solution of 3-hydroxyquinoline-2,4(1*H*,3*H*)-dione **2** (1 mmol) in Solvent (Table 2) at room temperature. The reaction mixture was stirred at the temperature and for the time indicated in Table 2. Then it was left overnight at 5–10 °C. The resulting precipitate was collected by filtration and repeatedly washed with small portions of water (totally 15–50 mL) to afford the first crop of product **3**. The filtrate was evaporated to dryness suspended in water and filtered. The filtrate was washed with water as described above to give the second crop of the product. Re-crystallisation of the combined crops from the solvent indicated below gave pure **3**.

4.5. Oxidation of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones 2 with sodium periodate into *N*-(α-ketoacyl)anthranilic acids 3

An aqueous solution of $NaIO_4$ (1.25 mL of water per 1 mmol of $NaIO_4$, Table 3) was added to the stirred solution of 3-hydroxyquinoline-2,4(1*H*,3*H*)-dione **2** (1 mmol) in ethanol (Table 3) at room temperature within 5 min. The stirring was continued for the time indicated in Table 3. The reaction mixture was left at 5–10 °C overnight. The precipitate was collected by filtration and washed repeatedly with small portions of water (totally 100–200 mL) to give the first crop of product **3**. The above water filtrates were combined, solvents were evaporated in vacuo and the residue was suspended in water (40 mL). The precipitate was collected by filtration and washed with water (3×5 mL) to give the second crop of product **3**. Re-crystallisation of the combined crops from the solvent indicated below gave pure **3**.

*4.5.1. 2-[(2-Oxopropanoyl)amino]benzoic acid (**3a**).* For UV, IR and ^{1}H NMR (60 MHz) data, see Ref. 2 White solid, mp 207–210 °C

(ethyl acetate), mp[2] 194–196 °C (benzene). ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.45 (s, 3H, CH_3), 7.24 (dd, 1H, J=7.5, 7.5 Hz, H5), 7.67 (ddd, 1H, J=7.5, 7.5, 1.0 Hz, H4), 8.05 (dd, 1H, J=7.5, 1.0 Hz, H6), 8.67 (d, 1H, J=7.5 Hz, H3), 12.31 (br s, 1H, NH), 13.81 (br s, 1H, COOH); ^{13}C NMR (126 MHz, DMSO-d_6) δ 24.1 (CH_3), 117.1 (C1), 119.4 (C3), 123.7 (C5), 131.5 (C6), 134.3 (C4), 139.5 (C2), 158.8 (NCO), 169.2 (COOH), 196.2 ($COCH_3$); ^{15}N NMR (51 MHz, DMSO-d_6) δ 118; IR (cm^{-1}): ν 3260 m, 1725 s, 1700 s, 1673 s, 1585 m, 1520 s, 1451 m, 1419 s, 1281 s, 1253 s, 1138 s, 760 s; MS (EI) m/z (%): 208 ([M+1]$^+$, 1), 207 (M$^+$, 8), 164 (31), 146 (100), 119 (18), 90 (33), 65 (10), 43 (38). HRMS (ESI+): m/z calcd for $C_{10}H_{10}NO_4^+$ [M+H]$^+$ 208.0604, found 208.0610.

*4.5.2. 2-[(2-Oxobutanoyl)amino]benzoic acid (**3b**).* Off-white crystals, mp 179–182 °C (benzene); colourless needles, mp 194–196 °C (ethyl acetate); R_f=0.13 (5% ethanol in chloroform); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.04 (t, 3H, J=7.0 Hz), 2.96 (q, 2H, J=7.0 Hz), 7.24 (dd, 1H, J=7.6, 7.6 Hz), 7.67 (dd, 1H, J=7.6, 7.6 Hz), 8.05 (d, 1H, J=7.6 Hz), 8.67 (d, 1H, J=7.6 Hz), 12.31 (br s, 1H), 13.77 (br s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 7.0, 29.3, 117.0, 119.5, 123.6, 131.4, 134.2, 139.4, 158.6, 169.1, 198.6; IR (cm^{-1}): ν 2700–3300 br, 3266 w, 2983 w, 1721 m, 1693 s, 1672 s, 1602 m, 1584 m, 1519 s, 1416 m, 1277 s, 761 m, 662 w; MS (EI) m/z (%):222 ([M+1]$^+$, 1), 221 (M$^+$, 8), 164 (35), 146 (100), 119 (16), 90 (19), 57 (30). Anal. Calcd for $C_{11}H_{11}NO_4$ (221.21): C, 59.73; H, 5.01; N, 6.33%. Found: 59.72; H 5.03; N, 6.30%.

