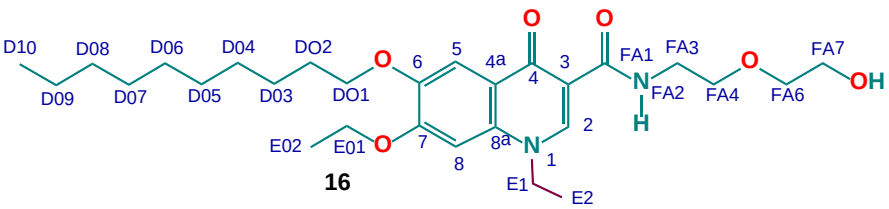
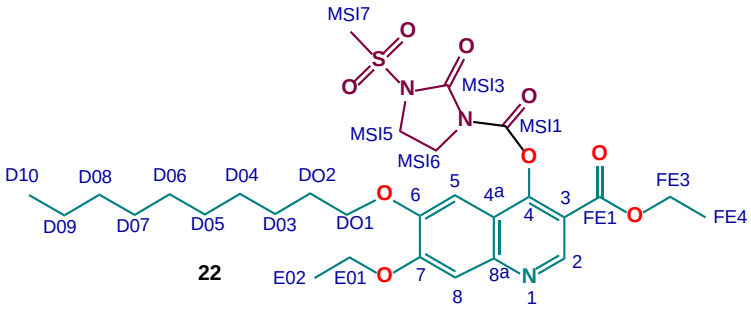
Supplementary Table 1 Summary of ^{1}H and ^{13}C NMR data for compound **16**.



16

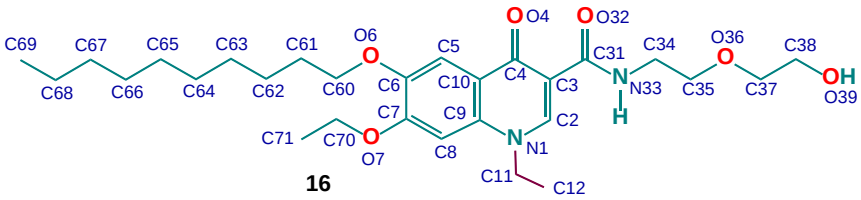
Atom	Carbon	δ (^{13}C)	δ (^{1}H)	H Multiplicity
2	CH	145.2	8.61	s
3	C	111.3		
4	C	175.3		
4a	C	122.3		
5	CH	107.6	7.77	s
6	C	147.8		
7	C	153.6		
8	CH	98.3	6.76	s
8a	C	134.1		
DO1	CH_2	69.2	4.06	t
DO2	CH_2	28.8	1.80	m
DO3	CH_2	25.9	1.41	m
DO4	CH_2	29.2	1.29	m
DO5	CH_2	29.5	1.21	bs
DO6	CH_2	29.4	1.20	bs
DO7	CH_2	29.3	1.20	bs
DO8	CH_2	31.8	1.19	bs
DO9	CH_2	22.6	1.21	bs
DO10	CH_3	14.0	0.80	t
EO1	CH_2	65.0	4.13	q
EO2	CH_3	14.5	1.47	t
E1	CH_2	49.1	4.20	q
E2	CH_3	14.5	1.46	t
FA1	C	165.5		
FA2			3.25	bs
FA3	CH_2	61.7	3.70	
FA4	CH_2	72.5	3.58	
FA6	CH_2	69.8	3.61	bs
FA7	CH_2	38.8	3.61	bs
FAOH			10.44	bs

Supplementary Table 2 Summary of ^{1}H and ^{13}C NMR data for compound **22**.



Atom	Carbon	δ(^{13}C)	δ (^{1}H)	H multiplicity
2	CH	148.8	9.13	s
3	C	112.3		
4	C	153.1		
4a*	C	117.2		
5	CH	100.4	7.20	s
6	C	150.8		
7	C	154.7		
8	CH	108.5	7.34	s
8a*	C	149.3		
DO1	CH2	69.3	4.07	t
DO2	CH2	28.8	1.84	m
DO3	CH2	25.9	1.45	m
DO4	CH2	29.2	1.32	m
DO5	CH2	29.4	1.23	bs
DO6†	CH2	29.4	1.22	bs
DO7†	CH2	29.3	1.20	bs
DO8	CH2	31.8	1.20	bs
DO9	CH2	22.6	1.20	bs
DO10	CH3	14.0	0.81	t
EO1	CH2	64.7	4.19	q
EO2	CH3	14.3	1.48	t
FE1	C	163.7		
FE3	CH2	61.3	4.31	q
FE4	CH3	14.1	1.34	t
MSI1	C	148.1		
MSI3	C	149.7		
MSI5†	CH2	40.1	3.97	bs
MSI6†	CH2	41.2	4.12	bs
MSI7	CH3	40.5	3.33	s

*C4a and C8a were assigned based on the reference shifts from Spectral Database for Organic Compounds (SDBS) (ref. 1); †signals due to DO6 and DO7 in the decyloxy side chain, and MSI5 and MSI6 in the imidazolidone cannot be unambiguously assigned.



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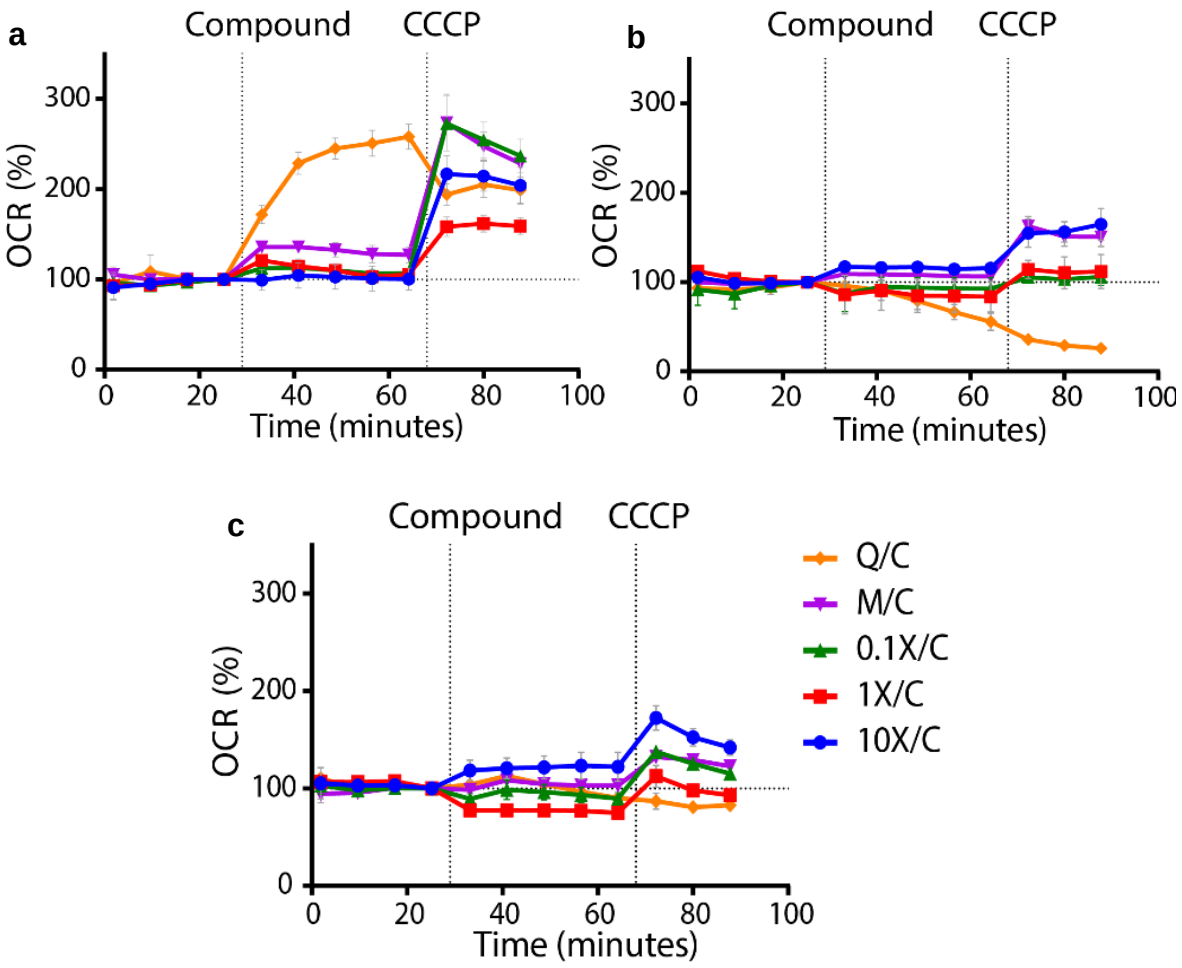
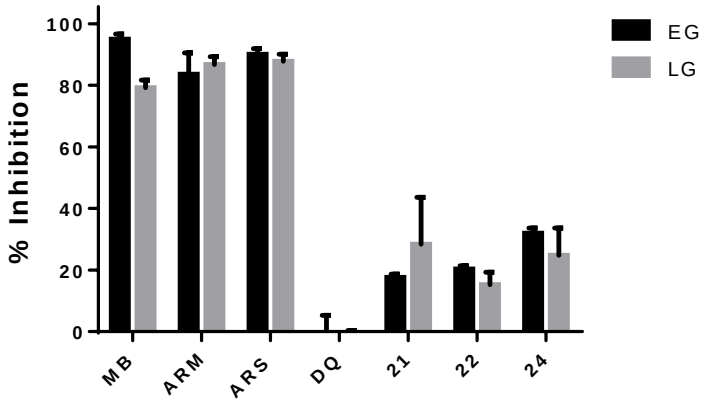
Supplementary Table 3 X-ray Structure determination summary for **16**

CCDC Deposition number	1525201
Empirical formula	$C_{28}H_{44}N_2O_6$
Formula weight	504.67
Temperature/K	173.15
Crystal system	triclinic
Space group	P-1 (no. 2)
a/Å	9.0688(4)
b/Å	12.6983(5)
c/Å	13.2548(6)
α/°	74.080(4)
β/°	72.309(4)
γ/°	82.112(4)
Volume/Å^3	1396.02(11)
Z	2
ρ_{calc} g/cm^3	1.2005
μ/ mm^{-1}	0.676
F(000)	548
Crystal size/mm^3	0.35 × 0.06 × 0.02
Radiation	Cu Kα (λ = 1.54178)
2Θ range for data collection/°	7.22 to 133.98
Index ranges	-10 ≤ h ≤ 9, -15 ≤ k ≤ 15, -15 ≤ l ≤ 15
Reflections collected	21145
Independent reflections	4942 [R_{int} = 0.0411, R_{sigma} = 0.0320]
Data/restraints/parameters	4942 / 0 / 332
Goodness-of-fit on F^2	1.044
Final R indexes [I>=2σ (I)]	R_1 = 0.0385, wR_2 = 0.0990
Final R indexes [all data]	R_1 = 0.0494, wR_2 = 0.1069
Largest diff. peak/hole / e Å^{-3}	0.23/-0.21

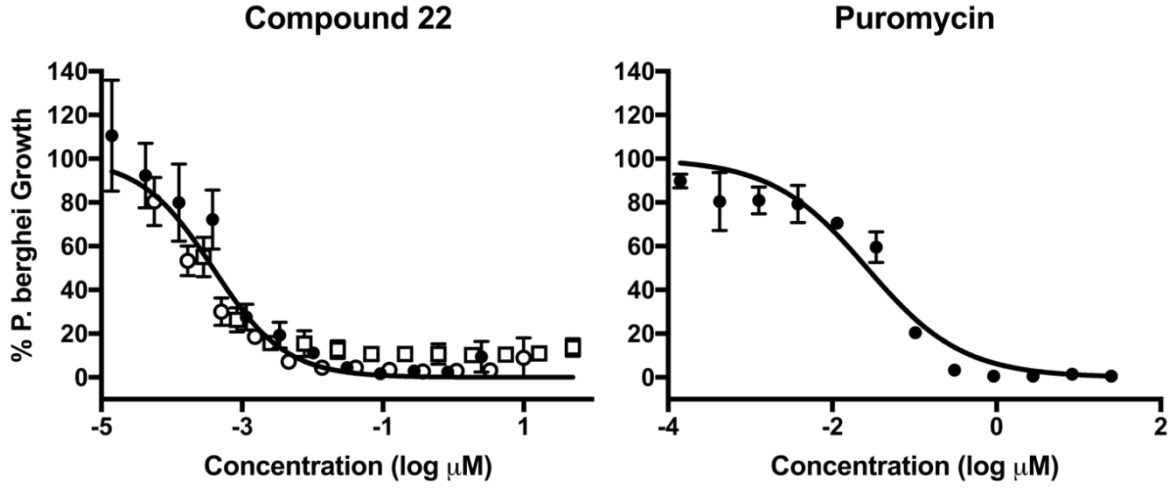


Supplementary Figure 1. Bioenergetic analysis of three *Mtb* strains. These include wild-type H37Rv **a**, an *Mtb* cytochrome *bd* knockout (*cydKO*); **b**, and an *Mtb* strain containing a complex 3 mutation (*qcrB*- A317T) **c**. At the indicated times, the compound (Q203, media or compound **16** at 0.1x, 1x and 10x MIC) was added, followed by the uncoupler, CCCP, to stimulate maximum respiration. No hypersensitivity was observed in all three strains following treatment with compound **16**. However, in all three strains, the compound at different concentrations had varying effects on uncoupling. OCR is indicated as a percentage of baseline values. Standard deviation of three replicate wells are indicated as calculated by the Seahorse XF Wave software. Q – Q203, M -Media, 0.1X – 0.1X compound **16** MIC, 1X – 1X compound **16** MIC, 10X – 10X Compound 16 MIC, C – CCCP. Q203 was used as a positive control as it binds to the QcrB subunit, thereby inhibiting cytochrome bc1 (ETC Complex III).[6,7,2] This results in an increase in OCR in the wild type (A) and a decrease in OCR in the *cydKO* strain (B).

