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Metallocene-Modified Uracils: Synthesis, Structure, and Biological Activity

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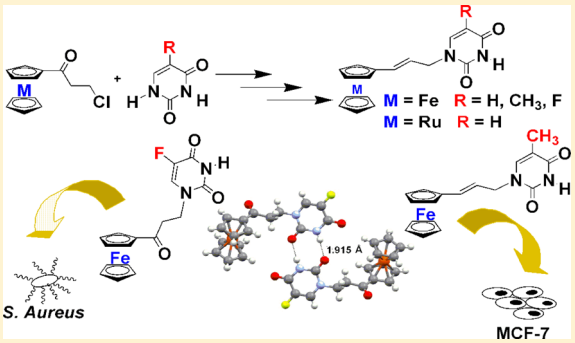
Supporting Information

ABSTRACT: A new family of metallocene−uracil conjugates, including [3-(*N*1-uracilyl)-1-(ferrocenyl)]propene (**2c**), [3-(*N*1-thyminyl)-1-(ferrocenyl)]propene (**3c**), [3-(*N*1-(5-fluorouracilyl))-1-(ferrocenyl)]propene (**4c**), and [3-(*N*1-uracilyl)-1-(ruthenocenyl)]-propene (**5c**), was obtained in three steps from (3-chloropropionyl)-ferrocene and (3-chloropropionyl)ruthenocene, respectively. The complexes **2c**−**5c** and their intermediates **2a**−**5a** and **2b**−**5b** were characterized by NMR and infrared spectroscopy, mass spectrometry, and elemental analysis. The molecular structures of the intermediates **2b** and **4a** were determined by single-crystal X-ray structure analysis. In the solid state, two molecules of **2b** or **4a** form a dimeric structure, which is held together by strong hydrogen bonds. Compounds **2c**−**5c** were also studied by cyclic voltammetry (CV). The ferrocenyl−uracil derivatives **2c**−**4c** revealed reversible uncomplicated oxidations, whereas the cyclic voltammogram of the ruthenocenyl derivative **5c** showed an irreversible oxidation. Compounds **2c**−**5c** were tested for their antiproliferative activity against human MCF-7 breast adenocarcinoma and HT-29 colon carcinoma cells. Compounds **3c**−**5c** were moderately active against MCF-7 cancerous cells. Atomic absorption spectroscopy measurements on compound **5c** revealed that the ruthenocenyl derivative is taken up by HT-29 cells in a time-dependent manner. However, the ruthenium cellular level remains relatively low. Compounds **2a**−**5a** were also tested against Gram-positive methicillin-sensitive *Staphylococcus aureus* (MSSA), methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Staphylococcus aureus* (VRSA) and *Staphylococcus epidermidis* bacterial strains. Compound **4a** showed significant antibacterial activity against all bacterial strains, while compounds **2a** and **3b** were only moderately active. No antibacterial activity was found for the ruthenocenyl derivative **5a**.



INTRODUCTION

Ferrocene was first reported in 1951 by Kealy and Pauson[1] and by Miller and co-workers.[2] The sandwich structure of ferrocene was disclosed soon after,[3] and ferrocene has remained at the forefront of organometallic chemistry for over 60 years. This popularity is clearly reflected by the large number of books and reviews focusing on various aspects of ferrocene chemistry.[4−6] One of the fields where ferrocene importance is steadily increasing is bioorganometallic chemistry.[7] This is due to the well-developed synthetic chemistry of ferrocene, the stability of the ferrocenyl group in aqueous and aerobic media, and the reversible electrochemistry of ferrocene.

Although ferrocene itself is considered to be a nontoxic, biologically inert compound, many ferrocenyl derivatives exhibit significant anticancer, antibacterial, antiparasitic, antifungal, and other biological activities. A common strategy for obtaining biologically active ferrocenyl derivatives is based on the conjugation of the ferrocenyl group with biologically relevant molecules. The conjugation strategy can be divided into two main groups. First, the ferrocenyl moiety is introduced or peripherally attached to a molecule of already known pharmacological significance. In such cases, the ferrocenyl fragment is intended to modulate or potentiate the biological activity of the conjugated pharmacophore. A good example of this strategy is provided by the ferrocenyl analogues of the antibreast cancer drug tamoxifen[8] and the antiparasite ferroquine derivatives.[9] In the second example, the ferrocenyl and the conjugated moiety do not exhibit biological activity on their own; however, after conjugation, the ferrocenyl−conjugate becomes biologically active. So far the ferrocenyl

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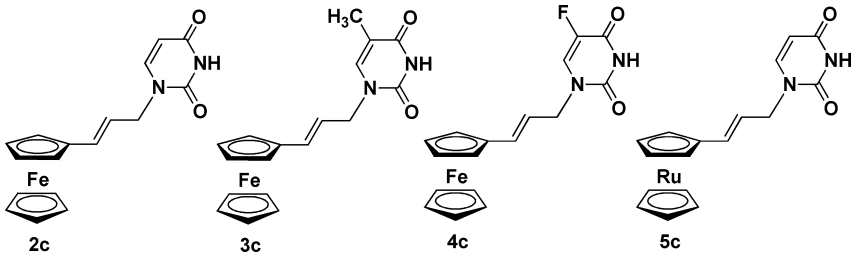
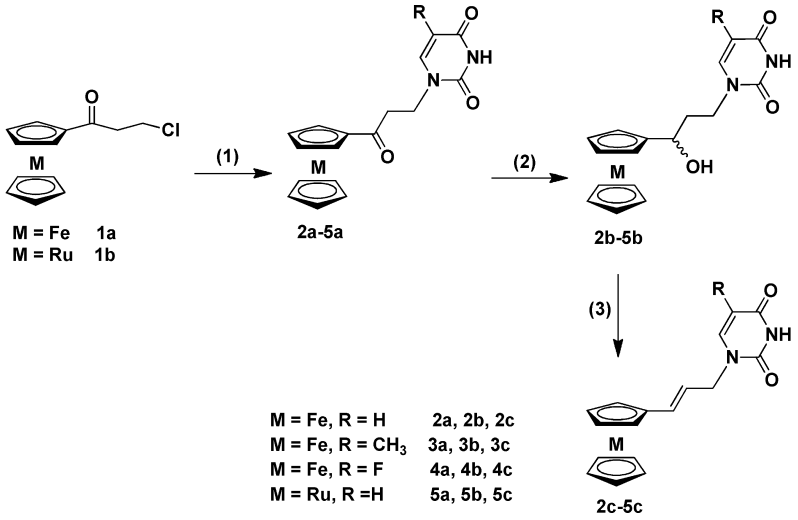


Figure 1. Metallocene-modified uracils prepared in this study.