*4.5.3. 5-Methoxy-2-[(2-oxobutanoyl)amino]benzoic acid (**3c**).* Colourless shiny crystals, mp 205–207° C (ethyl acetate); R_f=0.11 (5% ethanol in chloroform); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.03 (t, 3H, J=7.1 Hz), 2.94 (q, 2H, J=7.1 Hz), 3.80 (s, 3H), 7.27 (dd, 1H, J=9.2, 3.1 Hz), 7.52 (d, 1H, J=3.1 Hz), 8.60 (d, 1H, J=9.2 Hz), 12.05 (br s, 1H), 13.87 (br s, 1H); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 7.0, 29.4, 55.4, 115.4, 118.4, 120.1, 121.1, 132.7, 154.8, 158.2, 168.7, 198.9; IR (cm^{-1}): ν 2500–3300 br, 3270 w, 2978 w, 1722 m, 1697 s, 1689 s, 1673 s, 1525 s, 1439 s, 1299 s, 1287 s, 1251 s, 1216 s, 1045 m, 829 m; MS (EI) m/z (%): 251 (M$^+$, 4), 207 (15), 194 (17), 176 (51), 167 (46), 150 (28), 149 (70), 122(47), 107(15), 52(16), 45(24), 44(90); Anal. Calcd for $C_{12}H_{13}NO_5$ (251.24): C, 57.37; H, 5.22; N, 5.58%. Found: C, 57.53; H, 5.42; N, 5.58%.

*4.5.4. 4-Methoxy-2-[(2-oxobutanoyl)amino]benzoic acid (**3d**).* Off-white crystals, mp 201–203 °C (benzene–ethyl acetate), R_f=0.08 (5% ethanol in chloroform). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.03 (t, 3H, J=7.1 Hz), 2.94 (q, 2H, J=7.1 Hz), 3.23 (s, 3H), 6.80 (dd, 1H, J=8.9, 2.5 Hz), 7.99 (d, 1H, J=8.9 Hz), 8.30 (d, 1H, J=2.5 Hz), 12.46 (br s, 1H), 13.40 (br s, 1H); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 7.0, 29.3, 55.5, 104.6, 109.3, 109.4, 133.3, 141.4, 158.8, 163.5, 168.9, 198.4; IR (cm^{-1}): ν 2800–3400 br, 3180 w, 2972 w, 1698 s, 1688 s, 1661 s, 1608 s, 1583 s, 1530s, 1248 s, 1211 s, 1140 m, 1027 m, 830 m, 624 w; MS (EI) m/z (%): 252 ([M+1]$^+$, 2), 251 (M$^+$, 6), 176 (55), 97 (43), 85 (49), 83 (45), 71 (79), 69 (43), 57 (100), 43 (77). Anal. Calcd for $C_{12}H_{13}NO_5$ (251.24): C, 57.37; H, 5.22; N, 5.58%. Found: C, 57.28; H 5.43; N, 5.41%.

*4.5.5. 3-Methoxy-2-[(2-oxobutanoyl)amino]benzoic acid (**3e**).* Off-white crystals, mp 142–146 °C (benzene–cyclohexane), R_f=0.13 (5% ethanol in chloroform). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.03 (t, 3H, J=7.2 Hz), 2.87 (q, 2H, J=7.2 Hz), 3.81 (s, 3H), 7.27–7.41 (m, 3H), 9.83 (br s, 1H), 12.89 (br s, 1H); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 7.1, 30.2, 56.1, 115.3, 121.5, 124.3, 127.0, 128.8, 154.1, 159.5, 167.3, 199.2; IR (cm^{-1}): ν 2800–3400 br, 3330 m, 2974 w, 2943 w, 1716 s, 1679 s, 1537 m, 1479 m, 1287 m, 1203 m, 1054 m, 760 w, 760 w, 720 w, 647 w; Anal. Calcd for $C_{12}H_{13}NO_5 \cdot 0.25H_2O$ (255.74): C, 56.36; H, 5.32; N, 5.48%. Found: C, 56.31; H 5.25; N, 5.48%.

*4.5.6. 5-Methyl-2-(2-oxobutanamido)benzoic acid (**3f**).* Colourless shiny crystals, mp 199–205 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.03 (t, 3H, J=7.2 Hz), 2.32 (s, 3H), 2.95 (q, 2H, J=7.2 Hz), 7.47 (dd, 1H, J=7.5, 2.0 Hz), 7.86 (d, 1H, J=2.0 Hz), 8.57 (d, 1H, J=7.5 Hz), 12.23 (br s, 1H), 13.76 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6): 7.1, 20.3, 29.4, 116.9, 119.5, 131.6, 132.9, 134.8, 137.1, 158.5, 169.2, 198.7; IR (cm^{-1}): ν 3480 w, 3275 m, 1693 s, 1673 s, 1595 m, 1524 s, 1419 m, 1292 m, 1270 s, 1223 s, 916 m, 893 m, 794 m, 754 m, 665 m; HRMS (ESI+): m/z calcd for $C_{12}H_{14}NO_4^+$ [M+H]$^+$ 236.0917, found 236.0914.