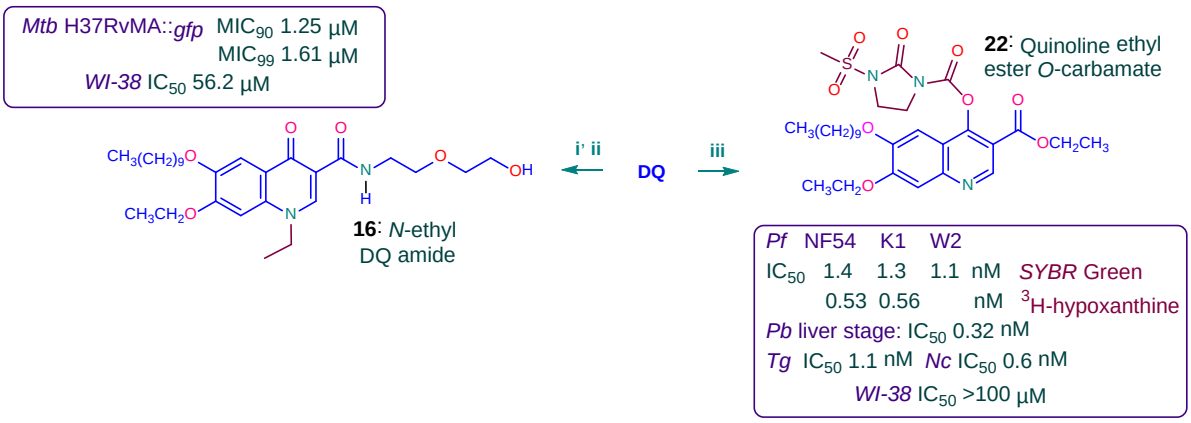
Supplementary Figure 2. Short-hand schematic of luminescence ('LUX') profiles following exposure of **a** PiniB-LUX and **b** PrecA-LUX reporter mutants to the indicated compounds. Isoniazid (INH) and ciprofloxacin (CIP) are used as controls, with a positive luminescence signal indicated by a solid red colour, which is plotted as a function of the time interval (Day1-4, Day 7, Day 10) and concentration relative to the measured MIC, as described previously.[5]



Supplementary Figure 3. *In vitro* gametocytocidal activity of DQ derivatives. Derivatives **21**, **22** and **24** at 1 µM screened against early and late stages of *P. falciparum* NF54 gametocytes as determined using the luciferase reporter gene assay. MB Methylene Blue, ARM artemether, ARS artesunate and DQ decoquinate. Data are from a single biological replicate (n=1) performed in technical triplicates, ±SD.



Supplementary Figure 4: *P. berghei* liver stage inhibition assay conducted in dose response using compound **22** and puromycin as a control. Compound activity was determined relative to the bioluminescent signal from DMSO (negative control) treated wells using luciferase expressing sporozoites and the Bright-Glo (Promega) reporter system. Three distinct 12-point titrations captured the potency range of **22** starting from 50 µM (□, i.e. empty squares), 10 µM (○, i.e. empty circles), and 2.5 µM (●, i.e. filled circles) ± SD. Biological duplicate (n=2) and technical quadruplicate measurements were performed.



Supplementary Figure 5. Summarizing data for optimal DQ derivatives **16** and **22** (Tables 1-5). **i**. Ethyl bromide (excess), K_2CO_3, DMF, gentle reflux, 10 h; **ii**. 2-Aminoethoxyethanol, DBU, $CHCl_3$, reflux, 24 h; **iii**. 3-Chlorocarbonyl-1-methanesulfonyl-2-imidazolidinone, DBU, $CHCl_3$, reflux, 15 h; *Mtb* - *Mycobacterium tuberculosis*, *Pf* – *Plasmodium falciparum* NF54 chloroquine (CQ) sensitive; K1 and W2 CQ resistant strains, *Pb* – *Plasmodium berghei*, *Tg* - *Toxoplasma gondii*, *Nc* - *Neospora caninum*, WI-38 - human fetal lung fibroblast cell line.

Supplementary Methods

Structural Assignments for Compounds 16 and 22 by 2D NMR spectroscopy

The *N*-ethyl DQ amide **16** and the quinoline ester carbamate **22** were examined by 2D NMR spectroscopy using correlation (COSY), total correlation (TOCSY), nuclear Overhauser effect (NOESY), heteronuclear multiple-bond correlation (HMBC) and heteronuclear single-quantum correlation spectroscopy (HSQC, gHSQCAD) edited to provide CH_2 signals in opposite phase to CH_3 and CH signals.

A Varian VNMRS-500 spectrometer was used with 10 mg samples in $CDCl_3$ (0.5 mL). Solvent signals were used as internal reference. 1D spectra were acquired at 25 °C using 32K data points and the 2D spectra using 2048 x 512 (COSY and TOCSY) and 4096 x 512 (NOESY, HSQCAD, and HMBC) data matrices, with spectral widths of 6010 and 22727 Hz for ^{1}H and ^{13}C, respectively; 4, 4, 16, 4, and 16 scans were used for COSY, TOCSY, NOESY, HSQCAD, and HMBC, respectively. Relaxation delays of 1.5 s were used for all 2D experiments and mixing times of 500 and 700 ms for the NOESY spectra. The Rance-Kay Fourier transform mode was used for the HSQCAD

experiments. Zero filling was used in all 2D experiments. Spectral were processed with VNMRJ software. The data for compounds **16** and **22** are summarized in Supplementary Tables 1 and 2.

Compound 16

The gHSQCAD spectrum revealed 21 carbons of which three are due to CH_3 groups (δ 14.0,14.5,14.5), fifteen are due to CH_2 groups (δ 22.6, 25.9, 28.8, 29.2, 29.3, 29.4, 29.5, 31.8, 38.8, 49.1, 61.7, 65.0, 69.2, 69.8, and 72.5), three are due to CH groups (δ 98.3, 107.6, 145.2) and seven are due to non-hydrogenated carbons (δ 111.3, 122.3, 134.1, 147.8, 153.6, 165.5, 175.3). The gHSQCAD experiment allowed one to distinguish the downfield singlet (δ 8.61) since C-2 of the quinolone is more deshielded than C-5 (δ 107.6) and C-8 (δ 98.3). Three proton spin systems were identified by COSY and TOCSY. Two ethyl group correlations were observed from H-1 (δ 4.20q)/H-2 (δ 1.46t) and H-1(δ 4.13q)/H-2 (δ 1.46t). The decyloxy spin system was observed on TOCSY with H-1 (δ 4.06t)/H-2 (δ 1.80m)/H-3 (δ 1.41m)/H-4(δ 1.29)/H-5(δ 1.21bs) and H-10 (δ 0.80t)/H-9 (δ 1.21bs). The side-chain attached to C-3 of the quinolone was observed with two spin systems OH (δ 10.44bs)/H-7,6 (δ 3.61bs) and NH (δ 3.25bs)/H-3 (δ 3.70)/H-4 (δ 3.58). Other ^{1}H and ^{13}C assignments to compound **16** were made and confirmed by HMBC correlations. The H-1 (δ 4.20) of one ethyl correlates with C-8a (δ 134.1) and C-2 (δ 145.2). C-1 (δ 49.1) of the ethyl correlated with H-2 (δ 8.61) of the quinolone. So this ethyl must be connected directly to N-1 of the quinolone. The H-1 (δ 4.13) of another ethyl correlated with C-7 (δ 153.6); this is thus the ethoxy group attached to the aromatic ring. The correlation of H-1 (δ 4.06) of the decyloxy group / the C-7(δ 153.6) can also be observed on HMBC. The H-4 (δ 3.58)/C-6 (δ 69.8) and H-6 (δ 3.61)/C-4 (δ 72.5) of the amido side chain confirms the connection of the two spin system of the side chain and distinguished C-6 (δ 69.8) from C-7 (δ 38.8), C-4 (δ 72.5) from C-3 (δ 61.7). The H-2 (δ 8.61) of the quinolone correlated with one of two carbonyl carbon, so this carbonyl carbon was assigned to C-1 (δ 165.5) of the amido side chain. Three quaternary carbons were observed to correlate respectively with H-2 (δ 8.61), H-5 (δ 7.77) and H-8(δ 6.76). So these quaternary carbons were assigned to C-8a (δ 134.1), C-6 (δ 147.8), and C-7 (δ 153.6). The NOESY experiment confirms the structural characterization by way of the observed correlations: H-8 (δ 6.76) of the quinolone/H-2 (δ 1.46t), H-1 (δ 4.13) of the ester ethoxy, and H-1 (δ 4.20) of the ethyl; H-5 (δ 7.77) of the quinolone/H-2 (δ 1.80m), H-1 (δ 4.06t) of the decyloxy; H-2 (δ 8.61) of the quinolone/H-2 (δ 1.46t), H-1 (δ 4.20) of the ethyl group.

Compound 22

The ^{13}C NMR spectrum in conjunction with the gHSQCAD spectrum revealed 20 carbons of which four are CH_3 groups (δ 14.0,14.1,14.3, and 40.5) correlated with ^{1}H NMR signals (δ 0.81, 1.34, 1.48, and 3.33 respectively), thirteen are CH_2 groups (δ 22.6, 25.9, 28.8, 29.2, 29.3, 29.4, 29.4, 31.8, 40.1, 41.2, 61.3, 64.7, and 69.3) correlated with ^{1}H NMR signals (δ 1.20, 1.45, 1.84, 1.32, 1.20, 1.22, 1.23, 1.20, 3.97, 4.12, 4.31, 4.19, and 4.07 respectively), three are CH groups (δ 100.4, 108.5, 148.8) correlated with ^{1}H NMR signals (δ 7.20, 7.34, 9.13 respectively) and nine are the non-hydrogenated carbons (δ 112.3, 117.2, 148.1, 149.3, 149.7, 150.8, 153.1, 154.7, and 163.7). The gHSQCAD experiment also allowed us to distinguish the downfield singlet (δ 9.13) since C-2 of the quinoline is more deshielded than C-5 (δ 100.4) and C-8 (δ 108.5). Due to the singlet (δ 3. 33) in the ^{1}H NMR spectrum and the unique chemical shift of C-7 (δ 40.5), the methylsulfonyl group attached to the imidazolidone was unambiguously assigned. Four proton spin systems were identified by use of COSY and TOCSY. Two ethyl group correlations can be observed from H-3 (δ 4.31q)/H-4 (δ 1.34t) of the carbethoxy group and H-1(δ 4.19q)/H-2 (δ 1.48t) of the ethoxyl group. The decyloxy spin system was observed on TOCSY with H-1 (δ 4.07t)/H-2 (δ 1.84m)/H-3(δ 1.45m)/H-4 (δ 1.32)/H-5 (δ 1.23bs) and H-10 (δ 0.81t)/H-9 (δ 1.20bs). The spin system of the imidazolidone was observed at H-5 (δ 3.97)/H-6 (δ 4.12). More ^{1}H and ^{13}C assignments were confirmed by HMBC correlations. The H-1 (δ 4.19) of one ethyl group correlated with C-7 (δ 154.7). This is thus associated with the ethoxyl group connected to C-7 of the quinoline. The H-1 (δ 4.31) of the second ethyl was found to correlate with the lowest field quaternary carbon C-1 (δ 163.7) of the carbethoxyl group. This carbon also correlated with H-2 (δ 9.13) of the quinolone. So this ethyl group is part of the carbethoxy group and the quaternary carbon is the carbonyl carbon. The correlation of the H-1(δ 4.07) of the decyloxy group/the C-6 (δ 150.8) can also be observed on HMBC. The H-5 (δ 3.97) and H-6 (δ 4.12)/(δ 149.7) indicates that the signal at δ 149.7 is due to C-3 of the imidazolidone. The quaternary carbon (δ 153.1) correlated with H-5 (δ 7.20) and H-2 (δ 9.13) and is assigned to C-4 of the quinoline. The quaternary carbon (δ 112.3) correlated with H-2(δ 9.13) only and is assigned to C-3 of the quinoline. The C-4a and C-8a signals were assigned by comparing with data in the SDBS.[1] The NOESY experiment confirms the structural characterization by way of the observed correlations: H-8 (δ 7.34) of the quinolone/H-1 (δ 4.19) of the ethoxy; H-5 (δ 7.20) of the quinolone/H-1 (δ 4.07t) of the decyloxy groups. Overall, signals due to C6, C7, and H6, H7 of the decyloxy chain, C5, C6, H5, H6 of the 4-imidazolin-2-one and C4a, C8a of the quinolone in compound **22** (for numbering, see structure above) cannot be unambiguously assigned. The data are summarized in Supplementary Table 2.

