

【公報種別】特許法第17条の2の規定による補正の掲載

【部門区分】第3部門第2区分

【発行日】平成27年5月21日(2015.5.21)

【公表番号】特表2014-510114(P2014-510114A)

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【出願番号】特願2014-502963(P2014-502963)

【国際特許分類】

| | | |
|---------|---------|-----------|
| C 0 7 D | 471/14 | (2006.01) |
| C 0 7 D | 487/04 | (2006.01) |
| A 6 1 K | 31/519 | (2006.01) |
| C 0 7 D | 491/147 | (2006.01) |
| A 6 1 K | 31/5377 | (2006.01) |
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| A 6 1 P | 35/00 | (2006.01) |
| A 6 1 P | 37/02 | (2006.01) |
| A 6 1 P | 29/00 | (2006.01) |
| A 6 1 P | 19/02 | (2006.01) |
| A 6 1 P | 17/06 | (2006.01) |
| A 6 1 P | 1/04 | (2006.01) |
| A 6 1 P | 25/00 | (2006.01) |
| A 6 1 P | 27/02 | (2006.01) |
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| A 6 1 P | 9/10 | (2006.01) |
| A 6 1 P | 11/06 | (2006.01) |
| A 6 1 P | 37/08 | (2006.01) |
| A 6 1 P | 17/00 | (2006.01) |

【F I】

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| C 0 7 D | 471/14 | 1 0 2 |
| C 0 7 D | 487/04 | 1 4 0 |
| A 6 1 K | 31/519 | |
| C 0 7 D | 491/147 | |
| A 6 1 K | 31/5377 | |
| A 6 1 P | 43/00 | 1 1 1 |
| A 6 1 P | 35/00 | |
| A 6 1 P | 37/02 | |
| A 6 1 P | 29/00 | |
| A 6 1 P | 19/02 | |
| A 6 1 P | 17/06 | |
| A 6 1 P | 1/04 | |
| A 6 1 P | 25/00 | |
| A 6 1 P | 27/02 | |
| A 6 1 P | 9/00 | |
| A 6 1 P | 9/10 | 1 0 1 |
| A 6 1 P | 11/06 | |
| A 6 1 P | 37/08 | |
| A 6 1 P | 17/00 | |

【誤訳訂正書】

【提出日】平成27年4月2日(2015.4.2)

【誤訳訂正1】

【訂正対象書類名】特許請求の範囲

【訂正対象項目名】全文

【訂正方法】変更

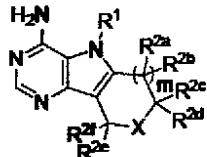
【訂正の内容】

【特許請求の範囲】

【請求項1】

式1：

【化1】



の化合物であって、

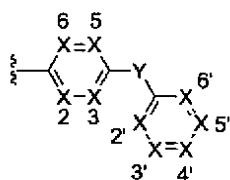
mは、0 - 1の整数であり、

Xは、CH₂、O、S(O)_n、NR⁶から選択され、

nは、0 - 2の整数であり、

R¹は、

【化2】



であり、

Yは、O又はCH₂から選択され、

X²、X³、X⁵、X⁶、X^{2'}、X^{3'}、X^{4'}、X^{5'}、X^{6'}は独立してCR及びNから選択され、

各Rは、独立して水素、ハロゲン、-NO₂、-CN、アルキル、アルケニル、アルキニル、-OR³、-OC(O)R³、-OC(O)NR⁴R⁵、-NR⁴R⁵、-S(O)_nR³、-C(O)R³、-C(O)OR³、-C(O)NR⁴R⁵、-S(O)₂NR⁴R⁵、-NR²C(O)R³、-NR²S(O)_nR³、-NR²C(O)NR⁴R⁵、-NR²S(O)₂N⁴R⁵、アリール、ヘテロアリール、カルボシクリル及びヘテロシクリルから選択され、R²は、水素、アルキル、アルケニル、アルキニル、ヘテロアルキル、カルボシクリル、ヘテロシクリル、アリール、ヘテロアリールから選択され、

R^{2a}、R^{2b}、R^{2c}、R^{2d}、R^{2e}、R^{2f}は独立して水素、アルキル、ヘテロアルキル、カルボシクリル、ヘテロシクリル、アリール又はヘテロアリールから選択され、R^{2a}及びR^{2b}、R^{2c}及びR^{2d}又はR^{2e}及びR^{2f}を縮合させて3 - 8員のシクロアルキル又はヘテロシクリル環系を形成することができ、

R³は、水素、アルキル、アルケニル、アルキニル、ヘテロアルキル、カルボシクリル、ヘテロシクリル、アリール、ヘテロアリールから選択され、

R⁴及びR⁵は独立して水素、アルキル、ヘテロアルキル、カルボシクリル、ヘテロシクリル、アリール、ヘテロアリールから選択され、あるいはR⁴及びR⁵を縮合させて3 - 8員のヘテロシクリル環系を形成することができ、

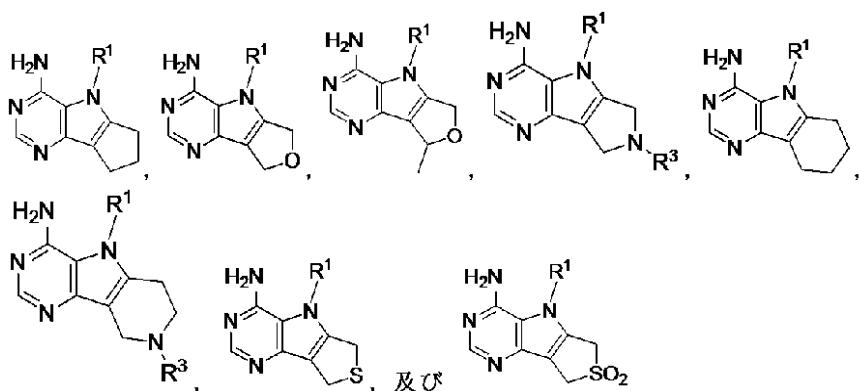
R⁶は、水素、アルキル、アルケニル、アルキニル、ヘテロアルキル、カルボシクリル、ヘテロシクリル、アリール、ヘテロアリール、-C(O)R⁴、-C(O)OR⁴、-S

$(O)_2R^4$ 、 $-C(O)NR^4R^5$ 、 $-S(O)_2NR^4R^5$ 、 $-C(S)NR^4R^5$ から選択される、ことを特徴とする化合物。

