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Ni–Pd Catalyzed Cyclization of Sulfanyl 1,6-Diynes: Synthesis of 1′-Homonucleoside Analogues

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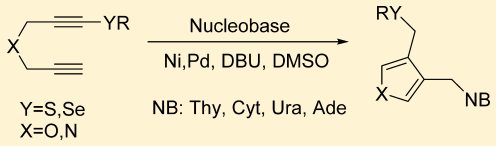
Supporting Information

ABSTRACT: The Ni–Pd catalyzed addition–cyclization of sulfanyl 1,6-diynes **2**–**9** with nucleobases is described. The reactions of *N*-tethered 1,6-diynes with N^3-benzoylthymine, N^4,N^4-bis(Boc)cytosine, N^3-benzoyluracil and N^6,N^6-bis(Boc)adenine exclusively afforded the pyrrolylmethyl and furylmethyl nucleotides in good yields. Deprotection of nucleobases was completed by treatment with acids or bases. Furthermore, the reactions of pyrroles and furans with nucleophiles such as alkoxides and amines underwent detosylation and conversion to the alkoxymethyl- and arylaminomethyl-pyrroles and furans in good yields.



INTRODUCTION

Modification of individual nucleosides is of major importance in the development of drugs.[1] A wide variety of clinically used nucleosides have been afforded by modification of sugar residues of nucleosides, including useful antiviral and anticancer agents such as azidothymidine (AZT),[2] dideoxycytidine (ddC),[3] dideoxyinosine (ddI),[4] and acyclovir as well as their analogues, in addition to lamivudine (3TC),[5] in which the carbohydrate is replaced by carbocyclic, acyclic and heterocyclic residues. To further increase the biological activity and selectivity of nucleoside analogues, much attention has been focused on enzymatically stable derivatives such as 1′-homo-*N*-nucleosides, which are tethered by a methylene group between the sugar moiety and the nucleobases.[6,7]

1′-Homo-*N*-nucleosides and their analogues are usually prepared from the nucleophilic displacement reactions of nucleobases with pentofuranose rings bearing a leaving group at the C-6′ position.[8] Another common method is the nucleobase being constructed by condensation from pentofuranosyl methylamines.[8c,9] These methods have a complex multistep procedure based on two fundamental processes: (i) preparation of carbohydrates, heterocyclic rings, and acyclic residues; (ii) introduction of nucleobases by nucleophilic displacement of carbohydrates or other residues bearing good leaving groups (Scheme 1). These multistep syntheses of homonucleosides gave rise to low yields and/or the formation of side-products. Recently, we developed a secondary amine-promoted cyclization of sulfanyl 1,6-diynes leading to polysubstituted heterocycles tethered by methylene groups between heterocycles and secondary amines.[10] Our strategy for the sulfanyl 1,6-diyne cyclization is highly regioselective due to the metal-coordinated effects between the sulfur atom on the terminal alkyne and the intramolecular alkynyl group. If the nucleobases were applicable to our amination–cyclization process, the 1′-homo-*N*-nucleosides bearing pyrroles and furans could be conveniently constructed from the readily available 1,6-diynes and nucleobases. 1′-Homonucleosides with pyrrolidine, isoxazolidine, and thiolane rings have been synthesized because of the interest in inhibiting glycosidases by modification of the spatial and electronic environment around the heterocycles in the five-membered rings.[11,12] However, nucleobases having a pyrrole ring have not yet been reported to the best of our knowledge. Here, we report a nucleobase-promoted cyclization reaction of sulfanyl and selanyl 1,6-diynes leading to new homonucleoside analogues and their antiviral and antiproliferative activities.

RESULTS AND DISCUSSIONS

First, we prepared nitrogen-tethered 1,6-diynes as shown in Scheme 2. Mitsunobu reactions of propargyl alcohols **1** with phenylsulfanyl and phenylselanyl propargyl alcohols provided the desired sulfanyl **2**, **3**–**9** and selanyl 1,6-diynes **3**. The other diynes **4**–**6** bearing substituents at the α-position of the nitrogen atom were also obtained from *N*-Boc tosylamide by a sequential process containing the Mitsunobu reaction.

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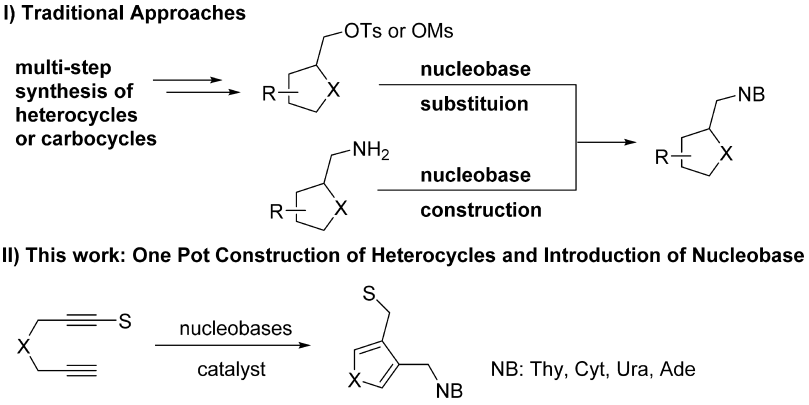
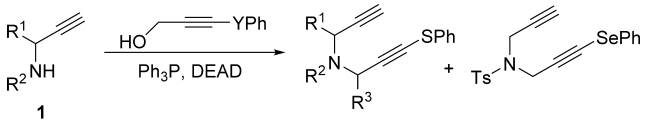
Scheme 1. Synthesis of Homonucleoside Analogues

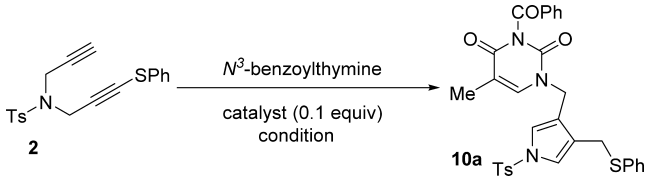


Scheme 2. Preparations of Sulfanyl and Selanyl 1,6-Diynes



2 (R^1=R^3=H; R^2=Ts)(85%)
4 (R^1=Me; R^2=Ts; R^3=H) (64%)
5 (R^1=pent; R^2=Ts; R^3=H)(77%)
6 (R^1=Ph; R^2=Ts; R^3=H) (46%)
7 (R^1=H; R^2=Ts; R^3=2-naph) (47%)
8 (R^1=R^3=H; R^2=*p*-$NO_2C_6H_4$)(57%)
9 (R^1=R^3=H; R^2=Ms)(21%)

Table 1. Screening for Catalysts of Thymine-Promoted Cyclization of 1,6-Diyne 2



entry	catalyst (equiv)[a]	yield of **10a**[b]
1	$NiCl_2(PPh_3)_2$, 2 h	87
2	$Pd(PPh_3)_4$, 1 h	77
3	$PdCl_2(PPh_3)_2$, 1.5 h	99
4	Nickelocene, 2 h	77
5	$NiCl_2$(dppe), 2.5 h	83
6	Ni(hfa)$_2$ H_2O, 2.5 h	89

[a]The commercially available catalysts were used without further purifications. [b]The isolated yields were listed in the table.

Next, we examined a reaction of *N*-tethered 1,6-diyne **2** with N^3-benzoylthymine in the presence of bis(hexafluoroacetylacetonato)nickel(II) hydrate (0.1 equiv), bis(triphenylphosphine)palladium(II) dichloride (0.1 equiv) and DBU (3 equiv) at 50 °C accordingly to our previous report.[10a] The cyclization-amination of **2** with N^3-benzoylthymine regioselectively proceeded to give 4-[(3-benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidyl)methyl]-3-(phenylsulfanylmethyl)-1-(*p*-tosyl)pyrrole (**10a**) in 74% yield. The structure of product **10a** was determined by its ^{1}H NMR spectrum, which shows the characteristic two doublet protons at δ 6.89 and 7.07 (J = 2.1 Hz) ppm due to the pyrrole ring and the other two singlet protons at δ 3.85 and 4.76 ppm due to the 3- and 5-methylene groups of the pyrrole. Since our process was found to be tolerated for the nucleobase-promoted cyclization reaction leading to the 1′-homonucleoside analogues, we next screened for optimized reaction conditions as shown in Table 1. Nickel or palladium metals were suitable for the nucleobase-promoted cyclizations. Bis(triphenylphosphine)palladium dichloride is the most convenient and suitable catalyst from the examination (entries 2−5). Water did not inhibit the formation of **10a** (entry 6). N^3-Benzoylthymine derivative **10a** easily underwent debenzoylation under the alkaline conditions to give 4-[(3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidyl)methyl]-3-(phenylsulfanylmethyl)-1-(*p*-tosyl)pyrrole (**11a**).

With the optimized reaction conditions in hand, we next screened the scope of 1,6-diynes and nucleobases. The results are shown in Table 2. A similar reaction of selenium analogue **3** afforded the selenomethylpyrrole **12a** in high yield (entry 1). The cyclization of *N*-3-butyn-2-ynyl diyne **4** successfully gave the 5-methylpyrrolyl derivative **13a** (entry 2), while the 5-pentylpyrrolyl homothymine **14a** was obtained (entry 3). 2-Naphthalen-1-ylpyrrole **16a** was obtained from naphthalen-1-yldiyne **7** in a similar manner. Next, we examined the effect of the substituent on nitrogen. *N*-*p*-Nitrophenyl- and methanesulfonyl 1,6-diynes **8** and **9** tolerated the thymine-promoted cyclizations (entries 6−7).

We next examined the cyclization of the similar 1,6-diynes with N^6,N^6-bis(Boc)adenine. Reaction of sulfanyl 1,6-diyne **2** with adenine afforded the pyrrolylmethyladenine **10b** in 65% yield. The reactions of the other 1,6-diynes **4**−**6** and **8** gave the products 5-methylpyrrolyl-**13b**, 5-pentylpyrrolyl-**14b**, and 5-phenylpyrrolylmethyladenine **15b**; however, most of these products yields were relatively low. Surprisingly, the use of *N*-nitrophenylsulfonyl-1,6-diyne **8** improved the yields of products (entry 12). On the other hand, it is difficult to yield the pyrrolylmethyluracil; however, the product **10c** was obtained in 73% yield as a sole uracil derivative (entry 13), while the reaction of **2**−**5** with N^4,N^4-bis(Boc)cytosine afforded 1-pyrrolylmethyl-N^4,N^4-bis(Boc)cytosines **10d**, **13d**, and **14d** in high yield (entry 14−16). Since we succeeded with the addition−cyclization of 1,6-diynes with four nucleobases, we next examined the deprotection of pyrrolylmethylnucleosides according to standard methods. Debenzoylation of both **14a** and **10c** easily proceeded under alkaline conditions to give 1-(*p*-tosyl)pyrroles **19a** and **11c**. Deprotection of the Boc groups of adenine and cytosine derivatives **10b**, **14b**, **10d**, and **14d** under the usual acid-mediated conditions was accomplished to give both adenines **11b** and **19b** and cytosines **11d** and **19d** in good yields.

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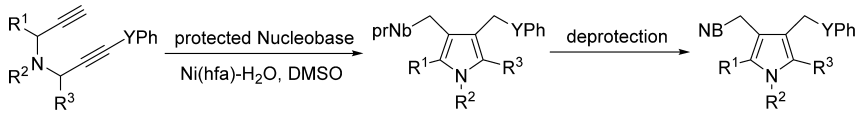
Table 2. Substrate Scope for Nucleobase-Promoted Cyclization of *N*-Tethered 1,6-Diynes

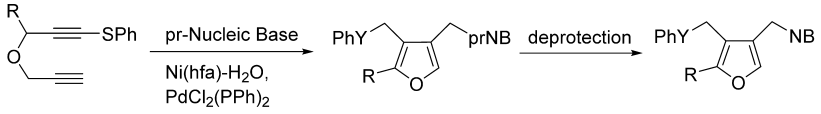


2, 4-9 (Y=S); **3** (Y=Se) | **12a-19a** (Y=S), **12a** (Y=Se), **10b-22b** (Y=S), **10c, 10d-14d** (Y=S) | **20a-22a**, **20b-21b**, **20d-21d**

entry	NB	PG	diyne	R^1	R^2	R^3	time (h)	yields (%)[a]
1	Thy	Bz	**3** (Y = Se)	H	Ts	H	2	**12a** (81)
2			**4** (Y = S)	Me	Ts	H	0.5	**13a** (62)
3			**5** (Y = S)	pent	Ts	H	0.33	**14a** (65/78)
4			**6** (Y = S)	Ph	Ts	H	3.5	**15a** (17)
5			**7** (Y = S)	H	Ts	^{1}naph	0.42	**16a** (57)
6			**8** (Y = S)	H	^{p}NO$_2$C$_6$H$_4$	H	1	**17a** (46)
7			**9** (Y = S)	H	Ms	H	2	**18a** (52)
8	Ade	Boc	**2** (Y = S)	H	Ts	H	2	**10b** (65/66)
9			**4** (Y = S)	Me	Ts	H	5	**13b** (45)
10			**5** (Y = S)	pent	Ts	H	6.7	**14b** (48/96)
11			**6** (Y = S)	Ph	Ts	H	9.5	**15b** (6)
12			**8** (Y = S)	H	^{p}NO$_2$C$_6$H$_4$	H	1	**17b** (63)
13	Ura	Bz	**2** (Y = S)	H	Ts	H	3	**10c** (73/49)
14	Cyt	Boc	**2** (Y = S)	H	Ts	H	2	**10d** (89/90)
15			**4** (Y = S)	Me	Ts	H	8	**13d** (39)
16			**5** (Y = S)	pent	Ts	H	6.25	**14d** (36/23)

[a]All products were isolated.

Table 3. Scope for Nucleobase-Promoted Cyclization of *O*-Tethered 1,6-Diynes



20 ($R=^p$MeOC$_6$H$_4$)
21 ($R=^p$ClC$_6$H$_4$)
22 ($R=^p$FC$_6$H$_4$)

23a-c ($R=^p$MeOC$_6$H$_4$)
24a-c ($R=^p$ClC$_6$H$_4$)
25a-c ($R=^p$FC$_6$H$_4$)

26a-27a ($R=^p$MeOC$_6$H$_4$)
28b ($R=^p$FC$_6$H$_4$)

entry	NB	PG	diyne	R	time (h)	yields (%)
1	Thy	Bz	**20**	^{p}MeOC$_6$H$_4$	20 min	**23a** (95/65)
2			**21**	^{p}ClC$_6$H$_4$	4.25	**24a** (67/78)
3			**22**	^{p}FC$_6$H$_4$	1.6	**25a** (43)
4	Ade	Boc	**21**	^{p}ClC$_6$H$_4$	2.8	**24b** (46)
5			**22**	^{p}FC$_6$H$_4$	20 min	**25b** (53/48)
6	Ura	Bz	**22**	^{p}FC$_6$H$_4$	1	**25c** (65/39)
7	Cyt	Boc	**20**	^{p}MeOC$_6$H$_4$	50 min	**23d** (38)
8			**22**	^{p}FC$_6$H$_4$	45 min	**25d** (48)

We next examined the addition−cyclization of *O*-tethered 1,6-diynes, which were easily prepared from the Lewis acid-catalyzed etherification of 1-arylpropargylic alcohol under similar conditions to that of the *N*-tethered derivatives (Table 3). The reaction of *p*-methoxyphenyl-substituted 4-oxahepta-1,6-diyne **20** with N^3-benzoylthymine gave the nucleobase-substituted furan **23a** in 95% yield (entry 1). Accordingly, the substrates bearing electron-withdrawing groups such as chlorine and fluorine atoms on aromatic rings accelerated the nucleobase-promoted cyclization to afford the unique furans **24a** and **25a** (entries 2 and 3). To screen the substrate scope using other bases, we selected the *p*-fluoro-, *p*-chloro-, and *p*-methoxyphenyl-substituted 1,6-diynes **20**−**22** as more reactive substrates and performed the reaction with N^6,N^6-bis(Boc)-adenine and N^4,N^4-bis(Boc)cytosine. The reactions were completed in 45 min-1 h, and the desired products **24b** and **25b** were obtained in moderate yield. Cytosine-promoted cyclization of sulfanyl 1,6-diynes **20** and **22** proceeded; however, the yield of products was relatively low (entries 6−8).