Structural Assignments to other derivatives and analogues by NMR spectroscopy.

Signals in the ^{1}H spectra of all of the other decoquinate derivatives of Fig. 2 are assigned based on the foregoing assignments. Thus the quinolone amide derivatives **3-10** (Fig. 2) show a singlet at *ca.* δ 12.5 ppm assigned to N1-H (H-1), a triplet (*J* = 5.8 Hz) at *ca* δ 11.0 ppm assigned to H-1' in the amide chain (except **10**), a singlet at *ca* δ 8.7 ppm assigned to H-2. The tertiary amide **10** shows a nine-proton multiplet between 3.68- 3.76 ppm due to the piperazinyl unit. For the *N*-alkyl DQ amides **11-20**, both the absence of the singlet at *ca* δ 12.0 ppm in the ^{1}H NMR spectra due to H-1 and the presence of the signal due to the quinolone carbonyl group (C-4) at *ca*. 175.3 ppm in the ^{13}C NMR spectra confirm that alkylation had taken place through N-1. The ^{1}H spectra of these compounds show a singlet at *ca*. δ 8.2 ppm assigned to H-2, two singlets in the range δ 6.8 – 7.5 ppm assigned to H-5 and H-8 of the quinolone nucleus, two triplets (*J* = 7.0, 6.9 Hz) in the range 4.0 – 4.4 ppm ascribed to H-13 and H-12 in the two alkoxy chains attached to C-6 and C-7. The ^{13}C NMR spectra of all compounds **3-20** contain a signal at ~175 ppm assigned to the quinolone carbonyl at C-4 and a signal at ~165 ppm assigned to the amide carbonyl carbon atom. The signals at ~69 and 65 ppm are due to C-13 and C-12 in the alkoxy chains attached to the quinolone nucleus. The ^{1}H spectra of the O-linked quinoline ester and amide carbamates **21-27**, show a singlet at *ca.* δ 8.2 ppm assigned to H-2, two singlets in the range δ 6.8 – 7.5 ppm assigned to H-5 and H-8 of the of the quinoline nucleus, two triplets (*J* = 7.0, 6.9 Hz) in the range 4.0 – 4.4 ppm due to H-13 and H-12 in the alkoxy chains attached to C-6 and C-7. Their ^{13}C NMR spectra also contain signals at ~ 69 and 65 ppm due to C-13 and C-12 in these alkoxy chains. The ^{1}H spectra of the short chain quinolone amide analogues **28** and **29** (Fig. 4) show two singlets at 3.85 – 3.95 ppm due to the two methoxy groups attached to C-6 and C-7 of the quinolone nucleus. The chain shortened haloaryl quinolone amides **31-33** (Fig.4) show a doublet (*J* = 8.8 Hz) at *ca* δ 8.0 ppm assigned to H-5, a doublet of doublets (*J* = 8.8, 2.4 Hz) at *ca* δ 7.79 ppm assigned to H-7, a doublet (*J* = 2.4 Hz) at *ca* δ 7.0 ppm assigned to H-8 of the of the quinolone nucleus. The ^{13}C NMR spectra of all compounds **28-33** contain a signal at ~175 ppm assigned to the quinolone carbonyl at C-4, a signal at ~165 ppm assigned to the amide carbonyl, and a signal at ~143 ppm assigned to C-2 of the quinolone nucleus.

X-Ray crystallography of compound 16.

A single needle specimen of **16** with dimensions 0.35 x 0.06 x 0.02 mm was protected by immersion in Paratone and mounted in a Cryoloop on a Rigaku-Oxford Diffraction Supernova diffractometer equipped with copper micro-source and Atlas detector. X-ray diffraction intensity data were collected at -100 °C to a 2-theta maximum of 135° (Cu-Kα radiation). The structure was solved by the charge-flipping algorithm of Olex-solve, refined using full matrix least squares with anisotropic

non-hydrogen atoms and in the Olex2 X-ray structure program suite.[3,4] The details are given in Supplementary Table 3.

Biological Activities for Tuberculosis

For the bioluminescence assays, the induction of either a cell wall (P*iniB*-LUX) or DNA damage (P*recA*-LUX) response following exposure to known and experimental compounds was determined using methods described previously.[5]

XF96 Extracellular Flux Analyser assay. All *Mtb* strains used in the extracellular flux assay were cultured in Middlebrock 7H9 media (Difco) supplemented with 10% OADC and 0.01% Tyloxapol at 37 °C, unless stated otherwise. *Mtb* H37Rv was obtained from BEI Resources (NR-123). The *Mtb* cydKO mutant (a cytochrome *bd* knockout) was a gift from Dr. Helena Boshoff. The drug MIC_{50} values used during this study were as follows: Q203 3 nM (Cmax 0.007–0.4 mM) (100 x MIC was used for XF experiments). Cell-Tak was purchased from from BD Biosciences. All other reagents were purchased from Sigma-Aldrich. The imidazopyridine Q203 was used as a control. Q203 binds to the QcrB subunit, thereby inhibiting cytochrome bc1 (ETC Complex III).[6] This forces the bacillus to use cytochrome bd, a less energetically efficient terminal oxidase. Carbonyl cyanide *m*-chlorophenyl hydrazone (CCCP) was also used in the assay in order to stimulate maximum respiration. CCCP is an uncoupler that depolarizes the cell membrane.[7] The dose used in this study was optimized to increase respiration and carbon catabolism to the maximum sustainable by the bacterium.

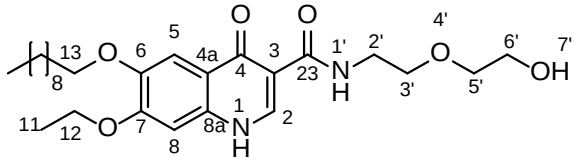
***Mtb* OCR measurements.** The OCR of *Mtb* bacilli adhering to the bottom of a Cell-Tak coated XF cell culture microplate (Seahorse Biosciences), at 2 x 10^6 bacilli per well were measured using a XF96 Extracellular Flux Analyser (Seahorse Biosciences). Cell-Tak has no effect on *Mtb* basal respiration. Assays were carried out in unbuffered 7H9 media (pH 7.35) without carbon source. *Mtb* bacilli were starved in liquid media, using 7H9 supplemented only with 0.01% Tyloxapol, for 24 h before being seeded into the XF cell culture microplate and the start of the experiment. In general, basal OCR were measured for ~21 min before the automatic addition of the ETC-targeting drugs through the drug ports of the sensor cartridge. The assays were concluded with the further addition of 2 mM CCCP (final concentration) after which OCR was measured for an additional 21–35 min. All OCR figures indicate the point of each addition as dotted lines. OCR data points are representative of the average OCR during 4 min of continuous measurement in the transient microchamber, with the error being calculated from the OCR measurements taken from three replicate wells by the Wave Desktop 2.2 software (Seahorse Biosciences). The transient microchamber is automatically re-equilibrated between

measurements through the up and down mixing of the probes of the XF96 sensor cartridge in the wells of the XF cell culture microplate.

Antimalarial assay *in vitro* of compound 22 against drug sensitive and atovaquone resistant *P. falciparum* asexual blood stages. *P. falciparum* was cultivated in a variation of the medium previously described[8,9] consisting of RPMI 1640 supplemented with 0.5% ALBUMAX® II, 25 mM Hepes, 25 mM $NaHCO_3$ (pH 7.3), 0.36 mM hypoxanthine, and 100 µg/mL neomycin. Human erythrocytes served as host cells. Cultures were maintained at 37 °C in an atmosphere of 3% O_2, 4% CO_2, and 93% N_2 in humidified modular chambers. Compounds were dissolved by sonication in DMSO (10 mg/mL) and diluted in hypoxanthine-free culture medium. Infected erythrocytes (100 microliter per well with 2.5% hematocrit and 0.3% parasitaemia) were added to each drug titrated in 100 microliter duplicates over a 64-fold range. After 48 h incubation, 0.5 microCi of ^{3}H-hypoxanthine in 50 microliter medium was added and plates were incubated for an additional 24 h. Parasites were harvested onto glass-fiber filters and radioactivity was counted using a Betaplate liquid scintillation counter (Wallac, Zurich). The results were recorded as counts per minute (cpm) per well at each drug concentration and expressed as a percentage of the untreated controls. Fifty percent inhibitory concentrations (IC_{50}) were estimated by linear interpolation.[10]

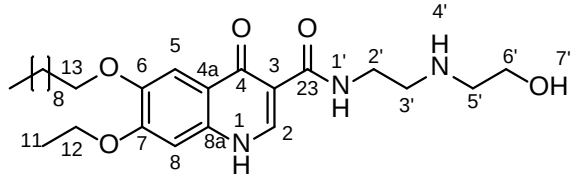
***In vitro* induction and gametocytocidal efficacy studies of sexual stage *P. falciparum* NF54 gametocytes.** *In vitro* gametocytogenesis was induced through glucose depletion and a drop in haematocrit using a >95% synchronised asexual ring stage parasite population (~10% parasitaemia). Following induction cultures were kept stationary at 37°C with 90% N_2, 5% CO_2 and 5% O_2 and treated with N-acetylglucosamine (Sigma-Aldrich).[11] Early (day 5 post-induction, ~90% stage I-III) and late stage (day 10 post-induction, ~95% stage IV-V) gametocytes (2% gametocytaemia and 2% haematocrit) were treated with the derivatives at 1 µM for 48 h at 37°C with 90% N_2, 5% CO_2 and 5% O_2. Gametocyte viability was determined through the luciferase reporter gene expressed by the transgenic parasite cell line NF54-PfS16-GFP-Luc with a luciferin substrate (Promega Luciferase Assay System). Methylene blue (MB), a known gametocytocidal compound, artemether (ARM), artesunate (ARS) and DQ were included as reference compounds. Data analysis was performed using GraphPad Prism 6. Data are from a single biological replicate, performed in technical triplicates.

Spectroscopic Data for Compound 3



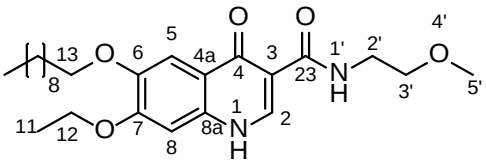
White powder, 0.680 g (68%), m.p. 133-136 °C; HPLC >96% purity, RT 8.79 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 11.99 (s, 1H, H-1), 10.73 (t, *J* = 5.3 Hz, 1H, H-1'), 8.64 (s, 1H, H-2), 7.39 (s, 1H, H-5), 6.80 (s, 1H, H-8), 4.43 (s, 1H, H-7'), 4.01 (q, *J* = 7.0 Hz, 2H, H-13), 3.86 (t, *J* = 6.8 Hz, 2H, H-12), 3.83 – 3.78 (t, *J* = 5.3 Hz, 2H, H-2'), 3.71 – 3.60 (m, 6H, H-3', H-5', H-6'), 1.76 (p, *J* = 7.0 Hz, 2H, H-14), 1.46 – 1.19 (m, 17H, H-11, H-15,-H-21), 0.87 (dt, *J* = 21.8, 7.3 Hz, 3H, H-22). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 175.76 (C-4), 166.62 (C-23), 153.66 (C-7), 147.86 (C-6), 141.49 (C-2), 134.73 (C-8a), 120.40 (C-4a), 110.13 (C-3), 105.39 (C-5), 99.88 (C-8), 72.38 (C-3'), 69.80 (C-5'), 68.54 (C-13), 64.63 (C-12), 61.73 (C-2'), 31.96 (C-6'), 31.90 (C-20), 29.65 (C-17, C-18) , 29.27 (C-19, C-16), 28.92 (C-14), 25.92 (C-15), 22.67 (C-21), 14.44 (C-11), 14.10 (C-22). APCI-HRMS *m/z* calcd for $C_{26}H_{41}N_20_6$ 477.2956, found 477.2911 $[M+H]^+$.