*4.5.7. 3-Methyl-2-[(2-oxobutanoyl)amino]benzoic acid (**3g**).* Yellowish solid, mp 130–136 °C (benzene). ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.03 (t, 3H, J=7.2 Hz), 2.20 (s, 3H), 2.90 (q, 2H, J=7.2 Hz), 7.29 (dd, 1H, J=7.7, 7.7 Hz), 7.48 (d, 1H, J=7.7 Hz), 7.69 (d, 1H, J=7.7 Hz), 10.29 (br s, 1H), 12.97 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 7.0, 18.2, 30.1, 126.2, 127.8, 127.9, 134.0, 134.5, 135.7, 159.4, 167.5, 199.0; IR (cm^{-1}): ν 2600–3400 br, 3343 w, 2985 w, 1724 s, 1697 s, 1678 s, 1597 m, 1515 s, 1468 m, 1431 m, 1405 m, 1291 s, 1193 m, 1113 m, 756 s; HRMS (ESI+): m/z calcd for $C_{12}H_{14}NO_4^+$ [M+H]$^+$ 236.0917; found 236.0922.

*4.5.8. 6-Chloro-3-methyl-2-[(2-oxobutanoyl)amino]benzoic acid (**3h**).* Colourless crystals, mp 189–191 °C (benzene). ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.02 (t, 3H, J=7.2 Hz, CH_3CH_2), 2.12 (s, 3H, CH_3–C_3), 2.87 (q, 2H, J=7.2 Hz, CH_2), 7.37 (d, J=8.3 Hz, 1H, H4), 7.41 (d, 1H, J=8.3 Hz, H5), 10.22 (br s, 1H, NH), 13.01 (br s, 1H, COOH); ^{13}C NMR (126 MHz, DMSO-d_6) δ 7.0 (CH_3CH_2), 17.2 (CH_3–C3), 30.4 (CH_2), 126.6 (C6), 128.1 (C5), 131.8 (C4), 133.2 (C2), 133.4 (C1), 135.6 (C3), 160.4 (NHCO), 165.9 (COOH), 199.0 ($COCH_2$); ^{15}N NMR (51 MHz, DMSO-d_6) δ 118; IR (cm^{-1}): ν 2700–3500 br, 3219 w, 2983 w, 2936 w, 1716 s, 1668 s, 1530 m, 1210 s, 1171 s, 1107 m, 694 m; HRMS (ESI–): m/z calcd for $C_{12}H_{11}ClNO_4^-$ [M–H]$^-$ 268.0382, found 268.0393.

*4.5.9. 2-[(2-Oxohexanoyl)amino]benzoic acid (**3i**).* Colourless shiny crystals, mp 147–151 °C (ethyl acetate); ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.90 (t, 3H, J=2.4 Hz, CH_3), 1.29–1.37 (m, 2H, CH_2CH_3), 1.50–1.57 (m, 2H, $CH_2CH_2CH_3$), 2.93 (t, 2H, J=7.3 Hz, $COCH_2$), 7.24 (ddd, 1H, J=7.7, 7.7, 1.0 Hz, H5), 7.67 (ddd, 1H, J=7.7, 7.7, 1.6 Hz, H4), 8.05 (dd, 1H, J=7.7, 1.6 Hz, H6), 8.67 (dd, 1H, J=7.7, 1.0 Hz, H3), 12.33 (br s, 1H, NH), 13.81 (br s, 1H, COOH); ^{13}C NMR (126 MHz, DMSO-d_6) δ 13.8 (CH_3), 21.6 (CH_2CH_3), 24.8 ($CH_2CH_2CH_3$), 35.4 (CH_2CO), 117.0 (C1), 119.5 (C3), 123.6 (C5), 131.5 (C6), 134.3 (C4), 139.4 (C2), 158.6 (NCO), 169.1 (COOH), 198.1 ($COCH_2$); ^{15}N NMR (51 MHz, DMSO-d_6) δ 119; IR (cm^{-1}): ν 2300–3300 br, 3252 w, 2957 w, 2871 w, 1723 m, 1695 s, 1668 s, 1603 m, 1586 s, 1521 s, 1412 m, 1283 s, 1265 s, 762 s, 662 m; MS (EI): m/z, (%) 249 (M$^+$, 6), 164 (43), 146 (100), 90 (19), 57 (32); HRMS (ESI+): m/z Calcd for $C_{13}H_{16}NO_4^+$ [M+H]$^+$ 250.1074; found 250.1075. Anal. Calcd for $C_{13}H_{15}NO_4$ (249.26): C, 62.64; H, 6.07; N, 5.62%. Found: C, 62.93; H 6.14; N, 5.70%.

*4.5.10. 3,5-Dimethyl-2-[(2-oxohexanoyl)amino]benzoic acid (**3j**).* Colourless crystals, mp 109–110 °C (cyclohexane). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.89 (t, 3H, J=7.4 Hz, CH_3CH_2), 1.28–1.36 (m, 2H, CH_2CH_3), 1.50–1.57 (m, 2H, $CH_2CH_2CH_3$), 2.15 (s, 3H, CH_3–C3), 2.31 (s, 3H, CH_3–C5), 2.86 (q, 2H, J=7.3 Hz, $COCH_2$), 7.29 (d, 1H, J=1.3 Hz, H4), 7.50 (d, 1H, J=1.3 Hz, H6), 10.17 (br s, 1H, NH), 12.89 (br s, 1H, COOH); ^{13}C NMR (126 MHz, DMSO-d_6) δ 13.7 (CH_2CH_3), 18.0 (CH_3–C3), 20.2 (CH_3–C5), 21.5 (CH_2CH_3), 24.8 ($CH_2CH_2CH_3$), 36.2 ($COCH_2$), 127.6 (C1), 128.3 (C6), 132.0 (C2), 134.5 (C4), 135.5 (C3), 135.6 (C1), 159.6 (NHCO), 167.6 (COOH), 198.8 ($COCH_2$); ^{15}N NMR (51 MHz, DMSO-d_6) δ 118; IR (cm^{-1}): ν 3332 w, 2500–3300 br, 2963 w, 2930 w, 1726 m, 1690 s, 1671 s, 1511 s, 1431 m, 1313 m, 1242 m, 1150 w, 727 w; HRMS (ESI–): m/z Calcd for $C_{15}H_{18}NO_4^-$ [M–H]$^-$ 276.1241, found 276.1248.