To clarify the synthetic utilization of nucleobase-substituted pyrrole derivatives, we performed transformations of thymine-substituted pyrroles as shown in Scheme 3. mCPBA oxidation and the following treatment with trifluoroacetic anhydride (the Pummerer reaction condition) gave the pyrrolemethanol **29**. CAN oxidation of **10a** in methanol afforded *N*-tosyl-methoxymethylpyrrole **30**, while the reaction with sodium hydroxide in alcohol gave the deprotected methoxymethyl-**31a** and **31d** and the ethoxymethylpyrroles **31b**; however, the bulky isopropyloxymethyl derivative **31c** was obtained in low yield. The reductive deselenenylation of **12a** (Y = Se) proceeded by treatment with Et_3SiH/Et_3B to give **32** in 40% yield. The reaction with *p*-anisidine in alkaline solution also underwent

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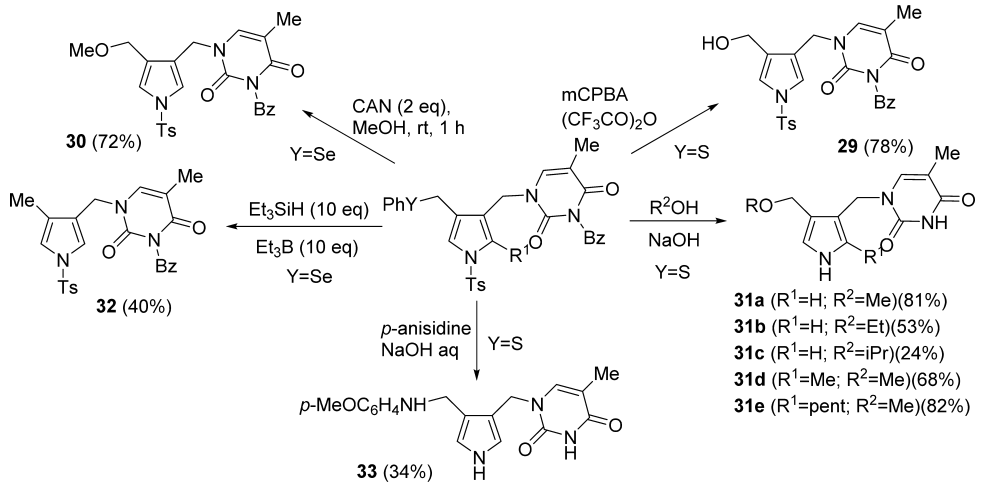
Scheme 3. Transformation of Thymine-Substituted Pyrroles



substitution to give **33** (Scheme 3). The 3-sulfanyl group of products were found to be replaced by other versatile nucleophiles. We were also interested in the biological activities and tested antiviral activity using Equine herpesvirus type 1 (EHV-1: family Herpesviridae, subfamily Alphaherpesvirinae, genus Varicellovirus); however, we could not find any noticeable activities at this stage.

Certain nucleoside analogues, fluorouracil and cytarabine, are commercially available as anticancer drugs. Fluorouracil, which includes the structure of pyrimidine, irreversibly inhibits the thymidylate synthase.[13] The cytosine arabinoside triphosphate, which is a metabolite of cytarabine, attenuated DNA synthase in malignant cells by convertion into cytosine arabinoside triphosphate.[14] In the present work, the antiproliferative activity of our synthesized nucleotide analogues against HCT-116 cells was assessed, and the data are shown in Figure 1. In 100 μM treatment of the derivatives, the 3-phenylsulfanylmethyl derivatives **27a** and **28b**, with 2-(*p*-chlorophenyl) and (*p*-fluorophenyl) moieties respectively, almost completely inhibited the tumor cell viability, while the derivatives without the 3-phenylsulfanylmethyl moiety scarcely attenuated the HCT-116 cell viability. Furthermore, the 4-pyrimidylmethyl derivatives with a 3-phenylsulfanylmethyl moiety, **11d**, **19a**, **27a**, and **28b**, demonstrated relatively good antiproliferative activity.

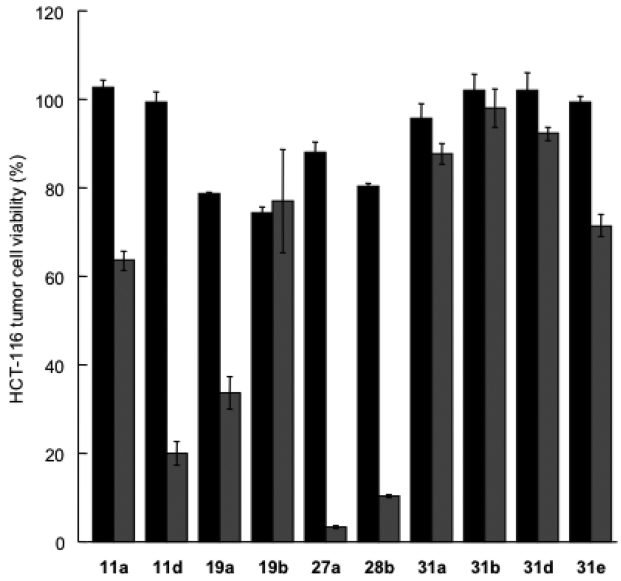


Figure 1. Antiproliferative activities of synthesized nucleotide derivatives against HCT-116 cells. HCT-116 cells were treated with 10 (filled column) and 100 μM (gray column) of the compounds, and then their viability was assessed using MTT method. Data are means ± SEM values (n = 3).

EXPERIMENTAL SECTION

General Experimental Methods. All nucleic base-promoted cyclization reactions were conducted using standard Erlenmeyer flask in 30 °C water bath. Analytical thin layer chromatography (TLC) was performed using silica gel precorted glass plates and visualized by ultraviolet radiation (254 nm). Flash column chromatography on silica gel was performed using silica gel (particle size 0.063−0.200 mm) under air pressure. Melting points were determined and uncorrected. ^{1}H and ^{13}C NMR spectra were determined with 600 MHz spectrometer. Chemical shifts are expressed in parts per million (ppm) with respect to tetramethylsilane as an internal standard. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet. IR spectra were determined on a FT-IR infrared spectrometer and are expressed in reciprocal centimeters. EI mass spectra (MS) were obtained with direct-insertion probe at 70 eV. ESI measurements and their high reolution mass were performed using DART system. 4-Methyl-*N*-[3-(phenylthio)-2-proryn-1-yl]-*N*-2-propyn-1-ylbenzenesulfonamide (**1**) and the selenium analogue (**2**) were prepared according to the method for the previous report.[10a] N^3-Benzoylthymine was prepared from thymine, benzoyl chloride, pyridine in acetonitrile.[15] N^3-Benzoyluracil was prepared from uracil, benzoyl chloride, and trimethylamine in acetonitrile.[16] Both N^4,N^4-bis(Boc)cytosine and N^6,N^6-bis(Boc)adenine were prepared by the protection-monodeprotection procedure of the corresponding nucleic bases such as cytosine and adenine from the corresponding nucleic bases, di-*t*-butyl dicarbonate, and in THF and the following de protection process using $NaHCO_3$ in methanol or K_2CO_3 in dioxane.[17]

4-Methyl-N-prop-2-ynyl-N-(3-phenylselanylprop-2-ynyl)benzenesulfonamide (3). To a THF (3.0 mL) solution of *N*-propargyl-*N*-4-methylphenylsulfonamide (0.50 g, 2.39 mmol), 3-phenylselanylprop-2-yn-1-ol (0.51 g, 2.39 mmol) and triphenylphosphine (0.63 g, 2.39 mmol) was added diethyl azodicarboxylate (2.20 M THF solution, 1.10 mL, 2.39 mmol) under an Ar atmosphere. The reaction mixture was stirred for 15 min and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with AcOEt−*n*-hexane (1:10) to provide the titled compound **3** (0.44 g, 46%) as a yellow oil.

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IR (KBr, cm^{-1}) 3287, 3058, 2922, 2177, 1597, 1577, 1477, 1440, 1351, 1250, 1164, 1093, 1020, 893, 815; ^1H NMR (600 MHz, $CDCl_3$) δ 2.18 (1H, t, J = 2.7 Hz), 2.36 (3H, s), 4.15 (2H, d, J = 2.1 Hz), 4.41 (2H, s), 7.21−7.23 (2H, d, J = 8.3 Hz), 7.26−7.30 (3H, m), 7.38−7.39 (2H, d, J = 7.6 Hz), 7.69−7.71 (2H, d, J = 8.3 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.5(q), 36.5 (t), 37.9 (t), 66.3(s), 74.1 (d), 76.3 (s), 95.8 (s), 127.2 (d), 127.8 (d × 2), 127.9 (s), 129.0 (d × 2), 129.5 (d × 2), 129.5 (d × 2), 135.0 (s), 144.0 (s); EIMS m/z 403 (M^+), 247 (M^+-Tos). Anal. Calcd for $C_{19}H_{17}NO_2SSe$: C, 56.72; H, 4.26; N, 3.48. Found: C, 56.58; H, 4.25; N, 3.33.

*N-(But-3-yn-2-yl)-4-methyl-N-(3-phenylsulfanylprop-2-yn-1-yl)-benzenesulfonamide (**4**).* To a THF (0.9 mL) solution of *N*-(but-3-yn-2-yl)-4-methylbenzenesulfonamide[21] (200 mg, 0.900 mmol), 3-phenylsulfanyl-2-propyn-1-ol (148 mg, 0.900 mmol) and triphenylphosphine (236 mg, 0.900 mmol) was added diethyl azodicarboxylate (0.40 mL of 2.2 M THF solution, 0.900 mmol) under an Ar atmosphere. The reaction mixture was stirred for 15 min and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with AcOEt−*n*-hexane (1:10) to provide the titled compound **4** (213 mg, 64%) as white powders (mp 80−81 °C).

IR (KBr, cm^{-1}) 3299, 2970, 1713, 1582, 1478, 1442, 1354, 1328, 1287, 1222, 1108, 1084, 1062, 1035, 989, 894, 834, 821, 741, 663, 589, 545, 526; ^1H NMR (600 MHz, $CDCl_3$) δ 1.53 (3H, d, J = 7.6 Hz), 2.23 (1H, d, J = 2.0 Hz), 2.34 (3H, s), 4.33 (1H, d, J = 18.6 Hz), 4.44 (1H, d, J = 18.6 Hz), 4.93 (1H, dd, J = 2.7 and 6.9 Hz), 7.22 (3H, d, J = 7.6 Hz), 7.29−7.33 (4H, m), 7.77 (2H, d, J = 8.9 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.5 (q), 21.9 (q), 34.8 (t), 45.8 (d), 71.3 (s), 73.7 (s), 81.0 (d), 94.6 (s), 126.3 (d × 2), 126.6 (d), 127.6 (d × 2), 129.1 (d × 2), 129.5 (d × 2), 132.3 (s), 136.5 (s), 143.6 (s); EIMS m/z 369 (M^+), 354 (M^+-Me), 214 (M^+-Ts), 199 (M^+-Me-Ts); MS (ESI) m/z 392 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{20}H_{19}NNaO_2S_2$ 392.07549; Found 392.07621.

*4-Methyl-N-(oct-1-yn-3-yl)-N-(3-phenylsulfanylprop-2-yn-1-yl)-benzenesulfonamide (**5**).* To a THF (7.4 mL) solution of 4-methyl-*N*-(oct-1-yn-3-yl)benzenesulfonamide[22] (2.0 g, 7.16 mmol), 3-phenylsulfanyl-2-propyn-1-ol (1.18 g, 7.16 mmol) and triphenylphosphine (1.88 g, 7.16 mmol) was added diethyl azodicarboxylate (2.20 M THF solution, 3.25 mL, 7.16 mmol) under an Ar atmosphere. The residue was purified by column chromatography on silica gel eluting with AcOEt−*n*-hexane (1:10) to provide the titled compound **5** (2.35 g, 77%) as white powders (mp 83−84 °C).

IR (KBr, cm^{-1}) 3246, 2952, 2863, 1713, 1481, 1363, 1335, 1289, 1222, 1167, 1152, 1092, 1056, 878, 811, 736, 689, 666, 583, 532; ^1H NMR (600 MHz, $CDCl_3$) δ 0.85 (3H, t, J = 7.5 Hz), 1.23−1.28 (4H, m), 1.39−1.48 (2H, m), 1.78−1.87 (2H, m), 2.19 (1H, d, J = 2.0 Hz), 2.35 (3H, s), 4.25 (1H, d, J = 18.6 Hz), 4.38 (1H, d, J = 18.6 Hz), 4.72 (1H, dd, J = 2.8 and 8.3 Hz), 7.20−7.24 (3H, m), 7.29−7.34 (4H, m), 7.76 (2H, d, J = 8.3 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 13.9(q), 21.5 (q), 22.4 (t), 25.7 (t), 31.1 (t), 34.9 (t), 35.2 (t), 50.5 (d), 71.0 (s), 74.1 (s), 80.4 (d), 94.5 (s), 126.3 (d × 2), 126.5 (d), 127.7 (d × 2), 129.1 (d × 2), 129.4 (d × 2), 132.3 (s), 136.5 (s), 143.6 (s); MS m/z 426 (M^++1); MS (ESI) m/z 448 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{24}H_{27}NNaO_2S_2$ 448.13809; Found 448.13879.

*4-Methyl-N-(1-phenylprop-2-yn-1-yl)-N-(3-phenylsulfanylprop-2-yn-1-yl)benzenesulfonamide (**6**).* To a THF (0.30 mL) solution of 4-methyl-*N*-(1-phenylprop-2-yn-1-yl)benzenesulfonamide[23] (90 mg, 0.32 mmol), 3-phenylsulfanyl-2-propyn-1-ol (52.6 mg, 0.32 mmol) and triphenylphosphine (83.9 mg, 0.32 mmol) was added diethyl azodicarboxylate (0.15 mL of 2.20 M THF solution, 0.32 mmol) under an Ar atmosphere. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:15) to provide the titled compound **6** (63 mg, 46%) as pale yellow powders (mp 77−79 °C).

IR (KBr, cm^{-1}) 3290, 1712, 1598, 1583, 1494, 1479, 1452, 1442, 1353, 1163, 1092, 1062, 899, 814, 740, 696, 667, 584, 547; ^1H NMR (600 MHz, $CDCl_3$) δ 2.34 (3H, s), 2.40 (1H, d, J = 2.1 Hz), 3.99 (1H, d, J = 18.5 Hz), 4.29 (1H, d, J = 18.5 Hz), 6.14 (1H, d, J = 2.7 Hz), 7.16 (2H, d, J = 4.8 Hz), 7.19 (1H, t, J = 7.5 Hz), 7.23−7.27 (4H, m), 7.30 (1H, t, J = 7.5 Hz), 7.36 (2H, t, J = 7.5 Hz), 7.64 (2H, d, J = 7.5 Hz), 7.86 (2H, d, J = 8.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.5 (q), 35.2 (t), 52.7 (d), 71.4 (s), 76.9 (s), 77.9 (d), 93.5 (s), 126.2 (d × 2), 126.4 (d), 127.9 (d × 2), 128.0 (d × 2), 128.5 (d × 2), 128.6 (d), 129.0 (d × 2), 129.4 (d × 2), 132.3 (s), 135.1 (s), 136.3 (s), 143.8 (s); MS m/z 431 (M^+), 354 (M^+-Ph); MS (ESI) m/z 454 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{25}H_{21}NNaO_2S_2$ 454.09114; Found 454.08898.

4-Methyl-N-(1-naphthalen-1-yl-3-phenylsulfanylprop-2-yn-1-yl)-benzenesulfonamide.[24] To a toluene (4.5 mL) solution of ethynyl phenyl sulfide (134.2 mg, 1.0 mmol), diethyl zinc (0.90 mL of 1.06 M, 1.0 mmol), (*Z*)-4-methyl-*N*-(naphthalen-1-ylmethylene)-benzenesulfonamide[25] (133 mg, 0.500 mmol) under an Ar atmosphere. The workup procedure gave the titled compound (166 mg, 75%) as pale yellow needles (mp 177−179 °C).

IR (KBr, cm^{-1}) 3233, 1479, 1440, 1324, 1157, 1089, 1038, 1024, 932, 806, 779, 738, 723, 671, 581, 552, 486; ^1H NMR (600 MHz, $CDCl_3$) δ 2.27 (3H, s), 4.98 (1H, d, J = 8.2 Hz), 6.24 (1H, d, J = 8.3 Hz), 7.13 (2H, d, J = 8.3 Hz), 7.19−7.22 (3H, m), 7.27 (3H, t, J = 7.6 Hz), 7.39 (1H, t, J = 7.6 Hz), 7.52 (1H, t, J = 6.8 Hz), 7.58 (1H, t, J = 6.8 Hz), 7.72 (1H, d, J = 6.9 Hz), 7.75 (2H, d, J = 8.2 Hz), 7.82 (1H, d, J = 8.2 Hz), 7.86 (1H, d, J = 8.2 Hz), 8.29 (1H, d, J = 8.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4 (q), 48.5 (d), 74.3 (s), 94.8 (s), 123.4 (d), 125.0 (d), 126.1 (d), 126.2 (d), 126.3 (d × 2), 126.7 (d), 127.1 (d), 127.5 (d × 2), 128.8 (d), 129.2 (d × 2), 129.4 (d × 2), 129.9 (d), 130.1 (s), 131.9 (s), 132.0 (s), 134.0 (s), 137.0 (s), 143.7 (s); MS m/z 443 (M^+), 334 (M^+-SPh); MS (ESI) m/z 466 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{26}H_{21}NNaO_2S_2$ 466.09114; Found 466.09339.

*4-Methyl-N-(1-naphthalen-1-yl)-3-phenylsulfanylprop-2-yn-1-yl)-N-(prop-2-yn-1-yl)benzenesulfonamide (**7**).* To a DMF (1.0 mL) solution of 4-methyl-*N*-(1-(naphthalen-1-yl)-3-(phenylthio)prop-2-yn-1-yl)benzenesulfonamide (90 mg, 0.2 mmol), propargyl bromide (119.0 mg, 0.8 mmol), sodium hydride (16.0 mg, 0.4 mmol). The reaction mixture was stirred for 10 min at 0 °C. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:10) to provide the titled compound **7** (46 mg, 47%) as pale yellow powders (mp 93−95 °C, 74% purity). The compound **7** was contaminated with the unknown compounds.