Spectroscopic Data for Compound 4



White powder, 0.506 g (50%), m.p. 122.4-125.1 °C; HPLC >95% purity, RT 2 min; ^{1}H NMR (600 MHz, DMSO-*d6*) δ (ppm) : 10.27 (t, *J* = 5.6 Hz, 1H, H-1'), 8.58 (s, 1H, H-2), 7.55 (s, 1H, H-5), 7.08 (s, 1H, H-8), 4.62 (s, 1H, H-7'), 4.12 (q, *J* = 6.9 Hz, 2H, H-13), 4.03 (t, *J* = 6.6 Hz, 2H, H-12), 3.48 (dt, *J* = 5.6, 6.2 Hz, 2H, H-2'), 3.41 (q, *J* = 6.2 Hz, 3H, H-6' overlap with HDO peak), 2.75 (t, *J* = 6.2 Hz, 2H, H-3'), 2.67 (t, *J* = 6.2 Hz, 2H, H-5'), 1.74 (p, *J* = 6.8 Hz, 2H, H-14), 1.41 (dt, *J* = 17.4, 6.8 Hz, 5H, H-11, H-15), 1.36 – 1.17 (m, 15H, H-16,-H-22). ^{13}C NMR (151 MHz, DMSO-d6) δ (ppm): 174.74 (C-4), 165.05 (C-23), 152.91 (C-7), 146.99 (C-6), 141.98 (C-2), 137.50 (C-8a), 134.34 (C-4a), 109.99 (C-3) , 107.61 (C-5) , 105.61 (C-8) 68.39 (C-13), 64.20 (C-12), 59.72 (C-2'), 48.54 (C-3'), 40.04 (C-5'), 31.96 (C-6'), 31.34 (C-20), 29.03 (C-17) 28.99 (C-18), 28.74(C-19), 28.46 (C-14), 25.49 (C-15), 22.14 (C-16), 22.14 (C-21), 14.41 (C-11), 14.00 (C-22) . APCI-HRMS *m/z* calcd for $C_{26}H_{42}N_30_5$ 476.3119, found 476.3048 $[M+H]^+$.

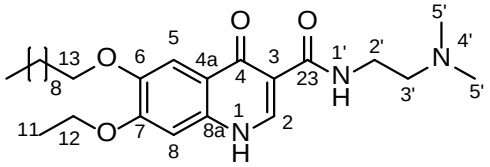
Spectroscopic Data for Compound 5



Light yellow powder, 0.620 g (62%), m.p. 167-170 °C; HPLC >97% purity, RT 11.4 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 12.01 (s, 1H, H-1), 10.83 (t, *J* = 5.6 Hz, 1H, H-1'), 8.67 (s, 1H, H-2), 7.68 (s, 1H, H-5), 6.89 (s, 1H, H-8), 4.11 – 4.01 (m, 4H, H-13, H-12), 3.70 (dd, *J* = 5.6, 5.6 Hz, 2H, H-2'), 3.56 (t, *J* = 5.6 Hz, 2H, H-3'), 3.33 (s, 3H, H-5'), 1.83 (p, *J* = 7.1 Hz, 2H, H-14), 1.44 (dt, *J* = 24.6, 7.1 Hz, 4H, H-15, H-16), 1.36 – 1.19 (m, 13H, H-11, H-17,-H-21), 0.85 (t, *J* = 6.9 Hz, 3H, H-22). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 176.06 (C-4), 166.97 (C-23), 153.84 (C-7), 148.04 (C-6), 141.18 (C-2), 134.87 (C-8a), 120.73 (C-4a), 110.16 (C-3), 105.93 (C-5), 99.98 (C-8), 71.18 (C-3'), 69.22 (C-13), 64.76 (C-12), 58.91 (C-2'), 39.30 (C-5'), 31.88 (C-20), 29.54 (C-17), 29.53 (C-18),

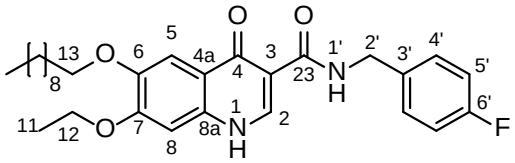
29.35 (C-19), 28.88 (C-14), 25.91 (C-15), 25.10 (C-16), 22.66 (C-21), 14.44 (C-11), 14.10 (C-22). APCI-HRMS *m/z* calcd for $C_{25}H_{39}N_20_5$ 447.2853, found 447.2814$[M+H]^+$.

Spectroscopic Data for Compound 6



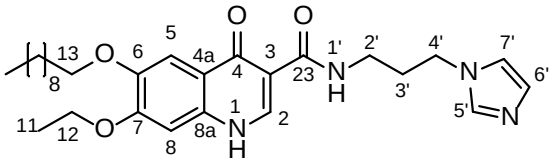
White powder, 0.928 g (92.8%), m.p. 151-155 °C; HPLC >95% purity, RT 4.9 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 12.01 (s, 1H, H-1), 10.64 (t, *J* = 5.6 Hz, 1H, H-1'), 8.47 (s, 1H, H-2), 7.36 (s, 1H, H-5), 6.73 (s, 1H, H-8), 4.15 – 4.06 (m, 2H, H-13), 3.90 (q, *J* = 7.2 Hz, 2H, H-12), 3.65 (dt, *J* = 5.6, 6.0 Hz, 2H, H-2'), 2.60 (t, *J* = 6.0 Hz, 2H, H-3'), 2.32 (s, 6H, H-5'), 1.90 – 1.76 (m, 2H, H-14), 1.53 – 1.42 (m, 2H, H-15), 1.30 – 1.19 (m, 15H, H-11, H-16,-H-21), 0.87 (dt, *J* = 14.0, 7.3 Hz, 3H, H-22). ^{13}C NMR (151 MHz, CDCl3) δ (ppm): 175.63 (C-4), 166.52 (C-23), 153.42 (C-7), 147.66 (C-6), 141.41 (C-2), 134.63 (C-8a), 120.29 (C-4a), 110.01 (C-3), 105.26 (C-5), 99.93 (C-8), 68.92 (C-13), 64.60 (C-12), 58.99 (C-2'), 45.28 (C-5'), 36.64 (C-3'), 31.88 (C-20), 29.58 (C-17), 29.55 (C-18), 29.32 (C-19), 28.92 (C-14), 28.92 (C-16), 25.91 (C-15), 22.65 (C-21), 14.50 (C-11), 14.09 (C-22). APCI-HRMS *m/z* calcd for $C_{26}H_{42}N_30_4$ 460.3170, found 460.3102 $[M+H]^+$.

Spectroscopic Data for Compound 7



White powder, 0.82 g (80%), m.p. 202-203 °C; HPLC >96% purity, RT 16.5 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 11.85 (s, 1H, H-1), 11.11 (t, *J* = 5.8 Hz, 1H, H-1'), 8.67 (s, 1H, H-2), 7.67 (s, 1H, H-5), 7.28 (dd, *J* = 8.4, 5.3 Hz, 2H, H-5',), 6.94 (t, *J* = 8.5 Hz, 2H, H-4',), 6.81 (s, 1H, H-8), 4.66 (d, *J* = 5.8 Hz, 2H, H-2'), 4.05 (t, *J* = 6.9 Hz, 2H, H-13), 3.92 (t, *J* = 6.9 Hz, 2H, H-12), 1.84 (dd, *J* = 7.4, 6.9 Hz, 2H, H-14,), 1.47 – 1.18 (m, 17H, H-11, H-15,-H-21,), 0.92 – 0.82 (m, 3H, H-22). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 176.11 (C-4), 166.87 (C-23), 162.83 (C-6'), 153.82 (C-7,) , 148.18 (C-6), 141.18 (C-2), 134.77 (C-8a), 133.94 (C-3'), 128.93 (C-4'), 120.70 (C-4a), 115.51 (C-5'), 110.05 (C-3), 105.92 (C-5), 99.85 (C-8), 69.26 (C-13), 64.70 (C-12) , 42.72 (C-2'), 31.87 (C-20), 29.53 (C-17, C-18), 29.31 (C-19, C-16), 28.85 (C-14), 25.90 (C-15), 22.66 (C-21), 14.38 (C-11) , 14.10 (C-22). APCI-HRMS *m/z* calcd for $C_{29}H_{38}FN_20_4$ 497.2810, found 497.2734 $[M+H]^+$.

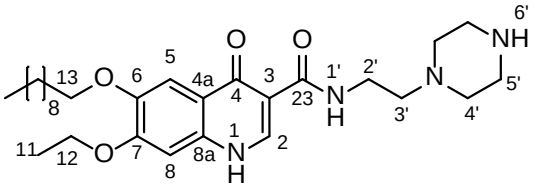
Spectroscopic Data for Compound 8



White powder, 0.956 g (95.6%), m.p. 124-127 °C; HPLC >96% purity, RT 5.0 min; ^{1}H NMR (600 MHz, DMSO-*d6*) δ (ppm): 12.01 (s, 1H, H-1), 10.29 (t, *J* = 5.8 Hz, 1H, H-1'), 8.60 (s, 1H, H-2), 7.65 (s, 1H, H-6'), 7.56 (s, 1H, H-5), 7.21 (s, 1H, H-7'), 7.08 (s, 1H, H-8), 6.89 (s, 1H, H-5'), 4.12 (q, *J* = 7.0 Hz, 2H, H-4'), 4.02 (dt, *J* = 13.7, 6.7 Hz, 4H, H-13, H-12), 3.27 (dt, *J* = 5.8, 6.9 Hz, 2H, H-2'), 1.95 (dt, *J* = 6.9, 7.0 Hz, 2H, H-3'), 1.74 (p, *J* = 13.7 Hz, 2H, H-14), 1.46 – 1.17 (m, 17H, H-11, H-15,-H-21), 0.87 – 0.81 (m, 3H, H-22). ^{13}C NMR (151 MHz, DMSO-*d6*) δ (ppm): 174.84 (C-4), 165.04 (C-23), 152.94 (C-7), 147.03 (C-6), 141.75 (C-2), 137.30 (C-6'), 134.45 (C-8a), 128.43 (C-5'), 120.84

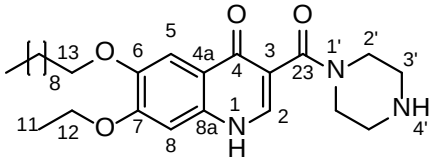
(C-4a), 119.35 (C-7'), 109.89 (C-3), 105.57 (C-5), 100.53 (C-8), 68.38 (C-13), 64.19 (C-12), 43.76 (C-2'), 39.08 (C-4'), 35.42 (C-3'), 31.32 (C-20), 31.03 (C-17), 29.02 (C-18), 28.98 (C-19), 28.73 (C-16), 28.44 (C-14), 25.48 (C-15), 22.12 (C-21), 14.39 (C-11), 13.98 (C-22). APCI-HRMS *m/z* calcd for $C_{28}H_{41}N_40_4$ 497.3170, found 497.3081$[M+H]^+$.

Spectroscopic Data for Compound 9



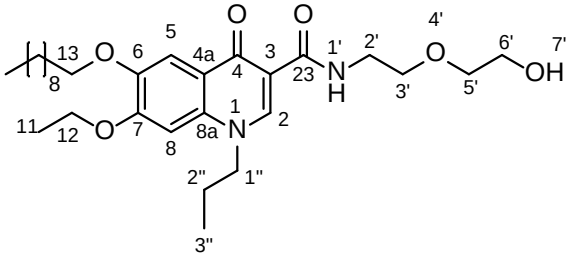
Off white powder, 0.750 g (75%), m.p. 168.-169 °C; HPLC >96% purity, RT 4.8 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 12.01 (s, 1H, H-1), 10.62 (t, *J* = 5.6 Hz, 1H, H-1'), 8.60 (s, 1H, H-2), 7.58 (s, 1H, H-5), 6.83 (s, 1H, H-8), 4.12 – 3.97 (m, 4H, H-13, H-12), 3.62 (dt, *J* = 5.6, 6.4 Hz, 2H, H-2'), 2.89 – 2.77 (m, 9H, H-4'- H-6'), 2.62 (t, *J* = 6.4 Hz, 2H, H-3'), 1.83 (p, *J* = 7.0 Hz, 2H, H-14), 1.49 – 1.18 (m, 17H, H-11, H-15,-H-21), 0.92 – 0.83 (m, 3H, H-22). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 175.94 (C-4), 166.60 (C-23), 153.72 (C-7), 147.95 (C-6), 141.15 (C-2), 134.71 (C-8a), 120.65 (C-4a), 110.26 (C-3), 105.84 (C-5), 99.91 (C-8), 69.16 (C-13), 64.74 (C-12), 58.03 (C-2'), 54.15 (C-4'), 45.76 (C-5'), 36.34 (C-3'), 31.88 (C-20), 29.56 (C-17), 29.54 (C-18), 29.38 (C-19), 29.32 (C-16), 28.91 (C-14), 25.93 (C-15), 22.66 (C-21), 14.50 (C-11), 14.11 (C-22). APCI-HRMS *m/z* calcd for $C_{28}H_{45}N_40_4$ 501.3435, found 501.3360$[M+H]^+$.