Scheme 1. Synthesis of Ferrocenyl−Uracils 2c−4c and Ruthenocenyl-Uracil 5c[a]



[a]Reagents and conditions: (1) nucleobase uracil, thymine, or 5-fluorouracil, NEt_3, DMF, 70 °C, 5 h; (2) $NaBH_4$, THF, room temperature, 30 min; (3) cat. H_2SO_4, DCM, reflux, 20 min.

moiety has been coupled to a plethora of biologically relevant vectors: for example, with biotin,[10] antibiotics,[11] peptides,[12] sugars,[13] drugs,[14] steroid hormones,[15] aurones,[16] and nucleosides.[17] In that respect, nucleobases, which are known to play a crucial role in biology and pharmacology, remain attractive targets for ferrocenyl conjugation. In contrast to the well-established classical medicinal chemistry of purely organic nucleobase derivatives,[18] the bioorganometallic chemistry of ferrocenyl−nucleobase conjugates is still an undeveloped area, as shown by the limited literature on the subject.[19] The main reasons behind the synthesis of ferrocenyl−nucleobase conjugates are to obtain new electrochemically active biomarkers[19c,d,g,h,m,n,p] or anticancer active agents[19h−k,p] or to investigate their self-assembly and supramolecular arrangement in the solid state.[19e−g]

Recently, we have started our own project in the chemistry of ferrocenyl−nucleobase conjugates. In a preliminary paper, we have reported on the *N*1-regioselective Michael addition of thymine to acryloylferrocene,[19p] followed by its reduction to the corresponding ferrocenyl−thymine acyclo-nucleoside. The ferrocenyl−thymine adduct has shown the ability to inhibit the growth of the estrogen receptor-responsive MCF-7 and the T lymphoblast-like CCRF-CEM human cancer cells.

In an extension of the above work, we report here the synthesis and electrochemistry of new olefinic ferrocenyl−nucleobase conjugates (nucleobase = uracil (**2c**), thymine (**3c**), 5-fluorouracil (**4c**)) and the corresponding ruthenocenyl−uracil conjugate **5c** (Figure 1). We also present the single-crystal X-ray structure analysis of two intermediates.

In addition, the anticancer activity of the ferrocenyl−uracil derivatives was evaluated in vitro against human estrogen receptor-responsive breast adenocarcinoma MCF-7 and colon carcinoma HT-29 cell lines. The cellular uptake of the ruthenocenyl-uracil derivative was estimated by atomic absorption spectroscopy. The antibacterial activity of selected ferrocenyl−nucleobases against Gram-positive methicillin-sensitive *Staphylococcus aureus* (MSSA), methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Staphylococcus aureus* (VRSA), and *Staphylococcus epidermidis* bacterial strains was also determined. To the best of our knowledge, this is the first report on the antibacterial activity of ferrocenyl−nucleobases ever published.

RESULTS AND DISCUSSION

Synthesis. The target compounds **2c−5c** were synthesized in a three-step strategy (Scheme 1).

First, the readily available (3-chloropropionyl)metallocenes **1a,b** underwent a dehydrohalogenation reaction to form the corresponding acryloyl derivatives. These in situ generated Michael acceptors reacted with the uracil donor to yield adducts **2a−5a**. Thus, the first step represents a one-pot, two-step process consisting of a dehydrohalogenation followed by a Michael addition reaction. This simple protocol allowed us to avoid a time-consuming (and costly) purification of acryloylferrocene and acryloylruthenocene (for an alternative synthesis of **3a** with one extra step, see ref 19p). In the second step the exocyclic carbonyl function in the Michael adducts **2a**, **4a**, and **5a** was reduced to a hydroxyl, thus affording racemic

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metallocenyl acyclo-nucleosides **2b**, **4b**, and **5b**. Compound **3b** has been obtained from **3a** by following a previously described procedure.[19p] In the key step, complexes **2b**−**5b** were dehydrated by treatment with a catalytic amount of concentrated H_2SO_4 in boiling dichloromethane solution. This simple and cheap method of dehydration took place with complete diastereoselectivity, affording exclusively the *E* isomers of the target conjugates **2c**−**5c** with ca. 35% isolated chemical yields.

Compounds **2c**−**4c** are orange-yellow air-stable solids, whereas derivative **5c** is a colorless air-stable solid. All newly obtained compounds were characterized by standard spectroscopic methods, including ^{1}H NMR, ^{13}C NMR, and IR spectroscopy, MS, and elemental analysis. The ^{1}H NMR and ^{13}C NMR spectra of the target compounds **2c**−**5c** are presented in Figures S1−S16 (Supporting Information). The solid-state structures of the intermediates **2b** and **4a** were determined by single-crystal X-ray structural analysis. All analytical data confirm the proposed structures.

Single-Crystal X-ray Structural Analysis of Compounds 2b and 4a. Crystals suitable for X-ray structural analysis were obtained by slow diffusion of gaseous *n*-hexane and diethyl ether into saturated chloroform solutions of **2b** and **4a**. ORTEP drawings with the atom-labeling scheme are presented in Figures 2 and 3 respectively, together with selected bond lengths and angles. In both structures the ferrocenyl group adopts an eclipsed conformation, with the uracil function pointing away from the ferrocenyl moiety. As a result, in the crystal packing of **2b** and **4a**, the uracil groups are available for hydrogen bonding with neighboring molecules.

In the solid state, each independent molecule of the ferrocenyl−uracil derivative **2b** forms a dimer, due to the presence of strong hydrogen bonds between the N1−H1 amino and C2═O2 carbonyl groups of the uracil moieties (Figure 4).

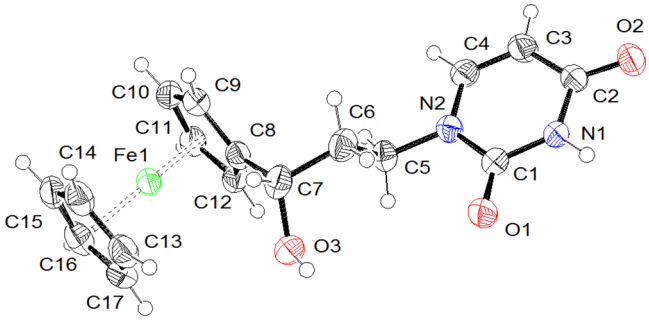

Figure 2. ORTEP diagram of **2b** with 50% probability level thermal ellipsoids. Selected bond lengths (Å) and angles (deg): O1−C1 = 1.224(4), C1−N1 = 1.372(4), C1−N2 = 1.375(4), C2−N1 = 1.379(4), C2−O2 = 1.237(4), C7−O3 = 1.466(4); N1−C1−N2 = 115.4(2), O1−C1−N1 = 122.2(3), O1−C1−N2 = 122.4(3), N1−C2−O2 = 119.5(3), O2−C2−C3 = 126.3(3).