IR (KBr, cm^{-1}) 3294, 1712, 1598, 1479, 1350, 1162, 1091, 1048, 892, 854, 792, 742, 704, 689, 665, 576, 545; ^1H NMR (600 MHz, $CDCl_3$) δ 1.25 (1H, t, J = 7.3 Hz), 2.27 (3H, s), 3.51 (1H, dd, J = 18.5 and 2.7 Hz), 4.09 (1H, dd, J = 18.5 and 2.7 Hz), 4.12 (1H, s), 7.03 (1H, s), 7.17 (2H, d, J = 8.2 Hz), 7.22−7.26 (1H, m), 7.27−7.31 (3H, m), 7.45−7.47 (1H, m), 7.53−7.55 (1H, m), 7.63−7.65 (1H, m), 7.85−7.89 (2H, m), 7.92 (2H, d, J = 8.3 Hz), 8.01 (1H, d, J = 7.5 Hz), 8.51 (1H, d, J = 9.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.5 (q), 33.6 (t), 52.0 (d), 72.9 (d), 75.5 (s), 77.8 (s), 93.3 (s), 123.5 (d), 124.8 (d), 126.2 (d), 126.6 (d × 2), 126.7 (d), 127.3 (d), 128.2 (d), 128.5 (d × 2), 128.6 (d), 129.1 (d × 2), 129.2 (d × 2), 129.9 (s), 130.3 (d), 131.0 (s), 132.0 (s), 133.8 (s), 135.7 (s), 143.9 (s); EIMS m/z 481 (M^+); MS (ESI) m/z 504 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{29}H_{23}NNaO_2S_2$ 504.10679; Found 504.10828.

*N-(3-Phenylsulfanylprop-2-yn-1-yl)-N-(prop-2-yn-1-yl)-methanesulfonamide (**9**).* To a THF (2.9 mL) solution of *N*-(prop-2-yn-1-yl)methanesulfonamide[21] (300 mg, 2.3 mmol), 3-phenylsulfanyl-2-propyn-1-ol (377.7 mg, 2.3 mmol) and triphenylphosphine (603.3 mg, 2.3 mmol) was added diethyl azodicarboxylate (1.0 mL of 2.20 M THF solution, 2.3 mmol) under an Ar atmosphere. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:6) to provide the titled compound **9** (119 mg, 21%) as yellow powders (mp 35−36 °C).

IR (KBr, cm^{-1}) 3285, 2929, 1712, 1582, 1479, 1441, 1347, 1257, 1222, 1156, 1024, 966, 895, 784, 742, 689, 512; ^1H NMR (600 MHz, $CDCl_3$) δ 2.41 (1H, t, J = 2.8 Hz), 2.98 (3H, s), 4.21 (2H, d, J = 2.7 Hz), 4.43 (2H, s), 7.25 (1H, t, J = 7.6 Hz), 7.35 (2H, t, J = 7.6 Hz), 7.41 (2H, d, J = 8.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 36.7 (t), 38.1 (t), 38.6 (q), 73.7 (s), 74.7 (d), 76.7 (s), 91.6 (s), 126.4 (d × 2), 126.9 (d), 129.0 (d × 2), 131.6 (s); MS m/z 279 (M^+); MS (ESI) m/z

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302 [M + Na]$^+$; HRMS (ESI-DART) m/z [M + Na]$^+$ calcd for $C_{13}H_{13}NNaO_2S_2$ 302.02854; Found 302.02825.

*Synthesis of 4-[(3-Benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidyl)methyl]-3-(phenylsulfanylmethyl)-1-(p-tosyl)pyrrole (**10a**), typical procedure (Table 1, Entry 1).* To a DMSO (0.50 mL) solution of 4-methyl-*N*-[3-(phenylthio)-2-propyn-1-yl]-*N*-2-propyn-1-ylbenzenesulfonamide (**2**) (50 mg, 0.14 mmol) were added N^3-benzoylthymine (55.3 mg, 0.24 mmol), bis(triphenylphosphine)-palladium(II) dichloride (5.6 mg, 0.008 mmol), and DBU(36.5 mg, 0.24 mmol). The reaction mixture was stirred for 1.5 h at 50 °C. The cooled mixture was poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:1) to give the titled compound **10a** (49.0 mg, 99%) as yellow powders.

Yellow crystals, mp 45−46 °C, IR (KBr, cm^{-1}) ν 3133, 3064, 2927, 1747, 1698, 1656, 1598, 1519, 1481, 1439, 1372, 1230, 1255, 1173, 1092, 1066, 993, 950, 814, 744, 673, 588, 539; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.86 (3H, s), 2.41 (3H, s), 3.85 (2H, s), 4.76 (2H, s), 6.89 (1H, brs), 7.07 (1H, brs), 7.18 (6H, s), 7.27 (2H, d, J = 9.0 Hz), 7.40 (2H, t, J = 7.6 Hz), 7.59 (1H, t, J = 6.8 Hz), 7.63 (2H, d, J = 7.6 Hz), 7.91 (2H, d, J = 7.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.3 (q), 21.6 (q), 29.4 (t), 42.0 (t), 111.0 (s), 120.6 (d), 121.2 (d), 121.6 (s), 123.0 (s), 126.8 (d × 2), 126.9 (d), 128.9 (d × 2), 129.0 (d × 2), 130.1 (d × 2), 130.4 (d × 2), 130.7 (d × 2), 131.4 (s), 134.8 (s), 134.9 (d), 135.3 (s), 138.9 (d), 145.4 (s), 149.9 (s), 163.0 (s), 169.0 (s); EIMS m/z 585 (M$^+$), 476 (M$^+$-SPh); MS (ESI) m/z 608 [M + Na]$^+$; HRMS (ESI-DART) m/z [M + Na]$^+$ calcd for $C_{31}H_{27}N_3NaO_5S_2$ 608.12898, found 608.13068.

*Synthesis of 4-[(3,4-Dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidyl)methyl]-3-(phenylsulfanylmethyl)-1-(p-tosyl)pyrrole (Entry 1, debenzoylation of **10a**).* To a NaOH (0.85 mL, 1.7 mmol) in MeOH (3.4 mL) was added 4-[(3-benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidyl)methyl]-3-(phenylsulfanylmethyl)-1-(*p*-tosyl)pyrrole (**10a**) (100 mg, 0.17 mmol). The reaction mixture was stirred for 2 h and poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:1) to give the titled compound **11a** (44.0 mg, 90%) as yellow powders (mp 54−56 °C).

IR (KBr, cm^{-1}) ν 2927, 1678, 1470, 1372, 1305, 1250, 1173, 1092, 1067, 813, 747, 674, 588, 539; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.85 (3H, s), 2.43 (3H, s), 3.87 (2H, s), 4.74 (2H, s), 6.91 (1H, d, J = 2.3 Hz), 6.95 (1H, d, J = 1.4 Hz), 7.11 (1H, d, J = 2.3 Hz), 7.19 (5H, brs), 7.29 (2H, d, J = 7.8 Hz), 7.65 (2H, d, J = 8.7 Hz), 8.77 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.4 (q), 21.7 (q), 29.4 (t), 41.8 (t), 111.1 (s), 120.6 (d), 120.7 (d), 122.2 (s), 122.9 (s), 126.9 (d × 2), 128.5 (s), 128.9 (d × 2), 130.1 (d × 2), 130.6 (d × 2), 135.0 (s), 135.4 (s), 139.1 (d), 145.4 (s), 150.7 (s), 163.8 (s); MS m/z 481 (M$^+$), 438 (M$^+$-CONH); high resolution mass (EI) calcd for $C_{24}H_{23}N_3O_4S_2$: 481.1130, found m/z 481.1135. MS (ESI) m/z 504 [M + Na]$^+$; HRMS (ESI-DART) m/z [M + Na]$^+$ calcd for $C_{24}H_{23}N_3NaO_4S_2$ 504.10277; Found 504.10074.

*Synthesis of 4-[(3-Benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidyl)methyl]-3-(phenylselanylmethyl)-1-(p-tosyl)pyrrole (**12a**) (Table 2, Entry 1).* To a DMSO (0.50 mL) solution of 4-methyl-*N*-[3-(phenylthio)-2-propyn-1-yl]-*N*-2-propyn-1-ylbenzeneselenoamide (**3**) (30 mg, 0.07 mmol) were added N^3-benzoylthymine (48.3 mg, 0.21 mmol), bis(triphenylphosphine)palladium(II) dichloride (4.9 mg, 0.007 mmol), and DBU(32.0 mg, 0.21 mmol). The reaction mixture was stirred for 2 h at 50 °C. The cooled mixture was poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:1) to give the titled compound **12a** (38 mg, 81%) as pale yellow powders (mp 67−70 °C).

IR (KBr, cm^{-1}) ν 3133, 3069, 2928, 1747, 1697, 1655, 1598, 1518, 1439, 1372, 1299, 1254, 1173, 1092, 1066, 1021, 993, 950, 904, 814, 740, 672, 587, 539, 478; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.89 (3H, s), 2.42 (3H, s), 3.82 (2H, s), 4.75 (2H, s), 6.77 (1H, d, J = 2.1 Hz), 7.06 (1H, s), 7.15 (3H, t, J = 7.6 Hz), 7.23 (1H, t, J = 7.6 Hz), 7.28−7.30 (4H, m), 7.41−7.43 (2H, m), 7.60 (1H, t, J = 7.5 Hz), 7.64 (2H, d, J = 8.3 Hz), 7.92 (2H, d, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.4 (q), 21.2 (t), 41.9 (t), 111.1 (s), 120.2 (d), 121.1 (d), 121.4 (s), 124.0 (s), 126.9 (d × 2), 127.7 (d), 128.9 (d × 2), 129.0 (d × 2), 129.2 (s), 130.1 (d × 2), 130.4 (d × 2), 131.4 (s), 133.9 (d × 2), 135.0 (d), 135.3 (s), 138.9 (d), 145.4 (s), 150.0 (s), 163.1 (s), 169.0 (s); EIMS m/z 633 (M$^+$) 476 (M$^+$-SePh); HRMS (EI) m/z [M]$^+$ calcd for $C_{31}H_{27}N_3O_5SSe$: 633.0836; Found 633.0858. Anal. Calcd for $C_{31}H_{27}N_3O_5SSe$ (+ 2 H_2O): C, 55.69; H, 4.67; N, 6.28. Found: C, 55.39; H, 4.31; N, 5.84.

*4-[(3-Benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidyl)-methyl]-5-methyl-3-(phenylsulfanylmethyl)-1-(p-tosyl)pyrrole (**13a**), Entry 2.* To a DMSO (1.0 mL) solution of 4-methyl-*N*-[3-(phenylsulfanyl)-2-propyn-1-yl]-*N*-(1-methyl-2-propyn-1-yl)-benzenesulfonamide (**4**)[18] (100 mg, 0.27 mmol) were added N^3-benzoylthymine (186.5 mg, 0.81 mmol), bis(triphenylphosphine)-palladium(II) dichloride (19.0 mg, 0.027 mmol), and DBU(123.3 mg, 0.81 mmol). The reaction mixture was stirred for 0.5 h at 50 °C. The cooled mixture was poured into water (50 mL). The workup procedure gave the titled compound **13a** (100 mg, 62%) as yellow powders (mp 68−70 °C).

IR (KBr, cm^{-1}) ν 3431, 2928, 1748, 1698, 1656, 1599, 1440, 1368, 1239, 1171, 1093, 1024, 817, 762, 671, 590, 542, 478; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.92 (3H, s), 1.94 (3H, s), 2.44 (3H, s), 3.77 (2H, s), 4.78 (2H, s), 7.10−7.13 (3H, m), 7.16−7.19 (3H, m), 7.31 (2H, d, J = 8.2 Hz), 7.35−7.38 (3H, m), 7.57 (1H, t, J = 7.6 Hz), 7.63 (2H, d, J = 8.2 Hz), 7.93 (2H, d, J = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.6 (q), 12.4 (q), 21.7 (q), 29.5 (t), 42.2 (t), 111.1 (s), 119.6 (s), 119.7 (s), 121.1 (d), 127.0 (d × 2), 127.3 (d), 128.8 (d × 2), 129.0 (d × 2), 130.1 (d × 2), 130.2 (s), 130.5 (d × 2), 131.6 (s), 132.1 (d × 2), 134.8 (s), 134.9 (d), 135.6 (s), 138.9 (s), 145.3 (s), 150.0 (s), 163.0 (s), 169.1 (s); MS m/z 599 (M$^+$), 490 (M$^+$-SPh), 230 (M$^+$-SPh−COPh-Ts). MS (ESI) m/z 622 [M + Na]$^+$, 638 [M + K]$^+$; HRMS (ESI-DART) m/z [M + Na]$^+$ calcd for $C_{32}H_{29}N_3NaO_5S_2$ 622.14463; Found 622.14452.

*4-[(3-Benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidyl)-methyl]-5-pentyl-3-(phenylsulfanylmethyl)-1-(p-tosyl)pyrrole (**14a**), Entry 3.* To a DMSO (0.50 mL) solution of 4-methyl-*N*-[3-(phenylsulfanyl)-2-propyn-1-yl]-*N*-(oct-1-yn-3-yl)benzenesulfonamide (**5**)[19] (30 mg, 0.07 mmol) were added N^3-benzoylthymine (48.3 mg, 0.21 mmol), bis(triphenylphosphine)palladium(II) dichloride (4.9 mg, 0.007 mmol), and DBU (32.0 mg, 0.21 mmol). The reaction mixture was stirred for 20 min at 40 °C. The cooled mixture was poured into water (50 mL). The workup procedure gave the titled compound **14a** (30 mg, 65%) as yellow powders (mp 51−54 °C).

IR (KBr, cm^{-1}) ν 3431, 2957, 2930, 1748, 1698, 1656, 1599, 1440, 1371, 1261, 1238, 1170, 1094, 1066, 995, 817, 762, 671, 589, 544; ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.84 (3H, t, J = 6.9 Hz), 1.21−1.36 (6H, m), 1.90 (3H, s), 2.43−2.45 (5H, m), 2.41−2.45 (2H, t, J = 6.9 Hz), 3.82 (2H, s), 4.78 (2H, s), 7.10 (1H, s), 7.14−7.18 (3H, m), 7.20−7.22 (2H, m), 7.28 (2H, d, J = 8.3 Hz), 7.32 (1H, s), 7.36 (2H, t, J = 8.3 Hz), 7.56 (1H, t, J = 7.6 Hz), 7.61 (2H, d, J = 8.3 Hz), 7.91 (2H, d, J = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.4 (q), 14.0 (q), 21.6 (q), 22.2 (t), 25.1 (t), 29.5 (t), 30.3 (t), 31.8 (t), 42.5 (t), 111.0 (s), 120.0 (s), 120.1 (s), 121.7 (d), 126.8 (d × 2), 127.1 (d), 128.9 (d × 2), 129.0 (d × 2), 130.1 (d × 2), 130.5 (d × 2), 131.2 (d × 2), 131.6 (s), 134.8 (d), 135.4 (s), 135.5 (s), 136.1 (s), 139.0 (d), 145.2 (s), 150.0 (s), 163.0 (s), 169.0 (s); EIMS m/z 655 (M$^+$), 546 (M$^+$-SPh), 286 (M$^+$-SPh-Ts-COPh). MS (ESI) m/z 678 [M + Na]$^+$, 694 [M + K]$^+$; HRMS (ESI-DART) m/z [M + Na]$^+$ calcd for $C_{36}H_{37}N_3NaO_5S_2$ 678.20723; Found 678.21118.

*Deprotection of **14a**.* To a NaOH (2N aq 0.40 mL, 0.8 mmol) in MeOH (1.6 mL) was added 4-[(3-benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidyl)methyl]-5-pentyl-3-(phenylsulfanylmethyl)-1-(*p*-tosyl)pyrrole (**14a**) (50 mg, 0.08 mmol). The reaction mixture was

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stirred at 70 °C for 20 min and poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:1) to give the titled compound **19a** (33 mg, 78%) as pale yellow powders(mp 57−60 °C).

IR (KBr, cm^{-1}) ν 3036, 2954, 2930, 2854, 1671, 1596, 1466, 1438, 1369, 1242, 1221, 1190, 1170, 1093, 1066, 815, 761, 739, 700, 673, 609, 587; ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.86 (3H, t, J = 6.9 Hz), 1.20−1.27 (4H, m), 1.31−1.36 (2H, m), 2.43−2.47 (5H, m), 3.84 (2H, s), 4.74 (2H, s), 6.97 (1H, s), 7.17 (3H, d, J = 6.2 Hz), 7.18−7.19 (1H, m), 7.22 (2H, dd, J = 2.1 and 7.6 Hz), 7.27 (1H, s), 7.31 (2H, d, J = 8.2 Hz), 7.62 (2H, d, J = 8.2 Hz), 9.01 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.3 (q), 13.9 (q), 21.6 (t), 22.2 (t), 25.1 (t), 29.1 (t), 30.4 (t), 31.8 (t), 42.0 (t), 111.0 (s), 119.4 (s), 120.7 (s), 121.2 (d), 126.7 (d × 2), 126.8 (d), 128.8 (d × 2), 130.0 (d × 2), 130.6 (d × 2), 135.4 (s), 135.7 (s), 136.2 (s), 139.2 (d), 145.2 (s), 150.9 (s), 164.0 (s); EIMS m/z 551 (M^+), 442 (M^+-SPh). Anal. Calcd for $C_{29}H_{33}N_3O_4S_2$ (+ 1/2 H_2O): C, 62.12; H, 6.11; N, 7.49. Found: C, 62.23; H, 6.07; N, 7.29.