Spectroscopic Data for Compound 10



Yellow powder, 0.28 g (28%), m.p. 182-184 °C; HPLC >98% purity, RT 4.38 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) : 12.00 (m, 1H, H-1), 7.67 (s, 1H, H-2), 7.52 (s, 1H, H-5), 6.70 (s, 1H, H-8), 4.01 – 3.92 (m, 4H, H-13, H-12), 3.76 – 3.68 (m, 9H, H-2',-H-4'), 1.81 (m, 2H, H-14), 1.45 – 1.35 (m, 4H, H-15, H-16), 1.37 – 1.18 (m, 13H, H-11, H-17,-H-21), 0.85 – 0.68 (m, 3H, H-22). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) : 172.75 (C-4), 167.79 (C-23), 153.61 (C-7), 147.80 (C-6), 138.63 (C-2), 135.00 (C-8a), 120.22 (C-4a), 115.47 (C-3), 105.57 (C-5), 99.84 (C-8), 69.17 (C-13), 67.23 (C-2'), 64.61 (C-12), 48.08 (C-3'), 31.88 (C-20), 29.54 (C-17, C-18), 29.35 (C-19, C-16), 28.97 (C-14), 25.93 (C-15), 22.66 (C-21), 14.45 (C-11), 14.10 (C-22). APCI-HRMS *m/z* calcd for $C_{26}H_{40}N_30_4$ 458.3013, found 458.2942 $[M+H]^+$.

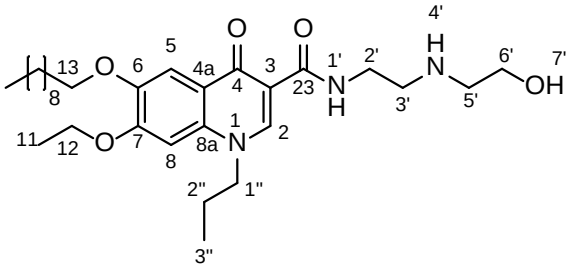
Spectroscopic Data for Compound 11



White powder, 0.38 g (76%), m.p. 162-164 °C; HPLC >98% purity, RT 4.30 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 10.45 (t, *J* = 5.4 Hz, 1H, H-1'), 8.61 (s, 1H, H-2), 7.80 (s, 1H, H-5), 6.76

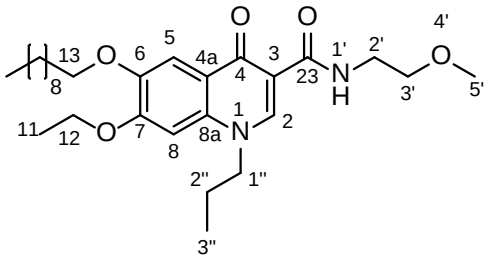
(s, 1H, H-8), 4.33 – 3.96 (m, 6H, H-12, H-13, H-1''), 3.74 – 3.48 (m, 4H, H-6', H-2'), 2.95 – 2.75 (m, 4H, H-5', H-3'), 2.37 (s, 1H, H-7'), 2.00 – 1.76 (m, 4H, H-2'', H-14), 1.59 – 1.37 (m, 4H, H-15, H-16), 1.35 – 1.17 (m, 13H, H-3'', H-17 - H-21), 0.98 (t, *J* = 7.4 Hz, 3H, H-11), 0.91 – 0.67 (m, 3H, H-22). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 175.35 (C-4), 165.77 (C-23), 153.54 (C-7), 147.78 (C-6), 145.88 (C-2), 134.32 (C-8a), 122.22 (C-4a), 110.87 (C-3), 107.40 (C-5), 98.59 (C-8), 69.60 (C-13), 64.98 (C-12), 60.94 (C-3'), 55.79 (C-5'), 50.66 (C-2'), 48.49 (C-1''), 38.89 (C-6'), 31.86 (C-2''), 29.52 (C-20), 29.49 (C-17), 29.30 (C-18), 29.28 (C-19), 28.87 (C-14), 25.92 (C-15), 22.64 (C-16), 22.09 (C-21), 14.51 (C-11), 14.08 (C-3''), 11.08 (C-22). APCI-HRMS *m/z* calcd for $C_{29}H_{47}N_2O_6$ 519.3429, found 519.3431 $[M+H]^+$.

Spectroscopic Data for Compound 12



White powder, 0.4 g (80%), m.p. 160-162 °C; HPLC >98% purity, RT 4.00 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 10.46 (t, *J* = 5.4 Hz, 1H, H-1'), 8.62 (s, 1H, H-2), 7.64 (s, 1H, H-5), 6.83 (s, 1H, H-8), 4.35 (s, 1H, H-7'), 4.22 – 4.09 (m, 2H, H-13), 4.06 – 3.97 (m, *J* = 6.9 Hz, 4H, H-12, H-1''), 3.73 (d, *J* = 6.5, 2H, H-6'), 3.63 – 3.57 (m, *J* = 6.5, 6H, H-3', H-5', H-2''), 3.44 (dd, *J* = 5.4, 6.5 Hz, 2H, H-2'), 1.88 – 1.78 (m, 2H, H-14), 1.56 – 1.42 (m, 6H, H-15 - H-17), 1.32 – 1.20 (m, 13H, H-3'', H-18 - H-22), 0.85 (t, *J* = 6.9 Hz, 3H, H-11). ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.12 (C-4), 166.27 (C-23), 153.58 (C-7), 147.69 (C-6), 146.69 (C-2), 134.75 (C-8a), 121.79 (C-4a), 110.34 (C-3), 107.12 (C-5), 98.56 (C-8), 72.62 (C-3'), 69.16 (C-13), 65.02 (C-12), 61.67 (C-5'), 59.78 (C-2'), 54.42 (C-1''), 38.87 (C-6'), 31.86 (C-20), 31.86 (C-2''), 29.49 (C-17), 29.30 (C-18), 29.28 (C-19), 28.87 (C-14), 25.92 (C-15), 22.64 (C-16), 22.09 (C-21), 14.50 (C-11), 14.08 (C-3''), 14.09 (C-22). APCI-HRMS *m/z* calcd for $C_{29}H_{48}N_3O_5$ 518.3221, found 518.3168 $[M+H]^+$.

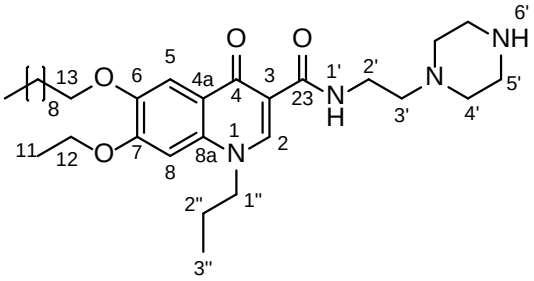
Spectroscopic Data for Compound 13



White powder, 0.45 g (90%), m.p. 152-153 °C; HPLC >97% purity, RT 6.70 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 10.35 (t, *J* = 5.3 Hz, 1H, H-1'), 8.62 (s, 1H, H-2), 7.84 (s, 1H, H-5), 6.77 (s, 1H, H-8), 4.21 – 4.00 (m, 6H, H-13, H-12, H-1''), 3.66 (dt, *J* = 5.3, 5.5 Hz, 2H, H-2'), 3.56 (t, *J* = 5.5 Hz, 2H, H-3'), 3.38 (s, 3H, H-5'), 2.00 – 1.86 (m, 2H, H-2''), 1.86 – 1.82 (m, 2H, H-14), 1.49 (dt, *J* = 16.2, 5.1 Hz, 4H, H-15, H-16), 1.48 – 1.37 (m, 2H, H-17), 1.30 – 1.17 (m, 11H, H-3'', H-18 - H-21), 0.98 (t, *J* = 7.4 Hz, 3H, H-11), 0.91 – 0.71 (m, 3H, H-22). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 175.35 (C-4), 165.53 (C-23), 153.54 (C-7), 147.71 (C-6), 145.92 (C-2), 134.31 (C-8a), 122.31 (C-4a), 110.84 (C-3), 107.52 (C-5), 98.55 (C-8), 71.35 (C-3') 69.19 (C-13), 64.99 (C-12), 58.82 (C-2'), 55.74 (C-1''), 38.91 (C-5'), 31.86 (C-20), 29.52 (C-17), 29.49 (C-18), 29.30 (C-19), 29.28 (C-14), 28.87 (C-

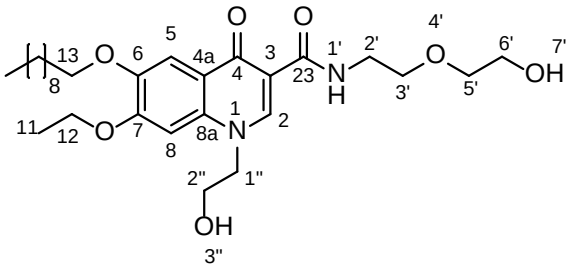
2"), 25.92 (C-15), 22.64 (C-16), 22.09 (C-21), 14.51 (C-11), 14.08 (C-3"), 11.08 (C-22). APCI-HRMS *m/z* calcd for $C_{28}H_{45}N_2O_5$ 489.3323, found 489.3302 $[M+H]^+$.

Spectroscopic Data for Compound 14



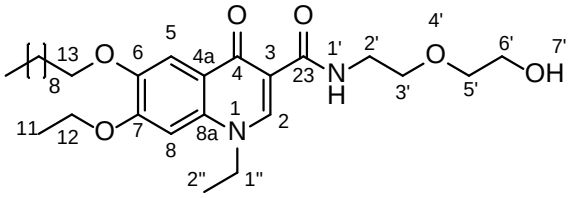
White powder, 0.47 g (94%), m.p. 168-169 °C; HPLC >96% purity, RT 5.18 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 10.32 (t, *J* = 5.8 Hz, 1H, H-1'), 8.61 (s, 1H, H-2), 7.82 (s, 1H, H-5), 6.77 (s, 1H, H-8), 4.13 (ddd, *J* = 21.8, 13.9, 6.9 Hz, 6H, H-13, H-12, H-1"), 3.58 (dd, *J* = 5.8, 4.8 Hz, 2H, H-2'), 2.90 (t, *J* = 4.8 Hz, 2H, H-3'), 2.71 – 2.36 (m, 9H, H-4', H-5', H-6'), 1.94 – 1.72 (m, 4H, H-2", H-14), 1.48 (dt, *J* = 33.4, 7.3 Hz, 4H, H-15, H-16), 1.50 – 1.37 (m, 2H, H-17), 1.27 – 1.21 (m, 11H, H-3", H-18 - H-21), 0.97 (t, *J* = 6.9 Hz, 3H, H-11), 0.84 (t, *J* = 7.0 Hz, 3H, H-22). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 175.33 (C-4), 165.40 (C-23), 153.45 (C-7), 147.70 (C-6), 145.88 (C-2), 134.31 (C-8a), 122.27 (C-4a), 110.96 (C-3), 107.49 (C-5), 98.52 (C-8), 69.17 (C-13), 64.97 (C-12), 58.01 (C-2'), 55.73 (C-4'), 54.37 (C-5'), 45.95 (C-1"), 36.34 (C-3'), 31.83 (C-2"), 29.50 (C-20), 29.47 (C-17), 29.27 (C-18), 29.26 (C-19), 28.84 (C-14), 25.89 (C-15), 22.61 (C-16), 22.19 (C-21), 14.50 (C-11), 14.06 (C-3"), 11.06 (C-22). APCI-HRMS *m/z* calcd for $C_{31}H_{51}N_4O_4$ 543.3905, found 543.3872 $[M+H]^+$.

