Base-Promoted Expedient Access to Spiroisatins: Synthesis and Antitubercular Evaluation of 1H-1,2,3-Triazole-Tethered Spiroisatin–Ferrocene and Isatin–Ferrocene Conjugates

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Base-Promoted Expedient Access to Spiroisatins: Synthesis and Antitubercular Evaluation of 1*H*-1,2,3-Triazole-Tethered Spiroisatin–Ferrocene and Isatin–Ferrocene Conjugates

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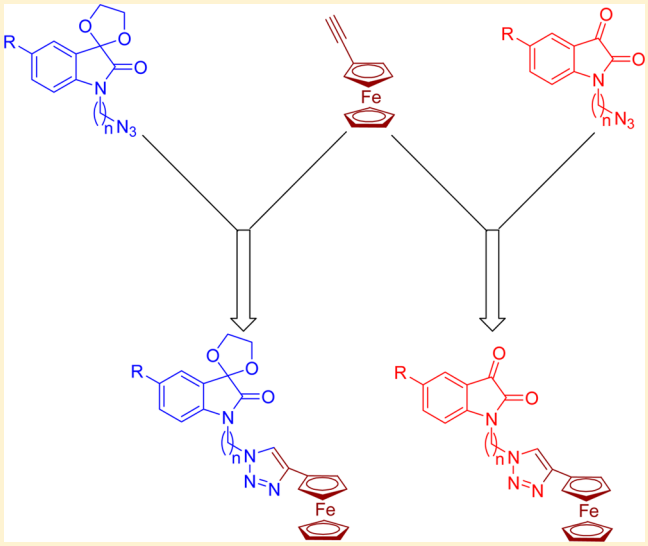
Supporting Information

ABSTRACT: The use of sodium hydride provides a convenient access to the synthesis of C-5-functionalized spiroisatins with the absence of the typical drawbacks associated with conventional protocols. The synthesized precursors, viz. *N*-alkylazido spiroisatins and their unprotected counterparts, were explored in Cu-mediated azide–alkyne cycloaddition reactions to probe the antitubercular structure–activity relationships (SAR) within the isatin–ferrocene–triazole conjugate family. The antitubercular evaluation studies of the synthesized conjugates revealed an improvement in the minimal inhibitory concentration (MIC) with the introduction of ferrocene nucleus, as evidenced by spiroisatin–ferrocene and isatin–ferrocene hybrids.



INTRODUCTION

Tuberculosis (TB) is a highly infectious disease caused by *Mycobacterium tuberculosis* (*M. tuberculosis*).[1] It is currently the second leading cause of death, claiming 1.4 million lives worldwide in 2011.[2] Over 95% of TB deaths occur in low- and middle-income countries, affecting mostly children and women aged between 15 and 44 years.[3] The chemotherapeutic options for the treatment of first-line TB have not changed for almost five decades, with the most recent drug, rifampin, being introduced in the early 1960s.[4] Moreover, factors such as inconsistent treatment, patient noncompliance, and the lack of available drugs especially in economically deprived countries have also contributed to the failure in achieving its cure.[5] The emergence of multidrug-resistant strains of tuberculosis (MDR-TB and XDR-TB) have increased the problems associated with TB treatment. The frequent coinfection of TB in HIV patients further complicates the selection of an appropriate treatment plan as a result of (a) drug–drug interactions which lead to subtherapeutic concentrations of antiretrovirals, (b) reduction of compliance due to the increased pill burden, and (c) increasing safety concerns due to overlapping toxic side effects.[6]

The United States Food and Drug Administration (FDA) recently approved TMC207 (bedaquiline),[7] the first anti-TB drug in over five decades, for the treatment of MDR-TB and XDR-TB in adults. Unfortunately, like other known second-line antitubercular drugs, it is associated with serious side effects.[7] Pertaining to the drug-resistant patterns, the synthesis of novel antimycobacterial scaffolds that work on characteristic targets with diverse mechanisms of action, with good potency, and

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with little or no toxicity as well as the lack of cross resistance with existing drugs remains pivotal.

Over the past few years, syntheses of organometallic analogues of biologically active compounds have emerged as an important strategy with potential advantages. These advantages include the preparation of stable metal complexes with predictable structures, the ability to tune ligand affinities according to their electron transfer properties, substitution rates, and reduction potentials, and efficient biological targeting.[8] Among the incredible number and variety of roles that metals play in contemporary medicine, the introduction of a ferrocenyl (Fc) moiety into a drug molecule has now been recognized as a useful approach for the development of more effective therapeutic applications: viz., ferrocenyl analogues of the commercial antiestrogen tamoxifen and antiandrogen nilutamide exhibited higher cytotoxicity on breast and prostate cancer cells with respect to the reference drugs, respectively.[9] The most symbolic example of the contribution of an Fc nucleus to enhance the activity of an organic molecule is that of ferroquine (FQ), a chloroquine (CQ) isostere with an Fc-based side chain that is highly active against CQ-resistant strains of malaria parasite and have the potential to express new organometallic-specific modes of action.[10] Using drug repositioning, FQ was also proven to be a new anti-hepatitis C virus molecule that could be used in combination with other direct-acting antivirals.[11]

Isatin is a privileged scaffold that is found as an endogenous molecule in humans, and its analogues display a diverse array of biological and pharmacological activities, which include anti-HIV,[12] antiviral,[13] antitumor,[14−16] antifungal,[17,18] antiangiogenic,[19] anticonvulsant,[20] anti-Parkinson's disease therapeutic,[21] and effective SARS coronavirus 3CL protease inhibitor.[22] The most enthralling application of isatins in organic synthesis is indisputably because of the highly reactive C-3 carbonyl group, which upon nucleophilic addition or spiroannulation transforms it into 2-oxoindole compounds.[23] 2-Oxoindoles have generated tremendous interest among synthetic organic and medicinal chemists not only because of their biological activities[24−30] but also because of their occurrence in natural products such as spirotryprostatins, horsfiline, gelsemine, gelseverine, rhynchophylline, elacomine, etc. Although a number of methods have been reported for the synthesis of spiroisatins, these methods are invariably associated with a number of drawbacks, including stringent reaction conditions, longer reaction times, moderate yields, and the use of toxic solvents such as benzene.[31]

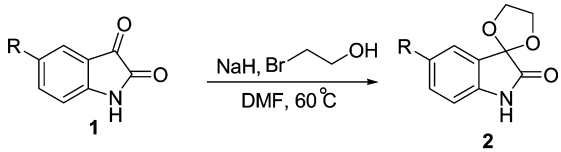
1*H*-1,2,3-Triazoles constitute an exhilarating class of compounds which has also attracted the attention of both synthetic and medicinal chemists due to their synthetic accessibility via azide−alkyne cycloaddition reactions as well as their great biological potential.[32] The molecular framework is highly stable under basic and acid hydrolysis and reductive and oxidative conditions, indicative of a high aromatic stabilization. The favorable properties of 1*H*-1,2,3-triazoles, including high dipole moment, capability of hydrogen bonding, and rigidity and stability under in vivo conditions are favorable factors in the binding of biomolecular targets.

Recent revelations from our group have shown the introduction of a ferrocene nucleus in the β-lactam family of therapeutics linked through the 1*H*-1,2,3-triazole ring with an extension toward the synthesis of mono and bis 1*H*-1,2,3-triazole-tethered β-lactam−ferrocene and β-lactam−ferrocenyl-chalcone hybrids and the evaluation of their antitubercular potential.[33,34] Further, isatin−ferrocene and isatin−ferrocenyl chalcones have been prepared and assayed for their antimycobacterial efficacy.[35] The anti-TB profiles revealed a marked improvement in the activity of isatins with the introduction of a ferrocene nucleus, with effects more pronounced at longer chain lengths: propyl chain tethered conjugates are more active than those with ethyl chains. In continuation, the present paper is a logical extension of the above protocol and involves the synthesis of isatin−ferrocene conjugates tethered via longer alkyl chain lengths (n = 4−8) along with their anti-TB potential. It was envisioned that the introduction of a longer nonhydrolyzable alkane spacer would enhance the lipophilicity, which is considered important for antitubercular efficacy because of its contribution toward increasing membrane permeability.[36] A convenient protocol was also developed for the preparation of spiroisatins with subsequent utilization in the synthesis of spiroisatin−ferrocene conjugates so as to ascertain the role of keto−carbonyl in the inhibition assays.

RESULT AND DISCUSSION

The methodology involved an initial treatment of C-5-substituted isatin with sodium hydride, resulting in the formation of an intensely purple anionic solution that was subsequently reacted with 2-bromoethanol. The reaction mixture was then heated to 60 °C until the completion of the reaction as evidenced by TLC. Then, the usual workup via quenching with water, extraction with ethyl acetate, and subsequent concentration under reduced pressure resulted in the isolation of the corresponding C-5-substituted spiroisatins in quantitative yields (Scheme 1).

Scheme 1. Synthesis of C-5-Substituted Spiroisatins 2



R = H, F, Cl, CH_3

Entry	Product
2a	R=H
2b	R=F
2c	R=Cl
2d	R=CH_3

Mechanistically, the reaction involved the initial generation of an anion by the treatment of isatin with sodium hydride followed by its nucleophilic attack on 2-bromoethanol to yield the corresponding 1-(2-hydroxyethyl)-1*H*-indole-2,3-dione **4**.[37] This species upon intramolecular cyclization via a facile nucleophilic addition of free −OH to the keto−carbonyl of isatin resulted in the formation of an intermediate, viz. C-5-substituted 8-hydroxy-9-oxa-1-azatricyclo[6.3.1.$0^{2,7}$]dodeca-2,4,6-trien-12-one **5** with subsequent ring opening to yield the desired spiroisatins **2**, as shown in Scheme 2.

The structure assigned to the product **2** was unambiguously confirmed using X-ray crystallographic studies, and the ORTEP diagram of compound **2b** is depicted in Figure 1.

The synthesized spiroisatins **2** were sufficiently pure and were utilized as such for further synthetic endeavors: i.e., an initial alkylation with dibromoalkanes with subsequent treatment with sodium azide in dry DMF at 60 °C. The *N*-

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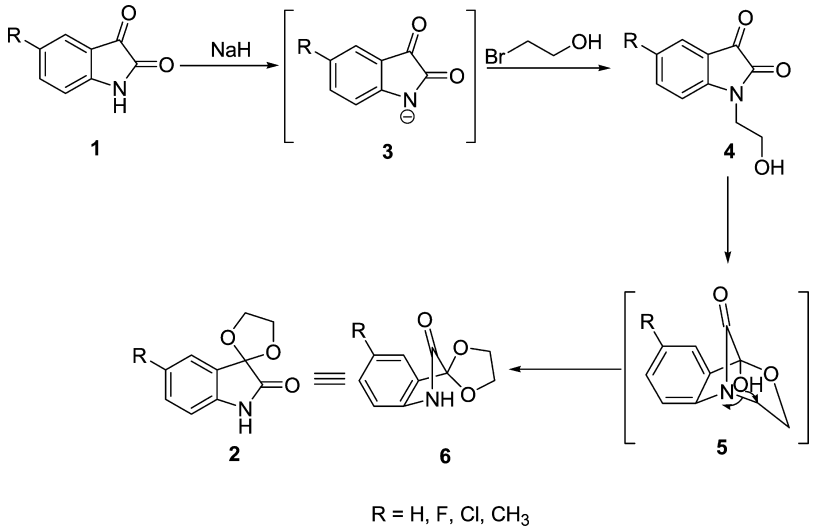
Scheme 2. Plausible Mechanism for the Formation of Spiroisatins 2



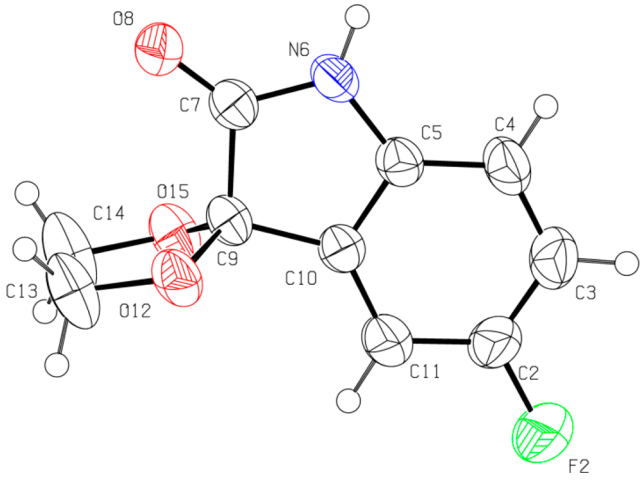
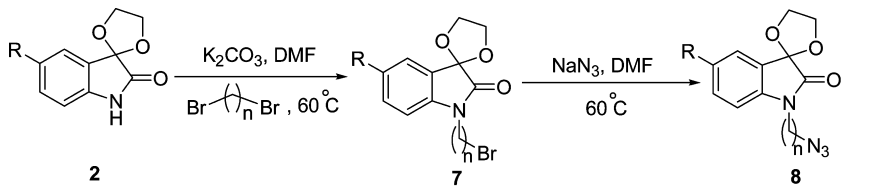


Figure 1. ORTEP diagram of spiroisatin **2b**.

alkylazido precursors **8** thus formed were subjected to Cu-promoted azide–alkyne cycloaddition reactions with ethynylferrocene (**9**) to yield the desired spiroisatin–ferrocene conjugates **10** (Scheme 3). The structures of these conjugates were assigned on the basis of analytical data and spectral evidence. Compound **10i**, for example, exhibited the molecular ion peak $[M]^+$ at m/z 498.1350 along with the characteristic peaks in the ^{1}H and ^{13}C NMR spectra. The ^{1}H NMR spectrum exhibited a singlet at δ 4.06 corresponding to 5H (ferrocene ring protons) along with the presence of two multiplets at δ 1.69–1.73 (2H) and 1.96–2.04 (2H) and two triplets at δ 3.69 (2H) and 4.41 (2H) corresponding to the butyl chain. The presence of a characteristic signal at 173.5 ppm corresponding to the spiroisatin ring carbonyl along with the requisite number of carbons in its ^{13}C NMR spectrum further corroborated the structure assigned to spiroisatin–ferrocene hybrids.