*4-[(3-Benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidyl)-methyl]-5-phenyl-3-(phenylsulfanylmethyl)-1-(p-tosyl)pyrrole (**15a**), Entry 4.* To a DMSO (0.50 mL) solution of 4-methyl-*N*-[3-(phenylsulfanyl)-2-propyn-1-yl]-*N*-(1-phethyl-2-propyn-1-yl)benzenesulfonamide (**6**) (50 mg, 0.1 mmol) were added N^3-benzoylthymine (69.1 mg, 0.3 mmol), bis(triphenylphosphine)palladium(II) dichloride (14.0 mg, 0.02 mmol), and DBU (45.7 mg, 0.3 mmol). The reaction mixture was stirred for 1.5 h at 50 °C. The cooled mixture was poured into water (50 mL). The workup procedure gave the titled compound **15a** (13 mg, 17%) as brown powders (mp 55−58 °C).

IR (KBr, cm^{-1}) ν 3444, 2925, 1748, 1698, 1658, 1598, 1440, 1374, 1239, 1175, 1092, 816, 761, 701, 670, 583, 542; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.94 (3H, s), 2.38 (3H, s), 3.65 (2H, s), 4.91 (2H, s), 6.85 (2H, d, J = 6.9 Hz), 7.05 (2H, d, J = 6.8 Hz), 7.09−7.16 (6H, m), 7.22 (4H, t, J = 7.6 Hz), 7.35 (1H, t, J = 7.6 Hz), 7.43 (2H, t, J = 7.6 Hz), 7.47 (1H, s), 7.60 (1H, t, J = 7.5 Hz), 7.95 (2H, d, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.5 (q), 21.6 (q), 29.4 (t), 43.0 (t), 111.0 (s), 120.0 (s), 121.5 (s), 122.3 (d), 127.0 (d), 127.3 (d × 2), 127.4 (d × 2), 128.6 (s), 128.9 (d × 3), 129.1 (d × 2), 129.5 (d × 2), 130.5 (d × 2), 131.2 (d × 2), 131.6 (s), 131.8 (d × 2), 134.1 (s), 134.8 (s), 134.9 (d), 135.1 (s), 139.3 (d), 145.1 (s), 150.0 (s), 163.1 (s), 169.1 (s); MS (ESI) m/z 684 [M + Na]$^+$, 700 [M + K]$^+$; HRMS (ESI-DART) m/z [M + Na]$^+$ calcd for $C_{37}H_{31}N_3NaO_5S_2$ 684.16028; Found 684.16301.

*4-[(3,4-Dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidyl)methyl]-3-(phenylsulfanylmethyl)-2-(1-naphthyl)-1-(p-tosyl)pyrrole (**16a**).* To a DMSO (0.50 mL) solution of 4-methyl-*N*-[2-(naphthalene-1-yl)-3-(phenylthio)-2-proryn-1-yl]-*N*-2-propyn-1-ylbenzenesulfonamide (**7**) (46 mg, 0.10 mmol) were added N^3-benzoylthymine (69.1 mg, 0.30 mmol) bis(triphenylphosphine)palladium(II) dichloride (7.0 mg, 0.01 mmol), and DBU (45.7 mg, 0.30 mmol). The reaction mixture was stirred at rt for 0.5 h. The mixture was poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with Et_2O-Hexane (1:3) to give the titled compound **16a** (39 mg, 57%) as yellow powders (mp 81−83 °C).

IR (KBr, cm^{-1}) ν 3442, 3060, 2925, 1748, 1699, 1656, 1598, 1439, 1372, 1237, 1174, 1112, 1092, 994, 953, 808, 776, 670, 584, 543, 445, 424, 403; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.97 (3H, s), 2.17 (3H, d, J = 13.1 Hz), 3.41 (1H, d, J = 13.1 Hz), 3.62 (1H, d, J = 13.1 Hz), 4.95 (1H, d, J = 15.8 Hz), 5.03 (1H, d, J = 15.1 Hz), 6.74 (2H, d, J = 7.6 Hz), 6.81 (1H, d, J = 8.2 Hz), 6.91−6.98 (6H, m), 7.04−7.13 (4H, m), 7.32−7.38 (3H, m), 7.43 (2H, t, J = 7.6 Hz), 7.58−7.63 (1H, m), 7.76 (1H, d, J = 8.2 Hz), 7.87 (1H, d, J = 8.3 Hz), 7.96 (2H, d, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.5 (q), 21.4 (q), 29.4 (t), 43.1 (t), 111.0 (s × 2), 119.4 (s), 122.1 (d), 122.6 (s), 124.5 (d), 125.1 (d), 125.4 (d), 125.7 (s), 126.2 (d), 126.8 (d), 127.4 (d × 2), 127.8 (d), 128.8 (d × 2), 129.1 (d × 2), 129.2 (d × 2), 129.8 (d), 130.5 (d × 2), 130.9 (d × 2), 131.6 (d), 131.6 (s), 132.8 (s), 133.3 (s), 134.2 (s), 134.8 (d), 134.9 (s), 139.6 (d), 144.9 (s), 150.0 (s), 163.2 (s), 169.1 (s); EIMS m/z 711 (M^+), 602 (M^+-SPh). MS (ESI) m/z 734 [M + Na]$^+$, 750 [M + K]$^+$; HRMS (ESI-DART) m/z [M + Na]$^+$ calcd for $C_{41}H_{33}N_3NaO_5S_2$ 734.17593; Found 734.17635.

*4-[(3-Benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidyl)-methyl]-3-(phenylsulfanylmethyl)-1-(p-nitrophenylsulfonyl)pyrrole (**17a**).* To a DMSO (0.50 mL) solution of 4-nitro-*N*-[3-(phenylthio)-2-propyn-1-yl]-*N*-2-propyn-1-ylbenzenesulfonamide (**8**) (30 mg, 0.08 mmol) were added N^3-benzoylthymine (55.3 mg, 0.24 mmol), bis(triphenylphosphine)palladium(II) dichloride (5.6 mg, 0.008 mmol), and DBU (36.5 mg, 0.24 mmol). The reaction mixture was stirred for 1.0 h at 50 °C. The workup procedure gave the titled compound **17a** (22 mg, 46%) as yellow powders.

IR (KBr, cm^{-1}) ν 3481, 2926, 1747, 1698, 1656, 1532, 1440, 1380, 1350, 1241, 1182, 1091, 1068, 856, 741, 684, 629, 583; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.91 (3H, s), 3.88 (2H, s), 4.78 (2H, s), 6.89 (1H, s), 7.12 (1H, s), 7.17 (1H, s), 7.20-7.22 (5H, m), 7.45 (2H, t, J = 7.6 Hz), 7.62 (1H, t, J = 7.6 Hz), 7.88 (2H, d, J = 8.3 Hz), 7.91 (2H, d, J = 7.6 Hz), 8.28 (2H, d, J = 8.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.4 (q), 29.4 (t), 42.7 (t), 111.3 (s), 120.5 (d), 121.4 (d), 123.2 (s), 124.4 (s), 124.8 (d × 2), 127.1 (d), 128.1 (d × 2), 129.0 (d × 2), 129.1 (d × 2), 130.5 (d × 2), 130.7 (d × 2), 131.5 (s), 134.5 (s), 135.1 (d), 139.0 (d), 143.6 (s), 149.9 (s), 150.7 (s), 162.9 (s), 168.9 (s); EIMS m/z 189 (M^+-Thy-*p*-$NO_2C_6H_4SO_2$). MS (ESI) m/z 639 [M + Na]$^+$; HRMS (ESI-DART) m/z [M + Na]$^+$ calcd for $C_{30}H_{24}N_4NaO_7S_2$ 639.09841; Found 639.09979.

*Synthesis of 4-[(3-Benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidyl)-methyl]-3-(phenylsulfanylmethyl)-1-(methanesulfonyl)-pyrrole (**18a**), Entry 7.* To a DMSO (0.50 mL) solution of *N*-[3-(phenylsulfanyl)prop-2yn-1-yl]-*N*-2-propyn-1-ylmethanesulfonamide (**9**) (30 mg, 0.08 mmol) were added N^3-benzoylthymine (103 mg, 0.45 mmol), bis(triphenylphosphine)palladium(II) dichloride (10.5 mg, 0.015 mmol), and DBU (685 mg, 0.45 mmol). The reaction mixture was stirred for 2.0 h at 50 °C. The workup procedure gave the titled compound **18a** (33 mg, 52%) as yellow powders (mp 54−56 °C).

IR (KBr, cm^{-1}) ν 2927, 1746, 1697, 1655, 1598, 1439, 1365, 1300, 1242, 1173, 1070, 987, 948, 819, 772, 692, 553, 474; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.94 (3H, s), 3.05 (3H, s), 3.94 (2H, s), 4.85 (2H, s), 6.83 (1H, d, J = 2.0 Hz), 7.12 (1H, d, J = 2.8 Hz), 7.17 (1H, d, J = 1.4 Hz), 7.22−7.28 (5H, m), 7.44 (2H, t, J = 7.5 Hz), 7.61 (1H, t, J = 7.6 Hz), 7.93 (2H, d, J = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.4 (q), 29.7 (t), 42.4 (t), 42.8 (q), 111.3 (s), 120.3 (d), 120.8 (d), 121.8 (s), 123.0 (s), 127.1 (d), 129.0 (d × 2), 129.1 (d × 2), 130.4 (d × 2), 131.1 (d × 2), 131.5 (s), 134.8 (s), 135.0 (d), 139.1 (d), 150.0 (s), 163.0 (s), 169.0 (s); EIMS m/z 509 (M^+). MS (ESI) m/z 532 [M + Na]$^+$; HRMS (ESI-DART) m/z [M + Na]$^+$ calcd for $C_{25}H_{23}N_3NaO_5S_2$ 532.09768; Found 532.09634.

*Synthesis of 4-[N^6,N^6-Bis(Boc)adenin-9-ylmethyl]-3-[(phenylsulfanyl)methyl]-2-pyrrole (**10b**), Entry 8.* To a DMSO (0.50 mL) solution of 4-methyl-*N*-[3-(phenylthio)-2-propyn-1-yl]-*N*-2-propyn-1-ylbenzenesulfonamide (**2**) (30 mg, 0.08 mmol) were added 4-[N^6,N^6-bis(Boc)amino]-9*H*-purine (80.5 mg, 0.24 mmol), 1,2-bis-(diphenylphosphino)ethane nickel(II) chloride (4.2 mg, 0.008 mmol), and DBU (36.5 mg, 0.24 mmol). The reaction mixture was stirred for 2 h at 50 °C. The cooled mixture was poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:2) to give the titled compound **10b** (38.0 mg, 65%) as pale yellow powders (mp 58−60 °C).

IR (KBr, cm^{-1}) 3435, 2980, 2928, 1788, 1758, 1602, 1456, 1370, 1335, 1280, 1254, 1173, 1144, 1109, 1067, 852, 814, 759, 673, 588, 539; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.43 (18H, s), 2.43 (3H, s), 3.82 (2H, s), 5.31 (2H, s), 6.88 (1H, d, J = 2.0 Hz), 7.15−7.20 (6H, m), 7.28 (2H, d, J = 8.3 Hz), 7.61 (2H, d, J = 8.3 Hz), 7.99 (1H, s), 8.84 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6 (q), 27.7 (qx6), 29.6 (t),

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38.5 (t), 83.8 (s), 120.5 (d), 120.8 (d), 121.5 (s), 122.7 (s), 126.8 (d × 2), 127.0 (d), 128.7 (s), 128.9 (d × 2), 130.1 (d × 2), 130.9 (d × 2), 134.6 (s), 135.3 (s), 144.4 (d × 2), 145.4 (s), 150.2 (s), 150.4 (s), 152.1 (d × 2), 153.1 (s); EIMS (*m*/*z*) 690 (small M^+), 535 (M^+-155). MS (ESI) *m*/*z* 713 $[M + Na]^+$, 729 $[M + K]^+$; HRMS (ESI-DART) *m*/*z* $[M + Na]^+$ calcd for $C_{34}H_{38}N_6NaO_6S_2$ 713.21919; Found 713.21728.

Deprotection of ***10b***. 1 N HCl (0.6 mL, 0.6 mmol) solution was added to a MeOH (1.2 mL) solution of **10b** (30 mg, 0.04 mmol) at room temperature. The reaction mixture was stirred for 7.5 h at 50 °C. The cooled mixture was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with $CHCl_3$−MeOH (45:1) to give the titled compound **11b** (14 mg, 66%) as white powders (mp 59−61 °C).

IR (KBr, cm^{-1}) ν 3626, 3408, 3272, 3115, 2924, 2853, 1676, 1604, 1521, 1480, 1420, 1370, 1335, 1305, 1247, 1188, 1171, 1089, 1067, 1016, 970, 906, 833, 809, 767, 674, 586, 542; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.42 (3H, s), 3.81 (2H, s), 5.23 (2H, s), 5.78 (2H, brs), 6.89 (1H, d, *J* = 2.0 Hz), 7.09 (1H, d, *J* = 2.0 Hz), 7.14−7.19 (5H, m), 7.28 (2H, s), 7.62 (2H, d, *J* = 8.2 Hz), 7.71 (1H, s), 8.34 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6 (q), 29.5 (t), 38.3 (t), 119.5 (s), 120.4 (d), 120.5 (d), 122.3 (s), 122.8 (s), 126.9 (d × 3), 128.8 (d × 2), 130.1 (d × 2), 130.7 (d × 2), 134.9 (s), 135.5 (s), 140.2 (d), 145.3 (s), 150.0 (s), 153.1 (d), 155.4 (s); EIMS *m*/*z* 490 (M^+), 381 (M^+-SPh), 335 (M^+-Tos), 226 (M^+-SPh-Tos); HRMS (EI) $[M]^+$ *m*/*z* calcd for $C_{24}H_{22}N_6O_2S_2$ 490.1245; Found 490.1263.

4-[7-(N^6*,*N^6*-Bis(Boc)amino)-9H-purin-9-yl]methyl-5-methyl-3-(phenylsulfanylmethyl)-1-tosylpyrrole (**13b**), Entry 9*. To a DMSO (0.50 mL) solution of 4-methyl-*N*-[3-(phenylsulfanyl)-2-propyn-1-yl]-*N*-(1-methyl-2-propyn-1-yl)benzenesulfonamide (**4**) (30 mg, 0.08 mmol) were added 4-[N^6,N^6-bis(Boc)amino]-9*H*-purine (81 mg, 0.24 mmol), bis(hexafluoroacetylacetonato)nickel(II) hydrate (3.8 mg, 0.008 mmol) and DBU (36.5 mg, 0.24 mmol). The reaction mixture was stirred for 5 h at 50 °C. The cooled mixture was poured into water (50 mL). The workup procedure gave the titled compound **13b** (26 mg, 45%) as pale yellow powders (mp 60−62 °C).

IR (KBr, cm^{-1}) ν 2979, 2932, 1789, 1725, 1577, 1452, 1370, 1335, 1280, 1250, 1170, 1145, 1105, 1094, 1049, 1000, 852, 816, 749, 669, 607, 584; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.43 (18H, s), 1.91 (3H, s), 2.45 (3H, s), 3.71 (2H, s), 5.30 (2H, s), 7.09−7.18 (5H, m), 7.31 (2H, d, *J* = 8.2 Hz), 7.34 (1H, s), 7.61 (2H, d, *J* = 8.2 Hz), 8.04 (1H, s), 8.85 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.5 (q), 21.6 (q), 27.8 (q × 6), 29.5 (t), 38.7 (t), 83.8 (s × 2), 119.4 (s), 119.6 (s), 120.9 (d), 127.0 (d × 2), 127.4 (d), 128.8 (d × 2), 128.9 (s), 129.9 (s), 130.1 (d × 2), 132.3 (d × 2), 134.5 (s), 135.6 (s), 144.5 (s), 145.3 (s), 150.2 (s), 150.5 (s × 2), 152.1 (d), 153.3 (s); EIMS *m*/*z* 370 (M + -Ade). MS (ESI) *m*/*z* 705 $[M + H]^+$, 727 $[M + Na]^+$, 743 $[M + K]^+$; HRMS (ESI-DART) *m*/*z* $[M + Na]^+$ calcd for $C_{35}H_{40}N_6NaO_6S_2$ 727.23484; Found 727.23226.

4-[7-(N^6*,*N^6*-Bis(Boc)amino)-9H-purin-9-yl]methyl-5-pentyl-3-(phenylsulfanylmethyl)-1-tosylpyrrole (**14b**), Entry 10*. To a DMSO (0.50 mL) solution of 4-methyl-*N*-[3-(phenylsulfanyl)-2-proryn-1-yl]-*N*-(1-pentyl-2-propyn-1-yl)benzenesulfonamide (**5**) (30 mg, 0.07 mmol) were added 4-[N^6,N^6-bis(Boc)amino]-9*H*-purine (70 mg, 0.21 mmol), bis(hexafluoroacetylacetonato)nickel(II) hydrate (3.3 mg, 0.007 mmol) and DBU (32 mg, 0.21 mmol). The reaction mixture was stirred for 7 h at 50 °C. The cooled mixture was poured into water (50 mL). The workup procedure gave the titled compound **14b** (26 mg, 48%) as pale yellow powders (mp 49−50 °C).