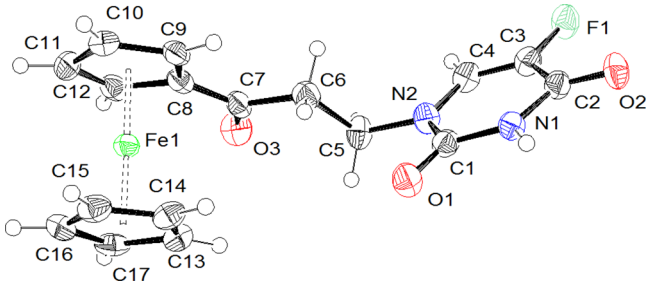

Figure 3. ORTEP diagram of **4a** with 50% probability level thermal ellipsoids. Selected bond lengths (Å) and angles (deg): O1−C1 = 1.234(10), C1−N1 = 1.382(10), C1−N2 = 1.371(10), C2−N1 = 1.386(10), C2−O2 = 1.228(10), C7−O3 = 1.213(10), C3−F1 = 1.351(9); N1−C1−N2 = 115.7(7), O1−C1−N1 = 121.7(7), O1−C1−N2 = 122.6(7), N1−C2−O2 = 122.6(8), O2−C2−C3 = 125.5(8), C2−C3−F1 = 116.8(7), C4−C3−F1 = 120.5(7).

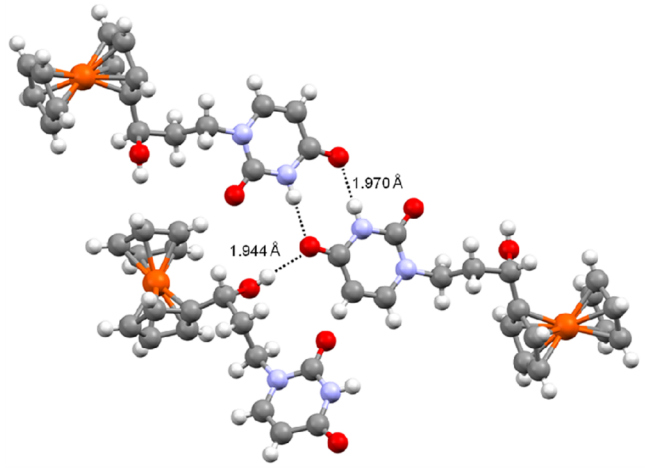

Figure 4. Intermolecular hydrogen bonding (H···O distance 1.944 Å) and dimeric structure (H···O distance 1.970 Å) observed in the crystal packing of **2b**.

The N1···O2 distances are 2.824(3) Å (H1···O2 distances 1.970 Å), with the N1−H1···O2 angles being almost linear at 171.9° (symmetry code: $-x + 1, -y - 1, -z$). A similar dimeric uracil system has been observed in the molecular structure of the uracil derivative 6-((4-bromo-3,5-bis((dimethylamino)-methyl)phenyl)ethynyl)-1-octylpyrimidine-2,4(1*H*,3*H*)-dione.[20] In addition, the O atom of the carbonyl group also makes a short contact with the alcohol function of a second neighboring molecule (symmetry code: $x, -y - {}^1/_2, z + {}^1/_2$). The O2···O3 distance is 2.745(4) Å with an O3−H3···O2 angle of 165.4°.

In the crystal packing of **4a**, a dimeric structure is also observed (Figure 5). However in **4a**, in comparison to **2b**, the C1═O1 carbonyl group is involved in the self-base pairing interaction, thus giving rise to a more close-compact arrange-

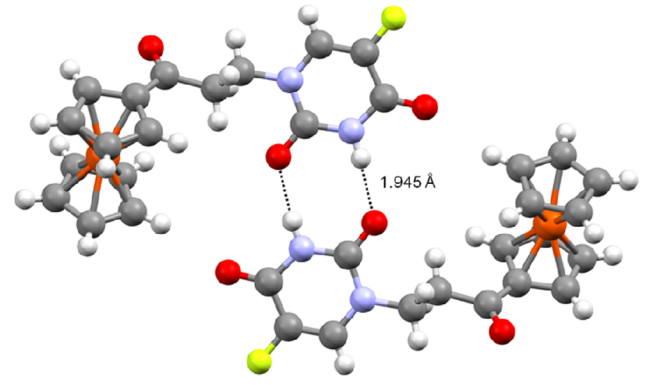

Figure 5. Dimeric structure observed in the crystal packing of **4a**.

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ment between the two ferrocenyl−nucleobase conjugates; the N1···O1 distances are slightly shorter at 2.785(9) Å, with the corresponding N1−H1···O1 angle being 164.9° (symmetry code: $-x + 1, -y + 1, -z + 1$).

Electrochemistry. The CV measurements of the products **2c−5c** were carried out in $CH_2Cl_2/[NBu_4][PF_6]$ with a platinum working electrode, a platinum-wire counter electrode, and a silver spiral as a pseudoreference electrode. The half-wave potentials $E_{1/2}^{0/+}$ of complexes **3a**,**b** have been reported previously.[19p] Pertinent electrochemical data are summarized in Table 1. Figures S17 and S18 (Supporting Information) show the voltammograms of compounds **4c** and **5c**, whereas Figures S19 and S20 (Supporting Information) show the voltammograms of **2c** and **3c**. Ferrocenyl derivatives **2c−4c** are oxidized in a single Nernstian one-electron process at half-wave potentials ($E_{1/2}^{0/+}$) of 30, 22, and 29 mV, respectively, versus the ferrocene/ferrocenium couple. Complex **5c**, upon anodic scans, shows a single, irreversible wave at $E_{p,a}$ = 511 mV that can be assigned to the oxidation of Ru^{2+} to Ru^{3+}. The reverse cathodic scan of **5c** displays no reduction wave for Ru^{3+} back to Ru^{2+}. Instead, the reduction wave at $E_{p,c}$ = −418 mV is recorded. The origin of this wave is likely due to the reduction of side products obtained from the decomposition of oxidized **5c**. The 17-electrons ruthenocenium cation is highly electrophilic and known to undergo follow-up reactions.[21] Chemical identification of the follow-up reaction products was outside the scope of this study.

Table 1. Cyclic Voltammetric Data for Compounds 2c−5c Obtained at a Scan Rate of 0.2 V s^{-1} at Room Temperature in CH_2Cl_2 with $[NBu_4][PF_6]$ (0.1 M) as the Supporting Electrolyte[a]

compd	$E_{p,a}$ (V)	$E_{p,c}$ (V)	$E_{1/2}^{0/+}$ (V)[b]	ΔE_p (mV)[c]
2c	0.065	−0.004	0.030	69
3c	0.052	−0.007	0.022	59
4c	0.064	−0.005	0.029	69
5c	0.511	−0.418		

[a]All potentials are reported relative to the ferrocene/ferrocenium redox couple. [b]$E_{1/2}^{0/+} = (E_{p,a} + E_{p,c})/2$. [c]$\Delta E_p = |E_{p,a} - E_{p,c}|$. ΔE_p values for decamethylferrocene were in the range 60−72 mV under the experimental conditions.