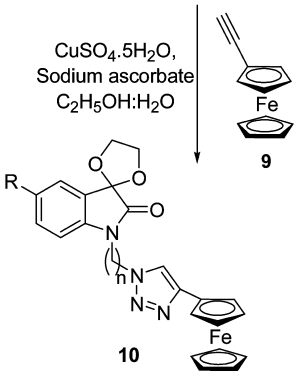
The synthesized conjugates **10** were then subjected to deprotection via refluxing in an HCl–methanol mixture.[38] However, the reaction resulted in the decomposition of the starting material without the isolation of the desired isatin–

Scheme 3. Cu-Promoted Synthesis of 1*H*-1,2,3-Triazole-Tethered Spiroisatin–Ferrocene Conjugates 10



Entry	n	R
8a/10a	2	H
8b/10b	2	F
8c/10c	2	Cl
8d/10d	2	CH_3
8e/10e	3	H
8f/10f	3	F
8g/10g	3	Cl
8h/10h	3	CH_3
8i/10i	4	H
8j/10j	4	F
8k/10k	4	Cl
8l/10l	4	CH_3

Entry	n	R
8m/10m	5	H
8n/10n	5	F
8o/10o	5	Cl
8p/10p	5	CH_3
8q/10q	6	H
8r/10r	6	F
8s/10s	6	Cl
8t/10t	6	CH_3
8u/10u	8	H
8v/10v	8	F
8w/10w	8	Cl
8x/10x	8	CH_3



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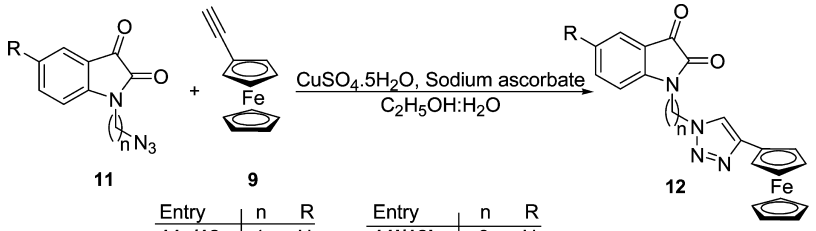
Scheme 4. Synthesis of 1*H*-1,2,3-Triazole-Tethered Isatin–Ferrocene Conjugates 12



Entry	n	R	Entry	n	R
11a/12a	4	H	**11i/12i**	6	H
11b/12b	4	F	**11j/12j**	6	F
11c/12c	4	Cl	**11k/12k**	6	Cl
11d/12d	4	CH_3	**11l/12l**	6	CH_3
11e/12e	5	H	**11m/12m**	8	H
11f/12f	5	F	**11n/12n**	8	F
11g/12g	5	Cl	**11o/12o**	8	Cl
11h/12h	5	CH_3	**11p/12p**	8	CH_3

Table 1. In Vitro Antimycobacterial Activity of Compounds 8a–x, 10a–x, 11a–p, and 12a–p against *M. tuberculosis* mc^{2}6230

compd	MIC (μM)	compd	MIC (μM)	compd	MIC (μM)	compd	MIC (μM)
8a	>385	**10a**	>213	**11a**	>410	**12a**	>220
8b	>360	**10b**	>205	**11b**	>382	**12b**	>212
8c	>340	**10c**	>198	**11c**	164–328	**12c**	>195
8d	ND	**10d**	ND	**11d**	>388	**12d**	>214
8e	>365	**10e**	>207	**11e**	>387	**12e**	>215
8f	>343	**10f**	>199	**11f**	>368	**12f**	>206
8g	>325	**10g**	>193	**11g**	171–242	**12g**	>199
8h	ND	**10h**	ND	**11h**	184–368	**12h**	>208
8i	>347	**10i**	>201	**11i**	>368	**12i**	>209
8j	>327	**10j**	>194	**11j**	172–344	**12j**	>200
8k	>311	**10k**	>188	**11k**	163–326	**12k**	>194
8l	ND	**10l**	ND	**11l**	174–348	**12l**	>201
8m	166–332	**10m**	>195	**11m**	175–350	**12m**	>202
8n	>313	**10n**	>187	**11n**	164–328	**12n**	>195
8o	>298	**10o**	>183	**11o**	158–312	**12o**	>189
8p	ND	**10p**	ND	**11p**	167–334	**12p**	>196
8q	158–316	**10q**	>190				
8r	>299	**10r**	>184				
8s	>286	**10s**	>179				
8t	ND	**10t**	ND				
8u	>303	**10u**	>185				
8v	144–287	**10v**	>179				
8w	137–274	**10w**	>174				
8x	ND	**10x**	ND				
cephalexin	72–144						
ethionamide	90.36						
isoniazid	2.92						
rifampicin	0.12						

ND= Not Determined.

ferrocene conjugates. Thus, in order to compare the antitubercular profiles of the spiroisatin–ferrocene conjugates with those of the deprotected isatin–ferrocene conjugates, a series of corresponding hybrids **12** were prepared following our recently reported protocol[35] involving Cu-promoted azide–alkyne cycloaddition reaction of *N*-alkylazido isatins **11**[39] and ethynylferrocene, as shown in Scheme 4. The structures of the hybrids were again confirmed using spectral data and analytical evidence, which are provided in detail in the Experimental Section; therefore, only the salient features are discussed here. The compound **12a**, for instance, showed a molecular ion peak $[M + H]^+$ at m/z 455.1181 along with the appearance of characteristic singlets at δ 4.05 (5H), 4.30 (2H), and 4.71 (2H) due to the ferrocene ring protons. The two multiplets at δ 1.73–1.80 and 2.01–2.05 and two triplets at δ 3.78 and 4.45 correspond to the protons of the butyl chain together with the presence of a singlet at δ 7.47 (1H) as a result of a triazole ring proton in the ^{1}H NMR spectrum. The presence of the requisite number of carbons along with the characteristic absorptions at δ 158.3 and 183.1 in the ^{13}C NMR spectrum further corroborate the assigned structure.

The synthesized spiroisatin–ferrocene (**10a–x**) and isatin–ferrocene (**12a–p**) molecular conjugates and their corresponding precursors (**8a–x**, **11a–p**) were evaluated for their antitubercular potential, and the results were compared with those for standard drugs: viz., cephalexin, ethionamide,

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rifampicin, and isoniazid (Table 1). As is evident from Table 1, although the synthesized conjugates and their precursors are not as active as the standard drugs used, the introduction of the ferrocene nucleus results in substantial enhancement in the activity profiles of both *N*-alkylazido spiroisatins and *N*-alkylazido isatins. Further, the activity profiles are shown to be independent of the nature of the substituent at the C-5 position of the isatin, the length of the alkyl chain, and the presence of either a keto−carbonyl or ketal unit at the C-3 position of the isatin ring.

In conclusion, the present paper describes a base-promoted straightforward access to C-5-functionalized spiroisatins without involving typical drawbacks of the conventional routes such as long reaction times, moderate yields, and the use of toxic solvents such as benzene. The synthesized precursors, viz. *N*-alkylazido spiroisatins and *N*-alkylazido isatins, were explored using Cu-promoted click chemistry approaches with ethnylferrocene, yielding the corresponding 1*H*-1,2,3-triazole-tethered spiroisatin−-ferrocene and isatin−ferrocene conjugates. The synthesized hybrids were assayed for their antitubercular potential, displaying enhancement in activity profiles with the introduction of a ferrocene nucleus in comparison to their organic precursors.

EXPERIMENTAL SECTION

General Information. Melting points were determined with open capillaries using a Veego Precision Digital Melting Point apparatus (MP-D) and are uncorrected. ^{1}H NMR spectra were recorded in deuteriochloroform (deuterated chloroform) with JEOL 300 (300 MHz) spectrometers using TMS as an internal standard. Chemical shift values are expressed as parts per million downfield from TMS, and *J* values are in hertz. Splitting patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; dd, doublet of doublets; ddd, doublet of doublets of doublets; br, broad peak. ^{13}C NMR spectra were recorded on JEOL 300 (75 MHz) spectrometers in deuteriochloroform using TMS as internal standard. Elemental analyses were performed with a Heraus CHN-O-Rapid Elemental Analyzer. Mass spectra were recorded on a Bruker high-resolution mass spectrometer (micrOTOF-QII). Column chromatography was performed using silica gel (60−120 mesh).

General Procedure for the Synthesis of Spiroisatins 2a−d. To a stirred suspension of NaH (1 mmol) in dry DMF (5 mL) was added dropwise a solution of isatin **1** (1 mmol) in dry DMF (10 mL) at 0 °C. The solution was stirred for 10 min, followed by the addition of 2-bromoethanol (1.1 mmol). The reaction mixture was stirred for 15 min at room temperature with subsequent heating at 70 °C for 60 min. The progress of the reaction was monitored using TLC. On completion, the reaction mixture was concentrated under reduced pressure, washed with brine solution, extracted with EtOAc (2 × 25 mL), and dried over anhydrous sodium sulfate. The combined organic layers were evaporated under reduced pressure, resulting in the isolation of crude products (91−97%) which were recrystallized using an 8/2 chloroform/hexane mixture.

Spiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**2a**): yield 95%; light yellow solid; mp 129−130 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.29−4.34 (m, 2H, $-OCH_2$), 4.54−4.57 (m, 2H, $-OCH_2$), 6.79−6.83 (m, 1H, −ArH), 7.03−7.07 (m, 1H, −ArH), 7.27−7.35 (m, 2H, −ArH), 8.24 (s, 1H, −NH, exchangeable with D_2O); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 65.8, 102.3, 110.7, 123.3, 124.3, 125.1, 131.6, 141.8, 175.6; HRMS calcd for $C_{10}H_9NO_3$ $[M]^+$ *m*/*z* 191.0582, found 191.0577. Anal. Calcd: C, 62.82; H, 4.74; N, 7.33. Found: C, 62.69; H, 4.71; N, 7.43.

5′-Fluorospiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**2b**): yield 91%; light brown solid; mp 157−158 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.27−4.38 (m, 2H, $-OCH_2$), 4.50−4.58 (m, 2H, $-OCH_2$), 6.76−6.80 (m, 1H, −ArH), 6.99−7.09 (m, 2H, −ArH), 8.35 (s, 1H, −NH, exchangeable with D_2O); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 65.9, 102.3, 111.4, 113.2, 118.2, 126.0, 137.7, 157.7, 175.9; HRMS calcd for $C_{10}H_8FNO_3$ $[M]^+$ *m*/*z* 209.0488, found 209.0483. Anal. Calcd: C, 57.42; H, 3.85; N, 6.70. Found: C, 57.51; H, 3.80; N, 6.58.

5′-Chlorospiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**2c**): yield 97%; light brown solid; mp 134−135 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.30−4.38 (m, 2H, $-OCH_2$), 4.52−4.65 (m, 2H, $-OCH_2$), 6.73−6.81 (m, 1H, −ArH), 7.04−7.09 (m, 1H, −ArH), 7.29−7.33 (m, 2H, −ArH), 8.31 (s, 1H, −NH, exchangeable with D_2O); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 65.4, 101.9, 110.1, 113.1, 122.3, 124.6, 131.5, 141.2, 173.5; HRMS calcd for $C_{10}H_8ClNO_3$ $[M]^+$ *m*/*z* 225.0193, found 225.0186. Anal. Calcd: C, 53.23; H, 3.57; N, 6.21. Found: C, 53.16; H, 3.51; N, 6.32.

5′-Methylspiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**2d**): yield 93%; light yellow solid; mp 152−153 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.24 (s, 3H, $-CH_3$), 4.25−4.34 (m, 2H, $-OCH_2$), 4.56−4.67 (m, 2H, $-OCH_2$), 6.60 (d, *J* = 8.4 Hz, 1H, −ArH), 7.27−7.38 (m, 2H, −ArH), 8.34 (s, 1H, −NH, exchangeable with D_2O); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.4, 65.1, 102.2, 110.3, 117.5, 121.6, 124.7, 131.5, 141.5, 174.8; HRMS calcd for $C_{11}H_{11}NO_3$ $[M]^+$ *m*/*z* 205.0739, found 205.0732. Anal. Calcd: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.49; H, 5.47; N, 6.71.

X-ray crystallographic data for **2b**: molecular formula $C_{10}H_8FNO_3$, formula weight 209.17, crystal system monoclinic, space group $P2_1/n$, a = 11.4436(6) Å, b = 5.2965(3) Å, c = 15.8782(9) Å, β = 97.601(3)°, V = 953.94(9) Å^3, T = 293 K, Z = 4, D_c = 1.456 g cm^{-3}, 14778 reflections measured, 1976 independent reflections, 1110 observed reflections ($I > 3.0\sigma(I)$), R1_obs = 0.0486, goodness of fit = 1.12. Crystallographic data (excluding structure factors) for spiroisatin **2b** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 953368.

General Procedure for the Synthesis of *N*-Alkylazidospiroisatins 8a−x. To a solution of **2** (1 mmol) in dry DMF (10 mL) was added K_2CO_3 (1.5 mmol), and the resulting suspension was stirred at room temperature for 10 min. A solution of the corresponding dibromoalkane (1.2 mmol) in dry DMF (5 mL) was added dropwise to the above reaction mixture with subsequent heating at 60 °C for 5 h. The progress of the reaction was monitored via TLC, and on completion the reaction mixture was concentrated under vacuum, washed with brine, and extracted with EtOAc (2 × 25 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure to result in the isolation of the crude product **7** (73−81%), which was purified by column chromatography (60−120 mesh) using EtOAc/hexane (10/90) as eluent. To a stirred solution of **7** (1 mmol) in dry DMF (5 mL) was added NaN_3 (2 mmol) at room temperature, and the reaction mixture was stirred at 60 °C for 1 h. On completion, the reaction mixture was concentrated under reduced pressure and extracted with EtOAc (2 × 25 mL). The combined organic layers were concentrated under vacuum, resulting in the isolation of the crude product **8** (88−95%), which was sufficiently pure for the next step.

1′-(2-Azidoethyl)spiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**8a**): yield 90%; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.51−3.55 (m, 2H, H^1), 3.72−3.78 (m, 2H, H^2), 4.26−4.37 (m, 2H, $-OCH_2$), 4.51−4.64 (m, 2H, $-OCH_2$), 6.77 (d, *J* = 8.1 Hz, 1H, −ArH), 7.03−709 (m, 1H, −ArH), 7.29−7.36 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 39.8, 48.4, 65.5, 102.7, 110.5, 123.1, 124.6, 125.5, 131.3, 141.6, 175.1; HRMS calcd for $C_{12}H_{12}N_4O_3$ $[M]^+$ *m*/*z* 260.0909, found 260.0901. Anal. Calcd: C, 55.38; H, 4.65; N, 21.53. Found: C, 55.27; H, 4.58; N, 21.67.

1′-(2-Azidoethyl)-5′-fluorospiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**8b**): yield 88%; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.54−3.59 (m, 2H, H^1), 3.74−3.79 (m, 2H, H^2), 4.29−4.34 (m, 2H, $-OCH_2$), 4.54−4.59 (m, 2H, $-OCH_2$), 6.81−6.85 (m, 1H, −ArH), 7.04−7.12 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 39.4, 48.9, 65.9, 101.6, 109.6, 112.9, 117.8, 125.5, 139.6, 157.9, 173.4; HRMS calcd for $C_{12}H_{11}FN_4O_3$ $[M]^+$ *m*/*z* 278.0815, found 278.0807. Anal. Calcd: C, 51.80; H, 3.98; N, 20.14. Found: C, 51.94; H, 3.93; N, 19.98.

1′-(2-Azidoethyl)-5′-chlorospiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**8c**): yield 89%; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ

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3.52−3.61 (m, 2H, H^1), 3.70−3.77 (m, 2H, H^2), 4.25−4.33 (m, 2H, $-OCH_2$), 4.51−4.58 (m, 2H, $-OCH_2$), 6.74−6.80 (m, 1H, −ArH), 7.03−7.11 (m, 1H, −ArH), 7.27−7.30 (m, 1H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 39.1, 48.4, 65.6, 102.0, 110.4, 113.7, 123.3, 124.6, 137.3, 141.3, 173.2; HRMS calcd for $C_{12}H_{11}ClN_4O_3$ $[M]^+$ m/z 294.0520, found 294.0508. Anal. Calcd: C, 48.91; H, 3.76; N, 19.01. Found: C, 48.73; H, 3.81; N, 18.87.

1′-(2-Azidoethyl)-5′-methylspiro[[1,3]dioxolane-2,3′-indolin]-2′-one ***(8d):*** yield 93%; colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.24 (s, 3H, $-CH_3$), 3.50−3.58 (m, 2H, H^1), 3.71−3.78 (m, 2H, H^2), 4.23−4.30 (m, 2H, $-OCH_2$), 4.54−4.59 (m, 2H, $-OCH_2$), 6.59 (d, J = 8.1 Hz, 1H, −ArH), 7.29−7.37 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 38.9, 48.6, 65.5, 102.3, 110.4, 117.7, 121.6, 124.2, 131.7, 141.7, 175.2; HRMS calcd for $C_{13}H_{14}N_4O_3$ $[M]^+$ m/z 274.1066, found 274.1075. Anal. Calcd: C, 56.93; H, 5.14; N, 20.43. Found: C, 57.12; H, 5.05; N, 20.26.

1′-(3-Azidopropyl)spiro[[1,3]dioxolane-2,3′-indolin]-2′-one ***(8e):*** yield 95%; colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.89 (t, J = 6.0 Hz, 2H, H^2), 3.35 (t, J = 5.7 Hz, 2H, H^1), 3.67 (t, J = 6.3 Hz, 2H, H^3), 4.25−4.31 (m, 2H, $-OCH_2$), 4.48−4.53 (m, 2H, $-OCH_2$), 6.79−6.86 (m, 1H, −ArH), 7.02−7.08 (m, 1H, −ArH), 7.29−7.38 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.8, 36.2, 46.5, 65.6, 102.4, 110.6, 123.0, 124.1, 125.8, 131.2, 141.7, 175.4; HRMS calcd for $C_{13}H_{14}N_4O_3$ $[M]^+$ m/z 274.1066, found 274.1071. Anal. Calcd: C, 56.93; H, 5.14; N, 20.43. Found: C, 56.82; H, 5.09; N, 20.56.