IR (KBr, cm^{-1}) ν 3434, 2926, 2856, 1790, 1749, 1601, 1577, 1456, 1370, 1283, 1250, 1171, 1107, 874, 745, 669, 606, 587; ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.83 (3H, t, *J* = 6.9 Hz), 1.17−1.32 (6H, m), 1.43 (18H, s), 2.39−2.43 (5H, m), 3.76 (2H, s), 5.30 (2H, s), 7.16−7.19 (5H, m), 7.29−7.31 (3H, m), 7.58 (2H, d, *J* = 8.2 Hz), 8.02 (1H, s), 8.83 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9 (q), 21.6 (q), 22.2 (t), 25.1 (t), 27.8 (q × 6), 29.4 (t), 30.4 (t), 31.7 (t), 38.8 (t), 83.9 (s × 2), 119.3 (s), 120.0 (s), 121.5 (d), 126.7 (d × 2), 127.2 (d), 128.9 (d × 2), 129.8 (s), 130.1 (d × 2), 131.4 (d × 2), 135.2 (s), 135.3 (s), 136.1 (s), 144.5 (d), 145.2 (s), 150.2 (s), 150.5 (s × 2), 152.0 (d), 153.3 (s); EIMS *m*/*z* 761 (M^++1). Anal. Calcd for $C_{39}H_{48}N_6O_6S_2$ (+1.5 H_2O): C, 59.45; H, 6.52; N, 10.67. Found: C, 59.18; H, 6.11; N, 10.25.

Deprotection of ***14b***. 1 N HCl (2.3 mL, 2.3 mmol) solution was added to a MeOH (4.6 mL) solution of **14b** (108 mg, 0.15 mmol) at room temperature. The reaction mixture was stirred for 8 h at 50 °C. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with $CHCl_3$−MeOH (10:1) to give the titled compound **19b** (78 mg, 96%) as white powders (mp 136−138 °C).

IR (KBr, cm^{-1}) ν 3300, 3136, 2956, 2925, 2858, 1677, 1645, 1604, 1573, 1539, 1480, 1419, 1362, 1330, 1302, 1282, 1234, 1170, 1092, 1068, 1026, 962, 905, 816, 748, 716, 676, 585, 536; ^{1}H NMR (600 MHz, DMSO) δ 0.78 (3H, t, *J* = 6.2 Hz), 1.13−1.16 (3H, m), 1.17−1.24 (3H, m), 2.36 (2H, t, *J* = 7.6 Hz), 2.51 (3H, s), 3.96 (2H, s), 5.22 (2H, s), 7.19−7.24 (7H, m), 7.39 (1H, s), 7.44 (2H, d, *J* = 8.2 Hz), 7.65 (2H, d, *J* = 9.0 Hz), 8.13 (2H, d, *J* = 13.8 Hz); ^{13}C NMR (125 MHz, DMSO) δ 13.8 (q), 21.1 (q), 21.7 (t), 24.4 (t), 27.9 (t), 30.0 (t), 31.1 (t), 37.3 (t), 119.7 (s), 121.5 (d), 122.3 (s), 126.5 (d × 2), 126.6 (d × 2), 128.8 (d × 2), 130.3 (d × 2), 130.4 (d × 2), 133.9 (s), 135.2 (s), 135.4 (s), 145.4 (s), 149.3 (s), 152.4 (d), 155.9 (s × 2); EIMS *m*/*z* 560 (small M^+), 451 (M^+-SPh), 405 (M^+-Ts). MS (ESI) *m*/*z* 561 $[M + H]^+$; HRMS (ESI-DART) *m*/*z* $[M + Na]^+$ calcd for $C_{29}H_{33}N_6O_2S_2$ 561.21064; Found 561.20937.

4-[7-(N^6*,*N^6*-Bis(Boc)amino)-9H-purin-9-yl]methyl-5-phenyl-3-(phenylsulfanylmethyl)-1-tosylpyrrole (**15b**), Entry 11*. To a DMSO (0.50 mL) solution of 4-methyl-*N*-[3-(phenylsulfanyl)-2-propyn-1-yl]-*N*-(1-phethyl-2-propyn-1-yl)benzenesulfonamide (**6**) (50 mg, 0.1 mmol) were added 4-[N^6,N^6-bis(Boc)amino]-9*H*-purine (100.6 mg, 0.3 mmol), bis(hexafluoroacetylacetonato)nickel(II) hydrate (9.5 mg, 0.02 mmol), and DBU(45.7 mg, 0.3 mmol). The reaction mixture was stirred for 9.5 h at 50 °C. The cooled mixture was poured into water (50 mL). The workup procedure gave the titled compound **15b** (5 mg, 6%) as pale yellow powders (mp 80−83 °C).

IR (KBr, cm^{-1}) ν 2925, 2853, 1751, 1609, 1466, 1369, 1323, 1232, 1175, 1146, 1093, 972, 814, 791, 751, 701, 668, 583, 543; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.57 (18H, s), 2.38 (3H, s), 3.58 (2H, s), 5.43 (2H, s), 6.81 (2H, d, *J* = 6.9 Hz), 7.02 (2H, d, *J* = 6.9 Hz), 7.10 (2H, d, *J* = 8.2 Hz), 7.12−7.17 (4H, m), 7.22 (2H, t, *J* = 7.6 Hz), 7.35 (1H, t, *J* = 7.6 Hz), 7.44 (1H, s), 7.97 (1H, brs), 7.99 (1H, s), 8.74 (1H, s); MS (ESI) *m*/*z* 789 $[M + Na]^+$, 805 $[M + K]^+$; HRMS (ESI-DART) *m*/*z* $[M + Na]^+$ calcd for $C_{40}H_{42}N_6NaO_6S_2$ 789.25049; Found 789.24628.

4-[7-(N^6*,*N^6*-Bis(Boc)amino)-9H-purin-9-yl]methyl-3-(phenylsulfanylmethyl)-1-(p-nitrophenylsulfonyl)pyrrole (**17b**), Entry 12*. To a DMSO (0.50 mL) solution of 4-nitro-*N*-[3-(phenylthio)-2-propyn-1-yl]-*N*-2-propyn-1-ylbenzenesulfonamide (**8**) (30 mg, 0.08 mmol) were added 9-[N^6,N^6-bis(Boc)amino]-9*H*-purine (80.5 mg, 0.24 mmol), bis(hexafluoroacetylacetonato)nickel(II) hydrate (4.2 mg, 0.008 mmol), and DBU (36.5 mg, 0.24 mmol). The reaction mixture was stirred for 1.0 h at 50 °C. The workup procedure gave the titled compound **17b** (32 mg, 63%) as pale yellow powders (mp 69−71 °C).

IR (KBr, cm^{-1}) ν 3106, 2981, 2928, 2853, 1789, 1720, 1604, 1577, 1535, 1453, 1370, 1349, 1280, 1250, 1211, 1183, 1141, 1108, 1067, 1108, 1067, 953, 854, 741, 683, 629, 586; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.46 (18H, s), 3.86 (2H, s), 5.33 (2H, s), 6.89 (1H, d, *J* = 2.0 Hz), 7.15 (1H, d, *J* = 2.0 Hz), 7.17−7.21 (5H, m), 7.86 (2H, d, *J* = 9.0 Hz), 8.04 (1H, s), 8.28 (2H, d, *J* = 9.0 Hz), 8.84 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.8 (q × 6), 29.3 (t), 38.4 (t), 83.9 (s × 2), 120.4 (d), 120.9 (d), 123.1 (s), 124.1 (s), 124.8 (d × 2), 127.1 (d), 128.1 (d × 2), 128.6 (s), 128.9 (d × 2), 130.8 (d × 2), 134.3 (s), 143.5 (s), 144.3 (d), 150.4 (s), 150.5 (s × 2), 150.7 (s), 152.1 (d), 153.1 (s); EIMS *m*/*z* 657 (M^+). MS (ESI) *m*/*z* 744 $[M + Na]^+$; HRMS (ESI-DART) *m*/*z* $[M + Na]^+$ calcd for $C_{33}H_{35}N_7NaO_8S_2$ 744.18862; Found 744.19164.

4-(N^3*-Benzoyluracil-1-yl)methyl-3-(phenylsulfanylmethyl)-1-tosylpyrrole (**10c**), Entry 13*. To a DMSO (0.50 mL) solution of 4-methyl-*N*-[3-(phenylthio)-2-propyn-1-yl]-*N*-2-propyn-1-ylbenzenesulfonamide (**2**) (50 mg, 0.14 mmol) were added N^3-benzoyluracil (90.8 mg, 0.42 mmol), bis(triphenylphosphine)palladium(II) dichloride (19.7 mg, 0.028 mmol), bis(hexafluoroacetylacetonato)nickel(II) hydrate (13.2 mg, 0.028 mmol), and DBU (63.9 mg, 0.42 mmol).

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The reaction mixture was stirred for 3 h at 40 °C. The cooled mixture was poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:1) to give the titled compound **10c** (59.0 mg, 73%) as pale yellow powders (mp 58−60 °C).

IR (KBr, cm^{-1}) ν 2924, 2853, 2360, 1748, 1704, 1665, 1597, 1519, 1439, 1374, 1300, 1254, 1173, 1092, 1067, 984, 942, 813, 745, 673, 587, 540; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.41 (3H, s), 3.85 (2H, s), 4.78 (2H, s), 5.75 (1H, d, J = 7.6 Hz), 6.87 (1H, d, J = 1.4 Hz), 7.18 (6H, brs), 7.25−7.28 (3H, m), 7.41 (2H, t, J = 7.6 Hz), 7.60 (1H, t, J = 7.6 Hz), 7.64 (2H, d, J = 8.2 Hz), 7.93 (2H, d, J = 7.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6 (q), 29.5 (t), 42.2 (t), 102.4 (d), 120.6 (d), 121.2 (s), 121.3 (d), 123.0 (s), 126.9 (d × 2), 127.0 (d), 128.9 (d × 2), 129.1 (d × 2), 130.1 (d × 2), 130.4 (d × 2), 131.0 (d × 2), 131.3 (s), 134.6 (s), 135.0 (d), 135.2 (s), 143.0 (d), 145.5 (s), 149.9 (s), 162.3 (s), 168.8 (s); EIMS m/z 571 (small M^+), 466 (M^+-COPh); MS (ESI) m/z 594 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{30}H_{25}N_3NaO_5S_2$ 594.11333; Found 594.11482.

Debenzoylation of ***10c****.* To a NaOH (0.9 mL, 1.7 mmol) in MeOH (3.4 mL) was added 4-(N^3-Benzoyluracil-1-yl)methyl-3-(phenylsulfanylmethyl)-1-tosylpyrrole (**10c**) (100 mg, 0.17 mmol). The reaction mixture was stirred for 2 h and poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:1) to give the titled compound **11c** (40 mg, 49%) as pale yellow powders (mp 55−57 °C).

IR (KBr, cm^{-1}) ν 3054, 1683, 1460, 1370, 1302, 1248, 1172, 1092, 1067, 812, 745, 673, 587, 540; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.43 (3H, s), 3.86 (2H, s), 4.77 (2H, s), 5.67 (1H, d, J = 8.2 Hz), 6.89 (1H, d, J = 2.1 Hz), 7.12 (1H, d, J = 2.1 Hz), 7.14 (1H, d, J = 8.3 Hz), 7.19 (5H, s), 7.29 (2H, d, J = 8.2 Hz), 7.65 (2H, d, J = 8.9 Hz), 9.12 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7 (q), 29.5 (t), 42.0 (t), 102.6 (d), 120.6 (d), 120.8 (d), 121.8 (s), 122.9 (s), 126.9 (d × 3), 128.9 (d × 2), 130.1 (d × 2), 130.7 (d × 2), 134.9 (s), 135.4 (s), 143.2 (d), 145.4 (s), 150.9 (s), 163.4 (s); MS (ESI) m/z 490 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{23}H_{21}N_3NaO_4S_2$ 490.08712; Found 490.08588.

Synthesis of 4-[N^4*,*N^4*-Bis(Boc)cytosin-1-ylmethyl]-3-[(phenylsulfanyl)methyl]-1-(p-tosyl)pyrrole (****10d****) (Entry 14).* To a DMSO (1.8 mL) solution of 4-methyl-*N*-[3-(phenylthio)-2-propyn-1-yl]-*N*-2-propyn-1-ylbenzenesulfonamide (**2**) (100 mg, 0.28 mmol) were added 4-[N^6,N^6-bis(Boc)amino]-1*H*-cytosine (261.5 mg, 0.84 mmol), bis-(hexafluoroacetylacetonato)nickel(II) hydrate (26.5 mg, 0.056 mmol), bis(triphenylphosphine)palladium(II) dichloride (39.3 mg, 0.056 mmol), and DBU(127.9 mg, 0.84 mmol). The reaction mixture was stirred for 2 h at 30 °C. The cooled mixture was poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:2) to give the titled compound **10d** (166.0 mg, 89%) as yellow powders (mp 54−56 °C).

IR (KBr, cm^{-1}) ν 2981, 2932, 1778, 1744, 1671, 1626, 1527, 1462, 1371, 1321, 1257, 1159, 1066, 969, 858, 790, 746, 673, 587, 540; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.55 (18H, s), 2.43 (3H, s), 3.86 (2H, s), 4.88 (2H, s), 6.89 (1H, s), 6.97 (1H, d, J = 7.6 Hz), 7.12 (1H, s), 7.20 (5H, s), 7.27−7.31 (2H, m), 7.50 (1H, d, J = 6.8 Hz), 7.64 (2H, d, J = 8.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6 (q), 27.7 (q × 6), 29.6 (t), 43.9 (t), 84.9 (s), 96.5 (d), 120.3 (d), 121.0 (d), 121.8 (s), 123.1 (s), 126.9 (d × 3), 128.9 (d × 2), 129.7 (s), 130.1 (d × 2), 130.9 (d × 2), 134.8 (s), 135.4 (s), 145.3 (d), 146.8 (s), 149.5 (s × 2), 155.0 (s), 162.1 (s); EIMS m/z 666 (M^+); MS (ESI) m/z 667 $[M + H]^+$, 689 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{33}H_{38}N_4NaO_7S_2$ 689.20796; Found 689.20968.

*Synthesis of 4-(Cytosin-1-yl)methyl-3-[(phenylsulfanyl)methyl]-1-(p-toluenesulfonyl)pyrrole (****11d****).* 1 N HCl (2.2 mL, 2.2 mmol) solution was added to a MeOH (2.2 mL) solution of **10d** (100 mg, 0.15 mmol) at room temperature. The reaction mixture was stirred for 20 min at reflux. The solvent was removed under reduced pressure. The residue was purified by column chromatography eluting with $CHCl_3$−MeOH (40:1 to 20:1) to give the titled compound **11d** (63 mg, 90%) as white powders (mp 78−80 °C).

IR (KBr, cm^{-1}) ν 3187, 2925, 2854, 2360, 2342, 1733, 1652, 1491, 1375, 1302, 1172, 1093, 1066, 809, 743, 670, 584, 409; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.38 (3H, s), 3.84 (2H, s), 4.77 (2H, s), 5.78 (1H, d, J = 6.9 Hz), 6.45 (1H, brs), 6.85 (1H, d, J = 2.0 Hz), 7.05 (1H, d, J = 1.4 Hz), 7.13−7.18 (6H, m), 7.24 (2H, d, J = 8.3 Hz), 7.60 (2H, d, J = 8.2 Hz), 7.92 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6 (q), 29.3 (t), 43.2 (t), 95.2 (d), 120.0 (d), 120.4 (d), 123.1 (s), 123.2 (s), 126.6 (d), 126.8 (d × 2), 128.8 (d × 2), 130.0 (d × 2), 130.5 (d × 2), 135.1 (s), 135.3 (s), 144.3 (d), 145.2 (s), 156.5 (s), 165.9 (s); EIMS m/z 384 (M^+-cytosine); HRMS (EI) $[M]^+$ m/z calcd for $C_{24}H_{22}N_6O_2S_2$: 490.1245; Found 490.1263. Anal. Calcd for $C_{23}H_{22}N_4O_3S_2$ (+ H_2O): C, 57.01; H, 4.99; N, 11.56. Found: C, 56.72; H, 4.66; N, 11.44.

Synthesis of 4-[N^4*,*N^4*-Bis(Boc)cytosin-1-ylmethyl]-5-methyl-3-[(phenylsulfanyl)methyl]-1-(p-tosyl)pyrrole (****13d****), Entry 15.* To a DMSO (0.50 mL) solution of 4-methyl-*N*-[3-(phenylsulfanyl)-2-propyn-1-yl]-*N*-(1-methyl-2-propyn-1-yl)benzenesulfonamide (**4**) (50 mg, 0.10 mmol) were added 4-[N^6,N^6-bis(Boc)amino]-1*H*-cytosine (93 mg, 0.30 mmol), bis(triphenylphosphine)palladium(II) dichloride (7.0 mg, 0.01 mmol), and DBU (45.7 mg, 0.30 mmol). The reaction mixture was stirred for 6 h at 50 °C. The cooled mixture was poured into water (50 mL). The workup procedure gave the titled compound **13d** (36 mg, 39%) as yellow powders (mp 57−60 °C).