Evaluation of Biological Activities. *Evaluation of Tumor Cell Growth Inhibition and Cellular Uptake.* The anticancer activity of ferrocenyl−nucleobases **2c−5c** and **4a** was evaluated on the basis of their ability to inhibit proliferation of human MCF-7 estrogen responsive human breast adenocarcinoma and HT-29 colon carcinoma cells. This was assessed by determining their IC_{50} concentrations (drug concentration necessary for 50% inhibition of cell viability) (Table 2). Though no activity (no IC_{50} value <100 μM) was observed in HT-29 cells, moderate effects were obtained in MCF-7 cells. Established cytostatics such as cisplatin reach IC_{50} values below 10 μM in the used assay, but for recently investigated ferrocene derivatives more moderate effects have also been observed.[28c] In our study complex **3c** was the most active derivative with an IC_{50} value of 23.8 μM, a value which is 2−3 times lower than those of the other compounds studied. It is also apparent that substitution of the hydrogen atom in the 5-position of the uracil ring in compound **2c**, by either a methyl group (**3c**) or a fluorine atom (**4c**), triggers the antiproliferative effect.

Table 2. IC_{50} Values of Antiproliferative Effects in MCF-7 and HT-29 Cells[a]

	IC_{50} (μM)	
compd	MCF-7	HT-29
4a	72.5 ± 0.5	>100
2c	>100	>100
3c	23.8 ± 0.1	>100
4c	59.2 ± 3.3	>100
5c	71.1 ± 3.9	>100
cisplatin[28]	2.0	7.0

[a]Results are expressed as means (± error) of repeated experiments.

It has been recently reported that ruthenium complexes can have low levels of cellular uptake.[22] In order to investigate if this was a reason for the relatively low cytotoxicity of the ruthenium complex **5c**, the cellular ruthenium levels in HT-29 cells—exposed to the high (but nontoxic) concentration of 100 μM of the complex—was measured by a method based on high-resolution continuum source atomic absorption spectroscopy.[22] These experiments confirmed that ruthenium was taken up by the cells in a time-dependent manner (Figure 6).

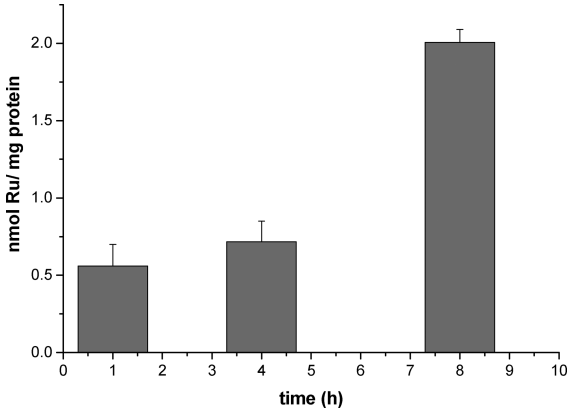

Figure 6. Cellular uptake of complex **5c** in HT-29 cells at a concentration of 100 μM incubated for 1, 4, and 8 h.

However, in comparison to a recently described, and substantially more cytotoxic, ruthenium NHC complex,[22b] the uptake values were low. This suggests that the cellular accumulation of **5c** is a limiting factor for the toxicity in tumor cells.

Evaluation of Antibacterial Activity. For a preliminary antibacterial activity study, fluorinated derivatives **4a−c** and the Gram-positive methicillin-sensitive *Staphylococcus aureus* (MSSA) bacterial strain were arbitrarily selected. This screening revealed a noticeable antibacterial activity for complex **4a**. Derivatives **4b**,**c** were inactive with minimal inhibitory concentrations (MIC) a higher than 256 μg mL^{-1}. On the basis of these initial results, further antibacterial activity studies were performed with derivatives **2a−5a**. The antibacterial activities of these compounds were tested against Gram-positive methicillin-sensitive *Staphylococcus aureus* (MSSA), methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Staphylococcus aureus* (VRSA), and *Staphylococcus epidermidis* bacterial strains. The antibacterial activity was evaluated by minimal inhibitory concentration (MIC) values. The pertinent MIC data are presented in Table 3. The detailed methodology

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of the antibacterial activity tests is provided in the Experimental Section and Supporting Information.

Table 3. In Vitro Antibacterial Activity of Ferrocenyl−Uracils 2a−5a[a]

microorganism	MIC (μg mL^{-1})			
	2a	3a	4a	5a
S. aureus subsp. *aureus* ATCC 29213 (MSSA)	128	128	32	>256
S. aureus subsp. *aureus* ATCC 43300 (MRSA)	128	128	32	>256
S. aureus subsp. *aureus* ATCC 700787 (VRSA)	128	128	32	>256
S. epidermidis ATCC 12228	128	128	16	>256

[a]The MIC value of the reference compound, penicillin G, against *S. aureus* ATCC 29213 is 0.31 μg mL^{-1}.

The most active compounds, **2a−4a**, were examined in vitro for hemolytic activity. No hemolytic activity was observed on human erythrocytes.

CONCLUSIONS

In conclusion, we have developed a cheap and effective three-step synthetic approach toward a new family of ferrocenyl−uracil derivatives **2c−4c**. The key step of our synthesis exploited an *N*1-regioselective Michael addition of the uracil group and an in situ generated acryloylferrocene complex. We have also showed that this strategy can be successfully utilized to obtain a ruthenocenyl−uracil derivative (**5c**). Single-crystal X-ray diffraction analysis of the intermediates **2b** and **4a** revealed the presence of dimers held together by strong hydrogen bonds. Cyclic voltammetry measurements of ferrocenyl−uracils **2c−4c** and ruthenocenyl−uracil **5c** revealed significant differences in their electrochemical behavior. Ferrocenyl−uracil derivatives **2c−4c** undergo a single reversible oxidation, whereas the ruthenocenyl derivative **5c** was found to exhibit an irreversible oxidation. Owing to the increasing importance of organometallics in biology, our compounds were subjected to anticancer and antibacterial screening studies. Anticancer activity studies have permitted to identify the thymine derivative **3c** as the most antiproliferative active agent (IC_{50} = 23.8 μM against MCF-7 cells). Compound **3c** can be considered as an attractive leading structure in the development of new, more active ferrocenyl−uracil derivatives. Atomic absorption spectroscopy gave us an unique set of data on cellular ruthenium levels after incubation of HT-29 cells with the ruthenocenyl−uracil derivative **5c**. These experiments confirmed the time-dependent uptake of ruthenium into the cancerous cells, though the measured cellular levels of ruthenium were relatively low. Antibacterial activity studies pointed out that fluorouracil derivative **4a** was the most active antibacterial compound against Gram-positive strains of *S. epidermidis* and *S. aureus*, including methicillin-resistant and vancomycin-resistant *S. aureus* strains. Work is in progress to further explore the chemistry of ferrocenyl−nucleobase derivatives and study their biological activity profiles.