1′-(3-Azidopropyl)-5′-fluorospiro[[1,3]dioxolane-2,3′-indolin]-2′-one ***(8f):*** yield 91%; colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.83 (t, J = 5.7 Hz, 2H, H^2), 3.38 (t, J = 6.0 Hz, 2H, H^1), 3.71 (t, J = 6.0 Hz, 2H, H^3), 4.24−4.32 (m, 2H, $-OCH_2$), 4.49−4.54 (m, 2H, $-OCH_2$), 6.84−6.89 (m, 1H, −ArH), 7.03−7.14 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.4, 37.2, 47.2, 65.5, 101.5, 109.3, 112.8, 117.6, 125.4, 139.4, 157.6, 173.2; Calcd for $C_{13}H_{13}FN_4O_3$ $[M]^+$ m/z 292.0972, found 292.0964. Anal. Calcd: C, 53.42; H, 4.48; N, 19.17. Found: C, 53.34; H, 4.40; N, 19.29.

1′-(3-Azidopropyl)-5′-chlorospiro[[1,3]dioxolane-2,3′-indolin]-2′-one ***(8g):*** yield 95%; colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.91 (t, J = 6.3 Hz, 2H, H^2), 3.33 (t, J = 6.3 Hz, 2H, H^1), 3.73 (t, J = 6.6 Hz, 2H, H^3), 4.27−4.35 (m, 2H, $-OCH_2$), 4.53−4.61 (m, 2H, $-OCH_2$), 6.76−6.82 (m, 1H, −ArH), 7.05−7.12 (m, 1H, −ArH), 7.33−7.35 (m, 1H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.3, 37.5, 47.8, 65.3, 102.4, 110.5, 113.6, 123.5, 124.3, 137.1, 141.2, 173.6; HRMS calcd for $C_{13}H_{13}ClN_4O_3$ $[M]^+$ m/z 308.0676, found 308.0665. Anal. Calcd: C, 50.58; H, 4.21; N, 18.15. Found: C, 50.72; H, 4.33; N, 18.01.

1′-(3-Azidopropyl)-5′-methylspiro[[1,3]dioxolane-2,3′-indolin]-2′-one ***(8h):*** yield 92%; colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.85 (t, J = 6.0 Hz, 2H, H^2), 2.21 (s, 3H, $-CH_3$), 3.36 (t, J = 6.6 Hz, 2H, H^1), 3.69 (t, J = 6.3 Hz, 2H, H^3), 4.24−4.33 (m, 2H, $-OCH_2$), 4.52−4.58 (m, 2H, $-OCH_2$), 6.61 (d, J = 7.8 Hz, 1H, −ArH), 7.32−7.38 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.2, 26.7, 38.6, 48.3, 65.4, 102.2, 110.7, 117.6, 121.9, 124.3, 131.9, 141.5, 175.0; HRMS calcd for $C_{14}H_{16}N_4O_3$ $[M]^+$ m/z 288.1222, found 288.1213. Anal. Calcd: C, 58.32; H, 5.59; N, 19.43. Found: C, 58.49; H, 5.68; N, 19.25.

1′-(4-Azidobutyl)spiro[[1,3]dioxolane-2,3′-indolin]-2′-one ***(8i):*** yield 88%; colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.72−1.84 (m, 4H, H^2 + H^3), 3.34 (t, J = 6.0 Hz, 2H, H^1), 3.66 (t, J = 6.6 Hz, 2H, H^4), 4.24−4.33 (m, 2H, $-OCH_2$), 4.44−4.53 (m, 2H, $-OCH_2$), 6.79−6.85 (m, 1H, −ArH), 7.04−7.11 (m, 1H, −ArH), 7.30−7.36 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.3, 29.0, 37.1, 48.3, 65.2, 102.7, 110.5, 123.3, 124.0, 125.7, 131.1, 147.4, 175.5; HRMS calcd for $C_{14}H_{16}N_4O_3$ $[M]^+$ m/z 288.1222, found 288.1215. Anal. Calcd: C, 58.32; H, 5.59; N, 19.43. Found: C, 58.15; H, 5.46; N, 19.62.

1′-(4-Azidobutyl)-5′-fluorospiro[[1,3]dioxolane-2,3′-indolin]-2′-one ***(8j):*** yield 94%; colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.79−1.88 (m, 4H, H^2 + H^3), 3.31 (t, J = 6.3 Hz, 2H, H^1), 3.63 (t, J = 6.9 Hz, 2H, H^4), 4.22−4.27 (m, 2H, $-OCH_2$), 4.48−4.52 (m, 2H, $-OCH_2$), 6.70−6.74 (m, 1H, −ArH), 6.98−7.07 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.5, 29.2, 36.9, 48.5, 65.8, 101.5, 109.2, 112.8, 117.6, 125.6, 139.5, 157.6, 173.1; HRMS calcd for $C_{14}H_{15}FN_4O_3$ $[M]^+$ m/z 306.1128, found 306.1126. Anal. Calcd: C, 54.90; H, 4.94; N, 18.29. Found: C, 54.81; H, 4.83; N, 18.45.

1′-(4-Azidobutyl)-5′-chlorospiro[[1,3]dioxolane-2,3′-indolin]-2′-one ***(8k):*** yield 92%; colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.74−1.84 (m, 4H, H^2 + H^3), 3.35 (t, J = 6.0 Hz, 2H, H^1), 3.62 (t, J = 6.6 Hz, 2H, H^4), 4.24−4.31 (m, 2H, $-OCH_2$), 4.48−4.50 (m, 2H, $-OCH_2$), 6.71−6.78 (m, 1H, −ArH), 7.02−7.08 (m, 1H, −ArH), 7.27−7.36 (m, 1H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.2, 29.0, 36.5, 48.6, 65.6, 102.1, 110.6, 113.5, 123.7, 124.2, 137.4, 141.5, 173.9; HRMS calcd for $C_{14}H_{15}ClN_4O_3$ $[M]^+$ m/z 322.1033, found 322.1037. Anal. Calcd: C, 52.10; H, 4.68; N, 17.36. Found: C, 52.22; H, 4.79; N, 17.17.

1′-(4-Azidobutyl)-5′-methylspiro[[1,3]dioxolane-2,3′-indolin]-2′-one ***(8l):*** yield 89%; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.79−1.88 (m, 4H, H^2 + H^3), 2.23 (s, 3H, $-CH_3$), 3.30 (t, J = 6.3 Hz, 2H, H^1), 3.66 (t, J = 6.3 Hz, 2H, H^4), 4.25−4.29 (m, 2H, $-OCH_2$), 4.48−4.55 (m, 2H, $-OCH_2$), 6.62 (d, J = 7.8 Hz, 1H, −ArH), 7.29−7.34 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.4, 26.6, 29.3, 36.8, 48.2, 65.5, 102.1, 107.5, 117.9, 121.7, 124.4, 131.8, 141.2, 175.3; HRMS calcd for $C_{15}H_{18}N_4O_3$ $[M]^+$ m/z 302.1379, found 302.1372. Anal. Calcd: C, 59.59; H, 6.00; N, 18.53. Found: C, 59.45; H, 5.86; N, 18.72.

1′-(5-Azidopentyl)spiro[[1,3]dioxolane-2,3′-indolin]-2′-one ***(8m):*** yield 91%; colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.30−1.36 (m, 2H, H^3), 1.46−1.59 (m, 4H, H^2 + H^4), 3.13 (t, J = 6.3 Hz, 2H, H^1), 3.58 (t, J = 6.6 Hz, 2H, H^5), 4.19−4.27 (m, 2H, $-OCH_2$), 4.47−4.54 (m, 2H, $-OCH_2$), 6.73−6.81 (m, 1H, −ArH), 7.06−7.12 (m, 1H, −ArH), 7.29−7.38 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.4, 26.6, 27.8, 39.6, 51.2, 66.0, 102.4, 110.4, 123.3, 124.1, 125.4, 131.6, 147.3, 175.4; HRMS calcd for $C_{15}H_{18}N_4O_3$ $[M]^+$ m/z 302.1379, found 302.1367. Anal. Calcd: C, 59.59; H, 6.00; N, 18.53. Found: C, 59.74; H, 6.19; N, 18.36.

1′-(5-Azidopentyl)-5′-fluorospiro[[1,3]dioxolane-2,3′-indolin]-2′-one ***(8n):*** yield 90%; colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.32−1.35 (m, 2H, H^3), 1.36−1.62 (m, 4H, H^2 + H^4), 3.18 (t, J = 6.6 Hz, 2H, H^1), 3.53 (t, J = 6.9 Hz, 2H, H^5), 4.21−4.25 (m, 2H, $-OCH_2$), 4.49−4.51 (m, 2H, $-OCH_2$), 6.67−6.68 (m, 1H, −ArH), 6.99−7.05 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.1, 26.8, 27.9, 39.7, 51.4, 66.2, 101.9, 109.7, 113.1, 117.9, 126.1, 140.0, 158.0, 173.3; HRMS calcd for $C_{15}H_{17}FN_4O_3$ $[M]^+$ m/z 320.1285, found 320.1282. Anal. Calcd: C, 56.24; H, 5.33; N, 17.49. Found: C, 56.35; H, 5.22; N, 17.29.

1′-(5-Azidopentyl)-5′-chlorospiro[[1,3]dioxolane-2,3′-indolin]-2′-one ***(8o):*** yield 89%; colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.29−1.36 (m, 2H, H^3), 1.39−1.57 (m, 4H, H^2 + H^4), 3.20 (t, J = 6.0 Hz, 2H, H^1), 3.58 (t, J = 6.0 Hz, 2H, H^5), 4.26−4.31 (m, 2H, $-OCH_2$), 4.46−4.54 (m, 2H, $-OCH_2$), 6.70−6.79 (m, 1H, −ArH), 7.06−7.11 (m, 1H, −ArH), 7.28−7.33 (m, 1H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.3, 26.7, 27.7, 39.4, 51.1, 65.9, 102.0, 110.5, 113.4, 123.8, 124.3, 137.5, 141.1, 173.8; HRMS calcd for $C_{15}H_{17}ClN_4O_3$ $[M]^+$ m/z 336.0989, found 336.0981. Anal. Calcd: C, 53.50; H, 5.09; N, 16.64. Found: C, 53.37; H, 4.96; N, 16.83.

1′-(5-Azidopentyl)-5′-methylspiro[[1,3]dioxolane-2,3′-indolin]-2′-one ***(8p):*** yield 88%; colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.29−1.38 (m, 2H, H^3), 1.41−1.55 (m, 4H, H^2 + H^4), 2.20, (s, 3H, $-CH_3$), 3.17 (t, J = 6.3 Hz, 2H, H^1), 3.54 (t, J = 6.6 Hz, 2H, H^5), 4.29−4.37 (m, 2H, $-OCH_2$), 4.44−4.55 (m, 2H, $-OCH_2$), 6.60 (d, J = 8.1 Hz, 1H, −ArH), 7.28−7.35 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.7, 24.0, 26.6, 27.5, 39.7, 51.4, 65.8, 102.0, 110.4, 117.8, 121.6, 124.5, 131.6, 141.1, 175.1; HRMS calcd for $C_{16}H_{20}N_4O_3$ $[M]^+$ m/z 316.1535, found 316.1539. Anal. Calcd: C, 60.75; H, 6.37; N, 17.71. Found: C, 60.90; H, 6.42; N, 17.56.

1′-(6-Azidohexyl)spiro[[1,3]dioxolane-2,3′-indolin]-2′-one ***(8q):*** yield 92%; colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.40−1.45 (m, 4H, H^3 + H^4), 1.55−1.67 (m, 2H, H^2), 1.71−1.77 (m, 2H, H^5), 3.25 (t, J = 6.6 Hz, 2H, H^1), 3.70 (t, J = 6.3 Hz, 2H, H^6), 4.20−4.27 (m, 2H, $-OCH_2$), 4.44−4.49 (m, 2H, $-OCH_2$), 6.68−6.73 (m, 1H, −ArH), 7.03−7.13 (m, 1H, −ArH), 7.27−7.37 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.0, 26.4, 27.1, 28.4, 40.3, 51.4, 65.8, 102.1, 110.7, 123.1, 124.3, 125.6, 131.5, 147.6, 175.2; Calcd for

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$C_{16}H_{20}N_4O_3$ $[M]^+$ m/z 316.1535, found 316.1541. Anal. Calcd: C, 60.75; H, 6.37; N, 17.71. Found: C, 60.91; H, 6.46; N, 17.53.

*1′-(6-Azidohexyl)-5′-fluorospiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**8r**):* yield 91%; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.37−1.46 (m, 4H, H^3 + H^4), 1.51−1.65 (m, 2H, H^2), 1.72−1.79 (m, 2H, H^5), 3.21 (t, J = 6.0 Hz, 2H, H^1), 3.66 (t, J = 6.6 Hz, 2H, H^6), 4.22−4.28 (m, 2H, $-OCH_2$), 4.48−4.53 (m, 2H, $-OCH_2$), 6.83−6.89 (m, 1H, −ArH), 7.02−7.11 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.5, 26.8, 27.3, 28.2, 40.2, 51.3, 66.0, 101.8, 109.6, 112.5, 117.4, 125.6, 139.8, 157.7, 173.6; HRMS calcd for $C_{16}H_{19}FN_4O_3$ $[M]^+$ m/z 334.1441, found 344.1449. Anal. Calcd: C, 57.48; H, 5.73; N, 16.76. Found: C, 57.34; H, 5.87; N, 16.90.

*1′-(2-Azidoethyl)spiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**8s**):* yield 93%; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.34−1.46 (m, 4H, H^3 + H^4), 1.49−1.57 (m, 2H, H^2), 1.74−1.81 (m, 2H, H^5), 3.24 (t, J = 5.7 Hz, 2H, H^1), 3.70 (t, J = 6.0 Hz, 2H, H^6), 4.18−4.24 (m, 2H, $-OCH_2$), 4.44−4.51 (m, 2H, $-OCH_2$), 6.70−6.78 (m, 1H, −ArH), 7.03−7.10 (m, 1H, −ArH), 7.29−7.36 (m, 1H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.1, 26.5, 27.2, 28.4, 40.5, 51.1, 65.9, 102.1, 110.8, 113.3, 123.6, 124.5, 137.2, 141.4, 173.7; HRMS calcd for $C_{16}H_{19}ClN_4O_3$ $[M]^+$ m/z 350.1146, found 350.1142. Anal. Calcd: C, 54.78; H, 5.46; N, 15.97. Found: C, 54.61; H, 5.36; N, 15.85.

*1′-(6-Azidohexyl)-5′-methylspiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**8t**):* yield 89%; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.34−1.41 (m, 4H, H^3 + H^4), 1.53−1.58 (m, 2H, H^2), 1.71−1.77 (m, 2H, H^5), 2.24 (s, 3H, $-CH_3$), 3.19 (t, J = 6.3 Hz, 2H, H^1), 3.68 (t, J = 6.0 Hz, 2H, H^6), 4.21−4.26 (m, 2H, $-OCH_2$), 4.45−4.52 (m, 2H, $-OCH_2$), 6.63 (d, J = 7.8 Hz, 1H, −ArH), 7.29−7.37 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 26.3, 26.4, 27.0, 28.3, 40.3, 51.0, 65.6, 102.4, 107.7, 117.5, 121.5, 124.4, 131.7, 141.4, 175.6; HRMS calcd for $C_{17}H_{22}N_4O_3$ $[M]^+$ m/z 330.1692, found 330.1699. Anal. Calcd: C, 61.80; H, 6.71; N, 16.96. Found: C, 61.86; H, 6.79; N, 16.86.

*1′-(8-Azidooctyl)spiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**8u**):* yield 93%; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.34−1.49 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.52−1.57 (m, 2H, H^2), 1.68−1.79 (m, 2H, H^7), 3.27 (t, J = 6.0 Hz, 2H, H^1), 3.63 (t, J = 5.7 Hz, 2H, H^8), 4.25−4.33 (m, 2H, $-OCH_2$), 4.44−4.56 (m, 2H, $-OCH_2$), 6.69−6.77 (m, 1H, −ArH), 7.04−7.10 (m, 1H, −ArH), 7.27−7.38 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.1, 26.4, 26.7, 28.4, 28.5, 29.4, 40.3, 50.5, 65.8, 102.2, 110.6, 123.4, 124.1, 125.8, 131.4, 147.3, 175.1; HRMS calcd for $C_{18}H_{24}N_4O_3$ $[M]^+$ m/z 344.1848, found 344.1841. Anal. Calcd: C, 62.77; H, 7.02; N, 16.77. Found: C, 62.71; H, 7.06; N, 16.68.