Spectroscopic Data for Compound 15



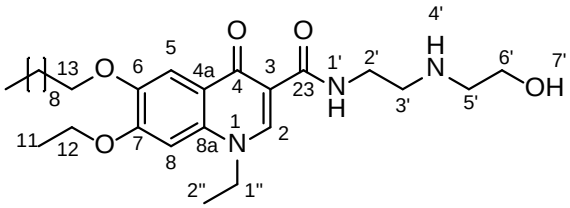
White powder, 0.47 g (94%), m.p. 155-157 °C; HPLC >96% purity, RT 4.02 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.46 (t, 1H, H-1'), 8.62 (s, 1H, H-2), 7.64 (s, 1H, H-5), 6.83 (s, 1H, H-8), 4.35 (s, 2H, H-3", H-7'), 4.22 – 4.09 (m, 2H, H-13), 4.06 – 3.97 (m, *J* = 6.9 Hz, 4H, H-12, H-1"), 3.73 (d, *J* = 16.5, 2H, H-6'), 3.63 – 3.57 (m, *J* = 16.5, 6H, H-3', H-5', H-2"), 3.44 (dd, 2H, H-2'), 1.88 – 1.78 (m, 2H, H-14), 1.56 – 1.42 (m, 6H, H-15 - H-17), 1.32 – 1.20 (m, 11H, H-18 - H-22), 0.85 (t, *J* = 6.9 Hz, 3H, H-11). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 175.12 (C-4), 166.27 (C-23), 153.58 (C-7), 147.69 (C-6), 146.69 (C-2), 134.75 (C-8a), 121.79 (C-4a), 110.34 (C-3), 107.12 (C-5), 98.56 (C-8), 72.62 (C-3'), 69.66 (C-2"), 69.16 (C-13), 65.02 (C-12), 61.67 (C-5'), 59.78 (C-2'), 54.42 (C-1"), 38.87 (C-6'), 31.86 (C-20), 29.49 (C-17), 29.30 (C-18), 29.28 (C-19), 28.87 (C-14), 25.92 (C-15), 22.64 (C-16), 22.09 (C-21), 14.50 (C-11), 14.09 (C-22). APCI-HRMS *m/z* calcd for $C_{28}H_{45}N_2O_7$ 521.3221, found 521.3168 $[M+H]^+$.

Spectroscopic Data for Compound 16



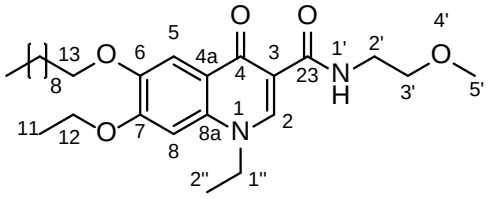
White powder, 0.42 g (84%), m.p. 158-160 °C; HPLC >96% purity, RT 4.18 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 10.50 (t, *J* = 5.8 Hz, 1H, H-1'), 8.65 (s, 1H, H-2), 7.81 (s, 1H, H-5), 6.78 (s, 1H, H-8), 4.18- 4.00 (ddd, *J* = 21.9, 13.0, 6.9 Hz, 6H, H-1", H-13, H-12), 3.86 – 3.71 (m, 2H, H-6'), 3.69 – 3.53 (m, 6H, H-2', H-3', H-5'), 3.30 (s, 1H, H-7'), 1.92 – 1.72 (m, 2H, H-14), 1.56 – 1.38 (m, 8H, H-11, H-22, H-15), 1.36 – 1.16 (m, 12H, H-16 - H-21), 0.84 (t, *J* = 6.9 Hz, 3H, H-2"). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 175.33 (C-4), 165.50 (C-23), 153.64 (C-7), 147.79 (C-6), 145.26 (C-2), 134.15 (C-8a), 122.28 (C-4a), 111.31 (C-3), 107.56 (C-5), 98.27 (C-8), 72.51 (C-3'), 69.85 (C-5'), 69.18 (C-13), 65.01 (C-12), 61.79 (C-2'), 49.11 (C-1"), 38.81 (C-6'), 31.86 (C-20), 29.52 (C-17), 29.49 (C-18), 29.30 (C-19), 29.28 (C-16), 28.87 (C-14), 25.92 (C-15), 22.63 (C-21), 14.54 (C-2"), 14.50 (C-11), 14.07 (C-22). APCI-HRMS *m/z* calcd for $C_{28}H_{45}N_2O_6$ 505.3272, found 505.3254 $[M+H]^+$.

Spectroscopic Data for Compound 17



White powder, 0.38 g (76%), m.p. 154-156 °C; HPLC >96% purity, RT 4.09 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 10.50 (t, *J* = 5.8 Hz, 1H, H-1'), 8.65 (s, 1H, H-2), 7.81 (s, 1H, H-5), 6.78 (s, 1H, H-8), 4.18- 4.00 (ddd, *J* = 28.9, 13.0, 6.9 Hz, 6H, H-1", H-13, H-12), 3.86 – 3.71 (m, 2H, H-6'), 3.69 – 3.53 (m, 6H, H-2', H-3', H-5'), 3.30 (s, 1H, H-7'), 1.92 – 1.72 (m, 2H, H-14), 1.56 – 1.38 (m, 8H, H-11, H-22, H-15), 1.36 – 1.16 (m, 12H, H-16 - H-21), 0.84 (t, *J* = 6.9 Hz, 3H, H-2"). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 175.33 (C-4), 165.50 (C-23), 153.64 (C-7), 147.79 (C-6), 145.26 (C-2), 134.15 (C-8a), 122.28 (C-4a), 111.31 (C-3), 107.56 (C-5), 98.27 (C-8), 72.51 (C-5'), 69.85 (C-3'), 69.18 (C-13), 65.01 (C-12), 61.79 (C-2'), 49.11 (C-1"), 38.81 (C-6'), 31.86 (C-20), 29.52 (C-17), 29.49 (C-18), 29.30 (C-19), 29.28 (C-16), 28.87 (C-14), 25.92 (C-15), 22.63 (C-21), 14.54 (C-2"), 14.50 (C-11), 14.07 (C-22). APCI-HRMS *m/z* calcd for $C_{28}H_{46}N_3O_5$ 504.3432, found 504.3426 $[M+H]^+$.

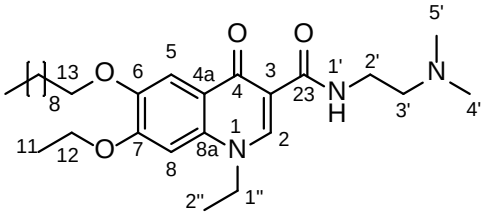
Spectroscopic Data for Compound 18



White powder, 0.4 g (80%), m.p. 157-159 °C; HPLC >96% purity, RT 4.33 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 10.35 (t, *J* = 5.5 Hz, 1H, H-1'), 8.66 (s, 1H, H-2), 7.84 (s, 1H, H-5), 6.79 (s, 1H, H-8), 4.32 – 4.20 (m, 2H, H-1"), 4.17 (q, *J* = 6.9 Hz, 2H, H-12), 4.10 (t, *J* = 6.8 Hz, 2H, H-13), 3.64 (t, *J* = 5.5 Hz, 2H, H-3'), 3.56 (dt, *J* = 5.5, 5.5 Hz, 2H, H-2'), 3.38 (s, 3H, H-5'), 1.90 – 1.80 (m, 2H, H-14), 1.60 – 1.40 (m, 10H, H-15- H-19), 1.30 – 1.18 (m, 10H, H-2", H-20 - H-22), 0.85 (t, *J* = 6.9 Hz, 3H, H-11). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 175.34 (C-4), 165.55 (C-23), 153.54 (C-7), 147.70 (C-6), 145.30 (C-2), 134.13 (C-8a), 122.30 (C-4a), 111.29 (C-3), 107.57 (C-5), 98.30 (C-8),

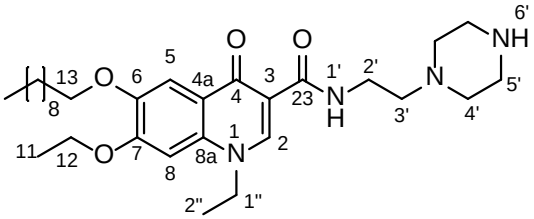
71.34 (C-3'), 69.19 (C-13), 65.05 (C-12), 58.82 (C-2'), 49.06 (C-1"), 38.93 (C-5'), 31.86 (C-20), 29.52 (C-17), 29.49 (C-18), 29.30 (C-19), 29.28 (C-16), 28.87 (C-14), 25.92 (C-15), 22.63 (C-21), 14.54 (C-2"), 14.51 (C-11), 14.08 (C-22). APCI-HRMS *m/z* calcd for $C_{27}H_{43}N_2O_5$ 475.3166, found 475.3169 $[M+H]^+$.

Spectroscopic Data for Compound 19



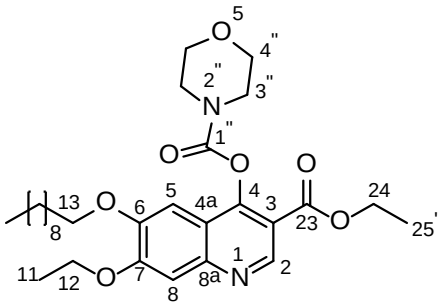
White powder, 0.25 g (51%), m.p. 155-156 °C; HPLC >96% purity, RT 4.11 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 10.35 (t, *J* = 5.8 Hz, 1H, H-1'), 8.65 (s, 1H, H-2), 7.83 (s, 1H, H-5), 6.80 (s, 1H, H-8), 4.25 (q, *J* = 7.2 Hz, 2H, H-1"), 4.18 (q, *J* = 7.0 Hz, 2H, H-13), 4.11 (t, *J* = 6.8 Hz, 2H, H-12), 3.70 (dt, *J* = 5.8, 6.1 Hz, 2H, H-2'), 2.73 (t, *J* = 6.1 Hz, 2H, H-3'), 2.44 (s, 6H, H-5'), 1.90 – 1.82 (m, 2H, H-14), 1.60 – 1.42 (m, 8H, H-15 - H-18), 1.34 – 1.16 (m, 12H, H-2", H-19 - H-22), 0.93 – 0.75 (m, *J* = 6.8 Hz, 3H, H-11). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 175.34 (C-4), 165.55 (C-23), 153.54 (C-7), 147.70 (C-6), 145.30 (C-2), 134.13 (C-8a), 122.30 (C-4a), 111.29 (C-3), 107.57 (C-5), 98.33 (C-8), 69.23 (C-13), 65.04 (C-12), 58.13 (C-3'), 49.13 (C-1"), 44.93 (C-5'), 36.44 (C-2'), 31.87 (C-20), 29.52 (C-17), 29.49 (C-18), 29.30 (C-19), 29.28 (C-16), 28.87 (C-14), 25.92 (C-15), 22.63 (C-21), 14.54 (C-2"), 14.51 (C-11), 14.08 (C-22). APCI-HRMS *m/z* calcd for $C_{28}H_{46}N_3O_4$ 488.3483, found 488.3490 $[M+H]^+$.

Spectroscopic Data for Compound 20



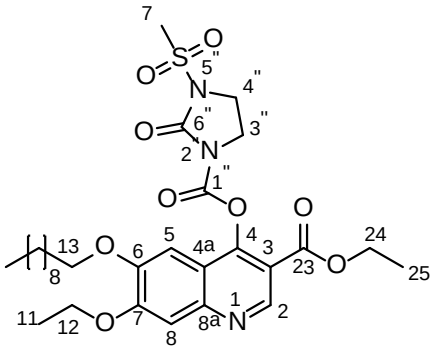
Yellow pallets, 0.3 g (60%), m.p. 145-147 °C; HPLC >97% purity, RT 3.96 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 10.35 (t, *J* = 5.8 Hz, 1H, H-1'), 8.64 (s, 1H, H-2), 7.83 (s, 1H, H-5), 6.79 (s, 1H, H-8), 4.32 – 4.20 (m, 2H, H-1"), 4.17 (q, *J* = 6.9 Hz, 2H, H-12), 4.10 (t, *J* = 6.8 Hz, 2H, H-13), 3.64 (t, *J* = 5.5 Hz, 2H, H-3'), 3.56 (dt, *J* = 5.5, 5.8 Hz, 2H, H-2'), 3.38 – 2.86 (m, 9H, H-4'- H-6'), 1.90 – 1.80 (m, 2H, H-14), 1.60 – 1.40 (m, 10H, H-15- H-19), 1.30 – 1.18 (m, 10H, H-2", H-20 - H-22), 0.85 (t, *J* = 6.9 Hz, 3H, H-11). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 175.34 (C-4), 165.55 (C-23), 153.54 (C-7), 147.70 (C-6), 145.30 (C-2), 134.13 (C-8a), 122.30 (C-4a), 111.29 (C-3), 107.57 (C-5), 98.30 (C-8), 69.19 (C-13), 65.05 (C-12), 58.82 (C-4'), 55.73 (C-1"), 54.37 (C-5',), 38.93 (C-3'), 36.43 (C-2'), 31.86 (C-20), 29.52 (C-17), 29.49 (C-18), 29.30 (C-19), 29.28 (C-16), 28.87 (C-14), 25.92 (C-15), 22.63 (C-21), 14.54 (C-2"), 14.51 (C-11), 14.08 (C-22). APCI-HRMS *m/z* calcd for $C_{30}H_{49}N_4O_4$ 529.3748, found 529.3760 $[M+H]^+$.