EXPERIMENTAL SECTION

General Comments. All syntheses were carried out using standard Schlenk techniques. Chromatographic separations were carried out using silica gel 60 (Merck, 230−400 mesh ASTM). Dichloromethane and dimethylformamide were distilled and deoxygenated prior to use. Other solvents were of reagent grade and were used without prior purification. All other chemicals were purchased from Aldrich Chemical Co. The NMR spectra were recorded on a Bruker AV600 Kryo (600 MHz) spectrometer. Chemical shifts are reported in δ (ppm) using residual DMSO (^{1}H δ 2.50 ppm, ^{13}C δ 39.70 ppm) and $CHCl_3$ (^{1}H δ 7.26 ppm, ^{13}C δ 77.00 ppm) signals as the reference. In order to unambiguously assign the acidic N−H and O−H protons in our compounds, their ^{1}H NMR spectra were additionally recorded after D_2O addition. Mass spectra were recorded using EI methods on a Finnigan MAT 710A mass spectrometer. IR spectra were recorded on a FTIR Nexus Nicolet apparatus. Microanalyses were determined by the Analytical Services of the Polish Academy of the Sciences (Łódź, Poland). Electrochemical work was performed on a Princeton Applied Research VersaStat3 potentiostat in a home-built vacuumtight one-compartment cell using a Pt electrodes as the working electrode, a platinum spiral as the counter electrode, and a silver spiral as a pseudoreference electrode. Each of the spiral-shaped electrodes was welded to Vycon wire and sealed into a glass tube. Counter and reference electrodes were introduced into the cell via appropriate fittings in the side wall and sealed using a Quickfit screw. CH_2Cl_2 for electrochemical use was distilled from CaH_2, deoxygenated by saturation with argon, and briefly stored over molecular sieves. Potential calibration was performed by adding decamethylferrocene ($E_{1/2}$ = −0.550 V vs $Cp_2Fe^{0/+}$) or ferrocene to the analyte solution as an internal standard. The added amount of the reference compound was adjusted until the peak current of its redox feature was comparable to that of the analyte. Potentials are reported against the ferrocene/ferrocenium couple.

General Procedure for the Synthesis of Michael Adducts 2a−5a. To a stirred solution of the appropriate (3-chloropropionyl)-metallocene (7.2 mmol) in DMF (20 mL) at room temperature was added 2053 μL (14.7 mmol) of triethylamine. After the mixture was stirred for 20 min, the appropriate uracil (7.5 mmol) was added in ∼7 mL of DMF and the mixture was stirred at a temperature of 70 °C for 5 h. Subsequently, the solvent was evaporated and the residue subjected to column chromatography on SiO_2 ($CHCl_3$/MeOH, 50/2). Chromatographically purified conjugates **2a−5a** were crystallized from chloroform/*n*-hexane to afford analytically pure samples. Complex **3a** was obtained and fully characterized in our previous work.[19p]

*[3-(N1-Uracilyl)propionyl]ferrocene (**2a**).* Red crystals. Yield: 73%. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.23 (s, 1H, NH), 7.698 (d, $J_{H,H}$ = 7.8 Hz, 1H, H-6 uracil), 5.55 (d, $J_{H,H}$ = 7.8 Hz, 1H, H-5 uracil), 4.81 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, α-C_5H_4), 4.59 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, β-C_5H_4), 4.20 (s, 5H, C_5H_5), 3.98 (t, $^3J_{HH}$ = 6.6 Hz, 2H, CH_2), 3.16 (t, $^3J_{HH}$ = 6.6 Hz, 2H, CH_2). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 201.3, 163.8, 151.0, 146.7, 100.5, 78.6, 72.5, 69.7, 69.2, 43.9, 37.6. MS (EI, 70 eV): *m*/*z* 352 (M^+), 240 (acryloyl ferrocene). FTIR (KBr; ν, cm^{-1}): 1695 (s, CO), 1647 (s, CO), 1459. Anal. Calcd for $C_{17}H_{16}N_2O_3Fe$: C, 57.98; H, 4.58; N, 7.95. Found: C, 58.01; H, 4.62; N, 7.91.

*[3-(N1-(5-Fluorouracilyl))propionyl]ferrocene (**4a**).* Red crystals,. Yield: 68%. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.79 (s, 1H, NH), 8.13 (d, $J_{H,F}$ = 7.2 Hz, 1H, H-6 5-fluorouracil), 4.81 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, α-C_5H_4), 4.58 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, β-C_5H_4), 4.21 (s, 5H, C_5H_5), 3.95 (t, J_{HH} = 6.6 Hz, 2H, CH_2), 3.18 (t, J_{HH} = 6.6 Hz, 2H, CH_2). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 201.4, 157.5 (d, $J_{C,F}$ = 25.5 Hz), 149.6, 139.3 (d, $J_{C,F}$ = 226.5 Hz), 131.2 (d, $J_{C,F}$ = 33.0 Hz), 78.6, 72.6, 69.8, 69.2, 44.2, 37.5. MS (EI, 70 eV): *m*/*z* 370 (M^+), 240 (acryloyl ferrocene). FTIR (KBr; ν, cm^{-1}): 1716 (s, CO), 1684 (s, CO), 1653 (s, CO), 1452, 1369, 1239, 817, 464. Anal. Calcd for $C_{17}H_{15}N_2O_3FFe$: C, 55.16; H, 4.08. Found: C, 55.39; H, 4.01.

*[3-(N1-Uracilyl)propionyl]ruthenocene (**5a**).* Yellow crystals. Yield: 70%. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.24 (s, 1H, NH), 7.622 (d, $J_{H,H}$ = 7.8 Hz, 1H, H-6 uracil), 5.535 (dd, $J_{H,H}$ = 7.8 Hz, 1.8 Hz, 1H, H-5 uracil), 5.12 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, α-C_5H_4), 4.85 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, β-C_5H_4), 4.59 (s, 5H, C_5H_5), 3.90 (t, J_{HH} = 6.6 Hz, 2H, CH_2), 3.03 (t, J_{HH} = 6.6 Hz, 2H, CH_2). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 199.0, 163.8, 150.9, 146.6, 100.5, 83.6, 73.9, 72.0, 70.7, 44.0, 36.9. MS (EI, 70 eV): *m*/*z* 398 (M^+), 286 (acryloylruthenocene). FTIR (KBr; ν, cm^{-1}): 3100, 1694 (s, CO), 1652 (s, CO), 1458. Anal.