*1′-(8-Azidooctyl)-5′-fluorospiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**8v**):* yield 94%; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.31−1.44 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.48−1.57 (m, 2H, H^2), 1.65−1.72 (m, 2H, H^7), 3.22 (t, J = 6.6 Hz, 2H, H^1), 3.61 (t, J = 6.3 Hz, 2H, H^8), 4.22−4.31 (m, 2H, $-OCH_2$), 4.45−4.53 (m, 2H, $-OCH_2$), 6.83−6.89 (m, 1H, −ArH), 7.07−7.10 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.2, 26.3, 26.8, 28.1, 28.3, 29.5, 40.4, 50.7, 65.4, 101.7, 109.6, 112.9, 117.5, 125.2, 139.1, 157.6, 173.3; HRMS calcd for $C_{18}H_{23}FN_4O_3$ $[M]^+$ m/z 362.1754, found 362.1759. Anal. Calcd: C, 59.66; H, 6.40; N, 15.46. Found: C, 59.73; H, 6.48; N, 15.55.

*1′-(8-Azidooctyl)-5′-chlorospiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**8w**):* yield 88%; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.34−1.42 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.43−1.55 (m, 2H, H^2), 1.64−1.73 (m, 2H, H^7), 3.23 (t, J = 5.7 Hz, 2H, H^1), 3.59 (t, J = 6.6 Hz, 2H, H^8), 4.26−4.34 (m, 2H, $-OCH_2$), 4.41−4.50 (m, 2H, $-OCH_2$), 6.71−6.79 (m, 1H, −ArH), 7.06−7.11 (m, 1H, −ArH), 7.28−7.38 (m, 1H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.4, 26.5, 26.9, 28.0, 28.2, 29.6, 40.5, 50.6, 65.7, 102.5, 110.3, 113.6, 123.3, 124.2, 137.0, 141.7, 173.4; HRMS calcd for $C_{18}H_{23}ClN_4O_3$ $[M]^+$ m/z 378.1459, found 378.1450. Anal. Calcd: C, 57.07; H, 6.12; N, 14.79. Found: C, 57.13; H, 6.17; N, 14.69.

*1′-(8-Azidooctyl)-5′-methylspiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**8x**):* yield 89%; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.31−1.42 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.45−1.57 (m, 2H, H^2), 1.61−1.74 (m, 2H, H^7), 2.21 (s, 3H, $-CH_3$), 3.21 (t, J = 6.9 Hz, 2H, H^1), 3.63 (t, J = 6.3 Hz, 2H, H^8), 4.24−4.31 (m, 2H, $-OCH_2$), 4.40−4.48 (m, 2H, $-OCH_2$), 6.66 (d, J = 8.4 Hz, 1H, −ArH), 7.30−7.39 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 26.1, 26.2, 26.4, 28.1, 28.5, 29.1, 40.0, 50.9, 65.8, 102.7, 110.8, 117.7, 121.2, 124.2, 131.6, 141.3, 175.8; HRMS calcd for $C_{19}H_{26}N_4O_3$ $[M]^+$ m/z 358.2005, found 358.2000. Anal. Calcd: C, 63.67; H, 7.31; N, 15.63. Found: C, 63.72; H, 7.28; N, 15.68.

General Procedure for the Synthesis of Spiroisatin−Ferrocene-Based Hybrids 10a−x. To a well-stirred solution of *N*-alkylazido spiroisatins **8** and ethynylferrocene **9** in a 9/1 ethanol/water mixture were added copper sulfate (0.05 mmol) and sodium ascorbate (0.13 mmol). The reaction mixture was stirred at room temperature for 7−10 h. After completion of the reaction, as indicated by TLC, water (20 mL) was added and the reaction mixture was extracted with dichloromethane (2 × 30 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure, resulting in the crude product **10**, which was purified via column chromatography using a 60/40 EtOAc/hexane mixture.

*1′-(2-(4-Ferrocenyl-1H-1,2,3-triazol-1-yl)ethyl)spiro[[1,3]-dioxolane-2,3′-indolin]-2′-one (**10a**):* yield 78%; dark brown oil; NMR ($CDCl_3$, 300 MHz) δ 3.93 (s, 5H, H^6), 4.15−4.17 (m, 2H, H^1), 4.25 (s, 2H, $-OCH_2$), 4.34 (s, 2H, H^5), 4.58−4.61 (m, 4H, $-OCH_2$ + H^4), 4.65−4.68 (m, 2H, H^2), 6.59−6.61 (m, 1H, −ArH), 7.01−7.05 (m, 1H, −ArH), 7.28−7.36 (m, 3H, H^3+2ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 40.3, 47.4, 65.9, 66.6, 68.6, 69.5, 74.6, 101.9, 108.3, 120.1, 123.6, 123.8, 125.1, 131.9, 143.1, 173.8; HRMS calcd for $C_{24}H_{22}FeN_4O_3$ $[M]^+$ m/z 470.1036, found 440.1034. Anal. Calcd: C, 61.28; H, 4.68; N, 11.91. Found: C, 61.25; H, 4.71; N, 11.85.

*5′-Fluoro-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)ethyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10b**):* yield 87%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.90 (s, 5H, H^6), 4.14−4.19 (m, 2H, H^1), 4.23 (s, 2H, $-OCH_2$), 4.37 (s, 2H, H^5), 4.54−4.59 (m, 4H, $-OCH_2$ + H^4), 4.62−4.69 (m, 2H, H^2), 6.80−6.87 (m, 1H, −ArH), 7.01−7.10 (m, 2H, −ArH), 7.49 (s, 1H, H^3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 40.4, 47.2, 65.5, 66.2, 68.4, 69.6, 74.3, 101.4, 109.8, 112.6, 117.7, 125.4, 131.1, 134.8, 139.2, 157.6, 173.7; HRMS calcd for $C_{24}H_{21}FFeN_4O_3$ $[M]^+$ m/z 488.0141, found 488.0135. Anal. Calcd: C, 59.02; H, 4.30; N, 11.48. Found: C, 58.91; H, 4.23; N, 11.55.

*5′-Chloro-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)ethyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10c**):* yield 79%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.86 (s, 5H, H^6), 4.11−4.18 (m, 2H, H^1), 4.20 (s, 2H, $-OCH_2$), 4.38 (s, 2H, H^5), 4.51−4.58 (m, 4H, $-OCH_2$ + H^4), 4.65−4.70 (m, 2H, H^2), 6.89−6.96 (m, 1H, −ArH), 7.28−7.35 (m, 2H, −ArH), 7.60 (s, 1H, H^3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 40.1, 47.0, 65.4, 66.6, 68.7, 69.4, 74.4, 102.4, 110.6, 113.5, 123.5, 124.7,130.7, 134.6, 137.3, 141.5, 173.7; Calcd for $C_{24}H_{21}ClFeN_4O_3$ $[M]^+$ m/z 504.0383, found 504.0377. Anal. Calcd: C, 57.14; H, 4.17; N, 11.11. Found: C, 57.06; H, 4.07; N, 11.19.

*5′-Methyl-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)ethyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10d**):* yield 75%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.20 (s, 3H, $-CH_3$), 3.86 (s, 5H, H^6), 4.14−4.19 (m, 2H, H^1), 4.24 (s, 2H, $-OCH_2$), 4.39 (s, 2H, H^5), 4.50−4.56 (m, 4H, $-OCH_2$ + H^4), 4.61−4.67 (m, 2H, H^2), 6.55 (d, J = 7.5 Hz, 1H, −ArH), 7.28−7.36 (m, 2H, −ArH); 7.58 (s, 1H, H^3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.4, 40.5, 47.6, 65.7, 66.9, 68.4, 69.5, 74.6, 102.1, 110.6, 117.9, 121.2, 124.0, 130.2, 131.6, 134.5, 141.4, 175.6; HRMS calcd for $C_{25}H_{24}FeN_4O_3$ $[M + H]^+$ m/z 485.0919, found 485.0915. Anal. Calcd: C, 61.98; H, 4.96; N, 11.57. Found: C, 61.90; H, 5.04; N, 11.64.

*1′-(2-(4-Ferrocenyl-1H-1,2,3-triazol-1-yl)propyl)spiro[[1,3]-dioxolane-2,3′-indolin]-2′ one (**10e**):* yield 81%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.26 (s, 2H, H^2), 3.64 (s, 2H, H^1), 4.01 (s, 5H, H^7), 4.22−4.31 (m, 6H, $-OCH_2$ + H^3 + H^6), 4.52 (s, 2H, H^5), 4.66 (s, 2H, $-OCH_2$), 6.72−6.74 (m, 1H, −ArH), 7.03−7.06 (m, 1H, −ArH), 7.30−7.33 (m, 2H, −ArH), 7.60 (s, 1H, H^4); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.9, 36.7, 47.4, 65.8, 66.6, 68.6, 69.6, 75.2, 101.9, 108.7, 119.9, 123.6, 124.0, 125.0, 131.8, 143.2, 173.7; HRMS calcd for $C_{25}H_{24}FeN_4O_3$ $[M]^+$ m/z 484.1192, found 484.1189. Anal. Calcd: C, 61.98; H, 4.96; N, 11.57. Found: C, 61.85; H, 4.88; N, 11.62.

*5′-Fluoro-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)propyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10f**):* yield 79%; dark brown oil;

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^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.29 (s, 2H, H^2), 3.66 (s, 2H, H^1), 4.04 (s, 5H, H^7), 4.20−4.27 (m, 6H, $-OCH_2$ + H^3 + H^6), 4.54 (s, 2H, H^5), 4.63 (s, 2H, $-OCH_2$), 6.83−6.89 (m, 1H, −ArH), 7.03−7.11 (m, 2H, −ArH), 7.44 (s, 1H, H^4); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.7, 36.8, 47.5, 65.5, 66.4, 68.7, 69.8, 75.0, 101.1, 109.5, 112.8, 117.8, 125.6, 130.4, 134.5, 139.0, 157.2, 173.3; HRMS calcd for $C_{25}H_{23}FFeN_4O_3$ $[M]^+$ m/z 502.1068, found 502.1060. Anal. Calcd: C, 59.76; H, 4.58; N, 11.16. Found: C, 59.85; H, 4.65; N, 11.09.

5′-Chloro-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)propyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10g**): yield 80%; dark brown oil;^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.26 (s, 2H, H^2), 3.61 (s, 2H, H^1), 4.07 (s, 5H, H^7), 4.23−4.29 (m, 6H, $-OCH_2$ + H^3 + H^6), 4.53 (s, 2H, H^5), 4.60 (s, 2H, $-OCH_2$), 6.88−6.97 (m, 1H, −ArH), 7.29−7.38 (m, 2H, −ArH), 7.63 (s, 1H, H^4); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.3, 36.5, 47.2, 65.3, 66.5, 68.9, 69.5, 75.7, 102.6, 110.4, 113.8, 123.9, 124.6, 130.2, 134.9, 137.3, 141.4, 173.3; HRMS calcd for $C_{25}H_{23}ClFeN_4O_3$ $[M]^+$ m/z 518.1058, found 518.1056. Anal. Calcd: C, 57.92; H, 4.44; N, 10.81. Found: C, 58.02; H, 4.49; N, 10.71.

5′-Methyl-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)propyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10h**): yield 87%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.23 (s, 3H, $-CH_3$), 2.29 (s, 2H, H^2), 3.68 (s, 2H, H^1), 4.10 (s, 5H, H^7), 4.24−4.31 (m, 6H, $-OCH_2$ + H^3 + H^6), 4.50 (s, 2H, H^5), 4.64 (s, 2H, $-OCH_2$), 6.51 (d, J = 7.8 Hz, 1H, −ArH), 7.29−7.39 (m, 2H, −ArH); 7.62 (s, 1H, H^4); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 27.2, 36.6, 47.7, 65.9, 66.3, 68.5, 69.8, 75.5, 102.0, 110.9, 117.6, 121.1, 124.5, 130, 131.8, 134.8, 141.1, 175.3; HRMS calcd for $C_{26}H_{26}FeN_4O_3$ $[M]^+$ m/z 498.1136, found 498.1141. Anal. Calcd: C, 62.65; H, 5.22; N, 11.24. Found: C, 62.76; H, 5.31; N, 11.29.

1′-(2-(4-Ferrocenyl-1H-1,2,3-triazol-1-yl)butyl)spiro[[1,3]-dioxolane-2,3′-indolin]-2′-one (**10i**): yield 87%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.69−1.73 (m, 2H, H^2), 1.96−2.04 (m, 2H, H^3), 3.69 (t, J = 6.3 Hz, 2H, H^1), 4.06 (s, 5H, H^8), 4.30−4.33 (m, 4H, $-OCH_2$ + H^7), 4.41 (t, J = 6.6 Hz, 2H, H^4), 4.53−4.64 (m, 2H, $-OCH_2$), 4.71 (s, 2H, H^6), 6.76−6.79 (d, J = 7.5 Hz, 1H, −ArH), 7.05−7.10 (m, 1H, −ArH), 7.32−7.41 (m, 2H, −ArH), 7.43 (s, 1H, H^5); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.9, 27.2, 38.5, 49.2, 65.8, 66.5, 68.5, 69.4, 75.3, 102.0, 108.8, 118.8, 123.3, 123.9, 124.9, 131.7, 143.4, 173.5; HRMS calcd for $C_{26}H_{26}FeN_4O_3$ $[M]^+$ m/z 498.1343, found 498.1350. Anal. Calcd: C, 62.65; H, 5.22; N, 11.24. Found: C, 62.57; H, 5.18; N, 11.21.

5′-fFluoro-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)butyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10j**): yield 86%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.66−1.76 (m, 2H, H^2), 1.95−2.01 (m, 2H, H^3), 3.66 (t, J = 6.6 Hz, 2H, H^1), 4.03 (s, 5H, H^8), 4.28−4.34 (m, 4H, $-OCH_2$ + H^7), 4.44 (t, J = 6.0 Hz, 2H, H^4), 4.54−4.63 (m, 2H, $-OCH_2$), 4.69 (s, 2H, H^6), 6.81−6.89 (m, 1H, −ArH), 7.04−7.10 (m, 2H, −ArH), 7.46 (s, 1H, H^5); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.5, 27.0, 38.4, 49.5, 65.4, 66.7, 68.6, 69.2, 75.6, 101.4, 109.4, 112.5, 117.7, 125.4, 130.2, 134.3, 139.1, 157.4, 173.6; HRMS calcd for $C_{26}H_{25}FFeN_4O_3$ $[M]^+$ m/z 516.1373, found 516.1379. Anal. Calcd: C, 60.47; H, 4.84; N, 10.85. Found: C, 60.52; H, 4.89; N, 10.76.

5′-Chloro-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)butyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10k**): yield 77%; dark brown oil;^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.63−1.75 (m, 2H, H^2), 1.98−2.04 (m, 2H, H^3), 3.69 (t, J = 6.3 Hz, 2H, H^1), 4.01 (s, 5H, H^8), 4.29−4.37 (m, 4H, $-OCH_2$ + H^7), 4.42 (t, J = 6.3 Hz, 2H, H^4), 4.55−4.61 (m, 2H, $-OCH_2$), 4.68 (s, 2H, H^6),6.84−6.92 (m, 1H, −ArH), 7.31−7.39 (m, 2H, −ArH), 7.64 (s, 1H, H^5); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.1, 27.3, 38.3, 49.6, 65.7, 66.8, 68.4, 69.1, 75.4, 102.5, 110.6, 113.5, 123.3, 124.9, 130.3, 134.8, 137.2, 141.7, 173.8; HRMS calcd for $C_{26}H_{25}ClFeN_4O_3$ $[M]^+$ m/z 532.1372, found 532.1368. Anal. Calcd: C, 58.65; H, 4.69; N, 10.53. Found: C, 58.76; H, 4.77; N, 10.45.