*4.5.11. 3,5-Dimethoxy-2-[(2-oxohexanoyl)amino]benzoic acid (**3k**).* Pale yellow microcrystals, mp 101–105 °C (cyclohexane). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.89 (t, 3H, J=7.4 Hz), 1.28–1.35 (m, 2H), 1.50–1.55 (m, 2H), 2.83 (t, 2H, J=7.2 Hz), 3.78 (s, 3H), 3.81 (s, 3H),

6.84 (d, 1H, *J*=2.7 Hz), 6.89 (d, *J*=2.7 Hz), 9.66 (br s, 1H), 12.93 (br s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 13.8, 21.7, 25.0, 36.4, 55.6, 56.2, 102.5, 105.4, 117.5, 129.9, 155.5, 158.2, 159.9, 167.1, 199.2; IR (cm^{-1}): ν 3384 m, 2500–3200 br, 2964 w, 2875 w, 1698 s, 1601 m, 1510 s, 1465 m, 1355 m, 1299 m, 1211 s, 1154 s, 1070 m, 1048 m; HRMS (ESI+): *m*/*z* calcd for $C_{15}H_{20}NO_6^+$ $[M+H]^+$ 310.1285, found 310.1284; Anal. Calcd for $C_{15}H_{19}NO_6$ (309.31): C, 58.25; H, 6.19; N, 4.53%. Found: C, 58.07; H, 6.20; N, 5.02%.

*4.5.12. 1-[(2-Oxohexanoyl)amino]naphthalene-2-carboxylic acid (**3l**).* White powder, mp 98–105 °C (cyclohexane). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.92 (t, 3H, *J*=7.4 Hz, C*H*$_3$CH$_2$), 1.32–1.40 (m, 2H, C*H*$_2$CH$_3$), 1.56–1.62 (m, 2H, C*H*$_2$CH$_2$CH$_3$), 2.92 (t, 3H, *J*=7.3 Hz, COCH$_2$), 7.60 (ddd, 1H, *J*=7.6, 7.6, 1.0 Hz, H7), 7.66 (ddd, 1H, *J*=7.6, 7.6, 1.0 Hz, H6), 7.91 (d, 1H, *J*=8.6 Hz, H3), 7.96 (d, 1H, *J*=8.6 Hz, H4), 8.00 (br d, 1H, *J*=7.6 Hz, H8), 8.01 (d, 1H, *J*=8.1 Hz, H5), 10.76 (br s, 1H, NH), 13.17 (br s, 1H, COOH); ^{13}C NMR (126 MHz, DMSO-d_6) δ 13.8 (CH$_2$*C*H$_3$), 21.7 (*C*H$_2$CH$_3$), 25.0 (CH$_2$*C*H$_2$CH$_3$), 36.3 (CO*C*H$_2$), 124.9 (C2), 125.4 (C2), 126.0 (C3), 126.7 (C7), 126.8 (C4), 127.8 (C5), 128.1 (C6), 129.3 (C8a), 134.1 (C1), 135.0 (C4a), 160.8 (NCO), 167.6 (COOH), 198.6 (*C*OCH$_2$); IR (cm^{-1}): ν 2800–3300 br, 3294 w, 2961 w, 2877 w, 1694 s, 1675 s, 1571 m, 1501, 1409 m, 1284 m, 1258 m, 764 m; MS (EI, 70 eV) *m*/*z* (%): 300 ([M+1]$^+$, 2), 299 (M$^+$, 11), 214 (50), 197 (14), 196 (100), 187 (27), 169 (44), 141 (19), 140 (49), 115 (33), 114 (16), 85 (17), 57 (58), 43 (11), 41 (50). HRMS (ESI+): *m*/*z* calcd for $C_{17}H_{18}NO_4^+$ $[M+H]^+$ 300.1230, found 300.1229. Anal. Calcd for $C_{17}H_{17}NO_4$ (173.60): C, 68.21; H, 5.72; N, 4.68%. Found: C, 68.45; H 5.91; N, 5.71%.