Spectroscopic Data for Compound 21



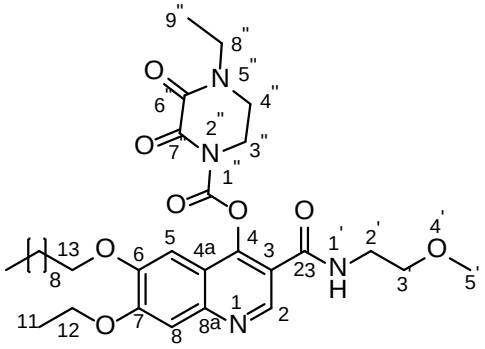
White powder, 0.46 g (92%), m.p. 164-166 °C; purity >97%, RT 10.3 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.19 (s, 1H, H-2), 7.40 (s, 1H, H-5), 7.23 (s, 1H, H-8), 4.35 (d, *J* = 15.6 Hz, 2H, H-24), 4.25 – 4.20 (m, 2H, H-13), 4.20 – 4.16 (t, *J* = 6.6 Hz, 2H, H-12), 4.12– 4.01 (m, 8H, H-3", H-4",), 1.96 – 1.82 (m, 2H, H-14), 1.51 (t, *J* = 15.5 Hz, 3H, H-25), 1.42 – 1.36 (m, 6H, H-15 - H-17), 1.30 – 1.18 (m, 11H, H-18 - H-22), 0.91 – 0.79 (t, 3H, *J* = 6.6 Hz, H-11). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 172.68 (C-23), 165.57 (C-7), 153.59 (C-4), 152.54 (C-6), 151.91 (C-1"), 145.82 (C-2), 138.72 (C-8a), 120.49 (C-4a), 117.94 (C-3), 108.59 (C-8), 100.25 (C-5), 69.30 (C-13), 69.19 (C-4"), 66.46 (C-3"), 64.51 (C-12), 61.40 (C-24), 31.85 (C-20), 29.67 (C-17), 29.54 (C-18), 29.50 (C-19), 28.81 (C-14), 25.98 (C-15), 25.65 (C-16), 22.64 (C-21), 14.37 (C-11), 14.19 (C-25), 13.09 (C-22). ESI-HRMS *m/z* calcd for $C_{29}H_{43}N_2O_7$ 531.3065, found 531.3035 $[M+H]^+$.

Spectroscopic Data for Compound 22



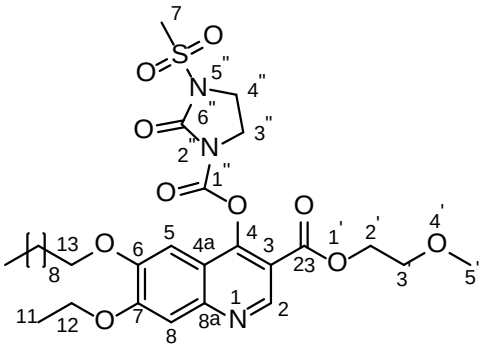
White powder, 0.4 6 g (92%), m.p. 160-162 °C; purity >97%, RT 9.8 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.19 (s, 1H, H-2), 7.40 (s, 1H, H-5), 7.23 (s, 1H, H-8), 4.35 (d, *J* = 15.6 Hz, 2H, H-24), 4.25 – 4.20 (m, 2H, H-13), 4.20 – 4.16 (t, *J* = 6.6 Hz, 2H, H-12), 4.12 (d, *J* = 6.6 Hz, 2H, H-3"), 4.01 (d, *J* = 6.6 Hz, 2H, H-4"), 3.39 (s, 3H, H-7"), 1.96 – 1.82 (m, 2H, H-14), 1.51 (t, *J* = 15.5 Hz, 3H, H-25), 1.42 – 1.36 (m, 6H, H-15 - H-17), 1.30 – 1.18 (m, 11H, H-18 - H-22), 0.91 – 0.79 (m, 3H, *J* = 6.6 Hz, H-11). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) 163.74 (C-23), 154.82 (C-7), 153.23 (C-4), 150.92 (C-6), 149.74 (C-6"), 149.28 (C-8a), 148.85 (C-2), 148.15 (C-1"), 117.32 (C-4a), 112.31 (C-3), 108.50 (C-8), 100.35 (C-5), 69.41 (C-13), 64.76 (C-12), 61.40 (C-24), 41.25 (C-4"), 40.69 (C-3"), 40.05 (C-7"), 31.87 (C-20), 29.55 (C-17), 29.54 (C-18), 29.30 (C-19), 28.80 (C-14), 25.94 (C-15), 25.21 (C-16), 22.65 (C-21), 14.37 (C-25), 14.09 (C-11), 13.49 (C-22),. ESI-HRMS *m/z* calcd for $C_{29}H_{42}N_3O_9S$ 608.2636, found 608.2609 $[M+H]^+$.

Spectroscopic Data for Compound 23



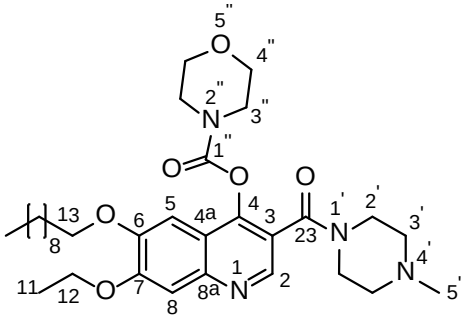
Yellow powder, 0.30 g (60%), m.p. 182-183 °C; Purity > 95%, RT 12.58 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.05 (s, 1H, H-2), 7.40 (s, 1H, H-5), 7.11 (s, 1H, H-8), 4.46 (d, *J* = 5.3 Hz, 2H, H-2'), 4.24 (q, *J* = 7.0 Hz, 2H, H-13), 4.10 (t, *J* = 6.7 Hz, 2H, H-12), 3.67 (d, *J* = 5.3, Hz, 2H, H-3'), 3.57 – 3.49 (m, 4H, H-3", H-4"), 3.41 (s, 3H, H-5'), 1.92 – 1.82 (m, 2H, H-14), 1.58 – 1.46 (m, 6H, H-15 - H-17), 1.40 – 1.20 (m, 16H, H-8", H-9", H-18 - H-22), 0.93 (t, *J* = 6.7 Hz, 3H, H-11). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.47 (C-23), 163.99 (C-1"), 158.85 (C-4), 157.07 (C-6", C-7"), 155.07 (C-7), 151.50 (C-6), 146.38 (C-2), 128.74 (C-8a), 122.21 (C-4a), 120.29 (C-3), 106.97 (C-8), 103.58 (C-5), 70.17 (C-3'), 69.40 (C-13), 68.09 (C-12), 64.82 (C-2'), 59.05 (C-5'), 48.55 (C-3"), 44.87 (C-4"), 43.73 (C-8"), 31.87 (C-20), 29.67 (C-17), 29.54 (C-18), 29.50 (C-19), 28.81 (C-14), 25.98 (C-15), 25.34 (C-16), 22.65 (C-21), 14.49 (C-11), 14.31 (C-9"), 13.09 (C-22). HRMS-ESI *m/z* calcd for $C_{32}H_{45}N_3O_9$ 616.3967, found 616.3926 $[M+H]^+$.

Spectroscopic Data for Compound 24



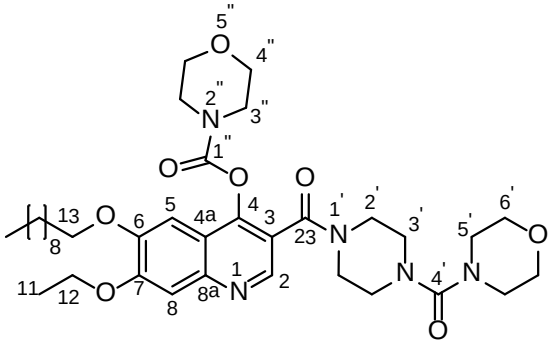
White powder, 0.20 g (40%), m.p. 170-173 °C; Purity > 96%, RT 10.13 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.03 (s, 1H, H-2), 7.50 (s, 1H, H-5), 7.23 (s, 1H, H-8), 4.58 – 4.50 (d, *J* = 5.3 Hz, 2H, H-2'), 4.24 (q, *J* = 7.0 Hz, 2H, H-13), 4.16 – 4.12 (t, *J* = 6.7 Hz, 2H, H-12), 3.95 – 3.90 (d, *J* = 5.3 Hz, 2H, H-3'), 3.79 – 3.71 (m, 4H, H-3", H-4"), 3.42 (s, 3H, H-5'), 3.31 (s, 3H, H-7"), 1.94 – 1.86 (m, 2H, H-14), 1.60 – 1.46 (m, 6H, H-15 - H-17), 1.38 – 1.23 (m, 11H, H-18 - H-22), 0.88 – 0.85 (t, *J* = 6.7 Hz, 3H, H-11). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.74 (C-23), 164.76 (C-7), 154.20 (C-4), 151.01 (C-6), 148.08 (C-2), 147.05 (C-6"), 141.21 (C-1") 128.77 (C-8a), 121.71 (C-4a), 120.35 (C-3), 108.59 (C-8), 103.64 (C-5), 70.31 (C-3'), 69.28 (C-13), 68.12 (C-12), 64.62 (C-2'), 59.05 (C-5'), 40.80 (C-3"), 40.52 (C-4"), 39.92 (C-7"), 31.87 (C-20), 29.67 (C-17), 29.54 (C-18), 29.50 (C-19), 28.81 (C-14), 25.98 (C-15), 25.28 (C-16), 22.65 (C-21), 14.49 (C-11), 13.09 (C-22). HRMS-ESI *m/z*) calcd for $C_{30}H_{44}N_3O_{10}S$ 638.3218, found 638.3193 $[M+H]^+$.

Spectroscopic Data for Compound 25



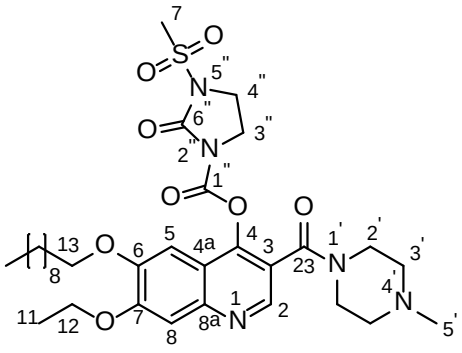
Brown powder, 0.3 g (60%), m.p. 172-174 °C; HPLC >95% purity, RT 7.24 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.48 (s, 1H, H-2), 7.24 (s, 1H, H-5), 6.74 (s, 1H, H-8), 4.26 – 4.20 (m, 2H, H-13), 4.09 (t, *J* = 6.8, 2H, H-12), 3.65 – 3.20 (m, 8H, H-2', H-3'), 2.59 – 2.31 (m, 8H, H-3", H-4"), 2.10 (s, 3H, H-5') 1.88 – 1.80 (m, 2H, H-14), 1.54 – 1.42 (m, 6H, H-15 - H-17), 1.30 – 1.16 (m, 11H, H-18 - H-21), 0.91 – 0.79 (m, *J* = 6.8, 3H, H-11). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 172.68 (C-23), 165.57 (C-7), 153.59 (C-4), 152.54 (C-6), 151.91 (C-1"), 145.82 (C-2), 138.72 (C-8a), 120.49 (C-4a), 117.94 (C-3), 108.59 (C-8), 100.25 (C-5), 69.30 (C-13), 69.19 (C-4"), 66.46 (C-3"), 64.51 (C-12), 54.49 (C-2'), 46.98 (C-3'), 41.90 (C-5'), 31.85 (C-20), 29.67 (C-17), 29.54 (C-18), 29.50 (C-19), 28.81 (C-14), 25.98 (C-15), 25.34 (C-16), 22.65 (C-21), 14.49 (C-22), 14.09 (C-11). ESI-HRMS *m/z* calcd for $C_{32}H_{49}N_4O_6$ 585.3647, 585.3604 $[M+H]^+$.