5′-Methyl-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)butyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10l**): yield 83%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.64−1.69 (m, 2H, H^2), 1.88−1.95 (m, 2H, H^3), 2.21 (s, 3H, $-CH_3$), 3.66 (t, J = 6.9 Hz, 2H, H^1), 4.04 (s, 5H, H^8), 4.20−4.29 (m, 4H, $-OCH_2$ + H^7), 4.46 (t, J = 6.0 Hz, 2H, H^4), 4.52−4.59 (m, 2H, $-OCH_2$), 4.66 (s, 2H, H^6),6.55 (d, J = 8.4 Hz, 1H, −ArH), 7.27−7.38 (m, 2H, −ArH), 7.60 (s, 1H, H^5); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 23.0, 27.2, 38.1, 49.5, 65.9, 66.4, 68.3, 69.5, 75.8, 102.2, 110.5, 117.9, 121.2, 124.4, 130.5, 131.7, 134.8, 141.4, 175.7; HRMS calcd for $C_{27}H_{28}FeN_4O_3$ $[M + H]^+$ m/z 513.0925, found 513.0917. Anal. Calcd: C, 63.28; H, 5.47; N, 10.94. Found: C, 63.23; H, 5.40; N, 11.02.

1′-(2-(4-Ferrocenyl-1H-1,2,3-triazol-1-yl)pentyl)spiro[[1,3]-dioxolane-2,3′-indolin]-2′-one (**10m**): yield 82%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.31−1.39 (m, 2H, H^3), 1.44−1.52 (m, 4H, H^2 + H^4), 3.17 (t, J = 6.0 Hz, 2H, H^1), 4.06 (s, 5H, H^9), 4.26−4.32 (m, 4H, H^5 + H^8), 4.44−4.51 (m, 2H, $-OCH_2$), 4.56 (s, 2H, H^7), 4.69−4.76 (m, 2H, $-OCH_2$), 6.73−6.78 (d, J = 7.8 Hz, 1H, −ArH), 7.02−7.09 (m, 1H, −ArH), 7.34−7.41 (m, 2H, −ArH), 7.47 (s, 1H, H^6); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.6, 26.4, 27.5, 39.3, 51.0, 65.4, 66.3, 68.8, 69.7, 75.7, 102.5, 108.3, 118.4, 123.6, 123.7, 124.8, 131.9, 143.2, 173.8; HRMS calcd for $C_{27}H_{28}FeN_4O_3$ $[M]^+$ m/z 512.1076, found 512.1074. Anal. Calcd: C, 63.28; H, 5.47; N, 10.94. Found: C, 63.24; H, 5.41; N, 11.07.

5′-Fluoro-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)pentyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10n**): yield 77%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.34−1.42 (m, 2H, H^3), 1.46−1.57 (m, 4H, H^2 + H^4), 3.15 (t, J = 6.9 Hz, 2H, H^1), 4.01 (s, 5H, H^9), 4.22−4.30 (m, 4H, H^5 + H^8), 4.46−4.52 (m, 2H, $-OCH_2$), 4.58 (s, 2H, H^7), 4.71−4.74 (m, 2H, $-OCH_2$), 6.80−6.90 (m, 1H, −ArH), 7.03−7.12 (m, 2H, −ArH), 7.48 (s, 1H, H^6); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.1, 26.3, 27.6, 39.2, 51.2, 65.3, 66.7, 68.5, 69.3, 75.4, 101.1, 109.5, 112.4, 117.9, 125.5, 130.5, 134.2, 139.5, 157.1, 173.2; HRMS calcd for $C_{27}H_{27}FFeN_4O_3$ $[M]^+$ m/z 530.1092, found 530.1088. Anal. Calcd: C, 61.13; H, 5.09; N, 10.56. Found: C, 61.21; H, 5.17; N, 10.45.

5′-Chloro-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)pentyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10o**): yield 84%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.33−1.45 (m, 2H, H^3), 1.48−1.56 (m, 4H, H^2 + H^4), 3.13 (t, J = 6.3 Hz, 2H, H^1), 4.03 (s, 5H, H^9), 4.21−4.31 (m, 4H, H^5 + H^8), 4.41−4.47 (m, 2H, $-OCH_2$), 4.56 (s, 2H, H^7), 4.67−4.71 (m, 2H, $-OCH_2$), 6.83−6.95 (m, 1H, −ArH), 7.30−7.37 (m, 2H, −ArH), 7.60 (s, 1H, H^6); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.4, 26.2, 27.4, 39.5, 51.0, 65.2, 66.4, 68.6, 69.8, 75.3, 102.4, 110.9, 113.8, 123.6, 124.3, 130.5, 134.5,137.7, 141.5, 173.3; HRMS calcd for $C_{27}H_{27}ClFeN_4O_3$ $[M]^+$ m/z 546.0519, found 546.0511. Anal. Calcd: C, 59.34; H, 4.95; N, 10.26. Found: C, 59.23; H, 4.87; N, 10.20.

5′-Methyl-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)pentyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10p**): yield 76%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.30−1.42 (m, 2H, H^3), 1.44−1.52 (m, 4H, H^2 + H^4), 2.22 (s, 3H, $-CH_3$), 3.20 (t, J = 6.3 Hz, 2H, H^1), 4.02 (s, 5H, H^9), 4.18−4.27 (m, 4H, H^5 + H^8), 4.42−4.47 (m, 2H, $-OCH_2$), 4.59 (s, 2H, H^7), 4.63−4.70 (m, 2H, $-OCH_2$), 6.53 (d, J = 8.7 Hz, 1H, −ArH), 7.31−7.37 (m, 2H, −ArH); 7.65 (s, 1H, H^6); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.4, 24.1, 26.0, 27.6, 39.9, 51.1, 65.3, 66.6, 68.8, 69.9, 75.1, 102.4, 110.6, 117.7, 121.3, 124.6, 130.4, 131.4, 134.2, 141.7, 175.5; HRMS calcd for $C_{28}H_{30}FeN_4O_3$ $[M]^+$ m/z 526.1080, found 526.1077. Anal. Calcd: C, 63.88; H, 5.70; N, 10.65. Found: C, 63.81; H, 5.82; N, 10.74.

1′-(2-(4-Ferrocenyl-1H-1,2,3-triazol-1-yl)hexyl)spiro[[1,3]-dioxolane-2,3′-indolin]-2′-one (**10q**): yield 87%; Brown Solid; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.38−1.48 (m, 4H, H^3 + H^4), 1.51−1.68 (m, 2H, H^2), 1.75−1.83 (m, 2H, H^5), 3.21 (t, J = 6.3 Hz, 2H, H^1), 4.03 (s, 5H, H^{10}), 4.21−4.29 (m, 4H, H^6 + H^9), 4.41−4.46 (m, 2H, $-OCH_2$), 4.51 (s, 2H, H^8), 4.64−4.69 (m, 2H, $-OCH_2$), 6.74−6.81 (d, J = 8.4 Hz,, 1H, −ArH), 7.04−7.11 (m, 1H, −ArH), 7.31−7.42 (m, 2H, −ArH), 7.45 (s, 1H, H^7); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.2, 26.3, 27.4, 28.1, 40.0, 51.1, 65.3, 66.7, 68.4, 69.8, 75.4, 102.4, 108.5, 118.5, 123.7, 123.9, 124.6, 131.8, 143.6, 173.5; HRMS calcd for $C_{28}H_{30}FeN_4O_3$ $[M]^+$ m/z 526.1184, found 526.1188. Anal. Calcd: C, 63.88; H, 5.70; N, 10.65. Found: C, 63.82; H, 5.74; N, 10.79.

5′-Fluoro-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)hexyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10r**): yield 87%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.33−1.41 (m, 4H, H^3 + H^4), 1.52−1.63 (m, 2H, H^2), 1.73−1.80 (m, 2H, H^5), 3.20 (t, J = 6.0 Hz, 2H, H^1), 4.05 (s, 5H, H^{10}), 4.22−4.28 (m, 4H, H^6 + H^9), 4.39−4.45 (m, 2H, $-OCH_2$), 4.56 (s, 2H, H^8), 4.65−4.69 (m, 2H, $-OCH_2$), 6.77−6.86 (m, 1H, −ArH), 7.07−7.14 (m, 2H, −ArH), 7.42 (s, 1H, H^7); ^{13}C

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NMR ($CDCl_3$, 75 MHz) δ 26.3, 26.5, 27.2, 28.0, 40.4, 51.5, 65.2, 66.4, 68.6, 69.7, 75.5, 101.2, 109.6, 112.6, 117.8, 125.4, 130.2, 134.7, 139.6, 157.2, 173.4; HRMS calcd for $C_{28}H_{29}FFeN_4O_3$ $[M + H]^+$ m/z 545.1170, found 545.1175. Anal. Calcd: C, 61.76; H, 5.33; N, 10.29. Found: C, 61.56; H, 5.21; N, 10.42.

*5′-Chloro-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)hexyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10s**):* yield 84%; dark brown oil; NMR ($CDCl_3$, 300 MHz) δ 1.37−1.48 (m, 4H, H^3 + H^4), 1.51−1.66 (m, 2H, H^2), 1.71−1.83 (m, 2H, H^5), 3.18 (t, J = 6.3 Hz, 2H, H^1), 4.03 (s, 5H, H^{10}), 4.22−4.29 (m, 4H, H^6 + H^9), 4.43−4.49 (m, 2H, $-OCH_2$), 4.58 (s, 2H, H^8), 4.63−4.70 (m, 2H, $-OCH_2$), 6.82−6.91 (m, 1H, −ArH), 7.33−7.38 (m, 2H, −ArH), 7.63 (s, 1H, H^7); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.4, 26.6, 27.4, 28.2, 40.5, 51.7, 65.1, 66.6, 68.7, 69.9, 75.4, 102.5, 110.8, 113.6, 123.7, 124.5, 130.7, 134.2, 137.6, 141.6, 173.4; HRMS calcd for $C_{28}H_{29}ClFeN_4O_3$ $[M]^+$ m/z 560.1284, found 560.1288. Anal. Calcd: C, 60.00; H, 5.18; N, 10.00. Found: C, 59.92; H, 5.17; N, 10.11.

*5′-Methyl-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)hexyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10t**):* yield 89%; dark brown oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.33−1.44 (m, 4H, H^3 + H^4), 1.52−1.63 (m, 2H, H^2), 1.74−1.80 (m, 2H, H^5), 2.21 (s, 3H, $-CH_3$), 3.20 (t, J = 6.9 Hz, 2H, H^1), 4.00 (s, 5H, H^{10}), 4.21−4.26 (m, 4H, H^6 + H^9), 4.47−4.51 (m, 2H, $-OCH_2$), 4.54 (s, 2H, H^8), 4.66−4.72 (m, 2H, $-OCH_2$), 6.57 (d, J = 8.1 Hz, 1H, −ArH), 7.30−7.39 (m, 2H, −ArH), 7.64 (s, 1H, H^7); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 26.2, 26.4, 27.5, 28.1, 40.3, 51.8, 65.0, 66.8, 68.3, 69.8, 75.3, 102.5, 110.3, 117.5, 121.4, 124.8, 130.7, 131.3, 134.8, 141.8, 175.2; HRMS calcd for $C_{29}H_{32}FeN_4O_3$ $[M]^+$ m/z 540.1510, found 540.1516. Anal. Calcd: C, 64.44; H, 5.93; N, 10.37. Found: C, 64.54; H, 5.99; N, 10.25.

*1′-(2-(4-Ferrocenyl-1H-1,2,3-triazol-1-yl)octyl)spiro[[1,3]-dioxolane-2,3′-indolin]-2′-one (**10u**):* yield 94%; dark brown oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.31−1.45 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.49−1.59 (m, 2H, H^2), 1.67−1.76 (s, 2H, H^7), 3.25 (t, J = 5.7 Hz, 2H, H^1), 4.01 (s, 5H, H^{12}), 4.19−4.28 (m, 4H, H^8 + H^{11}), 4.45−4.51 (m, 2H, $-OCH_2$), 4.54 (s, 2H, H^{10}), 4.60−4.64 (m, 2H, $-OCH_2$), 6.76−6.82 (d, J = 8.1 Hz, 1H, −ArH), 7.01−7.09 (m, 1H, −ArH), 7.29−7.39 (m, 2H, −ArH), 7.46 (s, 1H, H^9); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.2, 26.5, 26.6, 28.7, 28.8, 29.3, 40.1, 50.7, 65.1, 66.1, 68.5, 69.4, 75.5, 102.1, 108.6, 118.2, 123.5, 123.9, 124.7, 131.6, 143.0, 173.4; HRMS calcd for $C_{30}H_{34}FeN_4O_3$ $[M + H]^+$ m/z 555.1273, found 555.1271. Anal. Calcd: C, 64.98; H, 6.14; N, 10.11. Found: C, 65.07; H, 6.20; N, 10.03.

*5′-Fluoro-1′-(2-(4-Ferrocenyl-1H-1,2,3-triazol-1-yl)octyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10v**):* yield 89%; dark brown oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.27−1.39 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.44−1.55 (m, 2H, H^2), 1.66−1.77 (s, 2H, H^7), 3.21 (t, J = 5.4 Hz, 2H, H^1), 4.05 (s, 5H, H^{12}), 4.18−4.25 (m, 4H, H^8 + H^{11}), 4.43−4.48 (m, 2H, $-OCH_2$), 4.55 (s, 2H, H^{10}), 4.59−4.66 (m, 2H, $-OCH_2$), 6.75−6.85 (m, 1H, −ArH), 7.05−7.11 (m, 2H, −ArH), 7.46 (s, 1H, H^9); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.0, 26.4, 26.5, 28.6, 28.9, 29.0, 40.2, 50.5, 65.5, 66.6, 68.3, 69.6, 75.6, 101.4, 109.7, 112.5, 117.7, 125.7, 130.0, 134.6, 139.3, 157.5, 173.8; HRMS calcd for $C_{30}H_{33}FFeN_4O_3$ $[M]^+$ m/z 572.1291, found 572.1287. Anal. Calcd: C, 62.94; H, 5.77; N, 9.79. Found: C, 63.04; H, 5.84; N, 9.68.

*5′-Chloro-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)octyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10w**):* yield 90%; dark brown oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.24−1.38 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.41−1.55 (m, 2H, H^2), 1.63−1.76 (s, 2H, H^7), 3.27 (t, J = 5.7 Hz, 2H, H^1), 4.02 (s, 5H, H^{12}), 4.20−4.29 (m, 4H, H^8 + H^{11}), 4.45−4.53 (m, 2H, $-OCH_2$), 4.58 (s, 2H, H^{10}), 4.61−4.65 (m, 2H, $-OCH_2$), 6.84−6.93 (m, 1H, −ArH), 7.30−7.39 (m, 2H, −ArH), 7.65 (s, 1H, H^9); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.2, 26.3, 26.6, 28.7, 28.8, 29.1, 40.4, 50.8, 65.2, 66.2, 68.7, 69.3, 75.8, 102.1, 110.3, 113.9, 123.3, 124.9, 130.6, 1341, 137.4, 141.8, 173.6; HRMS calcd for $C_{30}H_{33}ClFeN_4O_3$ $[M]^+$ m/z 588.0280, found 588.0278. Anal. Calcd: C, 61.22; H, 5.61; N, 9.52. Found: C, 61.14; H, 5.55; N, 9.48.

*5′-Methyl-1′-(2-(4-ferrocenyl-1H-1,2,3-triazol-1-yl)octyl)spiro-[[1,3]dioxolane-2,3′-indolin]-2′-one (**10x**):* yield 80%; dark brown oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.21−1.35 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.43−1.58 (m, 2H, H^2), 1.62−1.74 (s, 2H, H^7), 2.24 (s, 3H, $-CH_3$), 3.23 (t, J = 5.4 Hz, 2H, H^1), 4.04 (s, 5H, H^{12}), 4.19−4.28 (m, 4H, H^8 + H^{11}), 4.43−4.47 (m, 2H, $-OCH_2$), 4.59 (s, 2H, H^{10}), 4.62−4.69 (m, 2H, $-OCH_2$), 6.59 (d, J = 8.4 Hz, 1H, −ArH), 7.33−7.38 (m, 2H, −ArH), 7.61 (s, 1H, H^9); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 26.1, 26.2, 26.7, 28.8, 28.9, 29.5, 40.8, 50.7, 65.1, 66.4, 68.4, 69.1, 75.5, 102.4, 110.5, 117.6, 121.4, 124.3, 130.1, 131.6, 134.9, 141.4, 175.6; HRMS calcd for $C_{31}H_{36}FeN_4O_3$ $[M]^+$ m/z 568.0418, found 568.0413. Anal. Calcd: C, 65.49; H, 6.34; N, 9.86. Found: C, 65.38; H, 6.45; N, 9.93.