*4.5.13. 2-{[Oxo(phenyl)acetyl]amino}benzoic acid (**3m**).*[9] For IR and ^{1}H NMR (60 MHz) data, see Ref. 9 Colourless crystals, mp 199–200 °C (ethanol), mp[9] 200 °C, *R*$_f$=0.18 (5% EtOH in CHCl$_3$). ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.29 (dd, 1H, *J*=7.5, 7.5 Hz), 7.60 (dd, 2H, *J*=7.5, 7.5 Hz), 7.68–7.78 (m, 2H), 8.08 (d, 1H, *J*=7.5 Hz), 8.24 (d, 2H, *J*=7.5 Hz), 8.67 (d, 1H, *J*=7.5 Hz), 12.43 (br s, 1H), 13.80 (br s, 1H); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 117.7, 120.1, 124.0, 128.6, 130.8, 131.4, 133.0, 134.1, 134.4, 139.3, 160.2, 169.1, 187.4; IR (cm^{-1}): ν 2600–3300 br, 3236 w, 3070 w, 1696 s, 1682 s, 1672 s, 1585 s, 1524 s, 1409 m, 1265 s, 758 m, 689 w, 660 w.

*4.5.14. 2-[Methyl(2-oxobutanoyl)amino]benzoic acid (**3n**).* Colourless crystals, mp 113–115 °C (ethanol). ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.75 (t, 3H, *J*=7.3 Hz), 2.50–2.71 (m, 2H), 3.17 (s, 3H), 7.44–7.50 (m, 2H), 7.64 (ddd, 1H, *J*=7.7, 7.7, 1.6 Hz), 7.90 (dd, 1H, *J*=7.7, 1.6 Hz), 13.29 (br s, 1H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 6.8, 31.9, 36.6, 128.4, 128.5, 130.0, 131.3, 133.4, 141.5, 165.6, 166.4, 200.6; IR (cm^{-1}): ν 2800–3200, 2985 w, 1732 m, 1709 s, 1632 s, 1598 m, 1237 s, 861 w, 644 w; MS (EI) *m*/*z* (%): 179 (11), 178 (100), 134 (61), 105 (35), 104 (20), 77 (32), 57 (43); HRMS (ESI+): *m*/*z* calcd for $C_{12}H_{14}NO_4^+$ $[M+H]^+$ 236.0917, found 236.0912.

*4.5.15. 2-[Methyl(2-oxohexanoyl)amino]benzoic acid (**3o**).* Colourless crystals, mp 101–105 °C (benzene), *Rf*=0.18 (5% ethanol in chloroform). ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.74 (t, 3H, *J*=7.2 Hz), 0.98–1.11 (m, 2H, C*H*$_2$CH$_3$), 1.19–1.31 (m, 2H, CH$_2$C*H*$_2$CH$_2$), 2.43–2.70 (m, 2H, COCH$_2$), 3.17 (s, 3H), 7.42–7.52 (m, 2H), 7.64 (ddd, 1H, *J*=7.7, 7.7, 1.3 Hz), 7.91 (dd, 1H, *J*=7.7, 1.3 Hz), 13.25 (br s, 1H); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 13.5, 21.2, 24.3, 36.5, 38.1, 128.5, 128.6, 130.2, 131.3, 133.3, 141.3, 165.7, 166.3, 200.1; IR (cm^{-1}): ν 2600–3300 br, 2959 w, 2623 w, 1714 s, 1620 s, 1595 m, 1396 m, 1247 m, 1140 w, 1083 w, 1067 w, 784 w, 710 w; Anal. Calcd for $C_{14}H_{17}NO_4$ (263.29): C, 63.87; H, 6.51; N, 5.32%. Found: C, 63.70; H 6.47; N, 5.26%.

*4.5.16. 2-(N-Methyl-2-oxo-2-phenylacetamido)benzoic acid (**3p**).* Colourless crystals, mp 145–146 °C (benzene-cyklohexane), *R*$_f$=0.21 (5% ethanol in chloroform), 0.05 (20% ethyl acetate in benzene); ^{1}H NMR (500 MHz, CD$_3$CN) δ 3.37 (s, 3H, CH$_3$), 7.34 (dd, 1H, *J*=7.8, 1.2 Hz, H3), 7.39 (ddd, *J*=7.8, 7.8, 1.2 Hz, H5), 7.44–7.50 (m, 3H, H4, H3′, H5′), 7.61–7.65 (m, 1H, H4′), 7.79–7.82 (m, 2H, H2′, H6′), 7.89 (dd, 1H, *J*=7.8, 1.2 Hz, H6), resonances for exchangeable protons in the baseline; ^{13}C NMR (126 MHz, CD$_3$CN) δ 36.9 (CH$_3$), 129.9 (C3′, C5′), 130.1 (C5), 130.2 (C1), 130.4 (C2′, C6′), 132.0 (C3), 132.9 (C6), 134.1 (C1′), 134.6 (C4), 135.6 (C4′), 141.9 (C2), 166.2 (COOH), 166.8 (NCO), 192.0 (COPh); IR (cm^{-1}): ν 2500–3300 br, 1719 s, 1680 s, 1616 s, 1593 s, 1576 m, 1249 s, 1236 s, 1220 s, 1081 s, 779 s, 715 s, 668 m; MS (EI) *m*/*z* (%): 105 (69), 77 (58), 57 (26), 45 (28), 44 (100), 43 (92), 42 (27), 41 (36); HRMS (ESI+): *m*/*z* calcd for $C_{16}H_{14}NO_4^+$ $[M+H]^+$ 284.0917, found 284.0918; Anal. Calcd for $C_{16}H_{13}NO_4$ (283.28): C, 67.84; H, 4.63; N, 4.94%. Found: C, 67.81; H 4.60; N, 4.90%.