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Calcd for $C_{17}H_{16}N_2O_3Ru$: C, 51.38; H, 4.06; N, 7.05. Found: C, 51.29; H, 4.12; N, 7.03.

General Procedure for the Synthesis of the Acyclo-Nucleosides 2b−5b. To vigorously stirred solutions of Michael adducts **2a−5a** (0.85 mmol) in THF (15 mL) was added $NaBH_4$ (32 mg, 0.85 mmol) at room temperature. After 30 min the reaction mixture turned yellow, whereby it was poured into water, extracted with chloroform, dried over $MgSO_4$, and evaporated to dryness. The residue was subjected to column chromatography on SiO_2 (eluent $CHCl_3$/MeOH, 10/2). Crystallization from chloroform/*n*-hexane gave the pure acyclo-nucleosides **2b−5b**. Complex **3b** was obtained and fully characterized in our previous work.[19p]

*Acyclo-Nucleoside **2b**.* Yellow crystals. Yield: 90%. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.18 (s, 1H, NH), 7.63 (d, $J_{H,H}$ = 7.8 Hz, 1H, H-6 uracil), 5.54 (d, $J_{H,H}$ = 7.8 Hz, 1H, H-5 uracil), 4.80 (d, $J_{H,H}$ = 6.0 Hz, 1H, OH), 4.34−4.31 (m, 1H, C*H*(OH)), 4.212 (pseudo-q, $J_{H,H}$ = 1.8 Hz, 1H, α-C_5H_4), 4.167 (pseudo-q, $J_{H,H}$ = 1.8 Hz, 1H, α-C_5H_4), 4.12 (s, 5H, C_5H_5), 4.09 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, β-C_5H_4), 3.90−3.86 (m, 1H, CH_2), 3.78−3.73 (m, 1H, CH_2), 2.17−2.11(m, 1H, CH_2), 1.87−1.81(m, 1H, CH_2). ^{1}H NMR (600 MHz, after D_2O addition, DMSO-d_6): δ 11.19 (s, NH, residual signal), 7.62 (d, $J_{H,H}$ = 7.8 Hz, 1H, H-6 uracil), 5.551 (d, $J_{H,H}$ = 7.8 Hz, 1H, H-5 uracil), 4.835 (d, $J_{H,H}$ = 6.0 Hz, OH, residual signal), 4.321 (dd, $J_{H,H}$ = 9.9 Hz, 3.0 Hz, 1H, C*H*(OH)), 4.207 (pseudo-q, $J_{H,H}$ = 1.8 Hz, 1H, α-C_5H_4), 4.161 (pseudo-q, $J_{H,H}$ = 1.8 Hz, 1H, α-C_5H_4), 4.11 (s, 5H, C_5H_5), 4.08 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, β-C_5H_4), 3.90−3.85 (m, 1H, CH_2), 3.77−3.73 (m, 1H, CH_2), 2.16−2.11 (m, 1H, CH_2), 1.87−1.81 (m, 1H, CH_2). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 163.9, 151.1, 146.2, 100.8, 92.6, 68.4, 67.3, 67.3, 67.2, 65.7, 65.6, 46.0, 35.9. MS (EI, 70 eV): *m*/*z* 354 (M^+), 336 ($M^+ - H_2O$). FTIR (KBr; ν, cm^{-1}): 3428 (OH), 1679 (s, CO). Anal. Calcd for 3 × $C_{17}H_{18}N_2O_3Fe$ + $CHCl_3$: C, 52.84; H, 4.69; N, 7.11. Found: C, 52.39; H, 5.03; N, 6.94.

*Acyclo-Nucleoside **4b**.* Yellow crystals. Yield: 70%. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.72 (s, 1H, NH), 8.06 (d, $J_{H,F}$ = 6.6 Hz, 1H, H-6 5-fluorouracil), 4.828 (d, $J_{H,H}$ = 6.0 Hz, 1H, OH), 4.36−4.33 (m, 1H, C*H*(OH)), 4.209 (pseudo-q, $J_{H,H}$ = 1.8 Hz, 1H, α-C_5H_4), 4.163 (pseudo-q, $J_{H,H}$ = 1.8 Hz, 1H, α-C_5H_4), 4.13 (s, 5H, C_5H_5), 4.08 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, β-C_5H_4), 3.88−3.83 (m, 1H, CH_2), 3.74−3.70 (m, 1H, CH_2), 2.16−2.10(m, 1H, CH_2), 1.89−1.81(m, 1H, CH_2). ^{1}H NMR (600 MHz, after D_2O addition, DMSO-d_6): δ 11.73 (s, NH, residual signal), 8.01 (d, $J_{H,F}$ = 6.6 Hz, 1H, H-6 5-fluorouracil), 4.89 (d, $J_{H,H}$ = 5.4 Hz, OH, residual signal), 4.334 (dd, $J_{H,H}$ = 9.9 Hz, 3.0 Hz, 1H, C*H*(OH)), 4.195 (pseudo-q, $J_{H,H}$ = 1.8 Hz, 1H, α-C_5H_4), 4.149 (pseudo-q, $J_{H,H}$ = 1.8 Hz, 1H, α-C_5H_4), 4.11 (s, 5H, C_5H_5), 4.08 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, β-C_5H_4), 3.86−3.82 (m, 1H, CH_2), 3.74−3.69 (m, 1H, CH_2), 2.15−2.10 (m, 1H, CH_2), 1.88−1.82 (m, 1H, CH_2). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 157.6 (d, $J_{C,F}$ = 25.5 Hz), 149.7, 139.5 (d, $J_{C,F}$ = 226.5 Hz), 130.7 (d, $J_{C,F}$ = 33.0 Hz), 92.7, 68.4, 67.28, 67.26, 67.21, 65.8, 65.6, 46.3, 35.71. MS (EI, 70 eV): *m*/*z* 372 (M^+). FTIR (KBr; ν, cm^{-1}): 3462 (OH), 1705 (s, CO), 1683 (s, CO), 1659 (s, CO), 1368, 1236, 820, 522. Anal. Calcd for $C_{17}H_{17}N_2O_3FFe$: C, 54.86; H, 4.60. Found: C, 54.38; H, 4.84.