IR (KBr, cm^{-1}) ν 3446, 2924, 2852, 1776, 1743, 1669, 1526, 1463, 1371, 1320, 1257, 1161, 1092, 908, 793, 738, 671, 587; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.55 (18H, s), 1.93 (3H, s), 2.45 (3H, s), 3.77 (2H, s), 4.88 (2H, s), 6.98 (1H, d, J = 7.5 Hz), 7.11−7.15 (2H, m), 7.17 (1H, d, J = 7.5 Hz), 7.20 (2H, d, J = 8.2 Hz), 7.28 (1H, s), 7.32 (2H, d, J = 8.2 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.63 (2H, d, J = 8.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.6 (q), 21.6 (q), 27.7 (q × 6), 29.6 (t), 44.0 (t), 84.8 (s × 2), 96.5 (d), 119.9 (s), 120.0 (s), 120.9 (d), 127.0 (d × 2), 127.4 (d), 128.8 (d × 2), 129.7 (s), 130.1 (d × 2), 132.5 (d × 2), 134.6 (s), 135.7 (s), 145.2 (s), 146.8 (d), 149.5 (s × 2), 155.0 (s), 162.1 (s); MS (ESI) m/z 703 $[M + Na]^+$, 719 $[M + K]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{34}H_{40}N_4NaO_7S_2$ 703.22361; Found 703.22401.

Synthesis of 4-[N^4*,*N^4*-Bis(Boc)cytosin-1-ylmethyl]-5-pentyl-3-[(phenylsulfanyl)methyl]-1-(p-tosyl)pyrrole (****14d****), Entry 16.* To a DMSO (2.0 mL) solution of 4-methyl-*N*-[3-(phenylsulfanyl)-2-propyn-1-yl]-*N*-(oct-1-yn-3-yl)benzenesulfonamide (**5**) (200 mg, 0.47 mmol) were added 4-[N^6,N^6-bis(Boc)amino]-1*H*-cytosine (409.7 mg, 1.32 mmol), bis(triphenylphosphine)palladium(II) dichloride (33.0 mg, 0.047 mmol), and DBU (214.7 mg, 1.41 mmol). The reaction mixture was stirred for 6 h at 50 °C. The cooled mixture was poured into water (50 mL). The workup procedure gave the titled compound **14d** (126 mg, 36%) as yellow powders (mp 55−57 °C).

IR (KBr, cm^{-1}) ν 3441, 2930, 2871, 1778, 1743, 1672, 1625, 1526, 1462, 1370, 1320, 1257, 1165, 1137, 1114, 1093, 1066, 1024, 969, 859, 813, 789, 744, 670, 588, 545; ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.84 (3H, t, J = 7.3 Hz), 1.20−1.35 (6H, m), 1.55 (18H, s), 2.42−2.45 (5H, m), 3.81 (2H, s), 4.87 (2H, s), 6.97 (1H, d, J = 7.4 Hz), 7.16−7.19 (3H, m), 7.24−7.26 (3H, m), 7.30−7.35 (2H, m), 7.50 (2H, d, J = 8.6 Hz), 7.61 (2H, d, J = 8.3 Hz) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9 (q), 21.6 (q), 22.2 (t), 25.1 (t), 27.7 (q × 6), 29.6 (t), 30.3 (t), 31.8 (t), 44.2 (t), 84.8 (s × 2), 96.5 (d), 119.8 (s), 120.4 (s), 121.5 (d), 126.8 (d × 2), 127.1 (d), 128.8 (d × 2), 130.0 (d × 2), 131.6 (d × 2), 135.0 (s), 135.3 (s), 136.1 (s), 145.1 (s), 146.9 (d), 149.5 (s × 2), 155.0 (s), 162.1 (s); EIMS m/z 736 (M^+). MS (ESI) m/z 759 $[M + Na]^+$, 775 $[M + K]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{38}H_{48}N_4NaO_7S_2$ 759.2862; Found 759.2876.

*4-(Cytosin-1-ylmethyl)-5-pentyl-3-[(phenylsulfanyl)methyl]-1-(p-tosyl)pyrrole (****19d****).* 1 N HCl (2.0 mL, 2.0 mmol) solution was added to a MeOH (2.0 mL) solution of **14d** (100 mg, 0.14 mmol) at room temperature. The reaction mixture was stirred for 20 min at reflux. The solvent was removed under reduced pressure. The residue was purified

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by column chromatography eluting with $CHCl_3$−MeOH (40:1 to 30:1) to give the titled compound **19d** (17 mg, 23%) as white powders (mp 71−73 °C).

IR (KBr, cm^{-1}) ν 3352, 3182, 2956, 2927, 2854, 1719, 1648, 1526, 1492, 1438, 1369, 1278, 1190, 1169, 1093, 1065, 975, 813, 741, 671, 587, 542; ^1H NMR (600 MHz, $CDCl_3$) δ 0.84 (3H, t, J = 6.9 Hz), 1.19−1.26 (5H, m), 1.29−1.33 (3H, m), 1.68 (2H, brs), 2.43 (3H, s), 3.83 (2H, s), 4.84 (2H, s), 5.68 (1H, d, J = 6.9 Hz), 7.17−7.19 (3H, m), 7.25−7.27 (4H, m), 7.30 (2H, d, J = 8.2 Hz), 7.61 (2H, d, J = 8.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9 (q), 21.6 (q), 22.2 (t), 25.1 (t), 29.4 (t), 30.4 (t), 31.8 (t), 43.5 (t), 94.8 (d), 119.6 (s), 120.9 (d), 121.6 (s), 126.7 (d × 2), 126.9 (d), 128.8 (d × 2), 130.0 (d × 2), 131.3 (d × 2), 134.9 (s), 135.6 (s), 136.2 (s), 144.6 (d), 145.0 (s), 156.6 (s), 165.8 (s); EIMS m/z 536 (small M^+). MS (ESI) m/z 559 $[M + Na]^+$, 575 $[M + K]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{28}H_{32}N_4NaO_3S_2$ 559.18135; Found 559.17943.

*Synthesis of 4-[(N^3-Benzoylthymin-1-yl)methyl]-2-(p-methoxyphenyl)-3-[(phenylsulfanyl)methyl]furan (**23a**), Table 2, Entry 1.* To a DMSO (1.1 mL) solution of 1-methoxy-4-[4-(2-propynyloxy)-3-(phenylsulfanyl)-2-propyn-1-yl]benzene (**20**) (70 mg, 0.023 mmol) were added N^3-benzoylthymine (139 mg, 0.60 mmol), bis(triphenylphosphine)palladium(II) dichloride (16.1 mg, 23 mmol), and DBU (105 mg, 0.69 mmol). The whole was stirred for 23 h at 30 °C and the workup procedure and purification by the preparative TLC on silica gel eluting with (AcOEt−*n*-hexane = 1:2) gave **23a** (116 mg, 95%) as pale yellow powders (mp 63−65 °C).

IR (KBr, cm^{-1}) ν 3065, 2928, 2854, 1747, 1697, 1657, 1600, 1507, 1440, 1349, 1307, 1254, 1179, 1029, 993, 950, 836, 762, 690, 628; ^1H NMR (600 MHz, $CDCl_3$) δ 1.91 (3H, s), 3.84 (3H, s), 4.12 (2H, s), 4.85 (2H, s), 6.94 (2H, d, J = 8.2 Hz), 7.21−7.26 (4H, m), 7.30−7.33 (4H, m), 7.52 (1H, s), 7.54 (1H, t, J = 7.6 Hz), 7.57 (2H, d, J = 8.3 Hz), 7.92 (2H, d, J = 7.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.4 (q), 29.0 (t), 40.8 (t), 55.3 (q), 111.0 (s), 113.1 (s), 114.2 (d × 2), 121.1 (s), 122.7 (s), 126.8 (d), 127.8 (d × 2), 128.96 (d × 2), 129.0 (d × 2), 130.2 (d × 2), 130.5 (d × 2), 131.4 (s), 134.8 (d), 135.4 (s), 138.9 (d), 140.8 (d), 150.1 (s), 153.0 (s), 159.6 (s), 163.2 (s), 169.1 (s); EIMS m/z 538 (M^+), 429 (M^+-SPh); MS (ESI) m/z 561 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{31}H_{26}N_2NaO_5S$ 561.14601; Found 561.14457.

*Debenzoylation of **23a**.* To a NaOH (0.47 mL, 0.93 mmol) in MeOH (1.9 mL) was added 4-[(N^3-benzoylthymin-1-yl)methyl]-2-(*p*-methoxyphenyl)-3-[(phenylsulfanyl)methyl]furan (23a) (50 mg, 0.093 mmol). The reaction mixture was stirred for 5.5 h at 40 °C and poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:1) to give the titled compound **26a** (26.0 mg, 65%) as (mp 148−150 °C).

IR (KBr, cm^{-1}) ν 3167, 3052, 2926, 2836, 1680, 1506, 1467, 1438, 1385, 1307, 1252, 1222, 1181, 1065, 1030, 953, 834, 761, 689, 623; ^1H NMR (600 MHz, $CDCl_3$) δ 1.88 (3H, s), 3.83 (3H, s), 4.13 (2H, s), 4.81 (2H, s), 6.94 (2H, d, J = 8.9 Hz), 7.06 (1H, d, J = 1.4 Hz), 7.20 (1H, t, J = 7.6 Hz), 7.28 (2H, d, J = 7.6 Hz), 7.32 (2H, d, J = 7.6 Hz), 7.47 (1H, s), 7.58 (2H, d, J = 9.0 Hz), 8.41 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.4 (q), 28.7 (t), 40.6 (t), 55.3 (q), 111.2 (s), 113.1 (s), 114.3 (d × 2), 121.8 (s), 122.9 (s), 126.6 (d), 127.8 (d × 2), 129.0 (d × 2), 129.6 (d × 2), 135.9 (s), 139.2 (d), 140.3 (d), 150.9 (s), 153.0 (s), 159.6 (s), 163.8 (s); EIMS m/z 434 (M^+), 325 (M^+-SPh). MS (ESI) m/z 457 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{24}H_{22}N_2NaO_4S$ 457.11980; Found 457.11876. Anal. Calcd for $C_{24}H_{22}N_2O_4S$ (+ 1/2 H_2O): C, 64.99; H, 5.00; N, 6.32. Found: C, 65.09; H, 5.49; N, 5.83.

*Synthesis of 4-[(N^3-Benzoylthymin-1-yl)methyl]-2-(p-chlorophenyl)-3-[(phenylsulfanyl)methyl]furan (**24a**), Entry 2.* To a DMSO (0.50 mL) solution of 1-chloro-4-[4-(2-propynyloxy)-3-(phenylsulfanyl)-2-propyn-1-yl]benzene (**21**) (30 mg, 0.10 mmol) were added N^3-benzoylthymine (69.1 mg, 0.30 mmol), bis(triphenylphosphine)palladium(II) dichloride (14.0 mg, 0.02 mmol), bis(hexafluoroacetylacetonato)nickel(II) hydrate (9.5 mg, 0.02 mmol), and DBU (45.7 mg, 0.30 mmol). The whole was stirred for 4 h at 30 °C and the workup procedure and purification by the preparative TLC on silica gel eluting with (AcOEt−*n*-hexane = 1:1) gave **24a** (35 mg, 67%) as pale yellow powders.

mp 71−73 °C, IR (KBr, cm^{-1}) ν 3061, 2928, 2364, 1746, 1697, 1656, 1599, 1488, 1439, 1350, 1315, 1259, 1236, 1152, 1093, 994, 949, 833, 762, 689, 620; ^1H NMR (600 MHz, $CDCl_3$) δ 1.91 (3H, s), 4.11 (2H, s), 4.85 (2H, s, 7.21 (2H, d, J = 7.8 Hz), 7.25 (2H, d, J = 6.6 Hz), 7.30−7.34 (4H, m), 7.37 (2H, d, J = 8.7 Hz), 7.54−7.57 (4H, m), 7.91 (2H, d, J = 7.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.4 (q), 28.9 (t), 40.7 (t), 111.2 (s), 115.2 (s), 121.5 (s × 2), 127.2 (d), 127.5 (d × 2), 128.4 (s), 129.0 (d × 3), 129.1 (d × 2), 130.5 (d × 2), 130.6 (d × 2), 131.4 (s × 2), 134.2 (s), 134.9 (d × 2), 138.9 (d), 141.6 (d), 151.7 (s × 2), 169.1 (s); EIMS m/z 543 (M^++1). MS (ESI) m/z 543 $[M + H]^+$, 565 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{30}H_{23}ClN_2NaO_4S$ 565.09647; Found 565.10123.

*Debenzoylation of **24a**.* To a NaOH (0.3 mL, 0.6 mmol) in MeOH (1.2 mL) was added 4-[(N^3-benzoylthymin-1-yl)methyl]-2-(*p*-chlorophenyl)-3-[(phenylsulfanyl)methyl]furan (**24a**) (30 mg, 0.06 mmol). The reaction mixture was stirred for 19 h at 40 °C and poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:1) to give the titled compound **27a** (19.0 mg, 78%) as pale yellow powders (mp 127−128 °C).

IR (KBr, cm^{-1}) ν 3433, 3053, 1679, 1481, 1354, 1219, 1120, 1094, 1012, 950, 833, 745, 692, 614, 542, 470; ^1H NMR (600 MHz, $CDCl_3$) δ 1.89 (3H, s), 4.12 (2H, s), 4.81 (2H, s), 7.06 (1H, s), 7.23 (1H, t, J = 7.5 Hz), 7.29 (2H, t, J = 7.5 Hz), 7.32 (2H, d, J = 7.6 Hz), 7.38 (2H, d, J = 8.2 Hz), 7.52 (1H, s), 7.57 (2H, d, J = 8.9 Hz), 8.08 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.4 (q), 28.6 (t), 40.5 (t), 111.3 (s), 115.0 (s), 122.1 (s), 126.9 (d), 127.5 (d × 2), 128.5 (d), 129.0 (d × 2), 129.1 (d × 2), 129.9 (d × 2), 134.1 (s), 135.4 (s), 139.1 (d), 141.1 (d), 151.0 (s), 151.6 (s), 163.9 (s); EIMS m/z 438 (M^+), 329 (M^+-SPh); MS (ESI) m/z 437 $[M-H]^-$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{23}H_{18}ClN_2O_3S$ 437.07267; Found 437.07303.

*Synthesis of 4-[(N^3-Benzoylthymin-1-yl)methyl]-2-(p-fluorophenyl)-3-[(phenylsulfanyl)methyl]furan (**25a**), Entry 3.* To a DMSO (0.50 mL) solution of 1-fluoro-4-[4-(2-propynyloxy)-3-(phenylsulfanyl)-2-propyn-1-yl]benzene (**22**) (30 mg, 0.10 mmol) were added N^3-benzoylthymine (69.1 mg, 0.30 mmol), bis(triphenylphosphine)palladium(II) dichloride (14.0 mg, 0.02 mmol), bis(hexafluoroacetylacetonato)nickel(II) hydrate (9.5 mg, 0.02 mmol), and DBU (45.7 mg, 0.30 mmol). The whole was stirred for 1.5 h at 30 °C and the workup procedure and purification by the preparative TLC on silica gel eluting with (AcOEt−*n*-hexane = 1:2) gave **25a** (22.6 mg, 43%) as yellow powders (mp 108−110 °C).

IR (KBr, cm^{-1}) ν 3427, 3063, 2929, 1747, 1698, 1657, 1599, 1504, 1440, 1350, 1314, 1235, 1158, 994, 950, 841, 763, 674, 628, 544; ^1H NMR (600 MHz, $CDCl_3$) δ 1.96 (3H, s), 4.11 (2H, s), 4.85 (2H, s, 7.10 (2H, t, J = 8.7 Hz), 7.19−7.25 (5H, m), 7.30−7.34 (3H, m), 7.52−7.61 (4H, m), 7.91 (2H, d, J = 7.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.4 (q), 28.9 (t), 40.7 (t), 111.1 (s), 114.4 (s), 115.7 (d), 115.9 (d), 121.3 (s × 2), 126.2 (s × 2), 127.0 (d), 128.2 (d), 128.3 (d), 129.0 (d × 2), 129.1 (d × 2), 130.4 (d × 3), 131.4 (s), 134.9 (d), 135.0 (s), 139.0 (d), 141.4 (d), 151.9 (s × 2), 162.5 (d, J = 248.5 Hz), 169.1 (s); EIMS m/z 526 (M^+), 417 (M^+-SPh); MS (ESI) m/z 549 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{30}H_{23}FN_2NaO_4S$ 549.12603; Found 549.12851.

*Synthesis of 4-[N^6,N^6-Bis(Boc)adenin-9-ylmethyl]-3-[(phenylsulfanyl)methyl]-2-(p-chlorophenyl)furan (**24b**), Entry 4.* To a DMSO (0.50 mL) solution of 1-chloro-4-[4-(2-propynyloxy)-3-(phenylsulfanyl)-2-propyn-1-yl]benzene (**21**) (50 mg, 0.16 mmol) were added N^6,N^6-bis(Boc)adenine (161 mg, 0.48 mmol), bis(triphenylphosphine)palladium(II) dichloride (22 mg, 0.032 mmol), bis(hexafluoroacetylacetonato)nickel(II) hydrate (15 mg, 0.032 mmol), and DBU (73 mg, 0.48 mmol). The whole was stirred for 3 h at 30 °C and the workup procedure and purification by the

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preparative TLC on silica gel eluting with (AcOEt−*n*-hexane = 1:1) gave **24b** (48 mg, 46%) as white powders (mp 44−45 °C).