4.6. Hydrolysis of *N*-(α-ketoacyl)anthranilic acids 3

To a stirred suspension of *N*-(α-ketoacyl)anthranilic acids **3** (3 mmol) in water (10 mL) aqueous hydrochloric acid (37%, 15 mL) was added portion-wise at room temperature. The reaction mixture was refluxed, until the starting compound **3** was present according to TLC analysis (1–7 h). The reaction mixture was cooled down to room temperature and the precipitate (if formed) was removed by filtration. The filtrate was evaporated to dryness using rotary evaporator and the residue was recrystallized to give anthranilic acid hydrochloride (**4**·**HCl**).

*4.6.1. 2-Aminobenzoic acid hydrochloride (**4b**·**HCl**).* *N*-(α-Ketoacyl) anthranilic acids **3b**; Reaction time: 4 h. White crystalline solid, yield 443 mg (85%), mp 167–172 °C (ethanol–ethyl acetate), mp[47] 193–194 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 6.93 (dd, 1H, *J*=7.6, 7.6 Hz), 7.13 (d, 1H, *J*=7.6 Hz), 7.43 (dd, 1H, *J*=7.6, 7.6, 1.5 Hz), 7.8 (br s, 4H), 7.84 (dd, 1H, *J*=7.6, 1.5 Hz); ^{13}C NMR (126 MHz, DMSO-d_6) δ 115.5, 119.9, 120.2, 131.3, 133.9, 144.1, 168.4; IR (cm^{-1}): ν 2400–3300 br, 2980 w, 2681 w, 2569 w, 1693 s, 1561 m, 1494 m, 1460 m, 1393 m, 1219 s, 1100 m, 758 m, 752 m, 650 m; HRMS (ESI+): *m*/*z* calcd for $C_7H_8NO_2^+$ $[M+H]^+$ 138.0550, found 138.0548.

*4.6.2. 2-Amino-5-methoxybenzoic acid hydrochloride (**4c**·**HCl**).* *N*-(α-Ketoacyl)anthranilic acids **3c**; Reaction time: 6 h. Yellowish solid, yield 556 mg (91%), mp 211–214 °C (ethanol–ethyl acetate), mp[48] 213–214 °C (ethanol–diethyl ether); ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.80 (s, 3H), 7.25 (dd, 1H, *J*=8.8, 3.0 Hz), 7.45 (d, 1H, *J*=3.0 Hz), 7.50 (d, 1H, *J*=8.8 Hz), 9.8 (br s, 4H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 55.7, 115.5, 119.9, 122.8, 124.9, 128.8, 156.8, 166.8; IR (cm^{-1}): ν 2500–3300 br, 2845 w, 2617 w, 1698 s, 1614 s, 1509 s, 1404 m, 1273 s, 1234 s, 1025 m, 845 m, 741 m; HRMS (ESI+): *m*/*z* calcd for $C_8H_{10}NO_3^+$ $[M+H]^+$ 168.0655, found 168.0652.

*4.6.3. 2-Amino-4-methoxybenzoic acid hydrochloride (**4d**·**HCl**).* *N*-(α-Ketoacyl)anthranilic acids **3d**; Reaction time: 7 h. Colourless crystals, yield 391 mg (64%), mp 176–179 °C (ethanol–diethyl ether), mp[48] 178–180 °C; ^{1}H NMR (300 MHz, DMSO-d_6) 3.72 (s, 3H), 6.11 (dd, 1H, *J*=8.9, 2.5 Hz), 6.25 (d, 1H, *J*=2.5 Hz), 7.61 (d, 1H, *J*=8.9 Hz), resonances for exchangeable protons in the baseline; ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 54.9, 98.6, 103.16, 103.21, 132.9, 153.5, 163.6, 169.2; IR (cm^{-1}): ν 2600–3300 br, 2577 w, 1687 s, 1631 m, 1596 m; 1403 m, 1338 m, 1246 s, 1113 m, 1021 m; HRMS (ESI+): *m*/*z* calcd for $C_8H_{10}NO_3^+$ $[M+H]^+$ 168.0655, found 168.0653. Anal. Calcd for $C_8H_{10}ClNO_3$ (203.62): C, 47.19; H, 4.95; N, 6.88. Found: C, 47.38; H 5.10; N, 6.82.