*Acyclo-Nucleoside **5b**.* Yellow crystals. Yield: 90%. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.20 (s, 1H, NH), 7.59 (d, $J_{H,H}$ = 7.8 Hz, 1H, H-6 uracil), 5.535 (d, 1H, H-5 uracil), 4.66 (d, $J_{H,H}$ = 6.0 Hz, 1H, OH), 4.629−4.621 (m, 1H, α-C_5H_4), 4.601−4.594 (m, 1H, α-C_5H_4), 4.51 (s, 5H, C_5H_5), 4.47−4.45 (m, 2H, β-C_5H_4), 4.09−4.06 (m, 1H, C*H*(OH)), 3.82−3.80 (m, 1H, CH_2), 3.72−3.67 (m, 1H, CH_2), 2.039−1.98 (m, 1H, CH_2), 1.79−1.73 (m, 1H, CH_2). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 163.8, 151.0, 100.7, 96.4, 70.7, 70.2, 69.7, 68.6, 65.1, 46.0, 36.1. MS (EI, 70 eV): *m*/*z* 400 (M^+), 382 ($M^+ - H_2O$). FTIR (KBr; ν, cm^{-1}): 3442 (OH), 1694 (s, CO), 1682 (s, CO), 1423, 804. Anal. Calcd for 2 × $C_{17}H_{18}N_2O_3Ru$ + H_2O: C, 49.99; H, 4.69; N, 6.86. Found: C, 50.17; H, 4.76; N, 6.71.

General Procedure for the Synthesis of the Metallocenyl-Nucleobase Conjugates 2c−5c. To stirred solutions of the acyclo-nucleosides **2b−5b** (0.85 mmol) in DCM (7 mL) was added a catalytic amount of concentrated H_2SO_4 (4 drops from a pipet) at room temperature. The resultant reaction mixture was refluxed for 25 min, poured into water, extracted with chloroform, dried over $MgSO_4$, and evaporated to dryness. The residue was subjected to column chromatography on SiO_2 (eluent $CHCl_3$/ethyl acetate 1/1). Finally the analytically pure olefins **2c−5c** were obtained after recrystallization from a chloroform/*n*-hexane mixture.

*[3-(N1-Uracilyl)-1-(ferrocenyl)]propene (**2c**).* Orange crystals. Yield: 31%. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.25 (s, 1H, NH), 7.63 (d, $J_{H,H}$ = 8.4 Hz, 1H, H-6 uracil), 6.31 (d, $J_{H,H}$ = 15.6 Hz, 1H, Fc-C*H*═), 5.82 (dt, $J_{H,H}$ = 15.6 Hz, 6 Hz, 1H, ═C*H*-CH_2), 5.59 (dd, $J_{H,H}$ = 8.4 Hz, 1.8 Hz, 1H, H-5 uracil), 4.42 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, α-C_5H_4), 4.289 (dd, $J_{H,H}$ = 6.3 Hz, 1.2 Hz, 2H, CH_2), 4.23 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, β-C_5H_4), 4.09 (s, 5H, C_5H_5). ^{1}H NMR (600 MHz, after D_2O addition, DMSO-d_6): δ 11.27 (s, NH, residual signal), 7.62 (d, $J_{H,H}$ = 8.4 Hz, 1H, H-6 uracil), 6.31 (d, $J_{H,H}$ = 15.6 Hz, 1H, Fc-C*H*═), 5.81 (dt, $J_{H,H}$ = 15.6 Hz, 6 Hz, 1H, ═C*H*-CH_2), 5.59 (d, $J_{H,H}$ = 8.0 Hz, 1H, H-5 uracil), 4.41 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, α-C_5H_4), 4.28 (dd, $J_{H,H}$ = 6.3 Hz, 1.2 Hz, 2H, CH_2), 4.22 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, β-C_5H_4), 4.08 (s, 5H, C_5H_5). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.44 (s, 1H, NH), 7.19 (d, $J_{H,H}$ = 7.8 Hz, 1H, H-6 uracil), 6.41 (d, $J_{H,H}$ = 15.6 Hz, 1H, Fc-C*H*═), 5.76 (dt, $J_{H,H}$ = 15.6 Hz, 6.6 Hz, 1H, ═C*H*-CH_2), 5.71 (dd, $J_{H,H}$ = 7.8 Hz, 1.8 Hz, 1H, H-5 uracil), 4.36 (d, $J_{H,H}$ = 6.6 Hz, 2H, CH_2), 4.34 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, α-C_5H_4), 4.25 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, β-C_5H_4), 4.10 (s, 5H, C_5H_5). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 163.8, 150.9, 145.3, 131.2, 120.6, 101.3, 81.8, 69.1, 68.8, 66.9, 49.1. MS (EI, 70 eV): *m*/*z* 336 (M^+), 271 ($M^+ - C_5H_5$). FTIR (KBr; ν, cm^{-1}): 1720 (w, CO), 1687 (s, CO), 1666 (s, CO). Anal. Calcd for $C_{17}H_{16}N_2O_2Fe$: C, 60.74; H, 4.80; N, 8.33. Found: C, 60.51; H, 5.08; N, 8.05.

*[3-(N1-Thyminyl)-1-(ferrocenyl)]propene (**3c**).* Orange-yellow crystals. Yield: 32%. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.24 (s, 1H, NH), 7.50 (d, $J_{H,H}$ = 1.2 Hz, 1H, H-6 thymine), 6.32 (d, $J_{H,H}$ = 15.6 Hz, 1H, Fc-C*H*═), 5.81 (dt, $J_{H,H}$ = 15.6 Hz, 6.6 Hz, 1H, ═C*H*-CH_2), 4.43 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, α-C_5H_4), 4.25 (dd, $J_{H,H}$ = 6.6 Hz, 1.2 Hz, 2H, CH_2), 4.23 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, β-C_5H_4), 4.10 (s, 5H, C_5H_5), 1.76 (d, $J_{H,H}$ = 0.6 Hz, 3H, CH_3). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.39 (s, 1H, NH), 7.01 (s, 1H, H-6 thymine), 6.40 (d, $J_{H,H}$ = 15.6 Hz, 1H, Fc-C*H*═), 5.76 (dt, $J_{H,H}$ = 15.6 Hz, 6.6 Hz, 1H, ═C*H*-CH_2), 4.35−4.33 (m, 4H, overlap. signals of CH_2, α-C_5H_4), 4.25 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, β-C_5H_4), 4.10 (s, 5H, C_5H_5), 1.92 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 164.4, 150.8, 141.0, 131,2, 120.7, 108.8, 81.8, 69.1, 68.8, 66.9, 48.8, 12.0 MS (EI, 70 eV): *m*/*z* 350 (M^+), 285 ($M^+ - C_5H_5$). FTIR (KBr; ν, cm^{-1}): 1686 (s, CO), 1646 (s, CO). Anal. Calcd for $C_{18}H_{18}N_2O_2Fe$: C, 61.74; H, 5.18; N, 8.00. Found: C, 61.68; H, 5.45; N, 7.92.