Spectroscopic Data for Compound 26



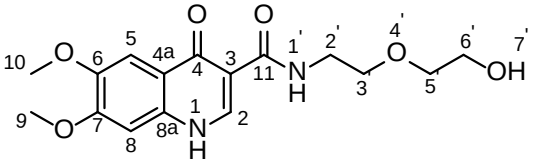
Yellow powder, 0.37 g (74%), m.p. 167-169 °C; HPLC purity >95% , RT 10.02 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.99 (s, 1H, H-2), 7.24 (s, 1H, H-5), 6.74 (s, 1H, H-8), 4.26 – 4.20 (m, 2H, H-13), 4.09 (t, *J* = 6.8, 2H, H-12), 3.85 – 3.20 (m, 24H, H-2', H-3', H-5', H-6', H-3", H-4"), 1.88 – 1.80 (m, 2H, H-14), 1.54 – 1.42 (m, 6H, H-15 - H-17), 1.30 – 1.16 (m, 11H, H-18 - H-21), 0.91 – 0.79 (m, *J* = 6.8, 3H, H-11). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 172.63 (C-23), 165.28 (C-7), 163.53 (C-4), 155.86 (C-4'), 153.82 (C-6), 152.14 (C-1"), 138.86 (C-2), 132.52 (C-8a), 120.42 (C-4a), 118.38 (C-3), 107.22 (C-8), 100.05 (C-5), 69.59 (C-13), 69.25 (C-12), 66.57 (C-4"), 66.46 (C-6'), 65.94 (C-3"), 49.42 (C-2'), 48.73 (C-5'), 46.45 (C-3'), 31.85 (C-20), 29.67 (C-17), 29.54 (C-18), 29.50 (C-19), 28.81 (C-14), 25.98 (C-15), 25.14 (C-16), 22.65 (C-21), 14.49 (C-11), 14.09 (C-22). ESI-HRMS *m/z* calcd for $C_{36}H_{54}N_5O_8$ 684.3967, found 684.3926 $[M+H]^+$.

Spectroscopic Data for Compound 27



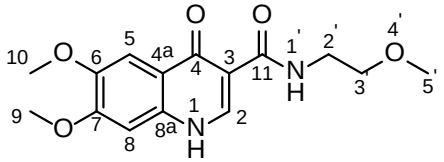
Brown powder, 0.28 g (56%), m.p. 170-173 °C; Purity > 96%, RT 6.94 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.48 (s, 1H, H-2), 7.24 (s, 1H, H-5), 6.74 (s, 1H, H-8), 4.26 – 4.20 (m, 2H, H-13), 4.09 (t, *J* = 6.8, 2H, H-12), 3.65 – 3.20 (m, 8H, H-2', H-3'), 3.09 (s, 3H, H-g), 2.59 – 2.31 (m, 4H, H-c, H-d,), 2.10 (s, 3H, H-5') 1.88 – 1.80 (m, 2H, H-14), 1.54 – 1.42 (m, 6H, H-15 - H-17), 1.30 – 1.16 (m, 11H, H-18 - H-21), 0.91 – 0.79 (m, *J* = 6.8, 3H, H-11). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 172.68 (C-23), 165.57 (C-7), 153.59 (C-4), 152.54 (C-f), 151.91 (C-6), 150.92 (C-8a), 145.82 (C-2), 138.72 (C-1"), 120.49 (C-4a), 117.94 (C-3), 108.59 (C-8), 100.25 (C-5), 69.30 (C-13), 69.19 (C-7"), 66.46 (C-3"), 65.04 (C-4"), 64.51 (C-12), 54.49 (C-2'), 46.98 (C-3'), 41.90 (C-5'), 31.85 (C-20), 29.67 (C-17), 29.54 (C-18), 29.50 (C-19), 28.81 (C-14), 25.98 (C-15), 25.14 (C-16), 22.65 (C-21), 14.49 (C-11), 14.09 (C-22). ESI-HRMS *m/z* calcd for $C_{32}H_{48}N_5O_8S$, 662.3218, found 662.3193 $[M+H]^+$.

Spectroscopic Data for Compound 28



White powder, 0.3 g (70%), m.p. 120-122 °C; HPLC >97% purity, RT 4.7 min; ^{1}H NMR (600 MHz, DMSO) δ 12.22 (s, 1H, H-1), 10.29 (t, *J* = 5.8 Hz, 1H, H-1'), 8.60 (s, 1H, H-2), 7.56 (s, 1H, H-5), 7.08 (s, 1H, H-8), 4.62 (s, 1H, H-7'), 3.90 (s, 3H, H-10), 3.85 (s, 3H, H-9), 3.52 (dd, *J* = 11.8, 5.8 Hz, 2H, H-2'), 3.43 (d, *J* = 11.7 Hz, 2H, H-3'), 3.40 – 3.34 (m, 4H, H-6', H-5'). ^{13}C NMR (151 MHz, DMSO) δ 174.76 (C-4), 164.82 (C-11), 153.61 (C-7), 147.61 (C-6), 141.72 (C-2), 134.86 (C-8a), 120.11 (C-4a), 110.05 (C-3), 104.40 (C-5), 99.73 (C-8), 72.29 (C-3'), 69.44 (C-5'), 60.24 (C-6'), 55.85 (C-10), 55.59 (C-9), 37.18 (C-2'). ESI-HRMS *m/z* calcd for $C_{16}H_{21}N_20_6$ 337.1394, found 337.1390 $[M+H]^+$.

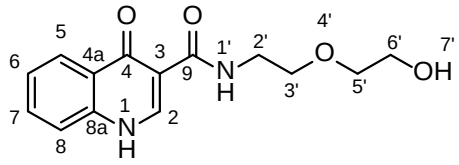
Spectroscopic Data for Compound 29



White powder, 0.3 g (70%), m.p. 125-126 °C; HPLC >97% purity, RT 5.0 min; ^{1}H NMR (600 MHz, DMSO) δ 12.40 (s, 1H, H-1), 10.30 (t, *J* = 5.4 Hz, 1H, H-1'), 8.59 (s, 1H, H-2), 7.52 (s, 1H, H-5), 7.09 (s, 1H, H-8), 3.87 (s, 3H, H-10), 3.84 (s, 3H, H-9), 3.54 – 3.42 (m, 4H, H-2', H-3'), 3.28 (s, 3H, H-5'). ^{13}C NMR (151 MHz, DMSO) δ 175.04 (C-4), 164.47 (C-11), 153.64 (C-7), 147.84 (C-6), 141.78 (C-2), 134.13 (C-8a), 120.57 (C-4a), 110.37 (C-3), 104.42 (C-5), 99.68 (C-8), 70.95 (C-3'),

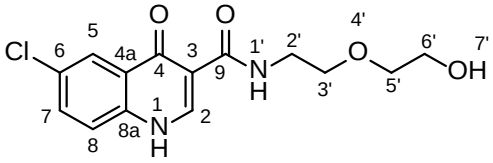
58.06 (C-5'), 55.84 (C-10), 55.46 (C-9), 38.16 (C-2'). ESI-HRMS *m/z* calcd for $C_{15}H_{19}N_20_5$ 307.1288, found 307.1260 $[M+H]^+$.

Spectroscopic Data for Compound 30



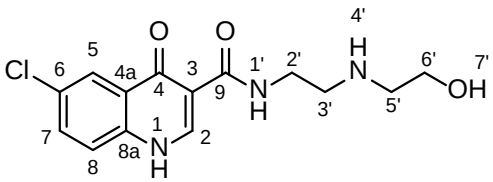
Pale brown powder, 0.2 g (50%), m.p. 114-116 °C; HPLC >95% purity, RT 3.2 min; ^{1}H NMR (600 MHz, DMSO) δ 12.76 (s, 1H, H-1), 10.11 (t, *J* = 5.4 Hz, 1H, H-1'), 8.71 (s, 1H, H-2), 8.25 – 8.19 (m, 1H, H-5), 7.79 – 7.63 (m, 1H, H-6), 7.44 – 7.40 (m, 2H, H-7, H-8), 4.64 (s, 1H, H-7'), 3.60 – 3.34 (ddd, *J* = 34.9, 10.1, 5.4 Hz, 8H, H-2' - H-5'). ^{13}C NMR (151 MHz, DMSO) δ 176.14 (C-4), 164.16 (C-9), 143.18 (C-2), 139.74 (C-8a), 132.35 (C-5), 126.14 (C-4a), 125.70 (C-6), 124.74 (C-7), 118.01 (C-8), 110.92 (C-3), 72.22 (C-3'), 69.39 (C-5'), 60.25 (C-6'), 38.48 (C-2'). ESI-HRMS *m/z* calcd for $C_{14}H_{17}N_20_4$ 277.1228, found 277.1215 $[M+H]^+$.

Spectroscopic Data for Compound 31



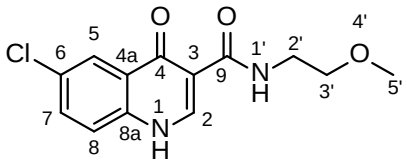
White powder, 0.2 g (40%), m.p. 117-118 °C; HPLC >96% purity, RT 3.8 min; ^{1}H NMR (600 MHz, DMSO) δ 12.45 (s, 1H, H-1), 9.97 (t, *J* = 5.4 Hz, 1H, H-1'), 8.76 (s, 1H, H-2), 8.16 (d, *J* = 8.8 Hz, 1H, H-5), 7.78 (dd, *J* = 8.8, 2.4 Hz, 1H, H-7), 7.72 (d, *J* = 2.4 Hz, 1H, H-8), 4.62 (s, 1H, H-6'), 3.56 – 3.36 (m, 8H, H-2' - H-5'). ^{13}C NMR (151 MHz, DMSO) δ 174.85 (C-4), 164.19 (C-9), 144.08 (C-2), 137.89 (C-6), 132.71 (C-5), 129.53 (C-8a), 127.29 (C-4a), 124.35 (C-7), 121.54 (C-8), 111.14 (C-3), 72.21 (C-3'), 69.31 (C-5'), 60.23 (C-6'), 38.49 (C-2'). ESI-HRMS *m/z* calcd for $C_{14}H_{17}ClN_30_3$ 309.1462, found 309.1461 $[M+H]^+$.

Spectroscopic Data for Compound 32



Brown powder, 0.3 g (60%), m.p. 115-117 °C; HPLC >96% purity, RT 3.4 min; ^{1}H NMR (600 MHz, DMSO) δ 12.45 (s, 1H, H-1), 10.03 (t, *J* = 5.4 Hz, 1H, H-1'), 8.72 (s, 1H, H-2), 8.15 (d, *J* = 8.8 Hz, 1H, H-5), 7.89 – 7.69 (m, 2H, H-7, H-8), 5.26 (s, 1H, H-7'), 3.74 – 3.62 (m, 2H, H-2'), 3.57 – 3.22 (m, 3H, H-4', H-6'), 3.04 – 2.94 (m, 2H, H-3') . ^{13}C NMR (151 MHz, DMSO) δ 174.73 (C-4), 165.20 (C-9), 143.89 (C-2), 137.97 (C-6), 132.80 (C-5), 129.62 (C-8a), 127.26 (C-4a), 124.21 (C-7), 121.66 (C-8), 110.83 (C-3), 56.50 (C-6'), 49.20 (C-5'), 46.78 (C-3'), 35.40 (C-2'). ESI-HRMS *m/z* calcd for $C_{14}H_{17}ClN_30_3$ 310.0926, found 310.0953 $[M+H]^+$.

Spectroscopic Data for Compound 33



White powder, 0.3 g (60%), m.p. 118-119 °C; HPLC >96% purity, RT 3.7 min; ^{1}H NMR (600 MHz, DMSO) δ 12.45 (s, 1H, H-1), 9.98 (t, *J* = 5.4 Hz, 1H, H-1'), 8.76 (s, 1H, H-2), 8.16 (d, *J* = 8.8 Hz, 1H, H-5), 7.79 (dd, *J* = 8.8, 2.4 Hz, 1H, H-7), 7.71 (d, *J* = 2.4 Hz, 1H, H-8), 3.54 – 3.42 (m, 4H, H-2', H-3'), 3.24 (s, 3H, H-4'). ^{13}C NMR (151 MHz, DMSO) δ 174.38 (C-4), 164.69 (C-9), 144.37 (C-2), 137.42 (C-6), 132.32 (C-5), 129.81 (C-8a), 127.41 (C-4a), 124.16 (C-7), 121.42 (C-8), 112.22 (C-3), 70.84 (C-3'), 58.06 (C-5'), 38.22 (C-2'). ESI-HRMS *m/z* calcd for $C_{13}H_{14}ClN_2O_3$ 281.0690, found 281.0687 $[M+H]^+$.

Supplementary References

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