【請求項 2】

式 1 が、

【化 3】

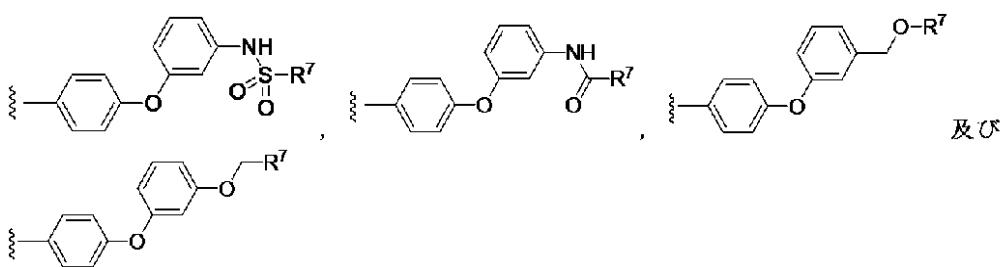


から選択される、請求項 1 に記載の化合物。

【請求項 3】

R¹ が、

【化 4】

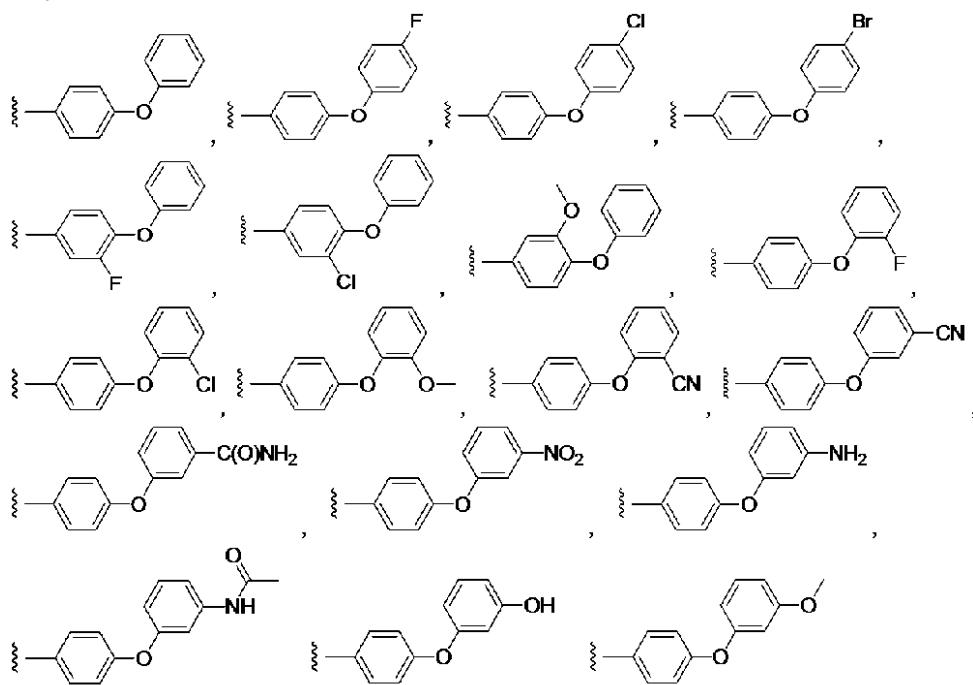


から成る群から選択され、R⁷ が置換又は非置換アルキル、アリール及びヘテロアリールである、請求項 1 又は 2 に記載の化合物。

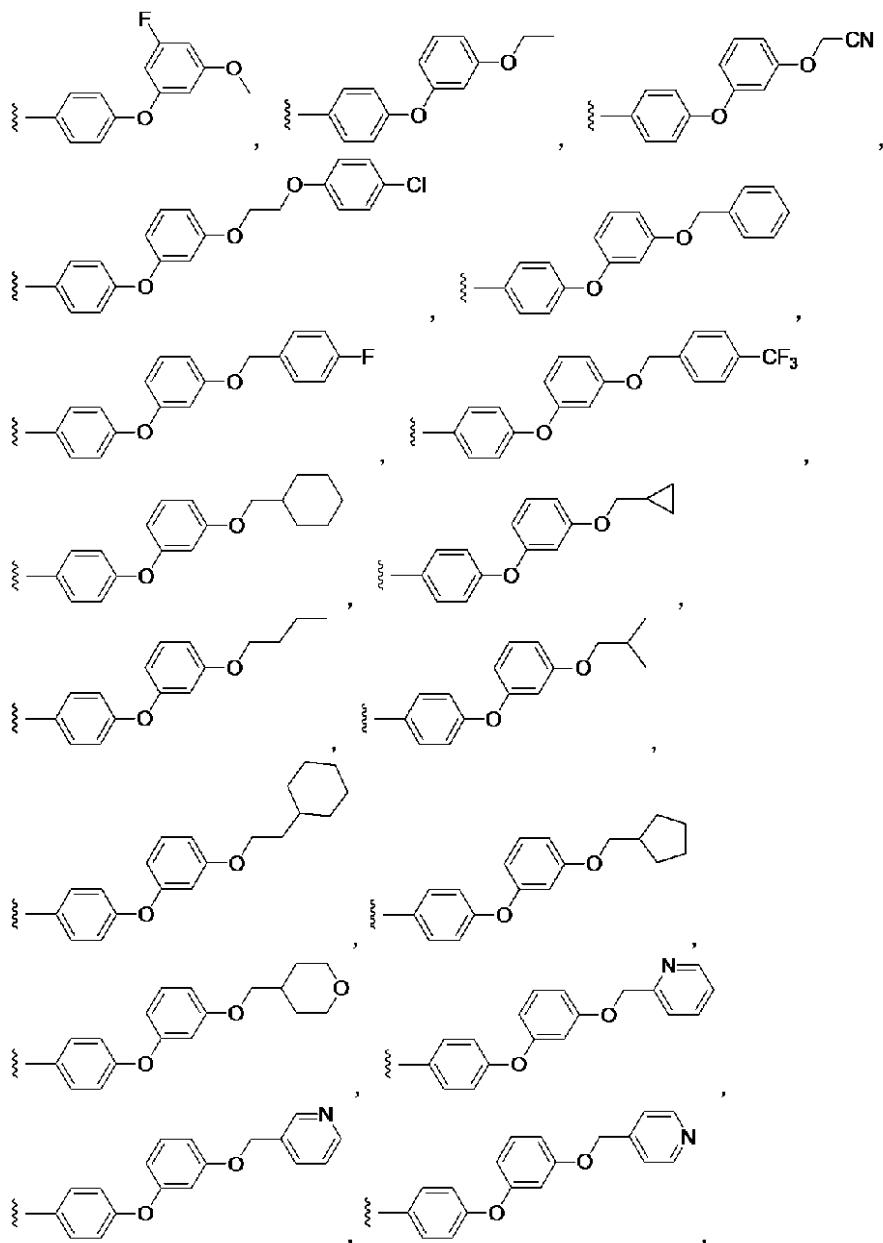
【請求項 4】

R¹ が、

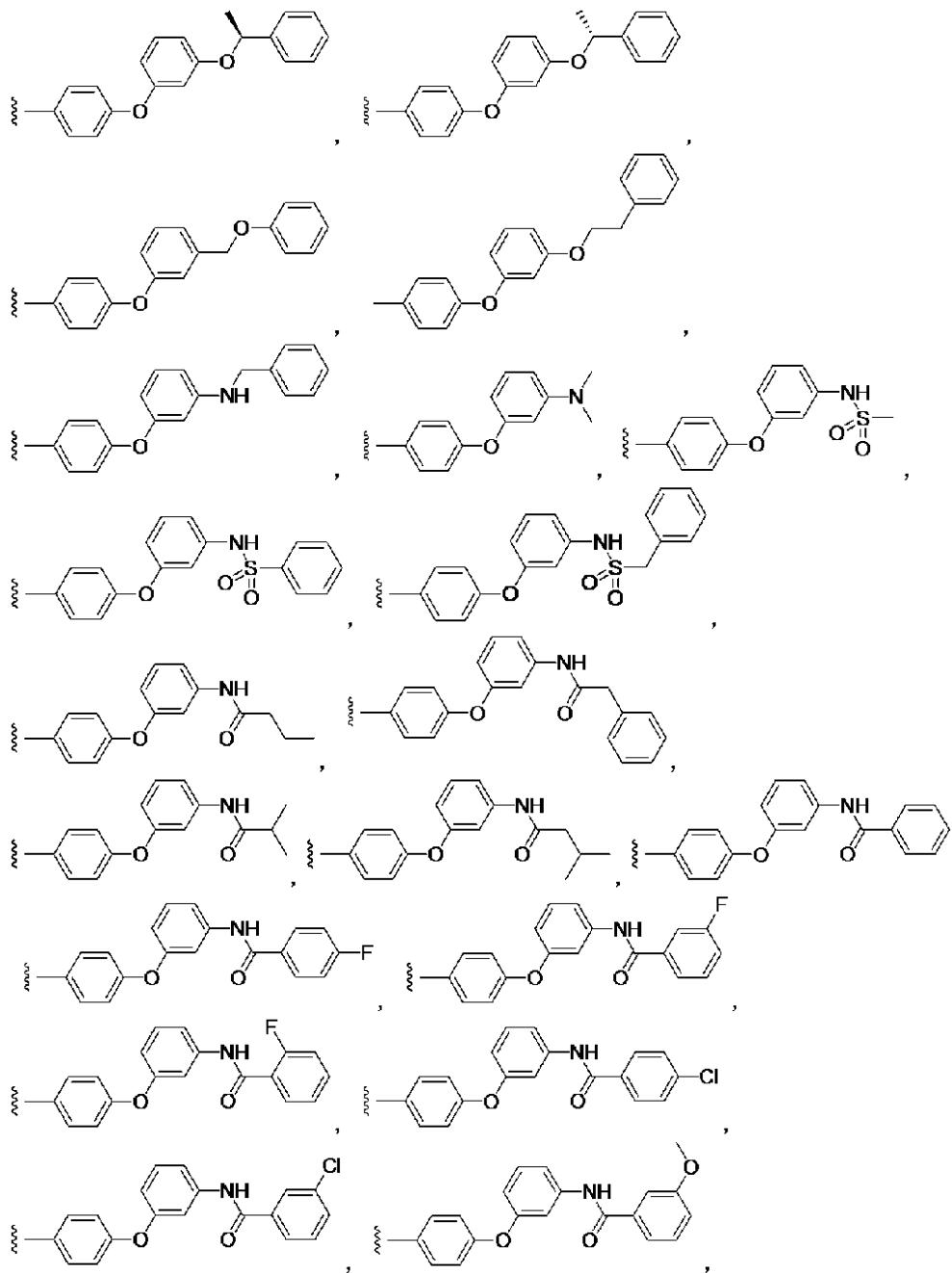
【化 5】



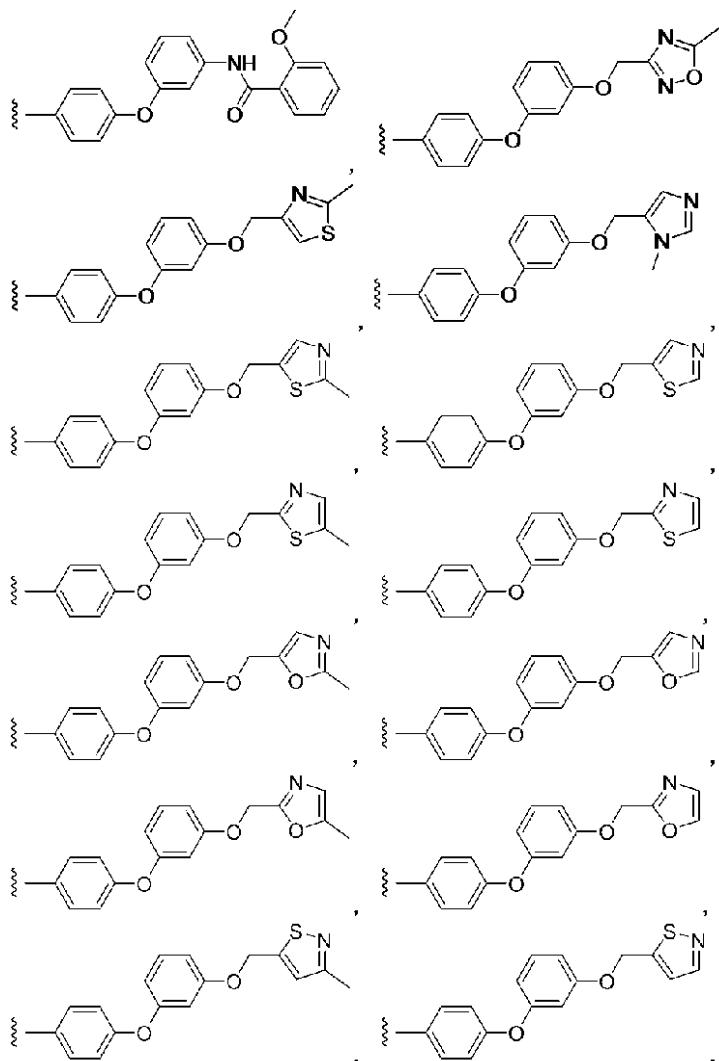
【化 6】



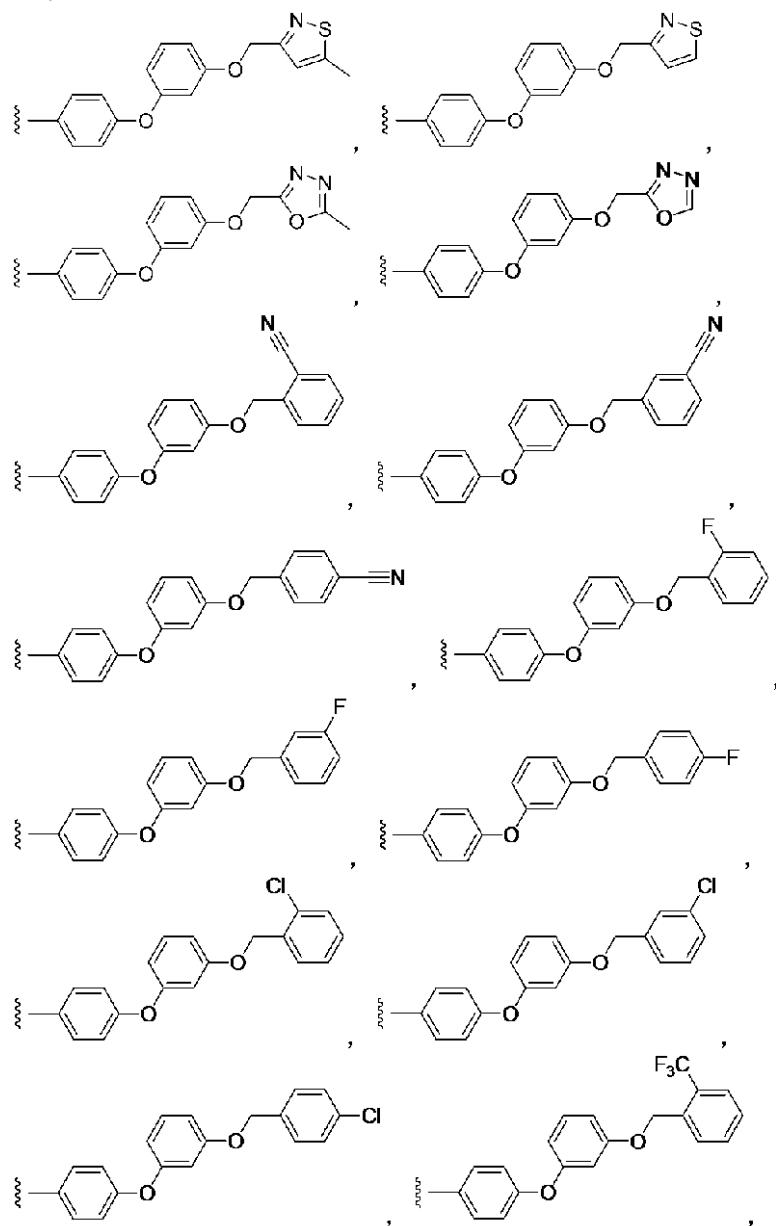
【化 7】



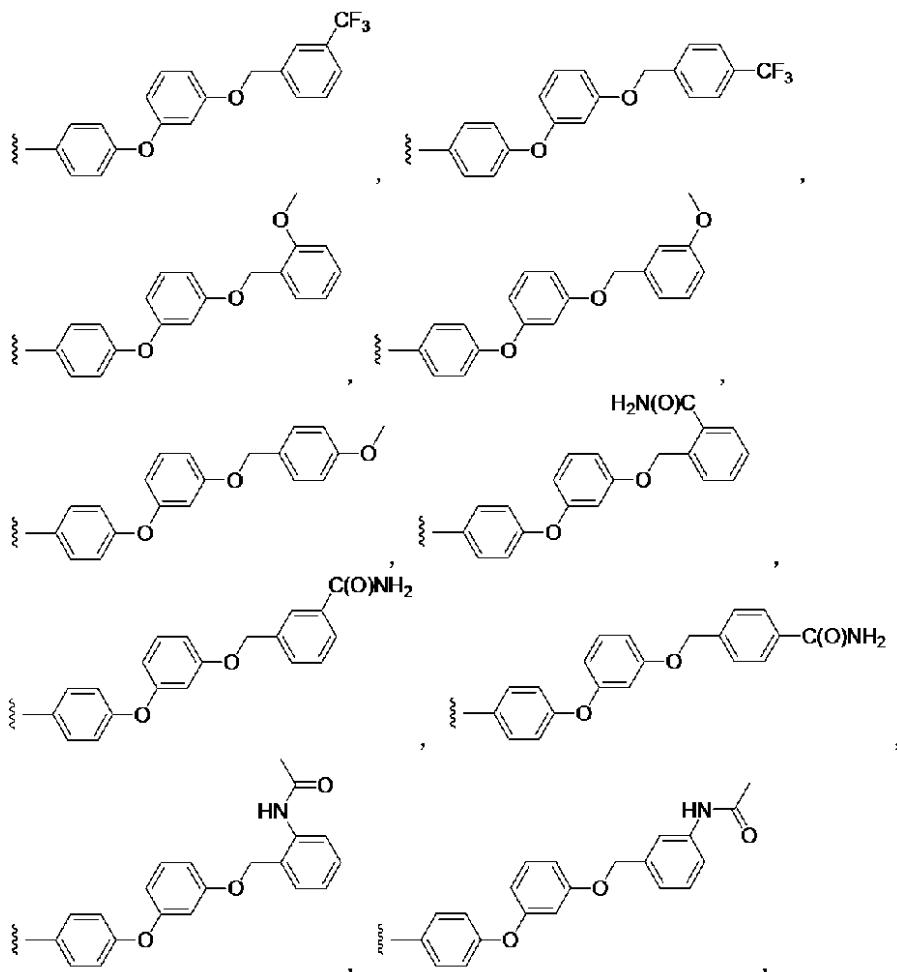
【化 8】



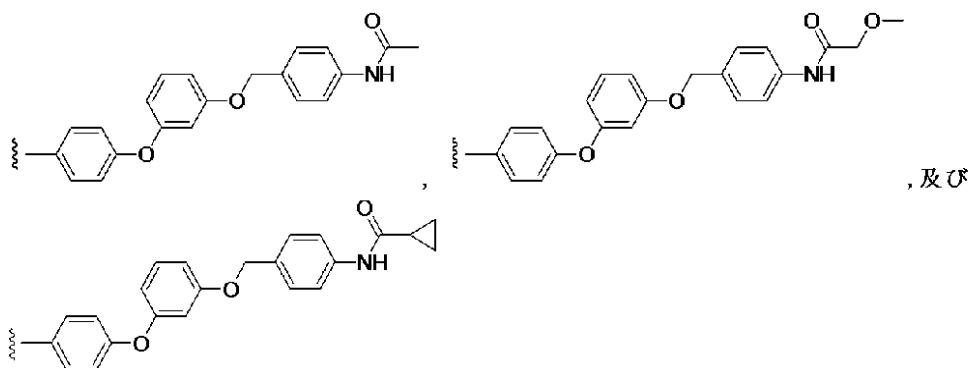
【化 9】



【化 1 0】



【化 1 1】

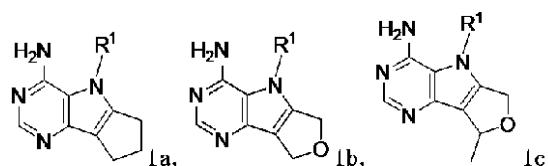


から成る群から選択される、請求項 1 又は 2 に記載の化合物。

【請求項 5】

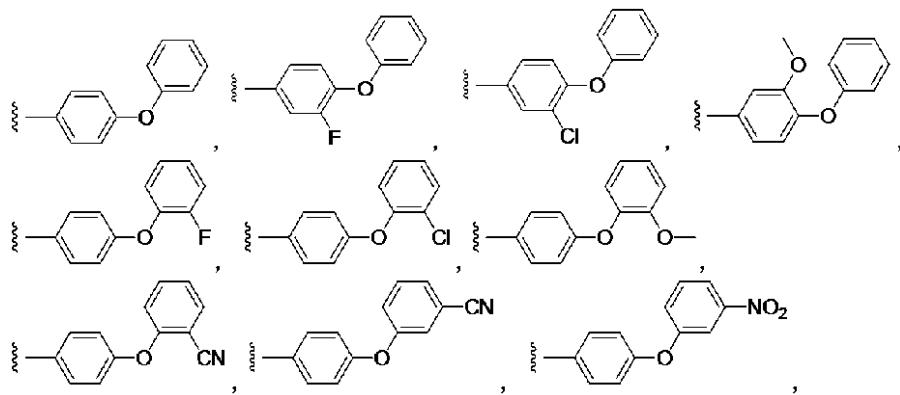
式 1 a、1 b 及び c :