*1-(4-Azidobutyl)-1H-indole-2,3-dione (**11a**):* yield 83%; red oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.75−1.85 (m, 4H, H^2 + H^3), 3.36 (t, J = 5.7 Hz, 2H, H^1), 3.61 (t, J = 6.3 Hz, 2H, H^4), 6.77−6.82 (m, 1H, −ArH), 7.02−7.10 (m, 1H, −ArH), 7.27−7.35 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.6, 29.3, 37.0, 48.7, 118.6, 123.4, 128.5, 130.7, 131.5, 138.3, 158.6, 183.5; HRMS calcd for $C_{12}H_{12}N_4O_2$ $[M]^+$ m/z 244.0960, found 244.0954. Anal. Calcd: C, 59.01; H, 4.95; N, 22.94. Found: C, 58.96; H, 4.88; N, 23.03.

*1-(4-Azidobutyl)-5-fluoro-1H-indole-2,3-dione (**11b**):* yield 82%; red oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.71−1.83 (m, 4H, H^2 + H^3), 3.33 (t, J = 6.6 Hz, 2H, H^1), 3.59 (t, J = 6.9 Hz, 2H, H^4), 6.78−6.85 (m, 1H, −ArH), 7.29−7.34 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.6, 29.7, 36.8, 48.3, 111.5, 118.5, 125.7, 129.7, 137.4, 149.6, 158.6, 182.8; HRMS calcd for $C_{12}H_{11}FN_4O_2$ $[M]^+$ m/z 262.0899, found 262.0892. Anal. Calcd: C, 54.96; H, 4.23; N, 21.36. Found: C, 55.03; H, 4.28; N, 21.42.

*1-(4-Azidobutyl)-5-chloro-1H-indole-2,3-dione (**11c**):* yield 85%; red oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.74−1.84 (m, 4H, H^2 + H^3), 3.34 (t, J = 5.7 Hz, 2H, H^1), 3.67 (t, J = 6.0 Hz, 2H, H^4), 6.76−6.79 (m, 1H, −ArH), 7.06−7.13 (m, 1H, −ArH), 7.32−7.38 (m, 1H, −ArH), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.4, 29.2, 36.4, 48.8, 110.6, 117.5, 121.7, 124.9, 146.3, 149.3, 158.3, 182.2; HRMS calcd for $C_{12}H_{11}ClN_4O_2$ $[M]^+$ m/z 278.0570, found 278.0573. Anal. Calcd: C, 51.72; H, 3.98; N, 21.10. Found: C, 51.69; H, 4.02; N, 21.18.

*1-(4-Azidobutyl)-5-methyl-1H-indole-2,3-dione (**11d**):* yield 83%; red oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.77−1.84 (m, 4H, H^2 + H^3), 2.22 (s, 3H, $-CH_3$), 3.36 (t, J = 6.0 Hz, 2H, H^1), 3.62 (t, J = 6.0 Hz, 2H, H^4), 6.67 (d, J = 8.1 Hz, 1H, −ArH), 7.27−7.37 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 26.7, 29.0, 36.5, 48.6, 111.5, 121.8, 124.8, 138.5, 146.4, 149.6, 158.6, 182.3; HRMS calcd for $C_{13}H_{14}N_4O_2$ $[M]^+$ m/z 258.1116, found 258.1113. Anal. Calcd: C, 60.45; H, 5.46; N, 21.69. Found: C, 60.37; H, 5.52; N, 21.63.

*1-(4-Azidopentyl)-1H-indole-2,3-dione (**11e**):* yield 81%; red oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.28−1.33 (m, 2H, H^3), 1.34−1.55 (m, 4H, H^2 + H^4), 3.21 (t, J = 6.0 Hz, 2H, H^1), 3.54 (t, J = 6.3 Hz, 2H, H^5), 6.77−6.84 (m, 1H, −ArH), 7.01−7.09 (m, 1H, −ArH), 7.29−7.35 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.1, 26.2, 27.4, 39.8, 51.3, 118.8, 123.3, 128.3, 130.1, 131.4, 138.4, 158.7, 183.1; HRMS calcd for $C_{13}H_{14}N_4O_2$ $[M]^+$ m/z 258.1116, found 258.1111. Anal. Calcd: C, 60.45; H, 5.46; N, 21.69. Found: C, 60.52; H, 5.50; N, 21.60.

*1-(4-Azidopentyl)-5-fluoro-1H-indole-2,3-dione (**11f**):* yield 88%; red oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.35−1.39 (m, 2H, H^3), 1.42−1.61 (m, 4H, H^2 + H^4), 3.16 (t, J = 6.0 Hz, 2H, H^1), 3.57 (t, J = 6.6 Hz, 2H, H^5), 6.73−6.81 (m, 1H, −ArH), 7.30−7.37 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.3, 26.6, 27.8, 39.9, 51.2, 111.8, 118.1, 125.5, 129.6, 137.8, 149.5, 158.5, 182.6; HRMS calcd for $C_{13}H_{13}FN_4O_2$ $[M]^+$ m/z 276.1022, found 276.1019. Anal. Calcd: C, 56.52; H, 4.74; N, 20.28. Found: C, 56.56; H, 4.72; N, 20.31.

*1-(4-Azidopentyl)-5-chloro-1H-indole-2,3-dione (**11g**):* yield 90%; red oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.25−1.33 (m, 2H, H^3), 1.38−1.59 (m, 4H, H^2 + H^4), 3.26 (t, J = 6.3 Hz, 2H, H^1), 3.55 (t, J = 6.3 Hz, 2H, H^5), 6.75−6.82 (m, 1H, −ArH), 7.09−7.14 (m, 1H, −ArH), 7.30−7.37 (m, 1H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.1, 26.3, 27.6, 39.7, 51.4, 110.9, 117.2, 121.5, 124.8, 146.1, 149.0, 158.6, 182.8; HRMS calcd for $C_{13}H_{13}ClN_4O_2$ $[M]^+$ m/z 292.0727, found 292.0721. Anal. Calcd: C, 53.34; H, 4.48; N, 19.14. Found: C, 53.26; H, 4.50; N, 19.09.

*1-(4-Azidopentyl)-5-methyl-1H-indole-2,3-dione (**11h**):* yield 81%; red oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.28−1.35 (m, 2H, H^3), 1.45−1.53 (m, 4H, H^2 + H^4), 2.24, (s, 3H, $-CH_3$), 3.19 (t, J = 6.9 Hz, 2H,

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H^1), 3.58 (t, J = 6.0 Hz, 2H, H^5), 6.64 (d, J = 8.4 Hz, 1H, −ArH), 7.29−7.38 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 24.4, 26.5, 27.2, 39.5, 51.3, 111.3, 121.7, 124.9, 138.2, 146.3, 149.2, 158.3, 182.5; HRMS calcd for $C_{14}H_{16}N_4O_2$ $[M]^+$ m/z 272.1273, found 272.1267. Anal. Calcd: C, 61.75; H, 5.92; N, 20.58. Found: C, 61.81; H, 5.99; N, 20.50.

*1-(4-Azidohexyl)-1H-indole-2,3-dione (**11i**):* yield 88%; red oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.43−1.48 (m, 4H, H^3 + H^4), 1.52−1.65 (m, 2H, H^2), 1.69−1.75 (m, 2H, H^5), 3.23 (t, J = 6.0 Hz, 2H, H^1), 3.74 (t, J = 6.6 Hz, 2H, H^6), 6.71−6.78 (m, 1H, −ArH), 7.06−7.15 (m, 1H, −ArH), 7.29−7.36 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.2, 26.3, 27.5, 28.1, 40.6, 51.5, 118.7, 123.1, 128.1, 130.4, 131.7, 138.2, 158.5, 183.3; HRMS calcd for $C_{14}H_{16}N_4O_2$ $[M]^+$ m/z 272.1273, found 272.1269. Anal. Calcd: C, 61.75; H, 5.92; N, 20.58. Found: C, 61.81; H, 5.89; N, 20.64.

*1-(4-Azidohexyl)-5-fluoro-1H-indole-2,3-dione (**11j**):* yield 92%; red oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.43−1.59 (m, 4H, H^3 + H^4), 1.60−1.62 (m, 2H, H^2), 1.70−1.74 (m, 2H, H^5), 3.27 (t, J = 6.3 Hz, 2H, H^1), 3.73 (t, J = 6.3 Hz, 2H, H^6), 6.86−6.90 (m, 1H, −ArH), 7.29−7.32 (m, 1H, −ArH), 7.55−7.57 (m, 1H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.2, 26.3, 27.0, 28.6, 40.1, 51.2, 111.1, 118.4, 125.3, 129.5, 137.6, 149.1, 157.6, 182.5; HRMS calcd for $C_{14}H_{15}FN_4O_2$ $[M]^+$ m/z 290.1179, found 290.1187. Anal. Calcd: C, 57.92; H, 5.21; N, 19.30. Found: C, 57.97; H, 5.15; N, 19.24.

*1-(4-Azidohexyl)-5-chloro-1H-indole-2,3-dione (**11k**):* yield 82%; red oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.34−1.46 (m, 4H, H^3 + H^4), 1.51−1.60 (m, 2H, H^2), 1.71−1.83 (m, 2H, H^5), 3.27 (t, J = 5.7 Hz, 2H, H^1), 3.66 (t, J = 6.3 Hz, 2H, H^6), 6.69−6.75 (m, 1H, −ArH), 7.03−7.12 (m, 1H, −ArH), 7.28−7.38 (m, 1H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.2, 26.6, 27.6, 28.5, 40.2, 51.0, 110.5, 117.3, 121.7, 124.5, 146.3, 149.3, 158.1, 182.5; HRMS calcd for $C_{14}H_{15}ClN_4O_2$ $[M]^+$ m/z 306.0854, found 306.0848. Anal. Calcd: C, 54.82; H, 4.93; N, 18.26. Found: C, 54.79; H, 4.88; N, 18.31.

*1-(4-Azidohexyl)-5-methyl-1H-indole-2,3-dione (**11l**):* yield 87%; red oil; ^{1}H NMR ($CDCl_3$, 300 MHz):δ 1.43−1.48 (m, 4H, H^3 + H^4), 1.53−1.59 (m, 2H, H^2), 1.75−1.79 (m, 2H, H^5), 2.22 (s, 3H, $-CH_3$), 3.27 (t, J = 6.0 Hz, 2H, H^1), 3.69 (t, J = 6.3 Hz, 2H, H^6), 6.66 (d, J = 8.1 Hz, 1H, −ArH), 7.30−7.39 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 26.6, 26.8, 27.3, 28.6, 40.8, 51.4, 111.7, 121.4, 124.5, 138.5, 146.4, 149.0, 158.6, 182.8; HRMS calcd for $C_{15}H_{18}N_4O_2$ $[M]^+$ m/z 286.1429, found 286.1422. Anal. Calcd: C, 62.92; H, 6.34; N, 19.57. Found: C, 62.87; H, 6.31; N, 19.55.

*1-(4-Azidooctyl)-1H-indole-2,3-dione (**11m**):* yield 91%; red oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.33−1.46 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.51−1.56 (m, 2H, H^2), 1.65−1.78 (m, 2H, H^7), 3.24 (t, J = 6.6 Hz, 2H, H^1), 3.66 (t, J = 5.7 Hz, 2H, H^8), 6.73−6.79 (m, 1H, −ArH), 7.02−7.07 (m, 1H, −ArH), 7.30−7.38 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.0, 26.3, 26.6, 28.7, 28.9, 29.1, 40.2, 50.8, 118.8, 123.0, 128.2, 130.6, 131.8, 138.3, 158.7, 183.7; HRMS calcd for $C_{16}H_{20}N_4O_2$ $[M]^+$ m/z 300.1586, found 300.1592. Anal. Calcd: C, 63.98; H, 6.71; N, 18.65. Found: C, 64.02; H, 6.67; N, 18.59.

*1-(4-Azidooctyl)-5-fluoro-1H-indole-2,3-dione (**11n**):* yield 88%; red oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.27−1.40 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.42−1.53 (m, 2H, H^2), 1.63−1.70 (m, 2H, H^7), 3.21 (t, J = 6.9 Hz, 2H, H^1), 3.66 (t, J = 6.6 Hz, 2H, H^8), 6.85−6.89 (m, 1H, −ArH), 7.29−7.33 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.0, 26.4, 26.9, 28.3, 28.7, 29.1, 40.7, 50.8, 111.1, 118.2, 125.6, 129.4, 137.2, 149.8, 157.6, 182.6; HRMS calcd for $C_{16}H_{19}FN_4O_2$ $[M]^+$ m/z 318.1525, found 318.1523. Anal. Calcd: C, 60.37; H, 6.02; N, 17.60. Found: C, 60.43; H, 5.99; N, 17.62.

*1-(4-Azidooctyl)-5-chloro-1H-indole-2,3-dione (**11o**):* yield 93%; red oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.31−1.44 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.47−1.54 (m, 2H, H^2), 1.66−1.72 (m, 2H, H^7), 3.24 (t, J = 6.9 Hz, 2H, H^1), 3.62 (t, J = 6.6 Hz, 2H, H^8), 6.67−6.74 (m, 1H, −ArH), 7.05−7.12 (m, 1H, −ArH), 7.27−7.34 (m, 1H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.1, 26.4, 26.6, 28.3, 28.5, 29.7, 40.2, 50.7, 110.7, 117.8, 121.3, 124.8, 146.2, 149.5, 158.4, 182.3; HRMS calcd for $C_{16}H_{19}ClN_4O_2$ $[M]^+$ m/z 334.1196, found 334.1188. Anal. Calcd: C, 57.40; H, 5.72; N, 16.73. Found: C, 57.47; H, 5.66; N, 16.69.

*1-(4-Azidooctyl)-5-methyl-1H-indole-2,3-dione (**11p**):* yield 91%; red oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.32−1.42 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.44−1.56 (m, 2H, H^2), 1.63−1.77 (m, 2H, H^7), 2.20 (s, 3H, $-CH_3$), 3.25 (t, J = 6.3 Hz, 2H, H^1), 3.66 (t, J = 6.6 Hz, 2H, H^8), 6.67 (d, J = 8.1 Hz, 1H, −ArH), 7.31−7.38 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 26.5, 26.7, 26.9, 28.2, 28.7, 29.5, 40.3, 50.8, 111.5, 121.7, 124.8, 138.4, 146.7, 149.2, 158.3, 182.7; HRMS calcd for $C_{17}H_{22}N_4O_2$ $[M]^+$ m/z 314.1742, found 314.1738. Anal. Calcd: C, 64.95; H, 7.05; N, 17.82. Found: C, 64.91; H, 7.08; N, 17.77.

*1-[2-(4-Ferrocenyl-[1,2,3]triazol-1-yl)butyl]-1H-indole-2,3-dione (**12a**):* yield 88%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.73−1.80 (m, 2H, H^2), 2.01−2.05 (m, 2H, H^3), 3.78 (t, J = 6.9 Hz, 2H, H^1), 4.05 (s, 5H, H^8), 4.30 (s, 2H, H^7), 4.45 (t, J = 6.9 Hz, 2H, H^4), 4.71 (s, 2H, H^6), 6.87−6.89 (m, 1H, −ArH), 7.08−7.14 (m, 1H, −ArH), 7.47 (s, 1H, H^5), 7.56−7.61 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.9, 27.3, 39.1, 49.1, 66.6, 68.7, 69.5, 75.3, 110.0, 117.4, 118.8, 123.4, 124.9, 131.7, 138.5, 150.4, 158.3, 183.1; HRMS calcd for $C_{24}H_{22}FeN_4O_2$ $[M + H]^+$ m/z 455.1165, found 455.1181. Anal. Calcd: C, 63.44; H, 4.85; N, 12.33. Found: C, 63.54; H, 4.92; N, 12.25.