*[3-(N1-(5-Fluorouracilyl))-1-(ferrocenyl)]propene (**4c**).* Orange-yellow crystals. Yield: 35%. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.78 (s, 1H, NH), 8.06 (d, $J_{H,F}$ = 6.6 Hz, 1H, H-6 5-fluorouracil), 6.35 (d, $J_{H,H}$ = 15.6 Hz, 1H, Fc-C*H*═), 5.82 (dt, $J_{H,H}$ = 15.6 Hz, 6.6 Hz, 1H, ═C*H*-CH_2), 4.43 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, α-C_5H_4), 4.25 (dd, $J_{H,H}$ = 6.6 Hz, 1.2 Hz, 2H, CH_2), 4.23 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, β-C_5H_4), 4.09 (s, 5H, C_5H_5). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 157.5 (d, $J_{C,F}$ = 33.0 Hz), 149.5, 139.8 (d, $J_{C,F}$ = 229.5 Hz), 131.6, 129.7 (d, $J_{C,F}$ = 33.0 Hz), 120.1, 81.7, 69.1, 68.8, 66.9, 49.4. MS (EI, 70 eV): *m*/*z* 354 (M^+), 289 ($M^+ - C_5H_5$). FTIR (KBr; ν, cm^{-1}): 1708 (s, CO), 1694 (s, CO), 1661 (s, CO), 1235, 820. Anal. Calcd for $C_{17}H_{15}N_2O_2FFe$: C, 57.65; H, 4.27. Found: C, 57.67; H, 4.31.

*[3-(N1-Uracilyl)-1-(ruthenocenyl)]propene (**5c**).* Colorless crystals. Yield: 32%. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.24 (s, 1H, NH), 7.54 (d, $J_{H,H}$ = 8.4 Hz, 1H, H-6 uracil), 6.18 (d, $J_{H,H}$ = 15.6 Hz, 1H, Fc-C*H*═), 5.76 (dt, $J_{H,H}$ = 15.6 Hz, 6.6 Hz, 1H, ═C*H*-CH_2), 5.57 (d, $J_{H,H}$ = 8.4 Hz,1H, H-5 uracil), 4.83 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, α-C_5H_4), 4.57 (pseudo-t, $J_{H,H}$ = 1.8 Hz, 2H, β-C_5H_4), 4.49 (s, 5H, C_5H_5), 4.228 (dd, $J_{H,H}$ = 6.6 Hz, 1.2 Hz, 2H, CH_2). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 163.7, 150.8, 145.2, 130.3, 120.4, 101.2, 85.7, 71.1, 70.8, 69.3, 48.8. MS (EI, 70 eV): *m*/*z* 382 (M^+), 271 ($M^+ - C_4H_3N_2O_2$). FTIR (KBr; ν, cm^{-1}): 1690 (s, CO), 1666 (s, CO), 1470, 803. Anal. Calcd for $C_{17}H_{16}N_2O_2Ru$: C, 53.54; H, 4.23; N, 7.34. Found: C, 53.59; H, 4.31; N, 7.19.

X-ray Structure Determination of 2b and 4a. Crystals of **2b** and **4a** were mounted on a Stoe Mark II-Image Plate Diffraction System, using Mo Kα graphite-monochromated radiation,an image

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plate distance of 135 mm, a 2θ range from 2.4 to 51.3°, and $D_{max}-D_{min}$ = 16.029−0.836 Å. The structures were solved by direct methods using the program SHELXS-97.[23] Refinement and all further calculations were carried out using SHELXL-97.[23] The H atoms were included in calculated positions and treated as riding atoms using the SHELXL default parameters. The non-H atoms were refined anisotropically, using weighted full-matrix least squares on F^2. In **2b**, the alcohol function is disordered over two positions, with occupancies of 0.75:0.25. Despite several attempts to get better crystals of complex **4a** and a better data set, only poor-quality data were obtained. Nevertheless, the molecular structure of **4a** confirms the structure suggested on the basis of the compiled NMR data. In **4a**, all residual electron densities >1 e $Å^{-3}$ are located near the Fe atom. Crystallographic details are summarized in Table S1 (Supporting Information). Figures 2 and 3 were drawn with ORTEP32,[24] while Figures 4 and 5 were prepared with the software Mercury CSD 3.0.[25] CCDC-927648 (**2b**) and CCDC-927649 (**4a**) contain supplementary crystallographic data for this paper. These can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, U.K.; fax, (internat.) +44-1223/336-033; e-mail, deposit@ccdc.cam.ac.uk).

Antiproliferative Effects and Cellular Uptake. Antiproliferative effects in HT-29 colon adenocarcinoma cells and MCF-7 breast cancer cells and the cellular ruthenium uptake were determined as described in recent reports.[22] Compounds were prepared as stock solutions in DMF and diluted 1000-fold with the assay media to the indicated concentrations.

Evaluation of Antibacterial Activity. The antibacterial activities of compounds **2a**, **3a**, **4a**−**c**, and **5a** were tested by the liquid microdilution method.[26] The antimicrobial spectra of ferrocenyl−uracils **2a**−**4a**, **2b**, **4b**, **2c**, and **4c** and ruthenocenyl−uracil **5a** were evaluated by the minimal inhibitory concentrations (MIC). Results were obtained with the use of Spectrostar Omega (BMG Labtech); the absorbance was measured at λ 540 and 595 nm. A panel of Gram-positive bacterial strains was used: *Staphylococcus aureus* ATCC 29213 (sensitive to methicillin, MSSA), *Staphylococcus aureus* ATCC 43300 (resistant to methicillin, MRSA), *Staphylococcus aureus* ATCC 700787 (resistant to vancomycin, VRSA), and *Staphylococcus epidermidis* ATCC 12228. The MIC value of the reference compound, penicillin G, against *S. aureus* ATCC 29213 was 4.8 $\mu g\ mL^{-1}$. A detailed methodology for these antibacterial activity tests is given in the Supporting Information.

Hemolysis. Hemolysis tests were evaluated following the literature method.[27] Red blood cells were obtained from a healthy donor. The erythrocytes prepared in the PBS were suspended so that they corresponded to a hematocrit of 1% in compounds **2a**−**4a** (final concentrations from 0.001 to 0.2 mM) and incubated for 30 min at 23 °C. After centrifugation (1000 rpm, 5 min) the absorbance of the supernatant was measured at 540 nm (Jasco V-630). A value of 100% hemolysis was determined by incubation of erythrocytes with double-distilled water (30 min at 23 °C).

■ ASSOCIATED CONTENT

Supporting Information

Table S1 and CIF files giving crystallographic data for **2b** and **4a**, figures giving ^1H and $^{13}C\{^1H\}$ NMR spectra for **2c**−**5c** and cyclic voltammograms for **2c** and **3c**, and text giving the detailed methodology of antibacterial and anticancer activity tests. 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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