【化 1 2】

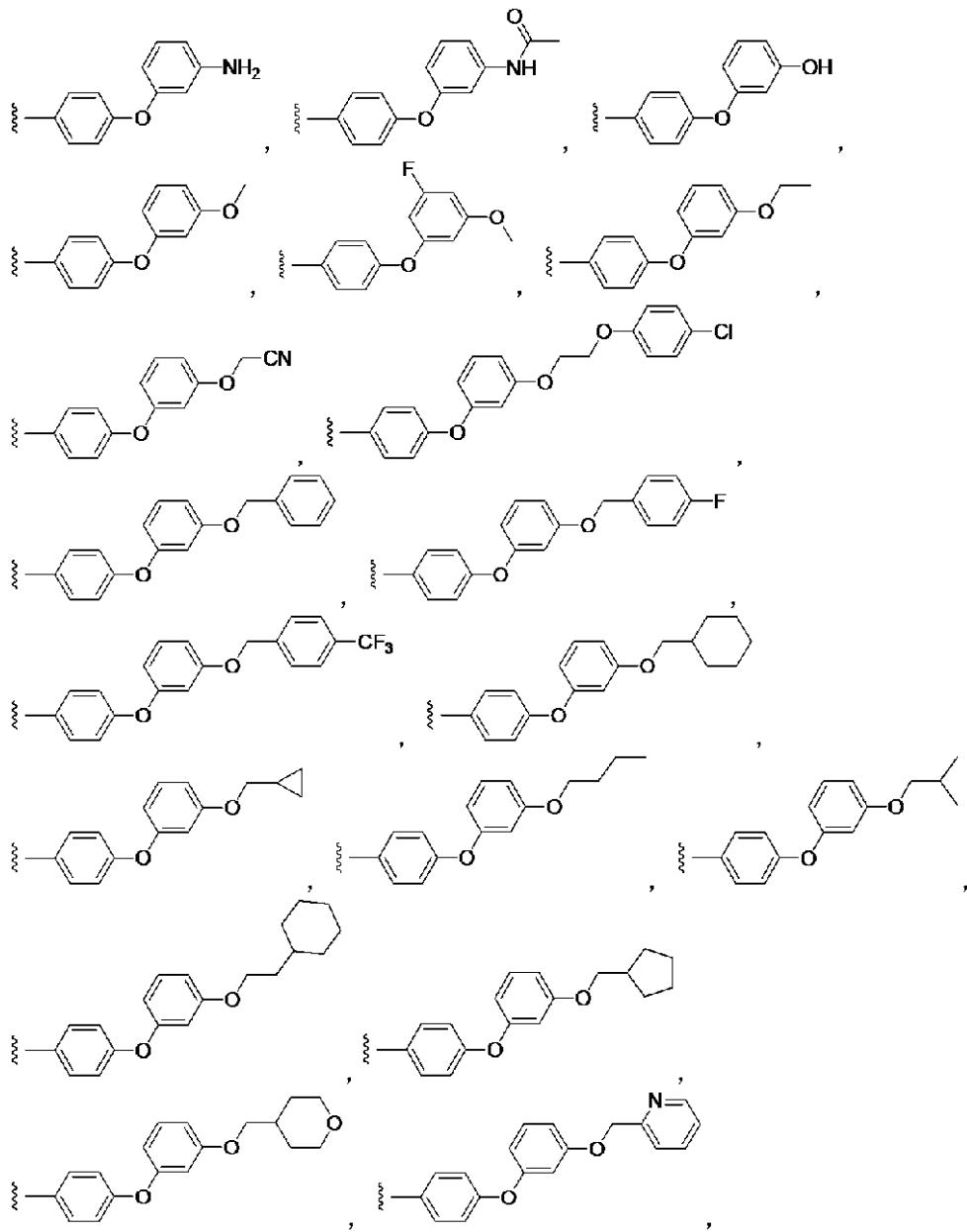


で表され、R¹が、

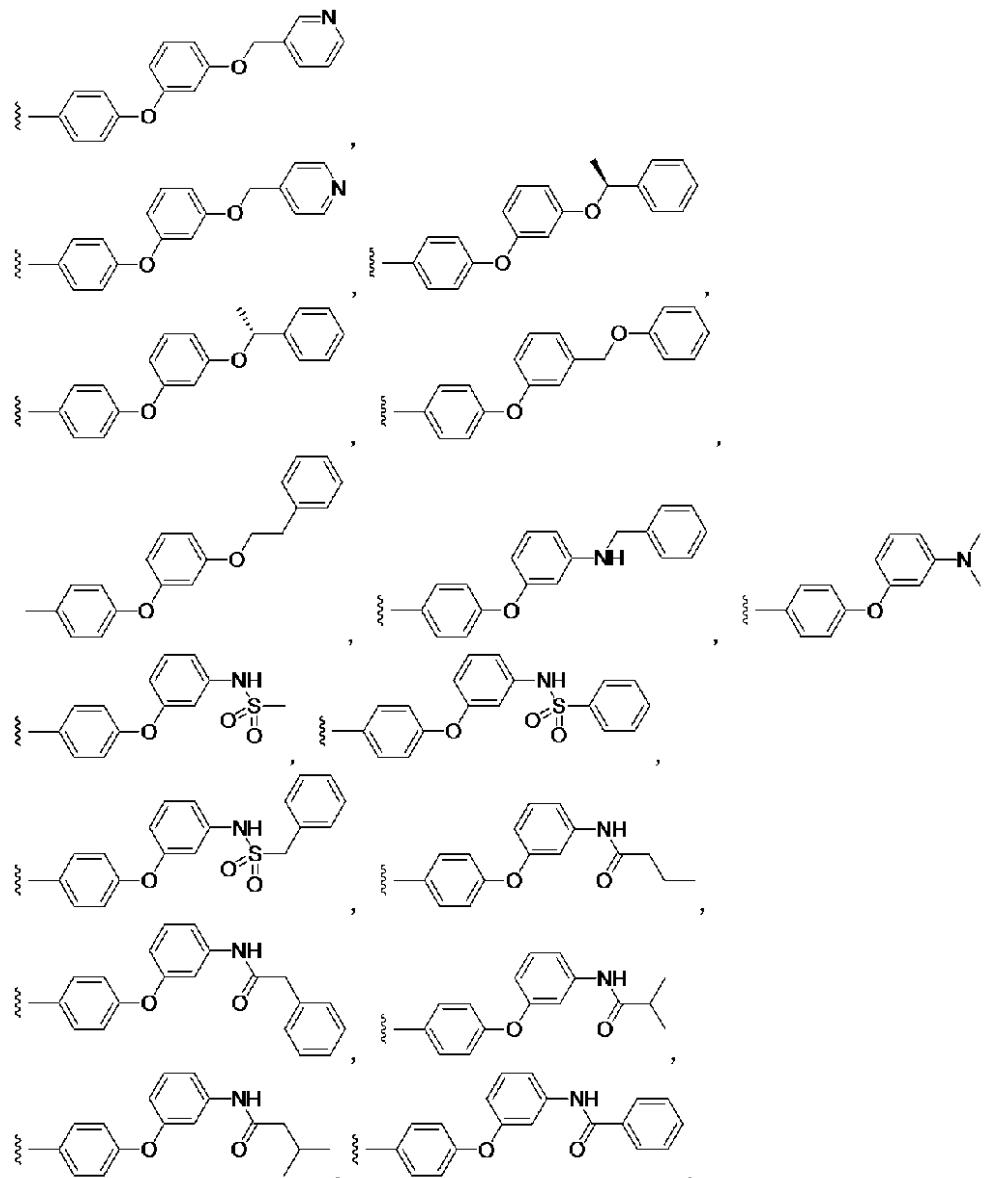
【化 1 3】



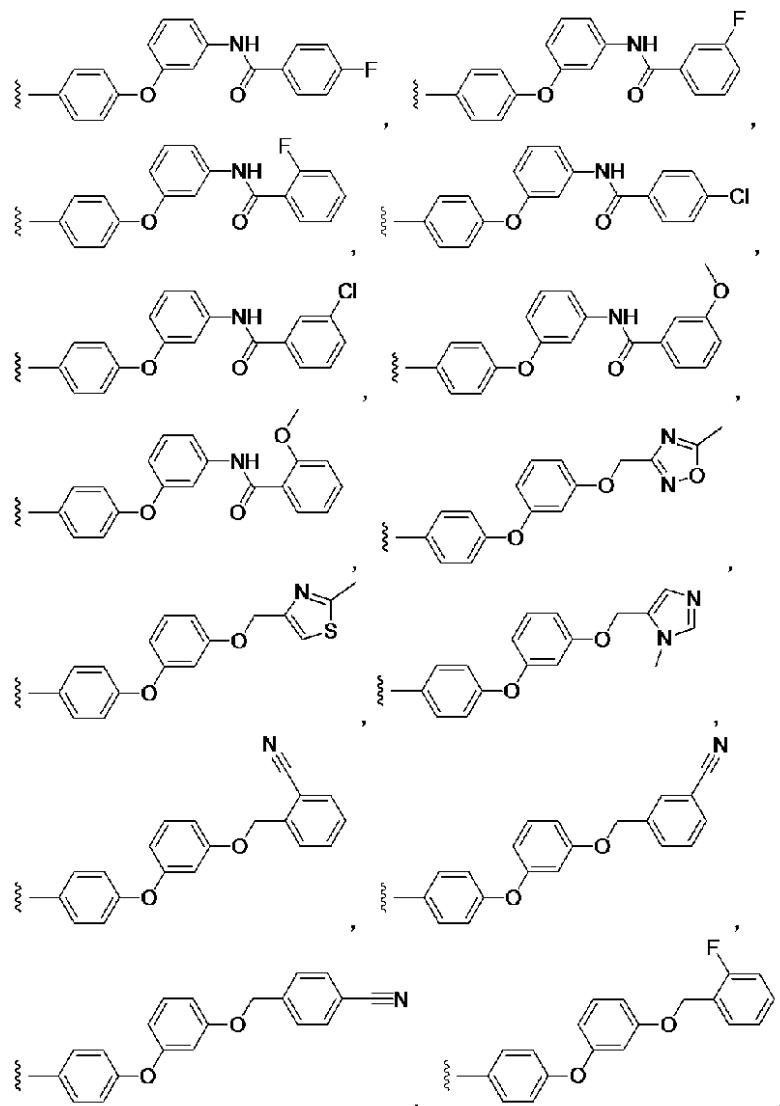
【化 1 4】



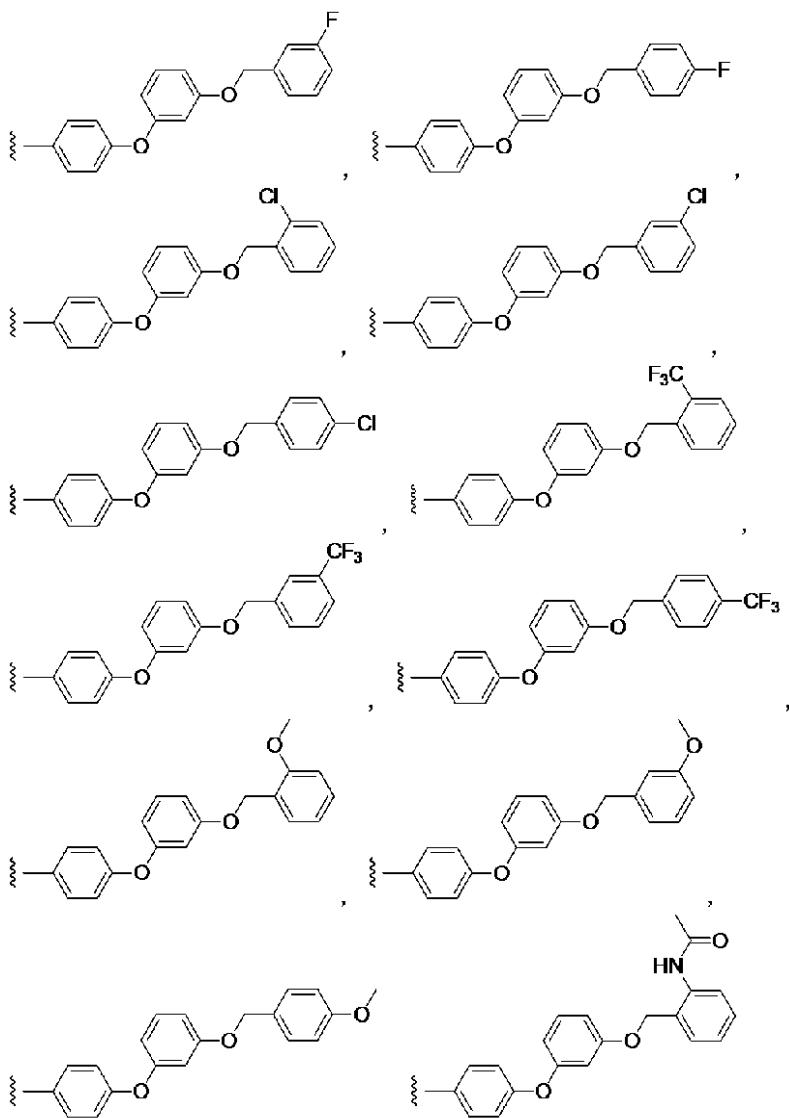
【化 1 5】



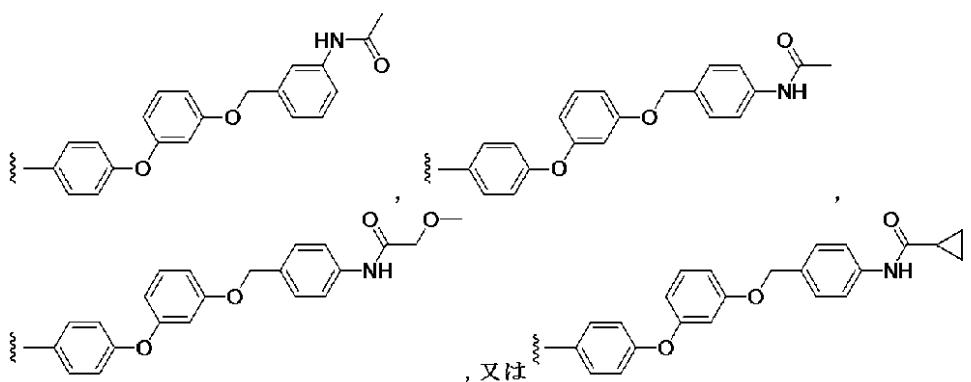
【化 1 6】



【化17】



【化18】

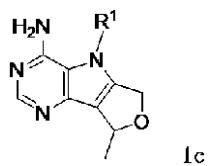


から成る群から選択される、請求項1-4のいずれかに記載の化合物。

【請求項6】

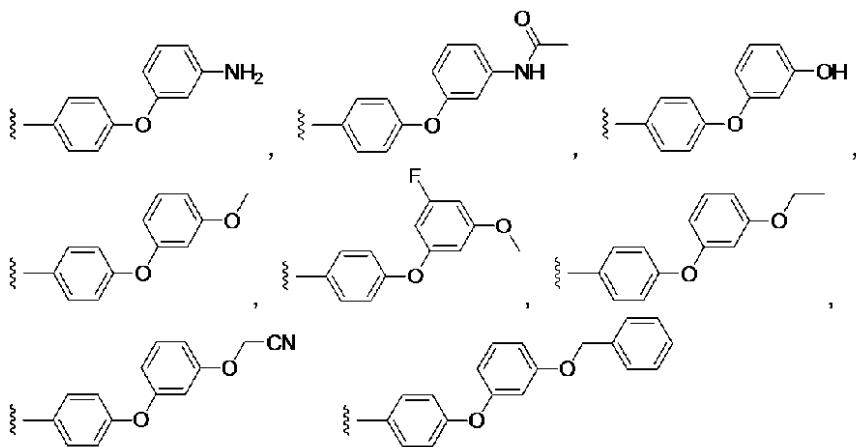
式1c：

【化19】

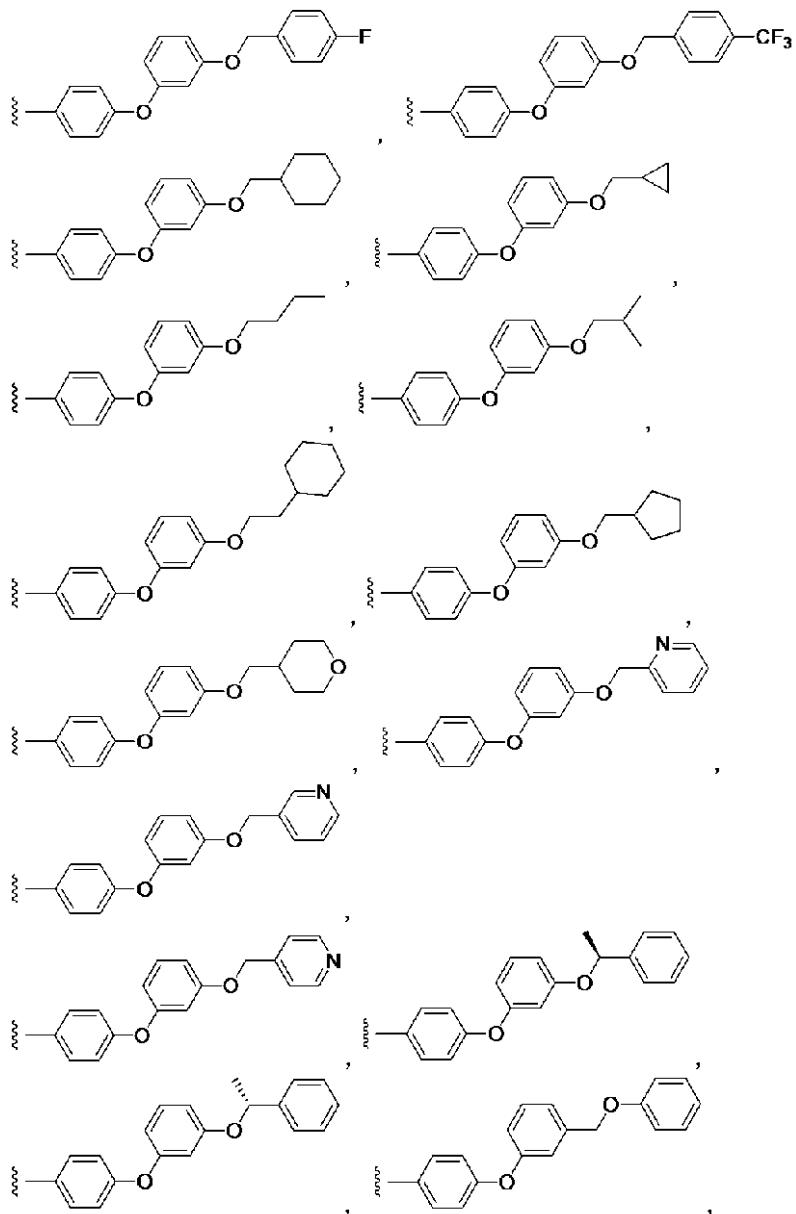


で表され、 R^1 が、

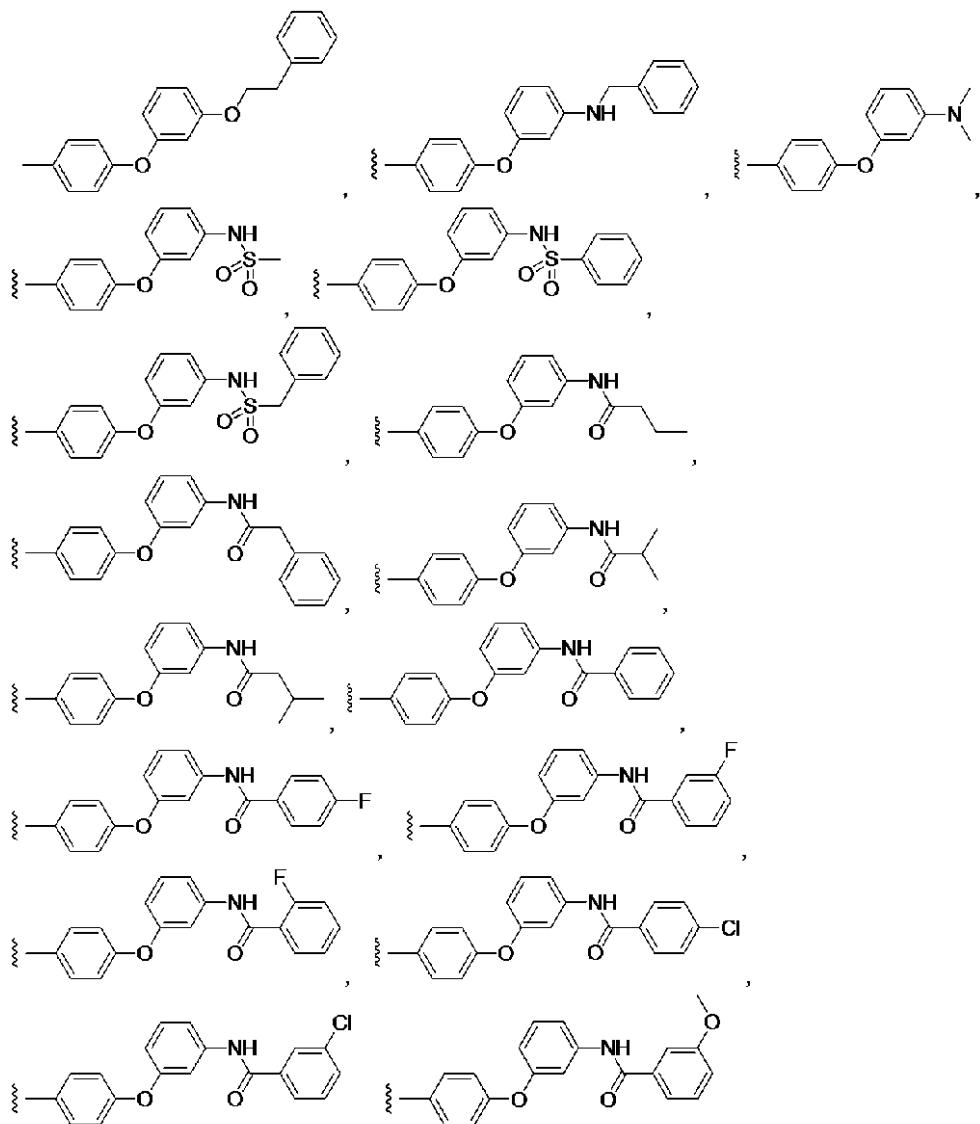