*4.6.4. 2-Amino-3-methoxybenzoic acid hydrochloride (**4e**·**HCl**).* *N*-(α-Ketoacyl)anthranilic acids **3e**; Reaction time: 1 h. White solid, yield 415 mg (68%) (crude, analytically pure product), mp

178–188 °C, mp[49] 205–206 °C (hydrochloric acid); ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.82 (s, 3H), 6.61 (dd, 1H, J=8.0, 8.0 Hz), 7.02 (dd, 1H, J=8.0, 1.0 Hz), 7.36 (dd, 1H, J=8.0, 1.0 Hz), resonances for exchangeable protons in the baseline; ^{13}C NMR (126 MHz, DMSO-d_6) δ 55.8, 111.1, 113.7, 115.4, 122.5, 139.6, 147.3, 169.4; IR (cm^{-1}): ν 3485 m, 3418 m, 2500–3400 br, 3064 w, 2616 w, 1699 s, 1651 s, 1589 m, 1478 s, 1362 s, 1286 s, 1213 s, 1049 s, 755 m; HRMS (ESI+): m/z calcd for $C_8H_{10}NO_3^+$ $[M+H]^+$ 168.0655, found 168.0653. Anal. Calcd for $C_8H_{10}ClNO_3$ (203.62): C, 47.19; H, 4.95; N, 6.88%. Found: C, 47.32; H 5.11; N, 6.85%.

*4.6.5. 2-(Methylamino)benzoic acid hydrochloride (**4n**·**HCl**).* *N*-(α-Ketoacyl)anthranilic acids **3n**; Reaction time: 2 h. Colourless needles, yield 411 mg (73%), mp 136–140 °C (ethanol–benzene), mp[50] 141 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.85 (s, 3H), 6.65 (dd, 1H, J=7.7, 7.7 Hz), 6.78 (d, 1H, J=7.7 Hz), 7.42 (ddd, 1H, J=7.7, 7.7, 1.6 Hz), 7.81 (dd, 1H, J=7.7, 1.6 Hz), resonances for exchangeable protons in the baseline; ^{13}C NMR (126 MHz, DMSO-d_6) δ 29.8, 111.0, 111.8, 115.2, 131.6, 134.5, 150.6, 169.7; IR (cm^{-1}): ν 3386 m, 2898 m, 2730 m, 2650 m, 1694 m, 1662 s, 1304 s, 1271 s, 1122 m, 772 m, 750 s, 699 m; HRMS (ESI−): m/z Calcd for $C_8H_8NO_2^-$ $[M-H]^-$ 150.0561, found 150.0558. Anal. Calcd for $C_8H_{10}ClNO_2$ (187.62): C, 51.21; H, 5.37; N, 7.47%. Found: C, 51.32; H 5.24; N, 7.71%.

Acknowledgements

This study was supported by the internal grant of the TBU in Zlin (No. IGA/FT/2013/003) funded from the resources of specific university research and the Ministry of Higher Education, Science and Technology of the Republic of Slovenia and the Slovenian Research Agency (Grant P1-0230-0103). This work was also partly supported through the infrastructure of the EN-FIST Centre of Excellence, Ljubljana.