*1-[2-(4-Ferrocenyl-[1,2,3]triazol-1-yl)butyl]-5-fluoro-1H-indole-2,3-dione (**12b**):* yield 81%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.70−185 (m, 2H, H^2), 2.04−2.10 (m, 2H, H^3), 3.69 (t, J = 6.6 Hz, 2H, H^1), 4.01 (s, 5H, H^8), 4.48 (s, 2H, H^7), 4.60 (t, J = 6.6 Hz, 2H, H^4), 4.74 (s, 2H, H^6), 6.79−6.85 (m, 1H, −ArH), 7.29−7.33 (m, 2H, −ArH), 7.48 (s, 1H, H^5); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.3, 29.5, 36.6, 39.4, 65.7, 68.2, 69.5, 72.2, 111.5, 112.7, 124.1, 125.8, 132.7, 136.4, 146.5, 157.3, 159.7, 182.8; HRMS calcd for $C_{24}H_{21}FFeN_4O_2$ $[M]^+$ m/z 472.0710, found 472.0716. Anal. Calcd: C, 61.02; H, 4.45; N, 11.86. Found: C, 60.90; H, 4.32; N, 11.98.

*5-Chloro-1-[2-(4-ferrocenyl-[1,2,3]triazol-1-yl)butyl]-1H-indole-2,3-dione (**12c**):* yield 81%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.73−1.85 (m, 4H, H^2 + H^3), 3.31 (t, J = 6.3 Hz, 2H, H^1), 3.64 (t, J = 5.7 Hz, 2H, H^4), 4.01 (s, 5H, H^8), 4.60 (s, 2H, H^7), 4.77 (s, 2H, H^6), 6.91−6.96 (m, 1H, −ArH), 7.29−7.37 (m, 2H, −ArH), 7.60 (s, 1H, H^5); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.5, 26.6, 36.3, 39.7, 66.4, 68.4, 69.7, 75.3, 110.4, 117.5, 121.8, 124.9, 132.8, 138.9, 146.3, 149.1, 158.6, 182.5; HRMS calcd for $C_{24}H_{21}ClFeN_4O_2$ $[M]^+$ m/z 488.1248, found 488.1253. Anal. Calcd: C, 59.02; H, 4.30; N, 11.48. Found: C, 58.92; H, 4.18; N, 11.56.

*1-[2-(4-Ferrocenyl-[1,2,3]triazol-1-yl)butyl]-5-methyl-1H-indole-2,3-dione (**12d**):* yield 75%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ1.73−183 (m, 2H, H^2), 2.00−2.08 (m, 2H, H^3), 2.21 (s, 3H, $-CH_3$), 3.64 (t, J = 6.0 Hz, 2H, H^1), 4.07 (s, 5H, H^8), 4.45 (s, 2H, H^7), 4.61 (t, J = 6.0 Hz, 2H, H^4), 4.70 (s, 2H, H^6), 6.60 (d, J = 8.4 Hz, 1H, −ArH), 7.30−7.37 (m, 2H, −ArH), 7.41 (s, 1H, H^5);^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 24.4, 26.7, 36.3, 39.5, 66.6, 68.3, 69.2, 75.5, 110.7, 117.8, 121.8, 124.9, 132.8, 138.7, 146.4, 149.5, 158.7, 182.2; HRMS calcd for $C_{25}H_{24}FeN_4O_2$ $[M]^+$ m/z 468.0624, found 468.0616. Anal. Calcd: C, 64.10; H, 5.13; N, 11.97. Found: C, 63.97; H, 5.06; N, 11.95.

*1-[2-(4-Ferrocenyl-[1,2,3]triazol-1-yl)pentyl]-1H-indole-2,3-dione (**12e**):* yield 79%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25−1.33 (m, 2H, H^3), 1.73−1.77 (m, 2H, H^2), 2.01−2.09 (m, 2H, H^4), 3.77 (t, J = 6.3 Hz, 2H, H^1), 4.06 (s, 5H, H^9), 4.30 (s, 2H, H^8), 4.45 (t, J = 6.3 Hz, 2H, H^5), 4.71 (s, 2H, H^7), 6.86−6.89 (m, 1H, −ArH), 7.08−7.13 (m, 1H, −ArH), 7.47 (s, 1H, H^6), 7.56−7.60 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.5, 26.1, 27.7, 39.4, 51.8, 66.8, 68.6, 69.8, 75.5, 110.4, 117.3, 118.7, 123.5, 124.6, 131.9, 138.2, 150.1, 158.0, 183.3; HRMS calcd for $C_{25}H_{24}FeN_4O_2$ $[M]^+$ m/z 468.1639, found 468.1631. Anal. Calcd: C, 64.10; H, 5.13; N, 11.97. Found: C, 64.23; H, 5.24; N, 11.86.

*1-[2-(4-Ferrocenyl-[1,2,3]triazol-1-yl)pentyl]-5-fluoro-1H-indole-2,3-dione (**12f**):* yield 85%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.28−1.35 (m, 2H, H^3), 1.71−1.79 (m, 2H, H^2), 2.01−2.11 (m, 2H, H^4), 3.70 (t, J = 5.7 Hz, 2H, H^1), 4.03 (s, 5H, H^9), 4.27 (s, 2H, H^8), 4.46 (t, J = 5.7 Hz, 2H, H^5), 4.67 (s, 2H, H^7), 6.74−6.83 (m, 1H, −ArH), 7.32−7.39 (m, 2H, −ArH), 7.50 (s, 1H, H^6); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.2, 26.6, 27.8, 39.1, 51.5, 66.6, 68.9, 69.7, 75.3, 111.3, 112.8, 124.0, 125.5, 132.9, 136.2, 146.6, 157.1, 159.6, 182.4;

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HRMS calcd for $C_{25}H_{23}FFeN_4O_2$ $[M]^+$ m/z 486.1482, found 486.1475. Anal. Calcd: C, 61.73; H, 4.73; N, 11.52. Found: C, 61.86; H, 4.85; N, 11.42.

*5-Chloro-1-[2-(4-ferrocenyl-[1,2,3]triazol-1-yl)pentyl]-1H-indole-2,3-dione (**12g**):* yield 83%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25−1.34 (m, 2H, H^3), 1.73−1.81 (m, 2H, H^2), 2.04−2.10 (m, 2H, H^4), 3.70 (t, J = 6.3 Hz, 2H, H^1), 4.04 (s, 5H, H^9), 4.27 (s, 2H, H^8), 4.49 (t, J = 6.3 Hz, 2H, H^5), 4.69 (s, 2H, H^7), 6.93−6.99 (m, 1H, −ArH), 7.30−7.39 (m, 2H, −ArH), 7.64 (s, 1H, H^6); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.4, 26.6, 27.3, 39.2, 51.4,, 66.3, 68.6, 69.2, 75.1, 110.1, 117.8, 121.4, 124.7, 135.6, 138.7, 146.1, 149.4, 158.3, 182.4; HRMS calcd for $C_{25}H_{23}ClFeN_4O_2$ $[M]^+$ m/z 502.1261, found 502.1268. Anal. Calcd: C, 59.76; H, 4.58; N, 11.16. Found: C, 59.85; H, 4.67; N, 11.04.

*1-[2-(4-Ferrocenyl-[1,2,3]triazol-1-yl)pentyl]-5-methyl-1H-indole-2,3-dione (**12h**):* yield 78%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.21−1.34 (m, 2H, H^3), 1.76−1.88 (m, 2H, H^2), 2.01−2.09 (m, 2H, H^4), 2.23 (s, 2H, $-CH_3$), 3.68 (t, J = 5.4 Hz, 2H, H^1), 4.02 (s, 5H, H^9), 4.27 (s, 2H, H^8), 4.45 (t, J = 5.4 Hz, 2H, H^5), 4.71 (s, 2H, H^7), 6.55 (d, J = 8.1 Hz, 1H, −ArH), 7.29−7.39 (m, 2H, −ArH), 7.48 (s, 1H, H^6); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.2, 24.4, 26.8, 27.4, 39.1, 51.8, 66.1, 68.3, 69.6, 75.2, 110.5, 117.4, 121.3, 124.7, 132.5, 138.6, 146.7, 149.4, 158.5, 182.6; HRMS calcd for $C_{26}H_{26}FeN_4O_2$ $[M]^+$ m/z 482.0736, found 482.0742. Anal. Calcd: C, 64.73; H, 5.39; N, 11.62. Found: C, 64.63; H, 5.31; N, 11.51.

*1-[2-(4-Ferrocenyl-[1,2,3]triazol-1-yl)hexyl]-1H-indole-2,3-dione (**12i**):* yield 82%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.29−1.38 (m, 4H, H^3 + H^4), 1.63−1.68 (m, 2H, H^2), 1.88−1.94 (m, 2H, H^5), 3.76 (t, J = 6.6 Hz, 2H, H^1), 4.04 (s, 5H, H^{10}), 4.29 (s, 2H, H^9), 4.39 (t, J = 6.3 Hz, 2H, H^6), 4.73 (s, 2H, H^8), 6.84−6.88 (m, 1H, −ArH), 7.03−7.11 (m, 1H, −ArH), 7.49 (s, 1H, H^7), 7.54−7.59 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.1, 26.2, 27.5, 28.7, 40.5, 51.2, 66.3, 68.2, 69.7, 75.2, 110.0, 117.6, 118.9, 123.3, 124.4, 131.8, 138.5, 149.7, 158.4, 182.2; HRMS calcd for $C_{26}H_{26}FeN_4O_2$ $[M]^+$ m/z 482.0581, found 482.0577. Anal. Calcd: C, 64.73; H, 5.39; N, 11.62. Found: C, 64.66; H, 5.30; N, 11.73.

*1-[2-(4-Ferrocenyl-[1,2,3]triazol-1-yl)hexyl]-5-fluoro-1H-indole-2,3-dione (**12j**):* yield 80%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25−1.36 (m, 4H, H^3 + H^4), 1.60−1.69 (m, 2H, H^2), 1.94−2.03 (m, 2H, H^5), 3.67 (t, J = 5.7 Hz, 2H, H^1), 4.01 (s, 5H, H^{10}), 4.34 (s, 2H, H^9), 4.41 (t, J = 5.7 Hz, 2H, H^6), 4.70 (s, 2H, H^8), 6.76−6.81 (m, 1H, −ArH), 7.30−7.38 (m, 2H, −ArH), 7.41 (s, 1H, H^7); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.0, 26.3, 27.2, 28.5, 40.4, 51.3, 66.0, 68.1, 69.5, 75.4, 111.1, 112.5, 124.4, 125.8, 132.6, 136.4, 146.8, 157.3, 159.4, 182.5; HRMS calcd for $C_{26}H_{25}FFeN_4O_2$ $[M + H]^+$ m/z 501.0483, found 501.0479. Anal. Calcd: C, 62.40; H, 5.00; N, 11.20. Found: C, 62.49; H, 5.11; N, 11.12.

*5-Chloro-1-[2-(4-ferrocenyl-[1,2,3]triazol-1-yl)hexyl]-1H-indole-2,3-dione (**12k**):* yield 76%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.31−1.38 (m, 4H, H^3 + H^4), 1.62−1.69 (m, 2H, H^2), 1.90−1.98 (m, 2H, H^5), 3.69 (t, J = 6.9 Hz, 2H, H^1), 4.05 (s, 5H, H^{10}), 4.33 (s, 2H, H^9), 4.41 (t, J = 6.9 Hz, 2H, H^6), 4.72 (s, 2H, H^8), 6.84−6.92 (m, 1H, −ArH), 7.29−7.38 (m, 2H, −ArH), 7.62 (s, 1H, H^7); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.3, 26.8, 27.3, 28.5, 40.2, 51.4, 66.5, 68.9, 69.8, 75.1, 110.5, 117.3, 121.2, 124.4, 135.8, 138.2, 146.0, 149.3, 158.4, 182.5; HRMS calcd for $C_{26}H_{25}ClFeN_4O_2$ $[M]^+$ m/z 516.0530, found 516.0522. Anal. Calcd: C, 60.47; H, 4.84; N, 10.85. Found: C, 60.57; H, 4.90; N, 10.76.

*1-[2-(4-Ferrocenyl-[1,2,3]triazol-1-yl)hexyl]-5-methyl-1H-indole-2,3-dione (**12l**):* yield 83%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.33−1.39 (m, 4H, H^3 + H^4), 1.61−1.73 (m, 2H, H^2), 1.90−1.97 (m, 2H, H^5), 2.20 (s, 3H, $-CH_3$), 3.69 (t, J = 6.3 Hz, 2H, H^1), 4.07 (s, 5H, H^{10}), 4.30 (s, 2H, H^9), 4.31 (t, J = 6.3 Hz, 2H, H^6), 4.69 (s, 2H, H^8), 6.56 (d, J = 8.7 Hz, 1H, −ArH), 7.32−7.38 (m, 2H, −ArH), 7.48 (s, 1H, H^7);^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.1, 26.2, 26.7, 27.6, 28.5, 40.4, 51.7, 66.3, 68.1, 69.8, 75.5, 110.1, 117.7, 121.5, 124.9, 132.2, 138.7, 146.8, 149.6, 158.4, 182.3; HRMS calcd for $C_{27}H_{28}FeN_4O_2$ $[M]^+$ m/z 496.1483, found 496.1474. Anal. Calcd: C, 65.32; H, 5.65; N, 11.29. Found: C, 65.40; H, 5.72; N, 11.51.

*1-[2-(4-Ferrocenyl-[1,2,3]triazol-1-yl)octyl]-1H-indole-2,3-dione (**12m**):* yield 75%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.27−1.39 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.67 (s, 2H, H^2), 1.95 (s, 2H, H^7), 3.63 (t, J = 6.0 Hz, 2H, H^1), 4.01 (s, 5H, H^{12}), 4.31 (s, 2H, H^{11}), 4.38 (t, J = 6.0 Hz, 2H, H^8), 4.69 (s, 2H, H^{10}), 6.80−6.87 (m, 1H, −ArH), 7.06−7.14 (m, 1H, −ArH), 7.45 (s, 1H, H^9), 7.53−7.61 (m, 2H, −ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.2, 26.6, 28.8, 28.9, 29.5, 30.3, 40.7, 50.0, 66.5, 68.7, 69.1, 75.4, 110.1, 117.3, 118.5, 123.6, 124.5, 131.7, 138.6, 149.4, 158.3, 182.7; HRMS calcd for $C_{28}H_{30}FeN_4O_2$ $[M]^+$ m/z 510.1483, found 510.1478. Anal. Calcd: C, 65.88; H, 5.88; N, 10.98. Found: C, 65.74; H, 5.73; N, 11.11.

*1-[2-(4-Ferrocenyl-[1,2,3]triazol-1-yl)octyl]-5-fluoro-1H-indole-2,3-dione (**12n**):* yield 88%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.26−1.33 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.66 (s, 2H, H^2), 1.91 (s, 2H, H^7), 3.68 (t, J = 6.9 Hz, 2H, H^1), 4.06 (s, 5H, H^{12}), 4.28 (s, 2H, H^{11}), 4.33 (t, J = 6.9 Hz, 2H, H^8), 4.72 (s, 2H, H^{10}), 6.81−6.86 (m, 1H, −ArH), 7.27−7.29 (m, 2H, −ArH), 7.46 (s, 1H, H^9); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.5, 27.0, 28.6, 28.8, 29.6, 30.0, 40.1, 50.1, 65.6, 68.6, 69.5, 75.4, 111.2, 112.2, 124.4, 124.7, 135.5, 136.8, 146.9, 157.8, 159.5, 182.9; HRMS calcd for $C_{28}H_{29}FFeN_4O_2$ $[M]^+$ m/z 528.1594, found 528.1587. Anal. Calcd: C, 63.64; H, 5.49; N, 10.61. Found: C, 63.59; H, 5.43; N, 10.75

*5-Chloro-1-[2-(4-ferrocenyl-[1,2,3]triazol-1-yl)octyl]-1H-indole-2,3-dione (**12o**):* yield 89%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.23−1.38 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.64 (s, 2H, H^2), 1.89 (s, 2H, H^7), 3.69 (t, J = 6.6 Hz, 2H, H^1), 4.07 (s, 5H, H^{12}), 4.27 (s, 2H, H^{11}), 4.35 (t, J = 6.6 Hz, 2H, H^8), 4.70 (s, 2H, H^{10}), 6.88−6.95 (m, 1H, −ArH), 7.31−7.37 (m, 2H, −ArH), 7.62 (s, 1H, H^9); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.5, 27.8, 28.2, 28.7, 29.4, 30.3, 40.1, 50.7, 66.2, 68.5, 69.7, 75.2, 110.2, 117.6, 121.7, 124.8, 135.3, 138.1, 145.6, 149.6, 158.9, 182.8; HRMS calcd for $C_{28}H_{29}ClFeN_4O_2$ $[M]^+$ m/z 544.1047, found 544.1041. Anal. Calcd: C, 61.76; H, 5.33; N, 10.29. Found: C, 61.65; H, 5.24; N, 10.40.