【化20】



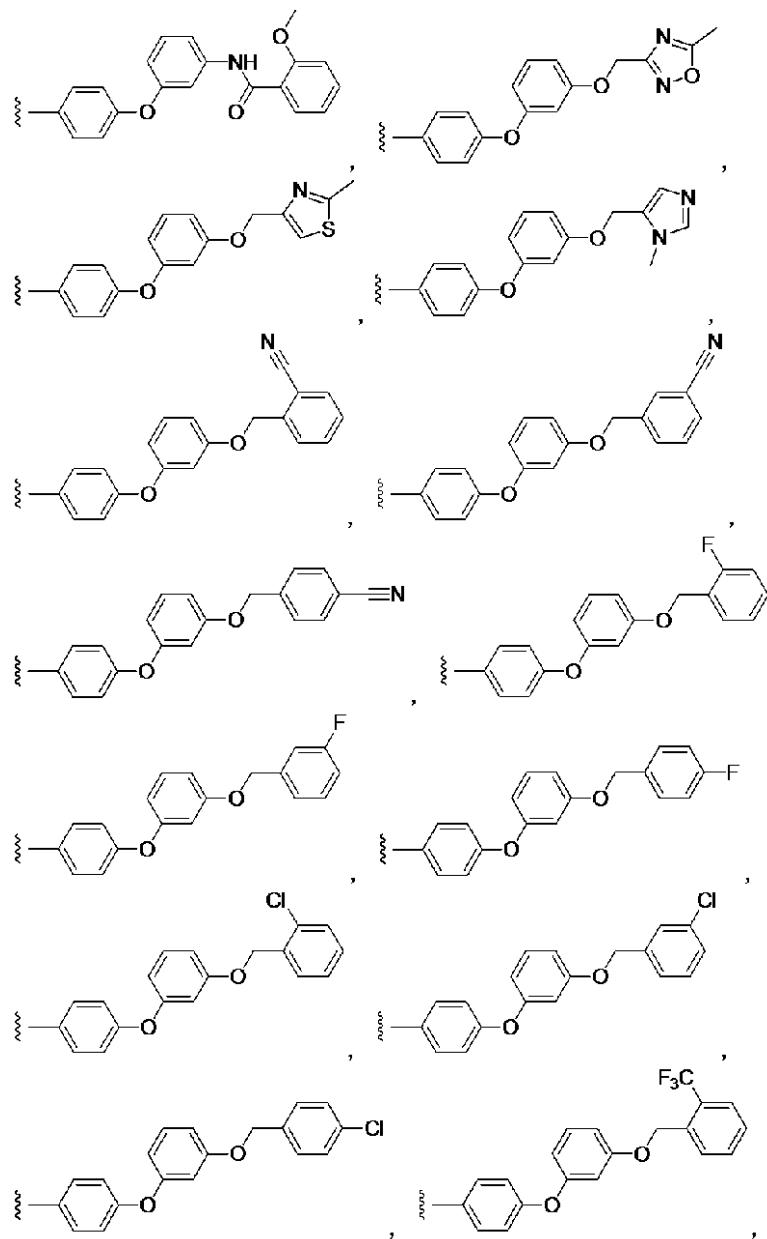
【化 2 1】



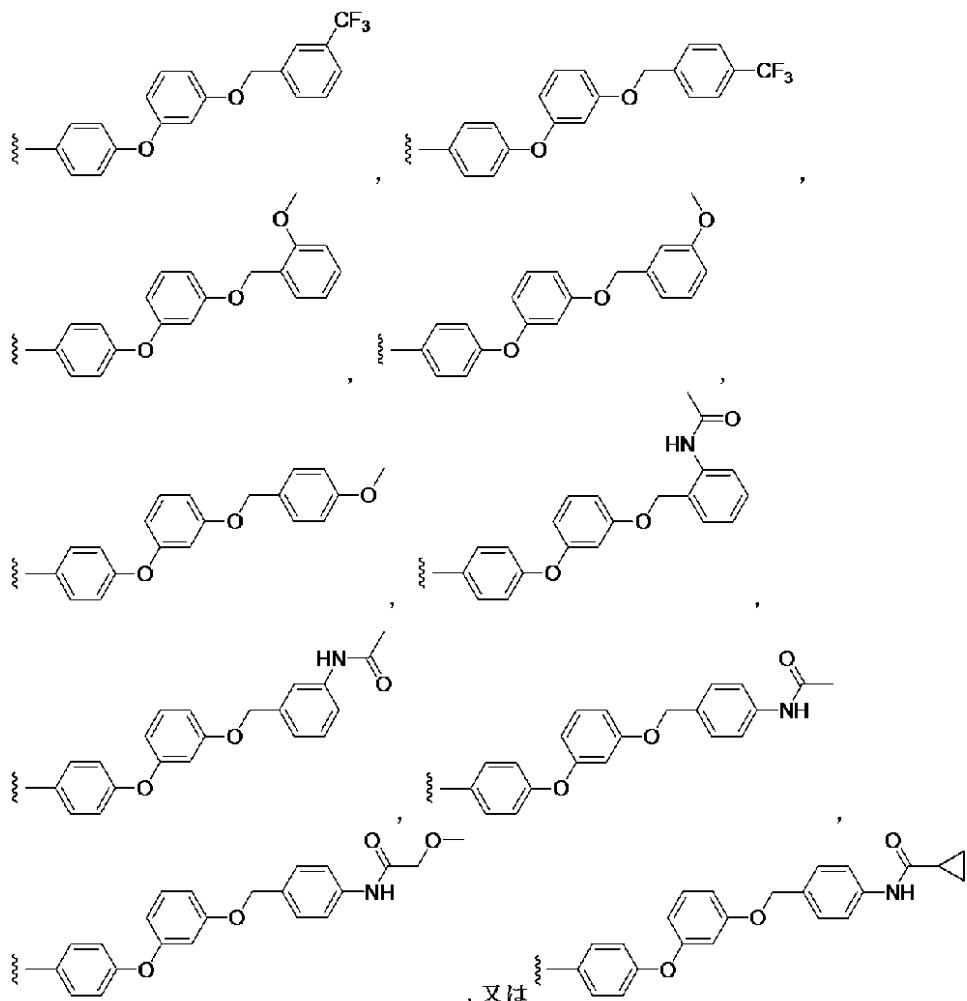
【化 2 2】



【化 2 3】



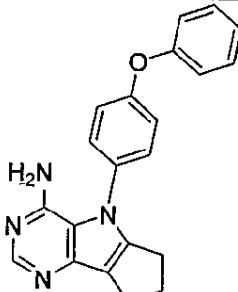
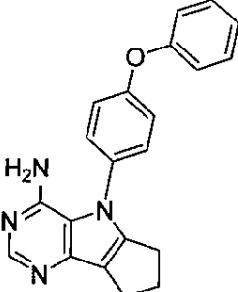
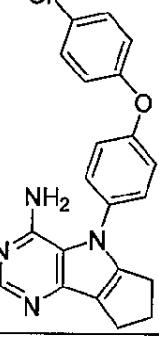
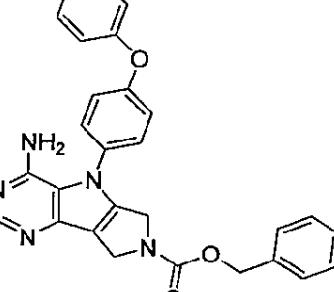
【化24】

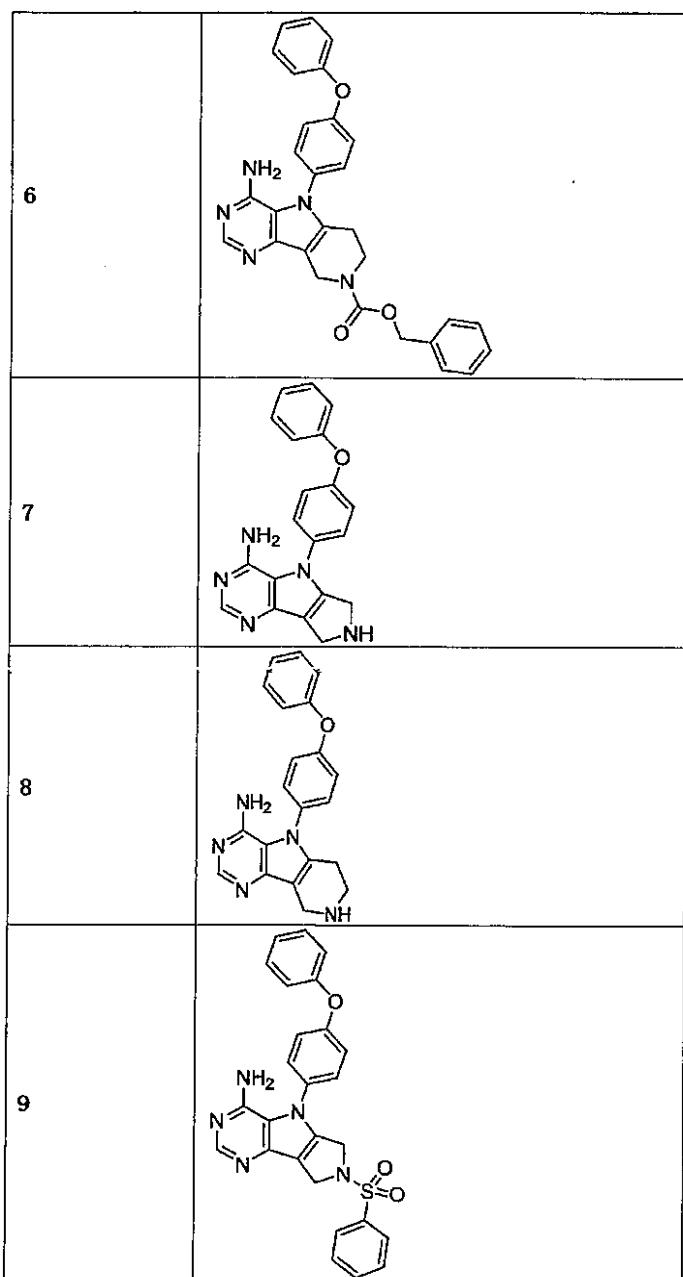


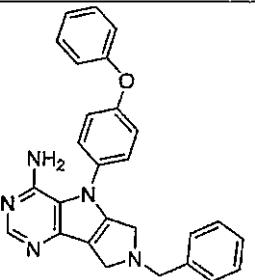
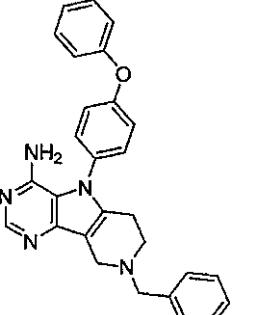
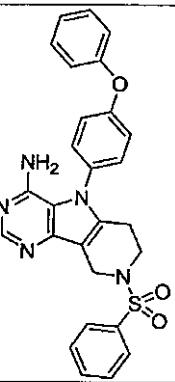
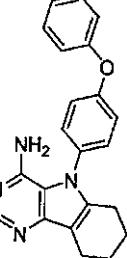
【請求項7】