References and notes

1. Andreichikov, Y. S.; Krylova, I. V. *Zh. Org. Khim.* **1988**, *24*, 2212–2216.
2. Lingens, F.; Sproessler, B. *Justus Liebigs Ann. Chem.* **1967**, *702*, 169–179.
3. Akbas, E.; Sonmez, M.; Celebi, M.; Aslanoglu, F. *J. Chem. Res.* **2008**, 256–259.
4. Wegfahrt, P. F.; Rapoport, H. *J. Org. Chem.* **1969**, *34*, 3035–3039.
5. Zhang, C.; Zong, X.; Zhang, L.; Jiao, N. *Org. Lett.* **2012**, *14*, 3280–3283.
6. Shibuya, M.; Sakurai, H.; Maeda, T.; Nishiwaki, E.; Saito, M. *Tetrahedron Lett.* **1986**, *27*, 1351–1354.
7. Filippo Rossi, P.; Massimino, A. *Gazz. Chim. Ital.* **1962**, *92*, 1478–1480.
8. Podesva, C.; Solomon, C.; Vagi, K. *Can. J. Chem.* **1968**, *46*, 435–439.
9. Rabilloud, G.; Sillion, B. *Bull. Soc. Chim. Fr.* **1975**, 2682–2686.
10. Fatiadi, A. J. *Synthesis* **1974**, 229–272.
11. Ermolinsky, B. S.; Mikhailov, S. N. *Russ. J. Bioorg. Chem.* **2000**, *26*, 429–504.
12. Klásek, A.; Kafka, S.; Kappe, T. *Collect. Czech. Chem. Commun.* **1995**, *60*, 2137–2146.
13. Klásek, A.; Kafka, S. *J. Heterocycl. Chem.* **1998**, *35*, 307–311.
14. Klásek, A.; Kořistek, K.; Polis, J.; Košmrlj, J. *Heterocycles* **1998**, *48*, 2309–2326.
15. Klásek, A.; Kořistek, K.; Polis, J.; Košmrlj, J. *Tetrahedron* **2000**, *56*, 1551–1560.
16. Kafka, S.; Klásek, A.; Košmrlj, J. *J. Org. Chem.* **2001**, *66*, 6394–6399.
17. Klásek, A.; Polis, J.; Mrkvička, V.; Košmrlj, J. *J. Heterocycl. Chem.* **2002**, *39*, 1315–1320.
18. Kafka, S.; Klásek, A.; Polis, J.; Košmrlj, J. *Heterocycles* **2002**, *57*, 1659–1682.
19. Klásek, A.; Kořistek, K.; Kafka, S.; Košmrlj, J. *Heterocycles* **2003**, *60*, 1811–1820.
20. Klásek, A.; Mrkvička, V.; Pevec, A.; Košmrlj, J. *J. Org. Chem.* **2004**, *69*, 5646–5651.
21. Košmrlj, J.; Kafka, S.; Leban, I.; Grad, M. *Magn. Reson. Chem.* **2007**, *45*, 700–704.
22. Pomeisl, K.; Kvíčala, J.; Paleta, O.; Klásek, A.; Kafka, S.; Kubelka, V.; Havlíček, J.; Čejka, J. *Tetrahedron* **2007**, *63*, 10549–10561.
23. Kafka, S.; Klásek, A.; Polis, J.; Rosenbreierová, V.; Palík, C.; Mrkvička, V.; Košmrlj, J. *Tetrahedron* **2008**, *64*, 4387–4402.
24. Kafka, S.; Kovář, M.; Klásek, A.; Kappe, T. *J. Heterocycl. Chem.* **1996**, *33*, 1977–1982.
25. Baumgarten, P.; Kärgel, W. *Ber. Dtsch. Chem. Ges.* **1927**, *60*, 832–842.
26. Bowman, R. E.; Campbell, A.; Tanner, E. M. *J. Chem. Soc.* **1959**, 444–447.
27. Stadlbauer, W.; Lutschounig, H.; Schindler, G.; Witoszynskyj, T.; Kappe, T. *J. Heterocycl. Chem.* **1992**, *29*, 1535–1540.
28. Kafka, S.; Pevec, A.; Proisl, K.; Kimmel, R.; Košmrlj, J. *Acta Crystallogr., Sect. E: Struct. Rep. Online* **2013**, *E69*, o231.
29. Kafka, S.; Pevec, A.; Proisl, K.; Kimmel, R.; Košmrlj, J. *Acta Crystallogr., Sect. E: Struct. Rep. Online* **2012**, *E68*, o3199–o3200.
30. Ficini, J.; Krief, A. *Tetrahedron Lett.* **1968**, 947–951.
31. Curd, F. H. S.; Raison, C. G.; Rose, F. L. *J. Chem. Soc.* **1947**, 899–909.
32. Kimmel, R.; Kafka, S.; Košmrlj, J. *Carbohydr. Res.* **2010**, *345*, 768–779.
33. Ukrainets, I. V.; Taran, S. G.; Evtifeeva, O. A.; Gorokhova, O. V.; Bezuglyi, P. A.; Turov, A. V.; Voronina, L. N.; Filimonova, N. I. *Khim. Geterotsikl. Soedin.* **1994**, 673–678.
34. McCorkindale, N. J. *Tetrahedron* **1961**, *14*, 223–229.
35. Stadlbauer, W.; Kappe, T. *Monatsh. Chem.* **1985**, *116*, 1005–1015.
36. Cooke, R. G.; Haynes, H. F. *Aust. J. Chem.* **1959**, *7*, 273–276.
37. Rapoport, H.; Holden, K. G. *J. Am. Chem. Soc.* **1959**, *81*, 3738–3743.
38. Kafka, S.; Pevec, A.; Proisl, K.; Kimmel, R.; Košmrlj, J. *Acta Crystallogr., Sect. E: Struct. Rep. Online* **2012**, *E68*, o3198.
39. Rügheimer, L.; Schramm, C. G. *Ber. Dtsch. Chem. Ges.* **1888**, *21*, 299–307.
40. Bezuglyi, P. A.; Ukrainets, I. V.; Treskach, V. I.; Turov, A. V. *Khim. Geterotsikl. Soedin.* **1992**, *4*, 522–524.
41. I. G. Farbenindustrie AG, Patent DE 490274, 1926.
42. Stadlbauer, W.; Laschober, R.; Lutschounig, H.; Schindler, G.; Kappe, T. *Monatsh. Chem.* **1992**, *123*, 617–636.
43. Stadlbauer, W.; Schmut, O.; Kappe, T. *Monatsh. Chem.* **1980**, *111*, 1005–1013.
44. Braeuniger, H.; Stens, B. *Pharmazie* **1963**, *18*, 585–600.
45. Stadlbauer, W.; Kappe, T. *Z. Naturforsch., B: Anorg. Chem., Org. Chem.* **1982**, *37*, 1196–1200.
46. Nishimura, H.; Nagai, Y.; Suzuki, T.; Sawayama, T. *Yakugaku Zasshi* **1970**, *90*, 818–828 *Chem. Abstr.* **1970**, *73*, 77020.
47. Fischer, E. *Ber. Dtsch. Chem. Ges.* **1896**, *29*, 2062–2064.
48. Karimov, A.; Telezhenetskaya, M. V.; Yunusov, S. *Khim. Prir. Soedin.* **1982**, *18*, 498–504.
49. Nyc, J. F.; Mitchell, H. K. *J. Am. Chem. Soc.* **1948**, *70*, 1847–1848.
50. Schultz, G.; Flachslaender, J. *Z. Farben- Text.-Chem.* **1902**, *1*, 353–354.