*1-[2-(4-Ferrocenyl-[1,2,3]triazol-1-yl)octyl]-5-methyl-1H-indole-2,3-dione (**12p**):* yield 75%; dark brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25−1.37 (m, 8H, H^3 + H^4 + H^5 + H^6), 1.61 (s, 2H, H^2), 1.93 (s, 2H, H^7), 2.24 (s, 3H, $-CH_3$), 3.70 (t, J = 6.0 Hz, 2H, H^1), 4.08 (s, 5H, H^{12}), 4.21 (s, 2H, H^{11}), 4.33 (t, J = 6.0 Hz, 2H, H^8), 4.68 (s, 2H, H^{10}), 6.55 (d, J = 7.5 Hz, 1H, −ArH), 7.30−7.39 (m, 2H, −ArH), 7.46 (s, 1H, H^9); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 26.3, 27.8, 28.4, 28.9, 29.5, 36.6, 40.8, 50.9, 66.0, 68.4, 69.5, 75.2, 110.6, 117.8, 121.1, 124.6, 132.8, 138.3, 146.4, 149.9, 158.7, 182.6; HRMS calcd for $C_{29}H_{32}FeN_4O_2$ $[M + H]^+$ m/z 525.0495, found 525.0488. Anal. Calcd: C, 66.41; H, 6.11; N, 10.69. Found: C, 66.34; H, 6.02; N, 10.73.

Bacterial Strains and Growth Conditions. *M. tuberculosis* mc^{2}7000, an unmarked version[40] of mc^{2}6230, was grown at 37 °C in Sauton's medium supplemented with 109 μM of pantothenic acid.

Drug Susceptibility Testing. The susceptibility of *M. tuberculosis* mc^{2}7000 to the various compounds was determined as reported previously.[41] In brief, Middlebrook 7H10 solid medium containing oleic-albumin-dextrose-catalase enrichment (OADC) and 109 μM of pantothenic acid was supplemented with increasing concentrations of the chemical analogues. Serial 10-fold dilutions of each actively growing culture were plated and incubated at 37 °C for 2−3 weeks. The MIC was defined as the minimum concentration required to inhibit 99% of the growth. All of the compounds were dissolved in DMSO to carry out the inhibition assay.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures giving ^{1}H and ^{13}C NMR spectra for the representative compounds **2a,b**, **8b,j,n**, **10a,e,i**, **11j**, and **12a,n** and a CIF file giving crystallographic data for **2b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ ABBREVIATIONS

TB, tuberculosis; MDR, multidrug resistant; XDR, extensively drug resistant; MIC, minimal inhibitory concentration; FQ, ferroquine; CQ, chloroquine

■ REFERENCES

(1) Zink, A. R.; Sola, C.; Reischl, U.; Grabner, W.; Rastogi, N.; Wolf, H.; Nerlich, A. G. *J. Clin. Microbiol.* **2003**, *41*, 359.

(2) Global Tuberculosis Report 2012; World Health Organisation: Geneva, Switzerland, 2012; http://apps.who.int/iris/bitstream/10665/75938/1/9789241564502_eng.pdf.

(3) Tuberculosis; Fact Sheet no. 104; World Health Organisation: Geneva, Switzerland, 2013; http://www.who.int/mediacentre/factsheets/fs104/en/index.html.

(4) Zhang, Y. *Annu. Rev. Pharmacol. Toxicol.* **2005**, *45*, 529.

(5) Jassal, M. S.; Bishai, W. R. *Clin. Infect. Dis.* **2010**, *50*, S156.

(6) Koul, A.; Arnoult, E.; Lounis, N.; Guillemont, J.; Andries, K. *Nature* **2011**, *469*, 483.

(7) FDA News Release; United States Food and Drug Administration: Silver Spring, MD, Dec 31, 2012; www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm333695.html.

(8) (a) Biot, C.; Castro, W.; Botte, C. Y.; Navarro, M. *Dalton Trans.* **2012**, *41*, 6335. (b) Hartinger, C. G.; Dyson, P. J. *Chem. Soc. Rev.* **2009**, *38*, 391. (c) Gasser, G.; Metzler-Nolte, N. *Curr. Opin. Chem. Biol.* **2012**, *16*, 84. (d) *Bioorganometallics: Biomolecules, Labeling, Medicine*; Jaouen, G., Ed.; Wiley-VCH: Weinheim, Germany, 2006.

(9) (a) Top, S.; Vessières, A.; Leclerq, G.; Quivy, J.; Tang, J.; Vaissermann, J.; Huché, M.; Jaouen, G. *Chem. Eur. J.* **2003**, *9*, 5223. (b) Hillard, E.; Vessières, A.; Thouin, L.; Jaouen, G.; Amatore, C. *Angew. Chem., Int. Ed.* **2006**, *45*, 285. (c) Payen, O.; Top, S.; Vessières, A.; Brulé, E.; Plamont, M. A.; McGlinchey, M. J.; Müller-Bunz, H.; Jaouen, G. *J. Med. Chem.* **2008**, *51*, 1791.

(10) (a) Dubar, F.; Slomianny, C.; Khalife, J.; Dive, D.; Kalamou, H.; Guérardel, Y.; Grellier, P.; Biot, C. *Angew. Chem., Int. Ed.* **2013**, *52*, 7690. (b) Dubar, F.; Bohic, S.; Slomianny, C.; Morin, J. C.; Thomas, P.; Kalamou, H.; Guérardel, Y.; Cloetens, P.; Khalife, J.; Biot, C. *Chem. Commun.* **2012**, *48*, 910.

(11) Vausselin, T.; Calland, N.; Belouzard, S.; Descamps, V.; Douam, F.; Helle, F.; François, C.; Lavillette, D.; Duverlie, G.; Wahid, A.; Fénéant, L.; Cocquerel, L.; Guérardel, Y.; Wychowski, C.; Biot, C.; Dubuisson, J. *Hepatology* **2013**, *58*, 86.

(12) Bal, T. R.; Anand, B.; Yogeeswari, P.; Sriram, D. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 4451.

(13) Jiang, T.; Kuhen, K. L.; Wolff, K.; Yin, H.; Bieza, K.; Caldwell, J.; Bursulaya, B.; Tuntland, T.; Zhang, K.; Karanewsky, D.; He, Y. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2109.

(14) Tripathy, R.; Reiboldt, A.; Messina, P. A.; Iqbal, M.; Singh, J.; Bacon, E. R.; Angeles, T. S.; Yang, S. X.; Albom, M. S.; Robinson, C.; Chang, H.; Ruggeri, B. A.; Mallamo, J. P. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2158.

(15) Cane, A.; Tournaire, M. C.; Barritault, D.; Crumeyrolle-Arias, M. *Biochem. Biophys. Res. Commun.* **2000**, *276*, 379.

(16) Silveira, V. Ch.; Luz, J. S.; Oliveira, C. C.; Graziani, I.; Ciriolo, M. R.; Costa-Ferreira, A. M. *J. Inorg. Biochem.* **2008**, *102*, 1090.

(17) Raj, A. A.; Raghunathan, R.; Sridevikumaria, M. R.; Raman, N. *Bioorg. Med. Chem.* **2003**, *11*, 407.

(18) Rodriguez-Arguelles, M. C.; Mosquera-Vazaquez, S.; Touron-Touceda, P.; Sanmartin-Matalobos, J.; Garcia-Deibe, A. M.; Belicchi-Ferraris, M.; Pelosi, G.; Pelizzi, C.; Zani, F. *J. Inorg. Biochem.* **2007**, *101*, 138.

(19) Maskell, L.; Blanche, E. A.; Colucci, M. A.; Whatmore, J. L.; Moody, Ch. J. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1575.

(20) Verma, M.; Pandyea, S. N.; Singh, K. N.; Stables, J. P. *Acta Pharm.* **2004**, *54*, 49.

(21) Igosheva, N.; Lorz, C.; O'Conner, E.; Glover, V.; Mehmet, H. *Neurochem. Int.* **2005**, *47*, 216.

(22) Chen, L. R.; Wang, Y. C.; Lin, Y. W.; Chou, S. Y.; Chen, S. F.; Liu, L. T.; Wu, Y. T.; Kuo, C. J.; Chen, T. S. S.; Juang, S. H. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3058.

(23) Singh, G. S.; Desta, Z. Y. *Chem. Rev.* **2012**, *112*, 6104.

(24) Fensome, A.; Adams, W. R.; Adams, A. L.; Berrodin, T. J.; Cohen, J.; Huselton, C.; Illenberger, A.; Karen, J. C.; Hudak, V. A.; Marella, M. A.; Melenski, E. G.; McComas, C. C.; Mugford, C. A.; Slayeden, O. D.; Yudt, M.; Zhang, Z.; Zhang, P.; Zhu, Y.; Winneker, R. C.; Wrobel, J. E. *J. Med. Chem.* **2008**, *51*, 1861.

(25) Kumari, G.; Nutan; Modi, M.; Gupta, S. K.; Singh, R. K. *Eur. J. Med. Chem.* **2011**, *46*, 1181.

(26) (a) Lo, M. M. C.; Newmann, C. S.; Nagayams, S.; Perlstein, E. O.; Schreiber, S. L. *J. Am. Chem. Soc.* **2004**, *126*, 16077. (b) Ding, K.; Lu, Y.; Nikolovska-Coleska, Z.; Qui, S.; Ding, Y.; Gao, W.; Stuckey, J.; Krajewski, K.; Roller, P. P.; Tomita, Y.; Parrish, D. A.; Deschamps, J. R.; Wang, S. *J. Am. Chem. Soc.* **2005**, *127*, 10130.

(27) Vintonyak, V. V.; Warburg, K.; Kruse, H.; Grimme, S.; Hubel, K.; Rauth, D.; Waldmann, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 5902.

(28) Yeung, B. K. S.; Zou, B.; Rottmann, M.; Lakshminarayana, S. B.; Ang, S. H.; Leong, S. Y.; Tan, J.; Wong, J.; Keller-Maerki, S.; Fischli, C.; Goh, A.; Schmitt, E. K.; Krastel, P.; Francotte, E.; Kuhen, K.; Plouffe, D.; Henson, K.; Wagner, T.; Winzeler, E. A.; Petersen, F.; Brun, R.; Dartois, V.; Diagana, T. T.; Keller, T. H. *J. Med. Chem.* **2010**, *53*, 5155.

(29) (a) Rottmann, M.; McNamara, C.; Yeung, B. K. S.; Lee, M. C. S.; Zhou, B.; Russell, B.; Seitz, P.; Plouffe, D. M.; Dharia, N. V.; Tan, J.; Cohen, S. B.; Spencer, K. R.; Gonzalez-Paez, G. E.; Lakshminarayana, S. B.; Goh, A.; Suwanarusk, R.; Jegla, T.; Schmitt, E. K.; Beck, H. P.; Brun, R.; Nosten, F.; Renia, L.; Dartois, V.; Keller, T. H.; Fidock, D. A.; Winzeler, E. A.; Diagana, T. T. *Science* **2010**, *329*, 1175. (b) Ang, S. H.; Crastel, P.; Leong, S. Y.; Tan, L. J.; Wong, W. L. J.; Yeung, B. K. S.; Zou, B. (Novartis AG) US Patent 2009/0275560 A1, 2009. (c) Liu, J. J.; Zhang, Z. (Hoffmann La Roche AG) spiroindolinone derivatives; PCT Int. Appl. WO 2008/055812, 2008.

(30) Ding, K.; Lu, Y.; Nikolovska-Coleska, Z.; Wang, G.; Qiu, S.; Shangary, S.; Gao, W.; Qin, D.; Stukey, J.; Krajewski, K.; Roller, P. P.; Wang, S. *J. Med. Chem.* **2006**, *49*, 3432.

(31) (a) Rajopadhyet, M.; Popp, F. D. *J. Med. Chem.* **1988**, *31*, 1001. (b) Zhou, N.; Polozov, A. M.; O'Connell, M.; Burgeson, J.; Yu, P.; Zeller, W.; Zhang, J.; Onua, E.; Ramirez, J.; Palsdottir, G. A.; Halldorsdottir, G. V.; Andresson, T.; Kiselyov, A, S.; Gurney, M.; Singh, J. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 2658. (c) Santos, E. L. D.; W, A. J., Jr.; Ribeiro, N. M.; Andrade, H. M. C. *J. Mol. Catal. A: Chem.* **2008**, *295*, 18.

(32) (a) Hou, J.; Liu, X.; Shen, J.; Zhao, G.; Wang, P. G. *Expert Opin. Drug Discov.* **2012**, *7*, 489. (b) Beal, D. M.; Jones, L. H. *Angew. Chem., Int. Ed.* **2012**, *51*, 6320. (c) He, X. P.; Xie, J.; Tang, Y.; Li, J.; Chen, G. R. *Curr. Med. Chem.* **2012**, *19*, 2399. (d) Kumar, K.; Sagar, S.; Esau, L.; Kaur, M.; Kumar, V. *Eur. J. Med. Chem.* **2012**, *58*, 153.

(33) Kumar, K.; Singh, P.; Kremer, L.; Guérardel, Y.; Biot, C.; Kumar, V. *Dalton Trans.* **2012**, *41*, 5778.

(34) Kumar, K.; Carrère-Kremer, S.; Kremer, L.; Guérardel, Y.; Biot, C.; Kumar, V. *Dalton Trans.* **2013**, *42*, 1492.
(35) Kumar, K.; Carrère-Kremer, S.; Kremer, L.; Guérardel, Y.; Biot, C.; Kumar, V. *Organometallics* **2013**, *32*, 5713.
(36) Hans, R. H.; Wiid, I. J. F.; Helden, P. D. V.; Wan, B.; Franzblau, S. G.; Gut, J.; Rosenthal, P. J.; Chibale, K. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 2055.
(37) Singh, P.; Kaur, S.; Kumar, V.; Bedi, P. M. S.; Mahajan, M. P.; Sehar, I.; Pal, H. C.; Saxena, A. K. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 3017.
(38) (a) Wang, C. H.; White, A. R.; Schwartz, S. N.; Alluri, S.; Cattabiani, T. M.; Zhang, L. K.; Chan, T. M.; Buevich, A. V.; Ganguly, A. K. *Tetrahedron* **2012**, *68*, 9750. (b) Vine, K. L.; Locke, J. M.; Ranson, M.; Pyne, S. G.; Bremner, J. B. *Bioorg. Med. Chem. Lett.* **2007**, *15*, 931.
(39) (a) Garden, S. J.; Torres, J. C.; da Silva, J. F. M.; Pinto, A. C. *Synth. Commun.* **1998**, *28*, 1679. (b) Bouhfid, R.; Joly, N.; Massoui, M.; Cecchelli, R.; Lequart, V.; Martin, P.; Essassi, E. M. *Heterocycles* **2005**, *65*, 2949. (c) Singh, P.; Sharma, P.; Anand, A.; Bedi, P. M. S.; Kaur, T.; Saxena, A. K.; Kumar, V. *Eur. J. Med. Chem.* **2012**, *55*, 455.
(40) Sambandamurthy, V. K.; Derrick, S. C.; Hsu, T.; Chen, B.; Larsen, M. H.; Jalapathy, K. V.; Chen, M.; Kim, J.; Porcelli, S. A.; Chan, J.; Morris, S. L.; Jacobs, W. R. *Vaccine* **2006**, *24*, 6309.
(41) Kremer, L.; Douglas, J. D.; Baulard, A. R.; Morehouse, C.; Guy, M. R.; Alland, D.; Dover, L. G.; Lakey, J. H.; Jacobs, W. R., Jr.; Brennan, P. J.; Minnikin, D. E.; Besra, G. S. *J. Biol. Chem.* **2000**, *275*, 16857.