化合物であつて、

【化 2 5】

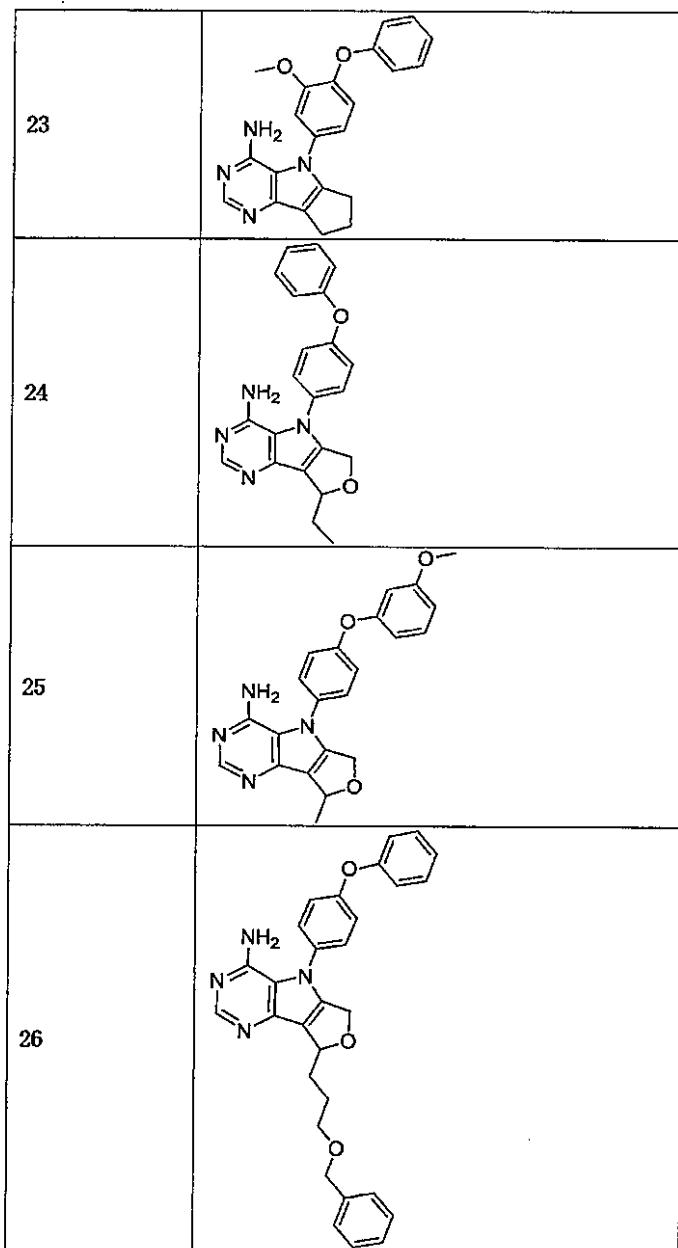
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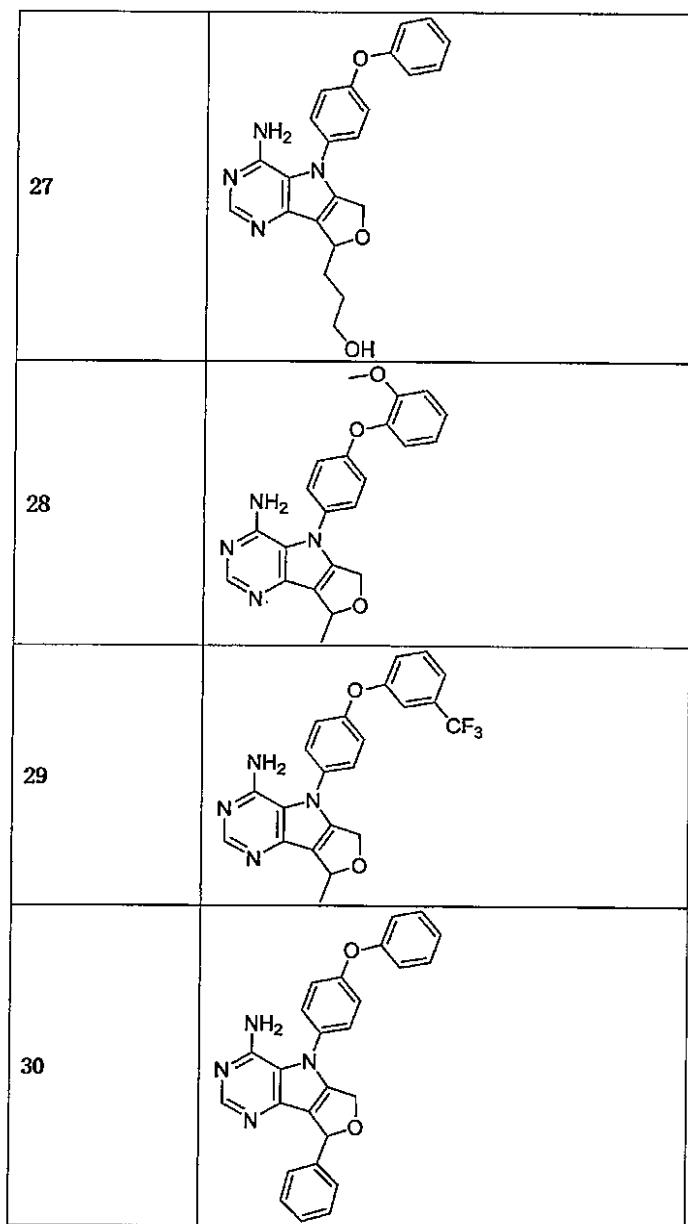


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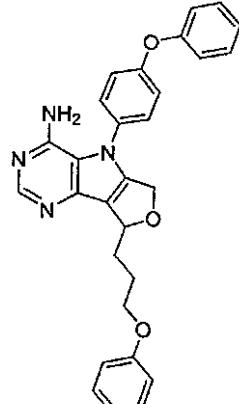
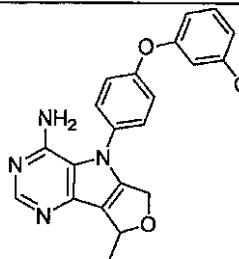
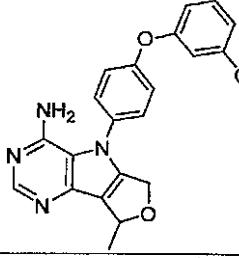
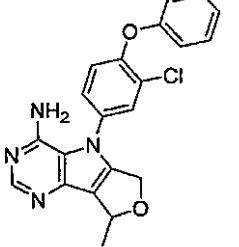
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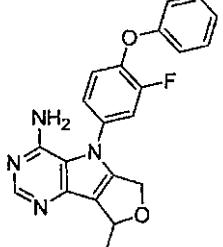
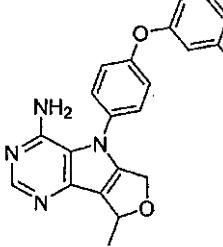
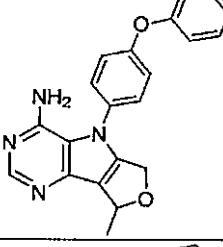
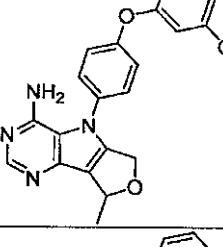
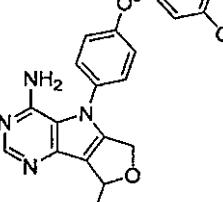
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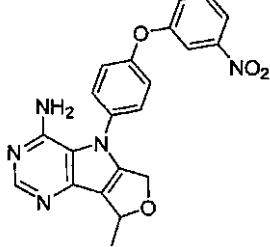
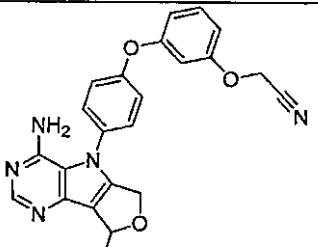
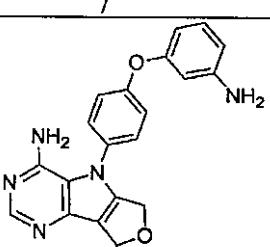
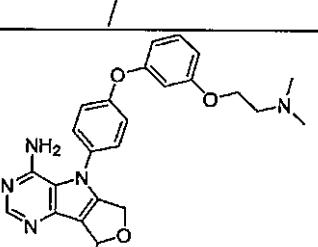
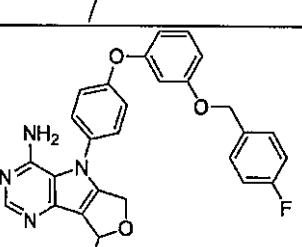


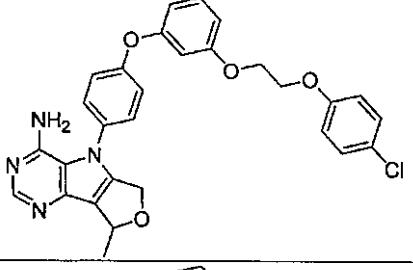
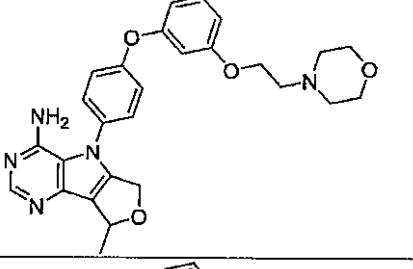
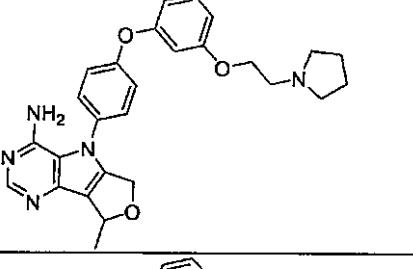
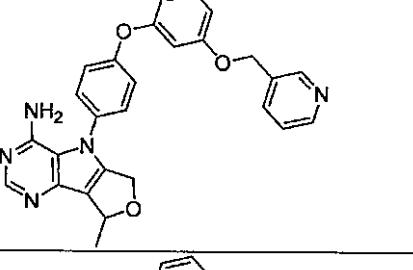
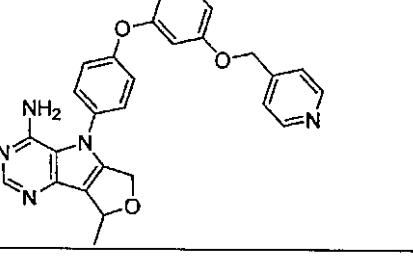