IR (KBr, cm^{-1}) ν 2980, 2934, 1787, 1758, 1602, 1578, 1531, 1489, 1455, 1409, 1394, 1370, 1335, 1279, 1254, 1211, 1144, 1108, 950, 851, 833, 753, 691, 640; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.43 (18H, s), 4.06 (2H, s), 5.35 (2H, s), 7.23−7.26 (5H, m), 7.35 (2H, d, J = 8.2 Hz), 7.48 (2H, d, J = 8.3 Hz), 7.54 (1H, s), 8.14 (1H, s), 8.82 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.7 (q × 6), 28.8 (t), 37.0 (t), 83.8 (s × 2), 115.1 (s), 121.5 (s), 127.2 (d), 127.5 (d × 2), 128.3 (s), 128.6 (s), 128.9 (d × 2), 129.0 (d × 2), 130.7 (d × 2), 134.1 (s), 134.7 (s), 141.1 (d), 144.4 (d), 150.2 (s), 150.4 (s × 2), 151.5 (s), 152.0 (d), 153.2 (s); EIMS m/z 647 (M^+). MS (ESI) m/z 670 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{33}H_{34}ClN_5NaO_5S$ 670.18669; Found 670.18729.

*Synthesis of 4-[N^6,N^6-Bis(Boc)adenin-9-ylmethyl]-3-[(phenylsulfanyl)methyl]-2-(p-fluorophenyl)furan (**25b**), Entry 5.* To a DMSO (0.70 mL) solution of 1-fluoro-4-[4-(2-propynyloxy)-3-(phenylsulfanyl)-2-propyn-1-yl]benzene (**22**) (70 mg, 0.20 mmol) were added N^6,N^6-bis(Boc)adenine (201 mg, 0.60 mmol), $PdCl_2(PPh_3)_2$ (14.0 mg, 0.02 mmol), and DBU (91.3 mg, 0.60 mmol). The whole was stirred for 3.5 h at 30 °C and the workup procedure and purification by the preparative TLC on silica gel eluting with (AcOEt−*n*-hexane = 1:1) gave **25b** (77 mg, 53%) as a pale yellow oil.

IR (KBr, cm^{-1}) 3060, 2981, 2933, 1787, 1760, 1602, 1578, 1532, 1504, 1481, 1454, 1409, 1394, 1370, 1336, 1310, 1279, 1252, 1211, 1143, 1108, 951, 847, 753, 692, 639, 590; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.43 (18H, s), 4.05 (2H, s), 5.36 (2H, s), 7.08 (2H, t, J = 8.6 Hz), 7.24−7.27 (5H, m), 7.52 (3H, t, J = 6.9 Hz), 8.14 (1H, s), 8.82 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.7 (q × 6), 28.8 (t), 37.1 (t), 83.9 (s × 2), 144.4 (s), 115.7 (d), 115.9 (d), 121.4 (s), 126.1 (s), 127.1 (d), 128.2 (d), 128.3 (d), 128.7 (s), 129.0 (d × 2), 130.7 (d × 2), 134.9 (s), 140.9 (d), 144.5 (d), 150.1 (s), 150.5 (s × 2), 151.9 (s), 152.1 (d), 153.3 (s), 162.0 (d, J = 250.0 Hz); EIMS m/z 631 (M^+); HRMS$[M]^+$ calcd for $C_{33}H_{34}N_5O_5SF$ 631.2264; Found 631.2227. MS (ESI) m/z 670 $[M + Na]^+$, 686 $[M + K]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{33}H_{34}ClN_5NaO_5S$ 670.18669; Found 670.18188.

*Synthesis of 4-(9H-Adenin-9-ylmethyl)-3-(phenylsulfanylmethyl)-2-(p-fluorophenyl)furan (**28b**).* 1 N HCl (2.0 mL, 2.0 mmol) solution was added to a MeOH (4.0 mL) solution of **25b** (80 mg, 0.13 mmol) at room temperature. The reaction mixture was stirred at 50 °C for 24 h. The workup procedure gave the titled compound **28b** (26 mg, 48%) as pale yellow powders (mp 66−68 °C).

IR (KBr, cm^{-1}) ν 3314, 3118, 2926, 1760, 1672, 1601, 1505, 1480, 1418, 1331, 1306, 1238, 1158, 1062, 1013, 953, 839, 756, 718, 691; ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.04 (2H, s), 5.29 (2H, s), 5.97 (2H, brs), 7.08 (2H, t, J = 8.3 Hz), 7.19−7.25 (5H, m), 7.49 (1H, s), 7.53−7.56 (2H, m), 7.85 (1H, s), 8.29 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.6 (t), 36.9 (t), 114.4 (s), 115.7 (d), 115.9 (d), 119.5 (s), 122.0 (s), 126.2 (s), 126.9 (d), 128.2 (d), 128.3 (d), 128.9 (d × 2), 130.2 (d × 2), 135.2 (s), 140.2 (d), 140.6 (d), 150.0 (s), 151.8 (s), 153.0 (d), 155.4 (s), 162.01 (d, J = 250.0 Hz); EIMS m/z 431 (M^+), 322 (M^+-SPh). Anal. Calcd for $C_{23}H_{18}N_5OSF$ (+ 2/5 H_2O): C, 62.97; H, 4.32; N, 15.96. Found: C, 63.17; H, 4.52; N, 15.66.

*Synthesis of 3-(N^3-Benzoyluracil-1-yl)-2-(p-fluorophenyl)-3-[(phenylsulfanyl)methyl]furan (**25c**), Entry 6.* To a DMSO (0.50 mL) solution of 1-fluoro-4-[4-(2-propynyloxy)-3-(phenylsulfanyl)-2-propyn-1-yl]benzene (**22**) (50 mg, 0.17 mmol) were added N^3-benzoyluracil (110.3 mg, 0.51 mmol), bis(triphenylphosphine)-palladium(II) dichloride (23.9 mg, 0.034 mmol), bis(hexafluoroacetylacetonato)nickel(II) hydrate (16.1 mg, 0.034 mmol), and DBU (77.6 mg, 0.51 mmol). The whole was stirred for 1 h at 40 °C and the workup procedure and purification by the preparative TLC on silica gel eluting with (AcOEt−*n*-hexane = 1:1) gave **25c** (56 mg, 65%) as pale yellow powders (mp 70−72 °C).

IR (KBr, cm^{-1}) ν 2925, 2360, 1748, 1704, 1665, 1598, 1504, 1439, 1383, 1255, 1237, 1179, 1146, 944, 842, 692, 544, 418; ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.10 (2H, s). 4.87 (2H, s), 5.83 (1H, d, J = 5.5 Hz), 7.10 (2H, t, J = 8.2 Hz), 7.20−7.26 (3H, m), 7.31−7.35 (4H, m), 7.38 (1H, d, J = 6.2 Hz), 7.55−7.59 (4H, m), 7.93 (2H, d, J = 7.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.9 (t), 40.9 (t), 102.5 (s), 114.4 (s), 115.8 (d), 115.9 (d), 120.9 (s × 2), 126.1 (s), 126.2 (s), 127.2 (d), 128.2 (d), 128.3 (d), 129.0 (d × 2), 129.1 (d × 2), 130.5 (d × 2), 130.7 (d × 2), 131.3 (s), 134.9 (s), 135.0 (d), 141.5 (d), 143.0 (d), 152.0 (s), 162.5 (d, J = 249.9 Hz), 168.8 (s); MS (ESI) m/z 535 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{29}H_{21}FN_2NaO_4S$ 535.11038; Found 535.11398.

*Debenzoylation of **25c**.* To a NaOH (0.35 mL, 0.7 mmol) in MeOH (1.4 mL) was added synthesis of 3-(N^3-Benzoyluracil-1-yl)-2-(*p*-fluorophenyl)-3-[(phenylsulfanyl)methyl]furan (**25c**) (42 mg, 0.08 mmol). The reaction mixture was stirred for 3.5 h at 40 °C and poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (2:1) to give the titled compound **28c** (13 mg, 39%) as pale yellow powders (mp 170−173 °C).

IR (KBr, cm^{-1}) ν 3182, 3058, 2924, 2852, 1681, 1500, 1457, 1391, 1322, 1236, 1158, 1120, 1092, 849, 783, 736, 691, 624, 543; ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.11 (2H, s), 4.84 (2H, s), 7.10 (2H, t, J = 8.9 Hz), 7.21 (1H, t, J = 7.5 Hz), 7.24−7.28 (4H, m), 7.31 (2H, d, J = 8.2 Hz), 7.52 (1H, s), 7.58−7.60 (2H, m), 8.72 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.6 (t), 40.7 (t), 102.8 (d), 114.3 (s), 115.8 (d), 116.0 (d), 121.6 (s), 126.2 (s), 126.9 (d), 128.2 (d), 128.3 (d), 129.1 (d × 2), 129.9 (d × 2), 135.3 (s), 141.0 (d), 143.2 (d), 150.9 (s), 152.1 (s), 163.2 (s), 163.4 (s); MS (ESI) m/z 431 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{22}H_{17}FN_2NaO_3S$ 431.08416; Found 431.08558.

*Synthesis of 4-[N^4,N^4-Bis(Boc)cytosin-1-ylmethyl]-3-[(phenylsulfanyl)methyl]-2-(p-methoxyphenyl)furan (**23d**), Entry 7.* To a DMSO (0.50 mL) solution of 1-methoxy-4-[4-(2-propynyloxy)-3-(phenylsulfanyl)-2-propyn-1-yl]benzene (**20**) (30 mg, 0.10 mmol) were added N^4,N^4-bis(Boc)cytosine (93.4 mg, 0.30 mmol), bis-(triphenylphosphine)palladium(II) dichloride (14.0 mg, 0.02 mmol), bis(hexafluoroacetylacetonato)nickel(II) hydrate (9.5 mg, 0.02 mmol), and DBU (45.7 mg, 0.30 mmol). The whole was stirred for 23 h at 30 °C and the workup procedure and purification by the preparative TLC on silica gel eluting with (AcOEt−*n*-hexane = 1:3) gave **23d** (23 mg, 38%) as pale yellow powders (mp 112−114 °C).

IR (KBr, cm^{-1}) 3441, 2981, 2934, 1777, 1744, 1670, 1625, 1529, 1507, 1463, 1371, 1321, 1255, 1157, 1028, 969, 837, 789, 749, 692; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.54 (18H, s), 3.84 (3H, s), 4.10 (2H, s), 4.93 (2H, s), 6.93 (2H, d, J = 8.7 Hz), 7.00 (1H, d, J = 7.4 Hz), 7.22−7.29 (3H, m), 7.35 (2H, d, J = 7.3 Hz), 7.50 (1H, s), 7.53 (2H, d, J = 8.2 Hz), 7.66 (1H, d, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.6 (q × 6), 29.1 (t), 43.0 (t), 55.3 (q), 84.9 (s × 2), 96.7 (d), 113.4 (s), 114.1 (d × 2), 121.1 (s), 122.9 (s), 127.0 (d), 127.9 (d × 2), 129.0 (d × 2), 130.6 (d × 2), 135.3 (s), 141.1 (d), 147.1 (d), 149.5 (s × 2), 152.5 (s), 155.2 (s), 159.5 (s), 162.2 (s); MS (ESI) m/z 642 $[M + Na]^+$, 658 $[M + K]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{33}H_{37}N_3NaO_7S$ 642.22499; Found 642.22116.

*Synthesis of 4-[N^4,N^4-Bis(Boc)cytosin-1-ylmethyl]-3-[(phenylsulfanyl)methyl]-2-(p-fluorophenyl)furan (**25d**), Entry 8.* To a DMSO (0.50 mL) solution of 1-fluoro-4-[4-(2-propynyloxy)-3-(phenylsulfanyl)-2-propyn-1-yl]benzene (**22**) (30 mg, 0.10 mmol) were added N^4,N^4-bis(Boc)cytosine (93.4 mg, 0.30 mmol), bis-(triphenylphosphine)palladium(II) dichloride (14.0 mg, 0.02 mmol), bis(hexafluoroacetylacetonato)nickel(II) hydrate (9.5 mg, 0.02 mmol), and DBU (45.7 mg, 0.30 mmol). The whole was stirred for 23 h at 30 °C and the workup procedure and purification by the preparative TLC on silica gel eluting with (AcOEt−*n*-hexane = 1:3) gave **25d** (35 mg, 57%) as pale yellow powders (mp 71−72 °C).

IR (KBr, cm^{-1}) 2980, 2933, 1775, 1740, 1573, 1505, 1446, 1395, 1370, 1340, 1304, 1239, 1160, 1121, 1004, 951, 841, 740, 691; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.55 (18H, s), 4.10 (2H, s), 4.93 (2H, s), 7.02 (1H, brs), 7.09 (2H, t, J = 8.2 Hz), 7.22 (1H, t, J = 7.6 Hz), 7.27 (2H, t, J = 7.6 Hz), 7.35 (2H, d, J = 7.6 Hz), 7.52−7.56 (3H, m), 7.65 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.7 (q × 6), 29.2 (t), 43.1 (t), 84.9 (s × 2), 114.7 (s), 115.7 (d), 115.9 (d), 121.4 (s × 2), 126.4 (s × 2), 127.2 (d), 128.3 (d), 128.4 (d), 129.1 (d × 2), 131.0 (d × 2),

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135.0 (s × 2), 141.5 (d), 147.0 (d), 149.6 (s), 151.5 (s × 2), 162.5 (d, J = 248.5 Hz); EIMS m/z 607 (M^+), 498 (M^+-SPh). MS (ESI) m/z 608 $[M + H]^+$, 630 $[M + K]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{32}H_{34}FN_3NaO_6S$ 630.20500; Found 630.20212.

Transformation of Nucleobase-Substituted Pyrroles and Furans As Shown in Scheme 3. *Pummerer Reaction of **10a**.* *m*-Chloroperbenzoic acid (58.6 mg, 0.34 mmol) was added over 1 h to a 1,2-dichloroethane (13.6 mL) solution of 4-[(3-benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidyl)methyl]-3-(phenylsulfanylmethyl)-1-(*p*-tosyl)pyrrole (**10a**) (200 mg, 0.34 mmol) at 0 °C. The whole was stirred for further 5 min and poured into a sat. $NaHCO_3$ (50 mL). Then the mixture was vigorously stirred for 15 min. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:1) to give the residue. To the residue (50 mg, 0.08 mmol) in dichloromethane (1 mL) were added trifluoroacetic anhydride (168 mg, 0.8 mmol) at 0 °C. The reaction mixture was stirred for 1 h and poured into a sat. $NaHCO_3$ (50 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:1) to give the titled compound **29** (32 mg, 78%) as white powders (mp 56−60 °C).

White powders, IR (KBr, cm^{-1}) ν 3477, 2930, 1748, 1698, 1655, 1599, 1520, 1443, 1371, 1297, 1252, 1173, 1093, 1068, 1019, 1002, 970, 950, 817, 777, 763, 704, 673, 589; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.61 (1H, brs), 1.90 (3H, s), 2.42 (3H, s), 4.45 (2H, s), 4.77 (2H, s), 7.10 (1H, d, J = 2.1 Hz), 7.18 (1H, s), 7.24 (1H, d, J = 2.1 Hz), 7.31 (2H, d, J = 8.3 Hz), 7.49 (2H, t, J = 8.3 Hz), 7.65 (1H, t, J = 6.8 Hz), 7.75 (2H, d, J = 8.3 Hz), 7.92 (2H, dd, J = 1.4 and 8.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.4 (q), 14.2 (q), 42.4 (t), 56.3 (t), 111.4 (s), 120.0 (d), 121.4 (d), 121.7 (s), 127.0 (s), 127.1 (d × 2), 129.2 (d × 2), 130.2 (d × 2), 130.4 (d × 2), 131.5 (s), 135.0 (d), 135.4 (s), 139.3 (d), 145.6 (s), 150.4 (s), 162.9 (s), 169.0 (s); EIMS m/z 493 (small M^+), 388 (M^+-COPh), 371 (M^+-COPh−OH). MS (ESI) m/z 516 $[M + Na]^+$, 532 $[M + K]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{25}H_{23}N_3NaO_6S$ 516.12053; Found 516.11812.

*Reaction of **12a** with Ammonium Cerium(IV) Nitrate (CAN).* To a MeOH (0.8 mL) solution of 4-[(3-benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidyl)methyl]-3-(phenylselanylmethyl)-1-(*p*-tosyl)-pyrrole (**12a**) (50 mg, 0.08 mmol) were added CAN (87.8 mg, 0.16 mmol). The reaction mixture was stirred for 1 h at room temperature and then poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:1) to give the titled compound **30** (29.0 mg, 72%) as white powders (mp 122−123 °C).