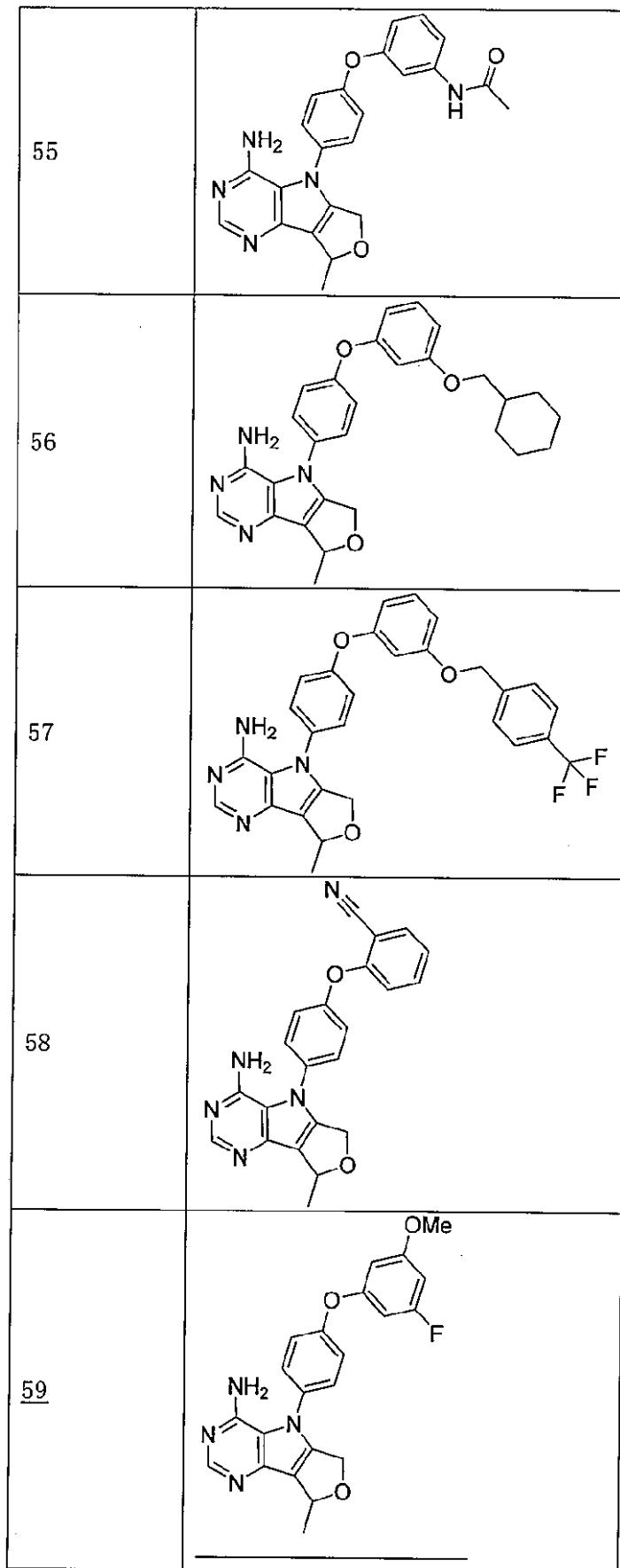
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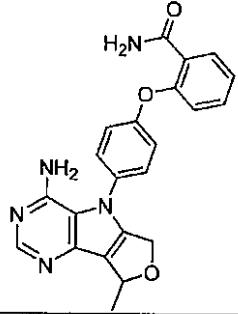
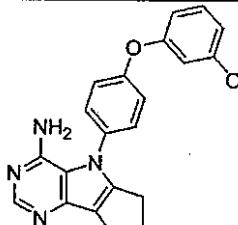
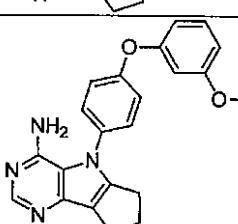
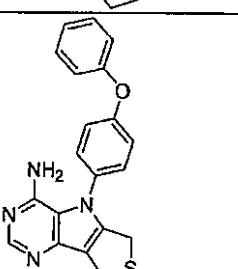
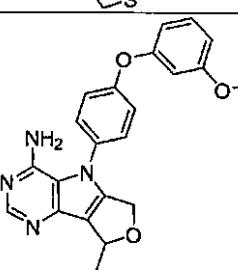
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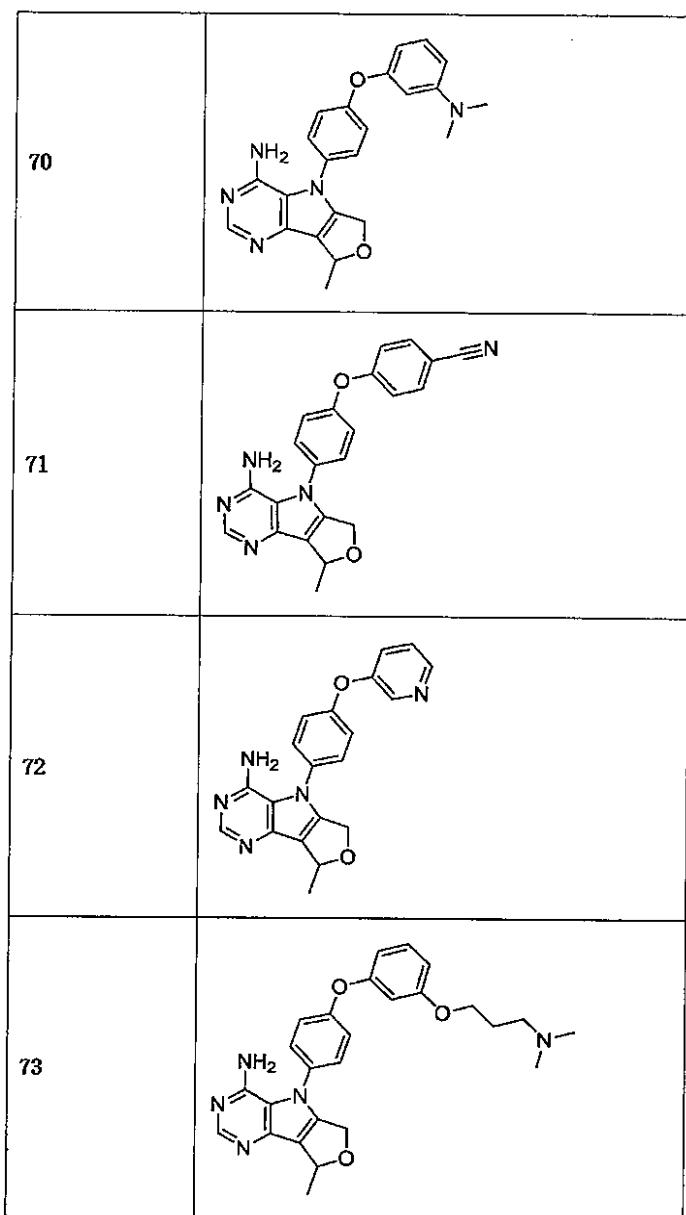
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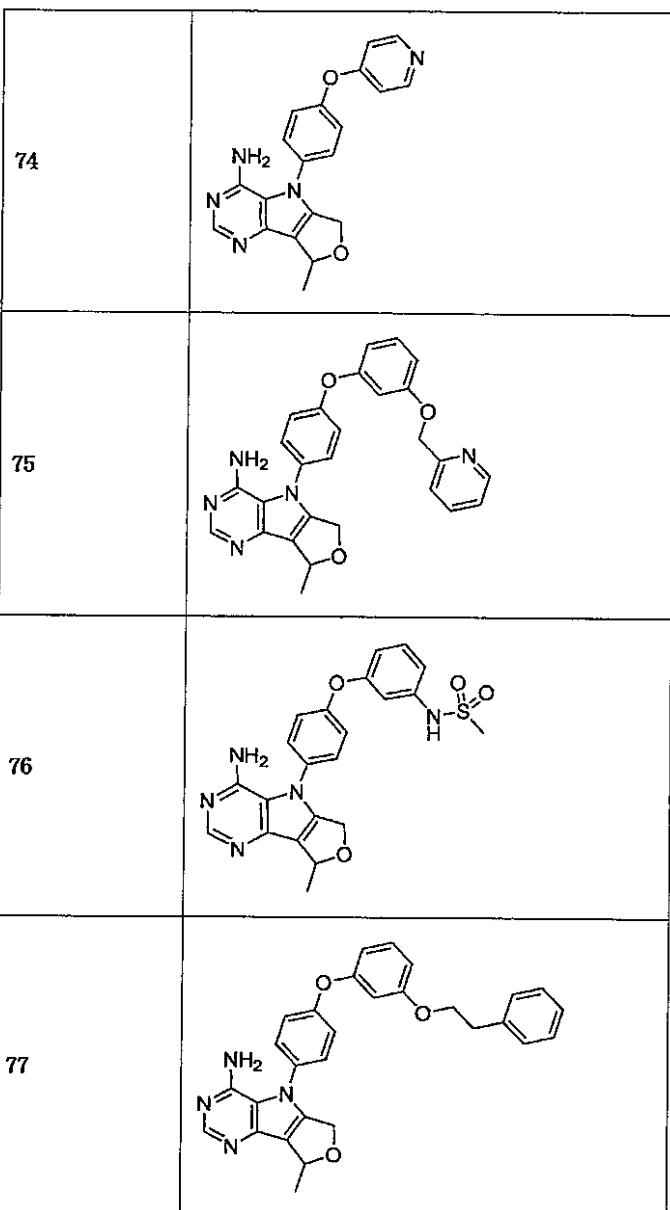
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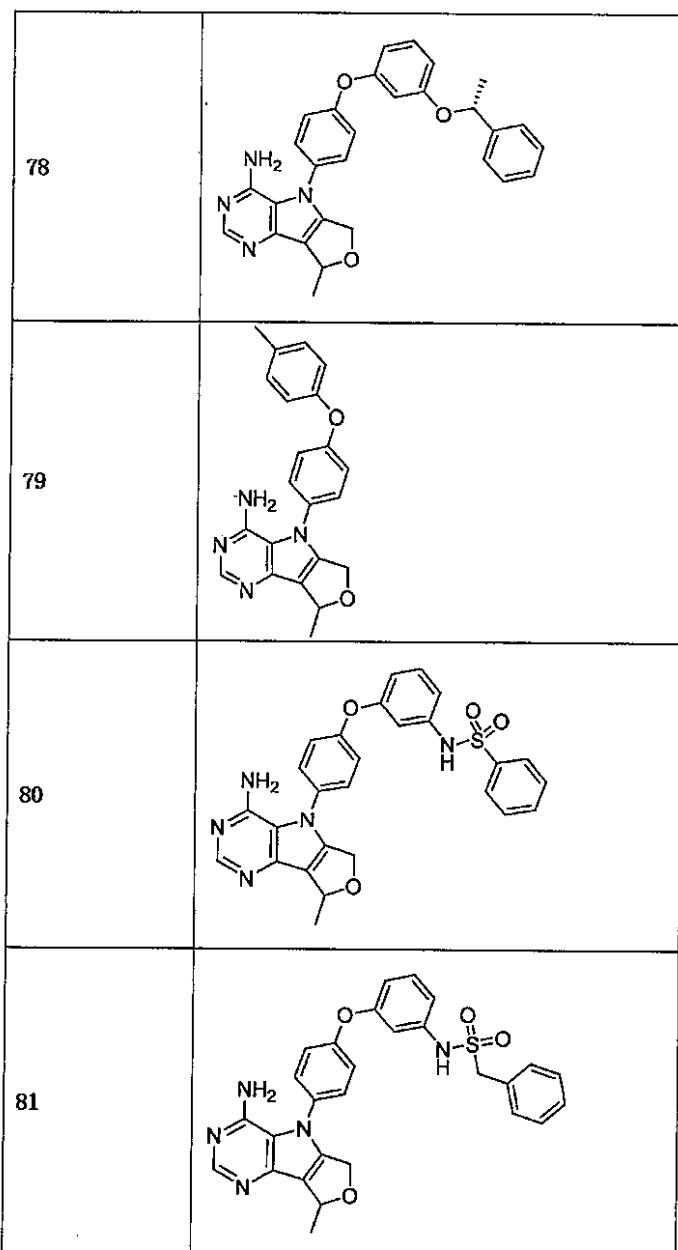


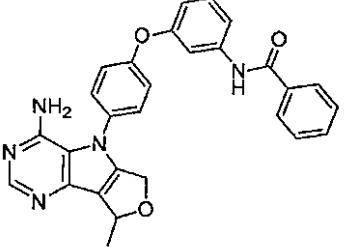
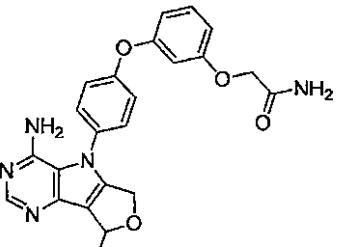
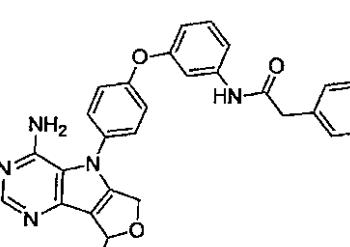
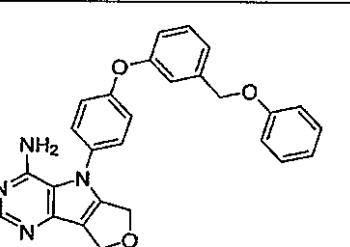
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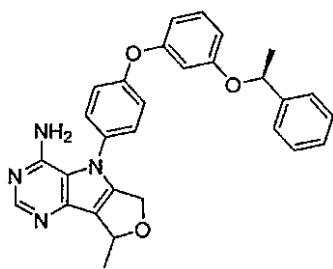
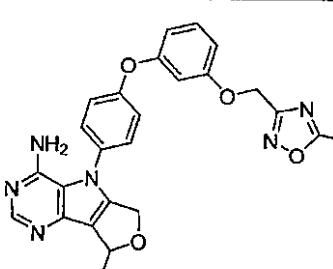
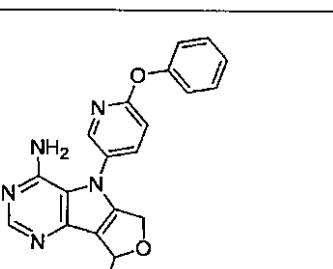
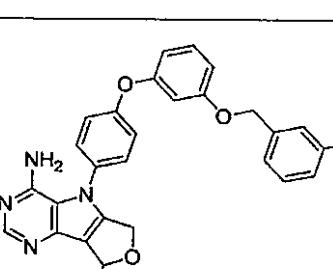
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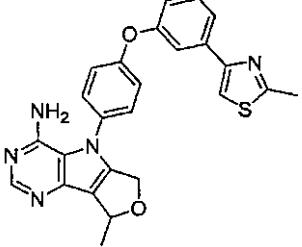
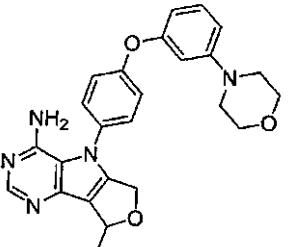
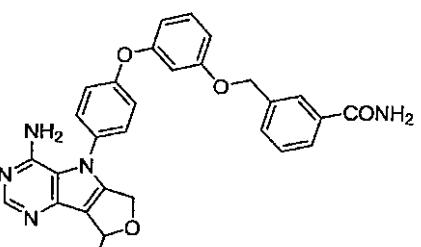
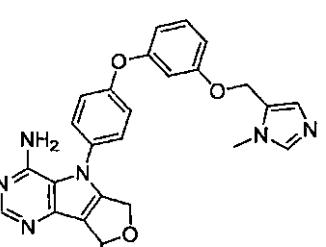


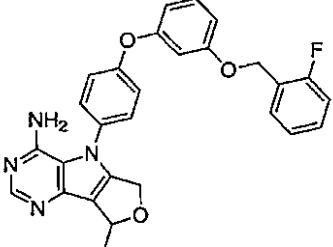
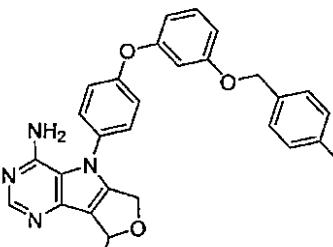
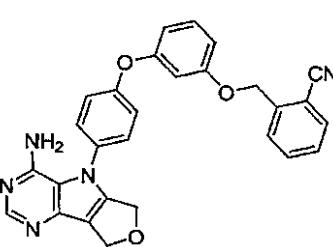
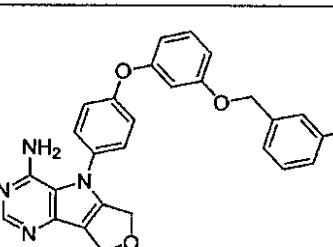


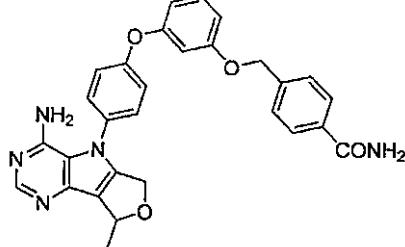
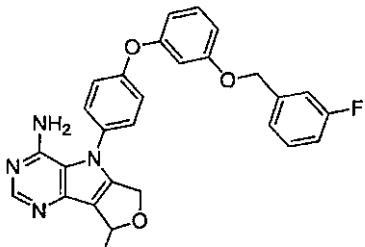
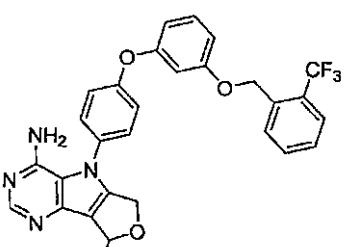
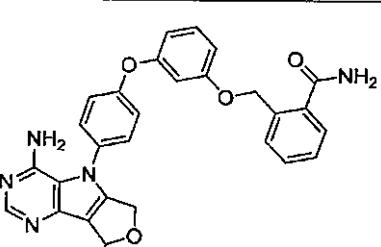


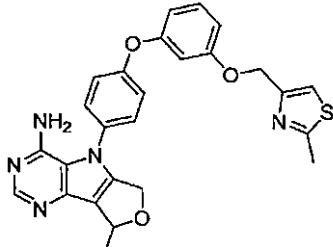
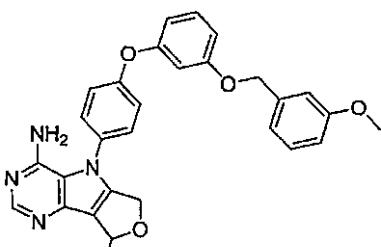
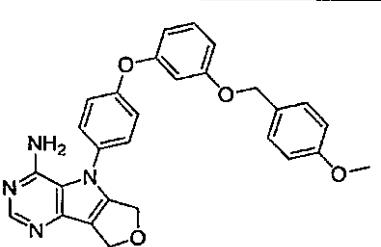
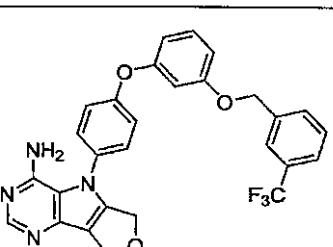
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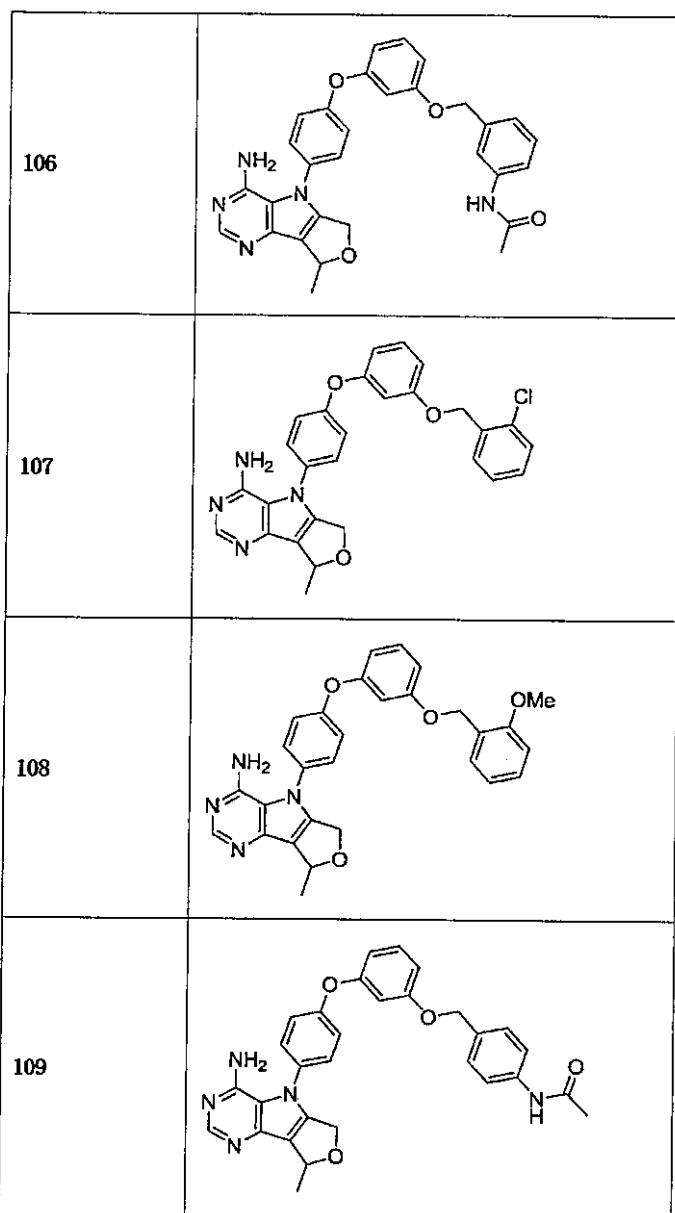
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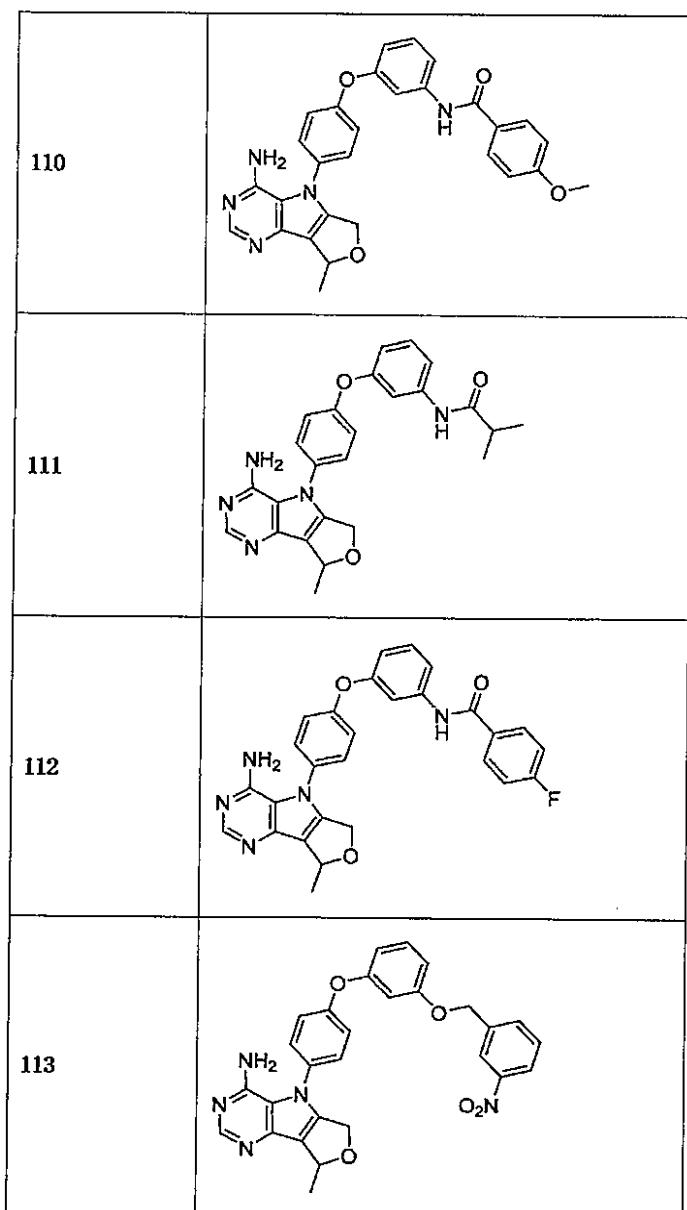
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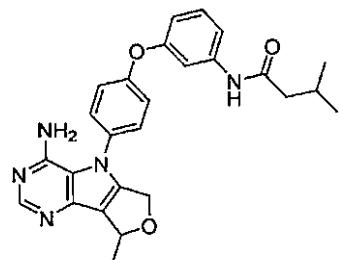
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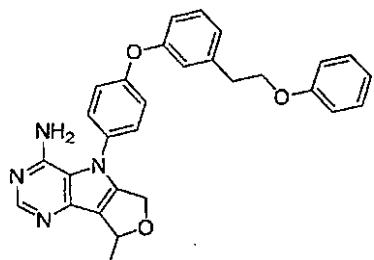




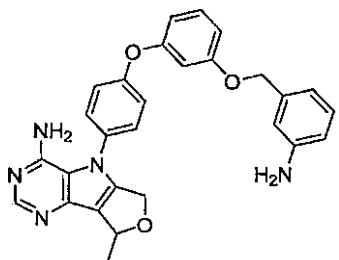
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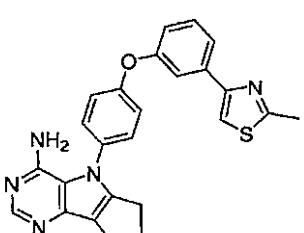
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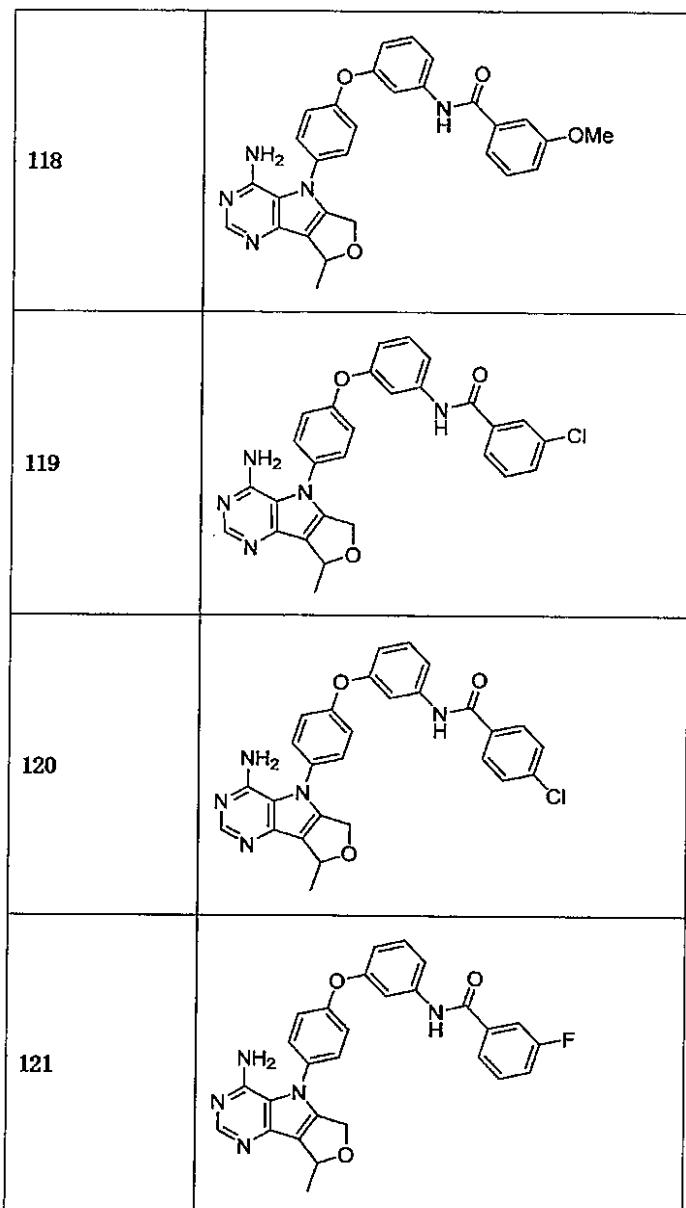


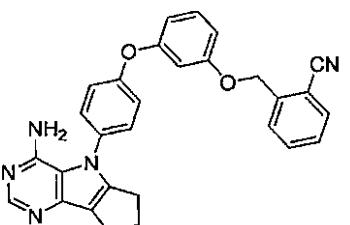
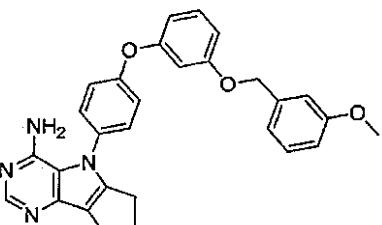
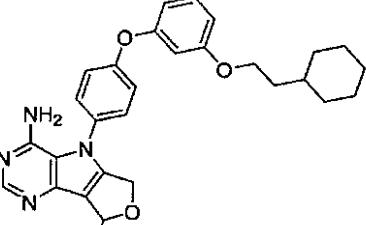
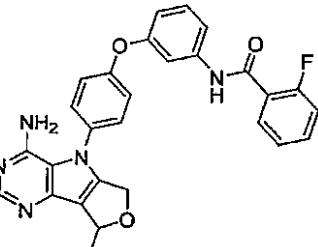
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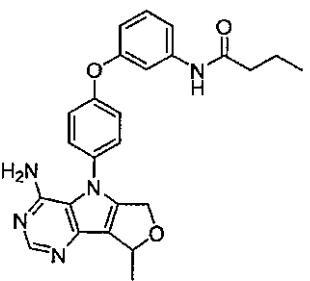
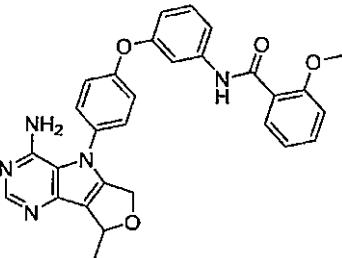
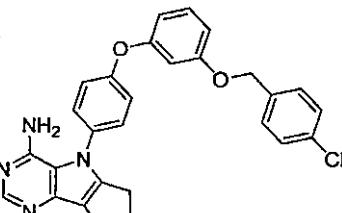
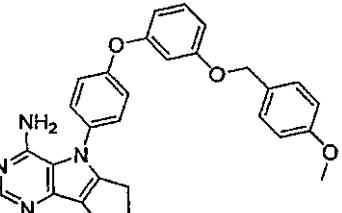


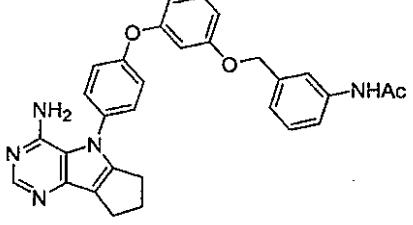
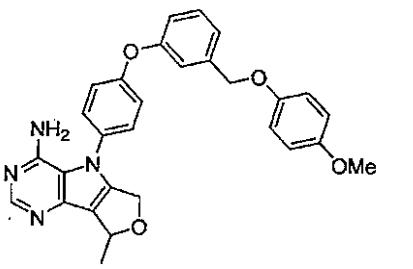
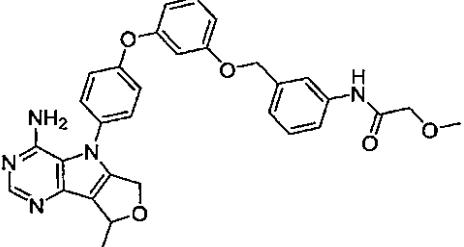
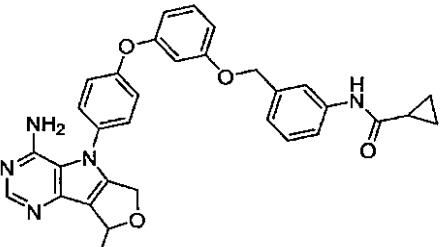
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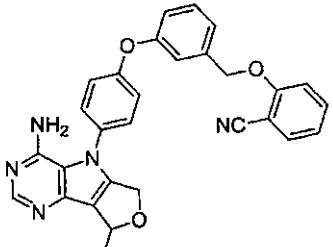
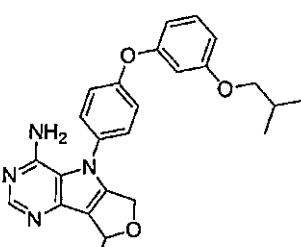
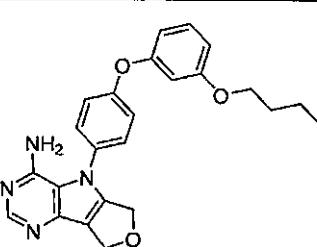
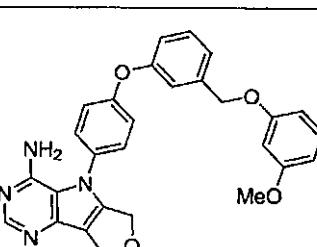