IR (KBr, cm^{-1}) ν 3444, 2925, 1748, 1699, 1656, 1598, 1441 1371, 1297, 1238, 1173, 1067, 817, 762, 598; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.89 (3H, s), 2.41 (3H, s), 3.28 (3H, s), 4.24 (2H, s), 4.73 (2H, s), 7.13 (1H, d, J = 2.7 Hz), 7.17 (1H, d, J = 1.4 Hz), 7.24 (1H, d, J = 2.1 Hz), 7.30 (2H, d, J = 8.2 Hz), 7.49 (2H, t, J = 7.6 Hz), 7.64 (1H, t, J = 7.6 Hz), 7.74 (2H, d, J = 8.3 Hz), 7.92 (2H, d, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.4 (q), 21.6 (q), 42.1 (t), 57.8 (q), 65.8 (t), 110.6 (s), 120.5 (d), 121.6 (d), 122.0 (s), 123.9 (s), 127.0 (d × 2), 129.1 (d × 2), 130.1 (d × 2), 130.4 (d × 2), 131.6 (s), 134.9 (d), 135.4 (s), 139.4 (d), 145.5 (s), 149.9 (s), 163.0 (s), 169.1 (s); EIMS m/z 507 (M^+), 352 (M^+-Ts); MS (ESI) m/z 507 M^+ 530 $[M + Na]^+$, 546 $[M + K]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{26}H_{25}N_3NaO_6S$ 530.13618; Found 530.13492. Anal. $C_{26}H_{25}N_3O_6S$ (+ 1/2 H_2O): C, 60.45; H, 5.07; N, 8.13. Found: C, 60.31; H, 5.12; N, 8.02.

*Synthesis of 4-[(Thymin-1-yl)methyl]-3-(methoxymethyl)pyrrole (**31a**).* To a NaOH (0.6 mL, 1.2 mmol) in MeOH (2.4 mL) was added 4-[(3-benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidyl)-methyl]-3-(phenylsulfanylmethyl)-1-(*p*-tosyl)pyrrole (**10a**) (70 mg, 0.12 mmol). The reaction mixture was stirred for 2.5 h at 70 °C and poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with $CHCl_3$−MeOH (40:1) to give the titled compound **31a** (24.0 mg, 81%) as white powders (mp 85−86 °C).

IR (KBr, cm^{-1}) ν 3329, 3032, 2927, 2820, 1687, 1532, 1473, 1384, 1328, 1258, 1218, 1190, 1076, 951, 893, 815, 766, 707, 602, 552, 491, 424; ^{1}H NMR (600 MHz, DMSO−D6) δ 1.71 (3H, s), 3.14 (3H, s), 4.22 (2H, s), 4.66 (2H, s), 6.72 (1H, s), 6.77 (1H, s), 7.36 (1H, s), 10.71 (1H, brs), 11.14 (1H, brs); ^{13}C NMR (125 MHz, DMSO−D_6) δ 12.0 (q), 41.4 (t), 56.4 (q), 65.6 (t), 108.0 (s), 116.9 (s), 118.0 (s), 118.6 (d × 2), 140.7 (d), 150.9 (s), 164.2 (s); EIMS m/z 249 (M^+), 218 (M^+-OMe); MS (ESI) m/z 272 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{12}H_{15}N_3NaO_3$ 272.10111; Found 272.09855.

*Synthesis of 4-[(Thymin-1-yl)methyl]-3-(ethoxymethyl)pyrrole (**31b**).* To a NaOH (0.45 mL, 0.9 mmol) in EtOH (1.8 mL) was added 4-[(3-benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidyl)methyl]-3-(phenylsulfanylmethyl)-1-(*p*-tosyl)pyrrole (**10a**) (50 mg, 0.09 mmol). The reaction mixture was stirred for 3 h at 80 °C and poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with $CHCl_3$−MeOH (40:1) to give the titled compound **31b** (12 mg, 53%) as white powders(mp 70−71 °C).

IR (KBr, cm^{-1}) ν 3314, 3052, 2976, 2927, 2857, 1681, 1531, 1473, 1352, 1262, 1216, 1076, 1001, 893, 786, 606, 555; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.20 (3H, t, J = 6.9 Hz), 1.84 (3H, s), 3.50 (2H, q, J = 6.9 Hz), 4.38 (2H, s), 4.80 (2H, s), 6.75 (1H, s), 6.83 (1H, s), 7.26 (1H, s), 8.46 (1H, brs), 9.03 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.3 (q), 15.2 (q), 42.2 (t), 64.3 (t), 65.4 (t), 109.8 (s), 116.9 (s), 118.5 (d), 119.3 (s), 119.5 (d), 140.5 (d), 151.2 (s), 164.3 (s); EIMS m/z 263 (M^+), 218 (M^+-OEt); HRMS (EI) $[M]^+$ m/z calcd for $C_{13}H_{17}N_3O_3$ 263.1270; Found 263.1292.

*Synthesis of 4-[(Thymin-1-yl)methyl]-3-(isopropoxymethyl)-pyrrole (**31c**).* To a NaOH (1.7 mL, 3.4 mmol) in *i*-PrOH (6.8 mL) was added 4-[(3-benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidyl)methyl]-3-(phenylsulfanylmethyl)-1-(*p*-tosyl)pyrrole (**10a**) (200 mg, 0.34 mmol). The reaction mixture was stirred for 7 h at reflux and then poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with $CHCl_3$−MeOH (40:1) to give the titled compound **31c** (23 mg, 24%) as pale yellow powders (mp 84−86 °C).

IR (KBr, cm^{-1}) ν 3245, 3164, 3051, 2971, 2925, 2856, 1670, 1529, 1472, 1369, 1328, 1267, 1245, 1215, 1124, 1072, 1041, 940, 765, 607, 554, 484; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.18 (3H, s), 1.19 (3H, s), 1.83 (3H, s), 3.69 (1H, q, J = 6.2 Hz), 4.38 (2H, s), 4.80 (2H, s), 6.73 (1H, s), 6.79 (1H, s), 7.28 (1H, s), 8.57 (1H, brs), 9.22 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.3 (q), 22.1 (q × 2), 42.3 (t), 61.8 (t), 70.8 (d), 109.8 (s), 116.6 (s), 118.2 (d), 119.5 (d), 119.7 (s), 140.5 (d), 151.3 (s), 164.5 (s); EIMS m/z 277 (M^+), 234 (M^+−$CH(CH_3)_2$), 218 (M^+-$OCH(CH_3)_2$). MS (ESI) m/z 300 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{14}H_{19}N_3NaO_3$ 300.13241; Found 300.13293.

*Synthesis of 4-[(Thymin-1-yl)methyl]-3-methoxymethyl-5-methylpyrrole (**31d**).* 4-[(3-Benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidyl)methyl]-5-methyl-3-(phenylsulfanylmethyl)-1-(*p*-tosyl)-pyrrole (**13a**) (50 mg, 0.08 mmol) was added to a MeOH (1.0 mL) solution of sodium hydroxide (2 N, 0.4 mL, 0.80 mmol). The reaction mixture was stirred at 70 °C. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$. The combined organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with $CHCl_3$−MeOH (40:1).

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The titled comound **31d** (15 mg, 68%) was obtained as white powders (mp 124−126 °C).

IR (KBr, cm^{-1}) ν 3434, 2925, 1681, 1471, 1355, 1250, 1225, 1122, 1097, 1043, 912, 875, 807, 750, 703, 606; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.83 (3H, s), 2.23 (3H, s), 3.30 (3H, s), 4.28 (2H, s), 4.75 (2H, s), 6.68 (1H, d, J = 2.7 Hz), 7.18 (1H, s), 8.19 (1H, brs), 9.01 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.0 (q), 12.3 (q), 42.5 (t), 57.2 (q), 64.9 (t), 109.8 (s), 114.7 (s), 116.8 (d), 117.4 (s), 127.7 (s), 140.4 (d), 151.2 (s), 164.4 (s); EIMS m/z 263 (M^+). MS (ESI) m/z 286 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{13}H_{17}N_3NaO_3$ 286.11676; Found 286.11721.

*Synthesis of 4-[(Thymin-1-yl)methyl]-3-methoxymethyl-5-pentylpyrrole (**31e**).* 4-[(3-Benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidyl)methyl]-5-pentyl-3-(phenylsulfanylmethyl)-1-(*p*-tosyl)-pyrrole (**14a**) (50 mg, 0.08 mmol) was added to a MeOH (1.6 mL) solution of sodium hydroxide (2 N aq, 0.4 mL, 0.80 mmol). The reaction mixture was stirred at 70 °C for 16 h. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$. The combined organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with $CHCl_3$−MeOH (40:1). The titled comound **31e** (20 mg, 82%) was obtained as white powders (mp 74−76 °C).

IR (KBr, cm^{-1}) ν 3260, 3063, 2954, 2928, 2857, 1684, 1469, 1356, 1250, 1223, 1080, 782, 769, 706, 614, 604, 592; ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 6.9 Hz), 1.26−1.34 (4H, m), 1.52−1.57 (2H, m), 1.84 (3H, s), 2.57 (2H, t, J = 8.3 Hz), 3.29 (3H, s), 4.28 (2H, s), 4.76 (2H, s), 6.69 (1H, d, J = 2.1 Hz), 7.19 (1H, d, J = 1.3 Hz), 8.14 (1H, brs), 8.98 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.3 (q), 13.9 (q), 22.4 (t), 25.7 (t), 29.8 (t), 31.5 (t), 42.6 (t), 57.2 (q), 64.8 (t), 109.7 (s), 114.3 (s), 116.8 (d), 117.2 (s), 132.6 (s), 140.5 (d), 151.2 (s), 164.4 (s); EIMS m/z 319 (M^+). Anal. Calcd for $C_{17}H_{25}N_3O_3$ (+ 4/3 H_2O): C, 59.46; H, 8.12; N, 12.24. Found: C, 59.18; H, 7.72; N, 12.00.

*Reaction of **10c** with NaOH in MeOH.* To a NaOH (1.2 mL, 2.4 mmol) in MeOH (4.8 mL) was added 4-(N^3-Benzoyluracil-1-yl)methyl-3-(phenylsulfanylmethyl)-1-tosylpyrrole (**10c**) (140 mg, 0.24 mmol). The reaction mixture was stirred for 2 h at 70 °C and poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with $CHCl_3$−MeOH (30:1) to give the titled compound **31f** (24 mg, 42%) as white powders (mp 153−154 °C).

IR (KBr, cm^{-1}) ν 3370, 3172, 3046, 2923, 2886, 2817, 2360, 1671, 1534, 1467, 1419, 1386, 1364, 1328, 1243, 1156, 1076, 949, 888, 810, 765, 730, 606, 556, 526, 474; ^{1}H NMR (600 MHz, DMSO−D_6) δ 3.13 (3H, s), 4.21 (2H, s), 4.68 (2H, s), 5.50 (1H, d, J = 7.6 Hz), 6.73 (1H, s), 6.78 (1H, s), 7.46 (1H, d, J = 8.3 Hz), 10.74 (1H, brs), 11.16 (1H, brs); ^{13}C NMR (125 MHz, DMSO−D_6) δ 41.7 (t), 56.4 (q), 65.6 (t), 100.5 (d), 116.6 (s), 118.0 (s), 118.7 (d), 118.8 (d), 144.9 (d), 151.0 (s), 163.7 (s); EIMS m/z 235 (M^+), 204 (M^+-OMe); MS (ESI) m/z 258 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{11}H_{13}N_3NaO_3$ 258.08546; Found 258.08559.

*Reaction of **12a** with Triethylsilane.* To a toluene (1.0 mL) solution of 4-[(3-benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidyl)methyl]-3-(phenylselanylmethyl)-1-(*p*-tosyl)pyrrole (**12a**) (50 mg, 0.08 mmol) were added Triethylborane (0.8 mL, 1 mol/L) and triethylsilane (93.0 mg, 0.8 mmol) under an Ar atmosphere. The whole was stirred for 32.5 h at 100 °C and the workup procedure and purification by the preparative TLC on silica gel eluting with (AcOEt−*n*-hexane = 1:2) gave **32** (15.0 mg, 40%) as yellow powders (mp 60−63 °C).

IR (KBr, cm^{-1}) ν 3444, 2926, 1747, 1699, 1656, 1598, 1519, 1439, 1370, 1294, 1241, 1172, 1092, 1066, 992, 949, 815, 776, 673, 587; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.90 (3H, s), 1.96 (3H, s), 2.42 (3H, s), 4.69 (2H, s), 6.94 (1H, s), 6.97 (1H, d, J = 1.4 Hz), 7.16 (1H, d, J = 2.0 Hz), 7.30 (2H, d, J = 8.2 Hz), 7.49 (2H, t, J = 7.5 Hz), 7.65 (1H, t, J = 7.5 Hz), 7.74 (2H, d, J = 8.3 Hz), 7.91 (2H, d, J = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.2 (q), 12.5 (q), 21.6 (q), 42.2 (t), 111.1 (s), 119.3 (d), 120.6 (d), 122.2 (s), 123.2 (s), 126.9 (d × 2), 129.1 (d × 2), 130.1 (d × 2), 130.4 (d × 2), 131.5 (s), 135.0 (d), 135.7 (s), 138.4 (d), 145.3 (s), 149.8 (s), 162.9 (s), 168.9 (s); EIMS m/z 477 (M^+), 322 (M^+-Ts). MS (ESI) m/z 500 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{25}H_{23}N_3NaO_5S$ 500.12561; Found 500.12349.

*Reaction of **10a** with Anisidine.* To a NaOH (0.45 mL, 0.9 mmol) and *p*-Anisidine (110.8 mg, 0.9 mmol) in dioxane (1.0 mL) was added 4-[(3-benzoyl-3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidyl)-methyl]-3-(phenylsulfanylmethyl)-1-(*p*-tosyl)pyrrole (**10a**) (50 mg, 0.09 mmol). The reaction mixture was stirred for 6.5 h at 100 °C and then poured into water (50 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with $CHCl_3$−MeOH (30:1) to give the titled compound **33** (10 mg, 34%) as brown powders (mp 151−153 °C).

IR (KBr, cm^{-1}) ν 3384, 2925, 2853, 1676, 1513, 1468, 1350, 1235, 1179, 1116, 1072, 1036, 822, 760; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.77 (3H, d, J = 1.4 Hz), 2.17 (2H, brs), 3.75 (3H, s), 4.10 (2H, s), 4.80 (2H, s), 6.60 (2H, d, J = 9.0 Hz), 6.78 (2H, d, J = 8.3 Hz), 6.87 (1H, brs), 7.12 (1H, brs), 8.18 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.3 (q), 40.5 (t), 42.9 (t), 55.8 (q), 110.0 (s), 114.2 (d × 2), 114.9 (d × 2), 116.6 (s), 117.8 (d), 119.5 (d), 120.2 (s), 140.5 (d), 142.3 (s), 151.0 (s), 152.3 (s), 164.1 (s); EIMS m/z 340 (M^+). MS (ESI) m/z 341 $[M + H]^+$, 363 $[M + Na]^+$; HRMS (ESI-DART) m/z $[M + Na]^+$ calcd for $C_{18}H_{20}N_4NaO_3$ 363.14331; Found 363.14342.

Antiviral Activity. The compounds **12a**, **14a**, **17a**, **18a**, **11b**, **19b**, **17b**, **11d**, **19d**, **24b**, **25b**, **28b**, **29**, **31b**, **31d**, **31e**, **33** were tested by using Rabbit Kidney 13 (RK-13) cell, which was cultivated with Eagle's minimum essential medial (MEM) (Nissui, Tokyo, Japan) supplemented with 5−10% fetal bovine serum (FBS), using Equine herpesvirus type 1 (EHV-1: family Herpesviridae, subfamily Alphaherpesvirinae, genus Varicellovirus). EHV-1 Cherry VP22, which was constructed from Ab4p BAC,[17] was used. EHV-1 Ab4p strain, which was provided by Dr. A. J. Davision, Glasgow University, Scotland.

Method. To evaluate antivirus activity, monolayers of RK 13 cells prepared in 24-well plates were inoculated with each virus at an m.o.i. of 0.01 pfu/cell. After 1 h adsorption, cells were washed once with PBS and incubated for 3 days at 37 °C in a 5% CO_2 atmosphere under a 1.5% methylcellulose overlay dissolved in 5 or 50 μg/mL each chemical compound.

Cell Viability Assay. The compounds **11a**, **11d**, **19a**, **27a**, **28b**, **31a**, **31b**, **31d**, **31e** were tested their antiproliferative activity by using human colon tumor (HCT-116) cell, which was cultivated with McCoy's 5A medial (Sigma-Aldrich, MO, USA) supplemented with 10% heat inactivated fetal bovine serum (FBS) at 37 °C under an atmosphere of 5%CO_2. The cells viability was assessed using by MTT method described by Mosmann.[20] HCT-116 cells were placed in 96 well flat bottomed tissue culture plated with 2.0 × 10^3 cells per well in 100 μL of culture medium. After the incubation of the cells for 24 h at 37 °C under an atmosphere of 5%CO_2 for attachment onto the wells, the cells were treated with the indicated concentrations of compounds in culture medium. Following a further 48 h incubation, 10 μL of MTT (5 mg/mL in PBS buffer) was added per well and the plate was incubated for 4 h to allow metabolism of MTT by cellular mitochondrial dehydrogenases. The excess MTT was aspirated, and the formazan crystals that were dissolved by the addition of 100 μL of DMSO. The absorbance of purple formazan was read at 570 nm using a microplate reader. The results following chemical exposure were calculated as a percentage relative to untreated controls. The data were expressed as means ± SEM, with n = 3.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02841.

^{1}H and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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