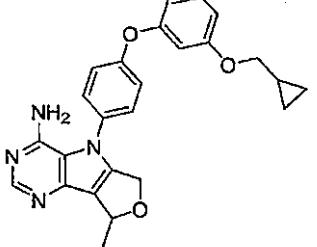
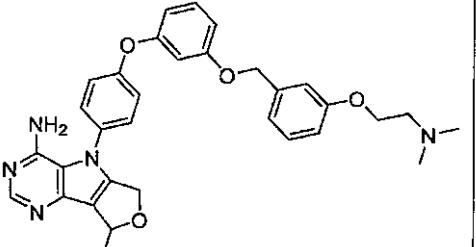
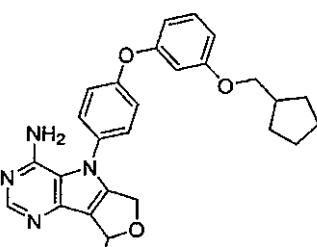
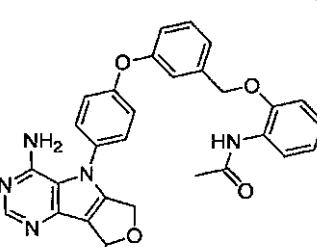


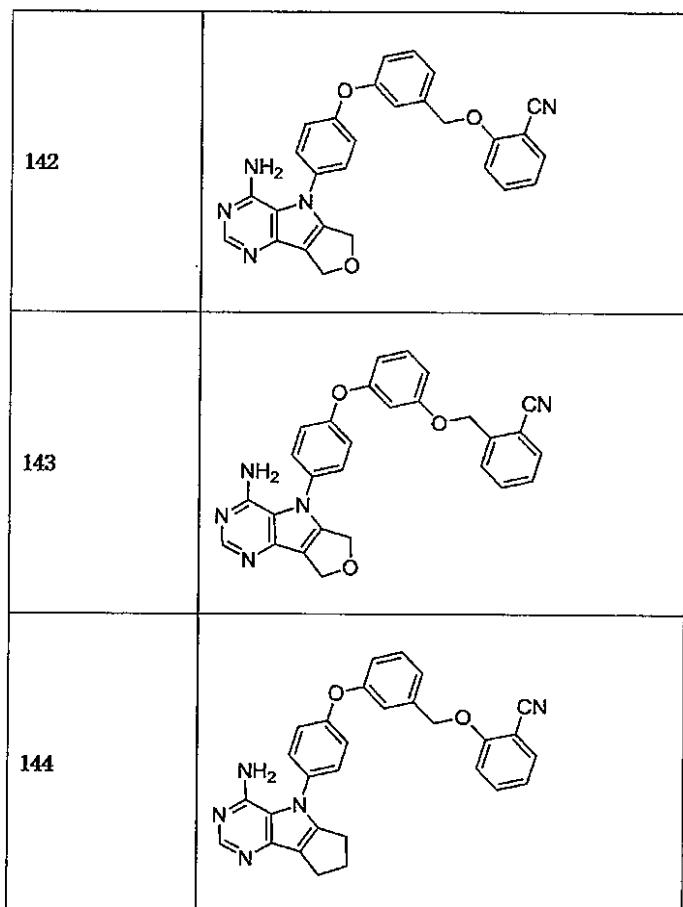
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から成る群から選択されることを特徴とする化合物。

【請求項 8】

化合物 1、20、21、23、24、28、29、31、32、33、34、35、37、39、40 及び 45 から成る群から選択される、請求項 7 に記載の化合物。

【請求項 9】

化合物 25、41、43、44、46、49、50、53、54、56、57、58、59、61、62、64、67、68、75、77、78、85、86、87、89、93、94、95、96、97、99、100、102、103、104、105、106、107、108、109、115、112、123、124、128、129、130、131、132、133、134、135、136、137、138、140、141、142、143 及び 144 から成る群から選択される、請求項 7 に記載の化合物。

【請求項 10】

化合物 47、66、69、70、76、80、81、82、84、111、112、114、118、119、120、121、125、126 及び 127 から成る群から選択される、請求項 7 に記載の化合物。

【請求項 11】

医薬組成物であって、
請求項 1 - 10 のいずれかに記載の化合物と、
薬学的に許容可能な担体又は希釈剤と、
を含むことを特徴とする医薬組成物。

【請求項 12】

標的キナーゼの阻害剤であって、請求項 1 ~ 10 のいずれか 1 項に記載の化合物を含むことを特徴とする阻害剤。

【請求項 13】

前記標的キナーゼが、Tec、Syk及びSrcキナーゼファミリーから成る群から選択される、請求項1-2に記載の阻害剤。

【請求項1-4】

前記標的キナーゼが、Btk及びLckから成る群から選択される、請求項1-2に記載の阻害剤。

【請求項1-5】

プローブであって、

請求項1-9のいずれかに記載の化合物と、

前記化合物用の検出可能なラベル又はアフィニティタグとを含む、ことを特徴とするプローブ。

【請求項1-6】

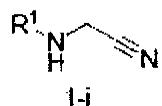
前記検出可能なラベルが、蛍光部分、化学発光部分、常磁性造影剤、金属キレート、放射性同位体含有部分及びビオチンから成る群から選択される、請求項1-5に記載のプローブ。

【請求項1-7】

式1-vの化合物を調製する方法であって、

(a) R¹NH₂をプロモアセトニトリルでアルキル化することによって中間体1-i:

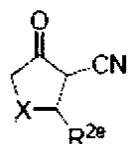
【化2-6】



を得て、

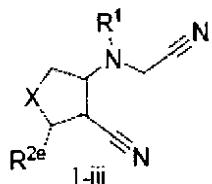
(b) 1-iを、酸の存在下で、1-ii、

【化2-7】



と縮合させることによって中間体1-iii、

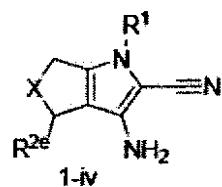
【化2-8】



を得て、

(c) 中間体1-iiiを塩基で処理することによって中間体1-iv、

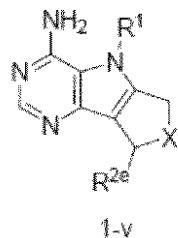
【化 2 9】



を得て、

(d) 中間体 1 - i v をアルコールのホルムアミンアセテートで処理することによって式 1 - v、

【化 3 0】



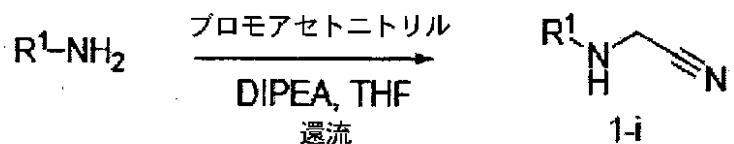
の化合物を得る工程を含むことを特徴とする方法。

【請求項 1 8】

以下の工程、

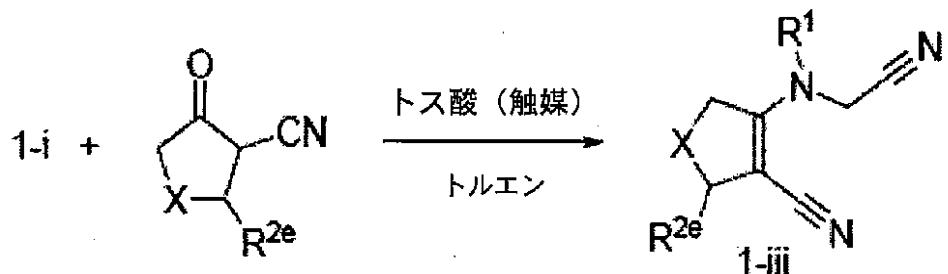
(a)

【化 3 1】



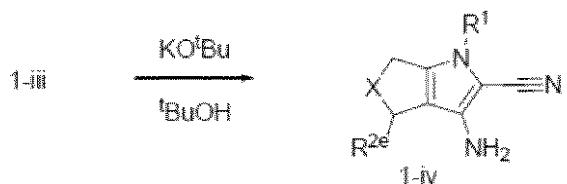
(b)

【化 3 2】

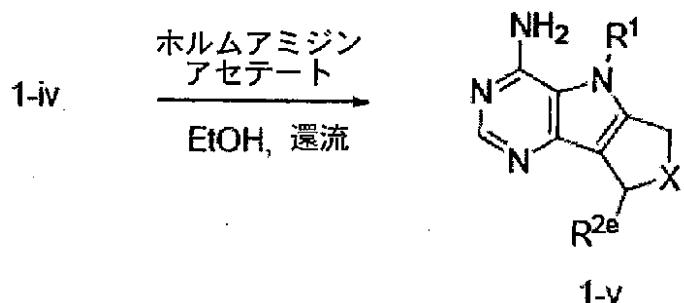


(c)

【化 3 3】



(d)
【化 3 4】

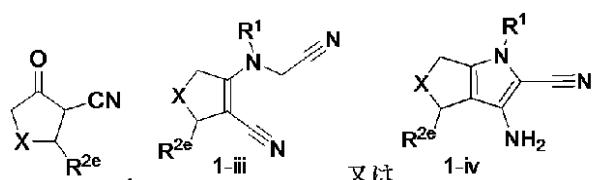


を含む、請求項 1 7 に記載の方法。

【請求項 1 9】

化合物であつて、以下の式、

【化 3 5】



で表されることを特徴とする化合物。

【誤訛訂正 2】

【訂正対象書類名】明細書

【訂正対象項目名】0 2 9 4

【訂正方法】変更

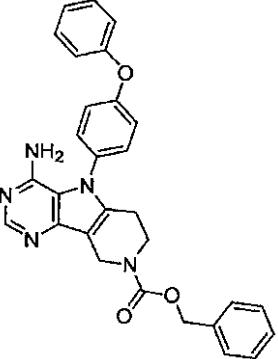
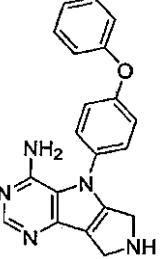
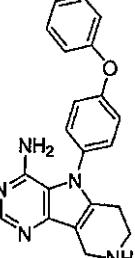
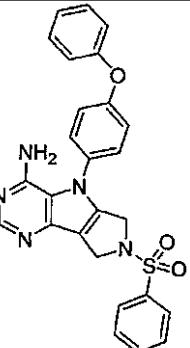
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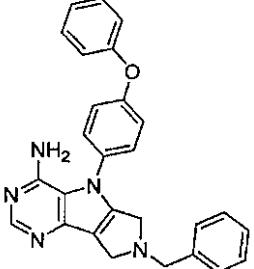
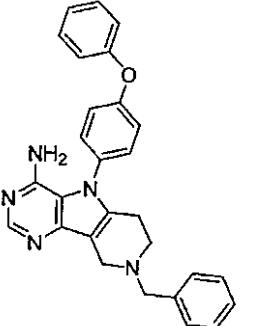
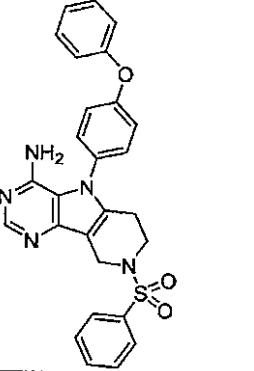
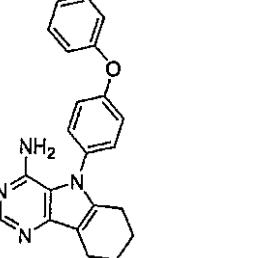
【0 2 9 4】

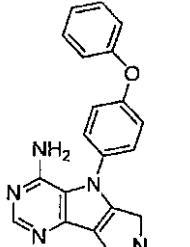
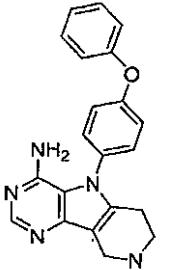
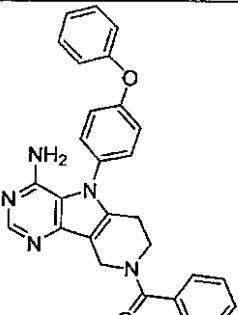
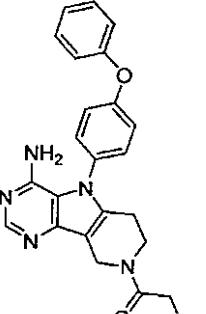
【表1】

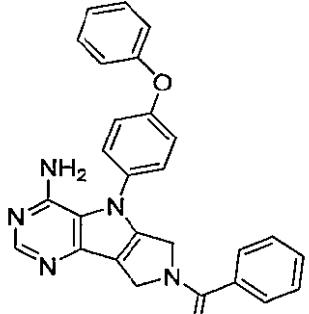
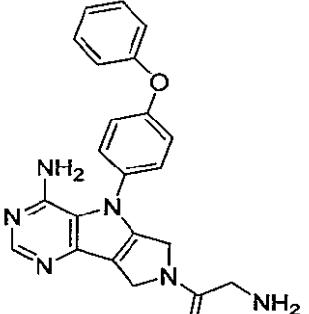
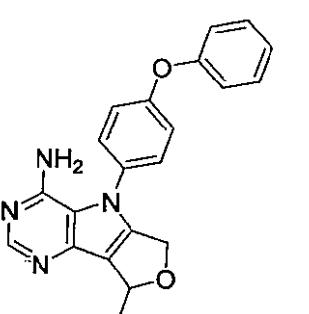
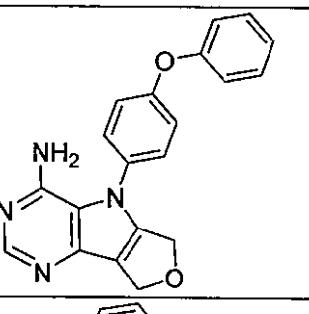
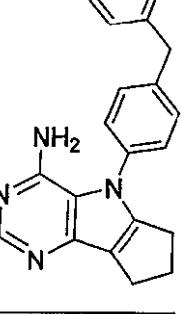
表1. 式1の化合物例

| 化合物 | 構造 | MS (m/z) |
|-----|----|-----------------------------------|
| 1 | | $[M+H]^+=343.2$ |
| 2 | | $[M+H]^+=361.2$ |
| 3 | | $[M+H]^+=421.6$ |
| 4 | | $[M+H]^+=377.2$ |
| 5 | | <u>$[M+H]^+=478.1$</u> |

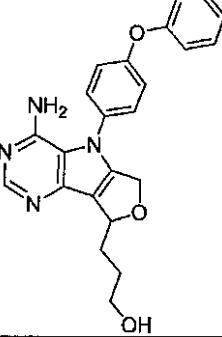
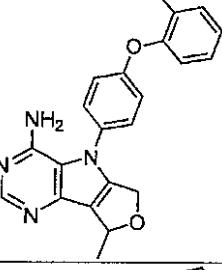
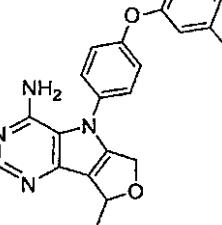
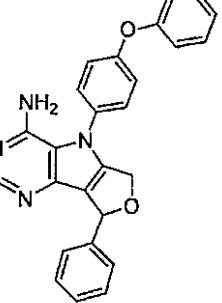
| | | |
|---|---|---------------------------|
| 6 |  | [M+H] ⁺ =492.1 |
| 7 |  | [M+H] ⁺ =344.2 |
| 8 |  | [M+H] ⁺ =358.2 |
| 9 |  | [M+H] ⁺ =484.1 |

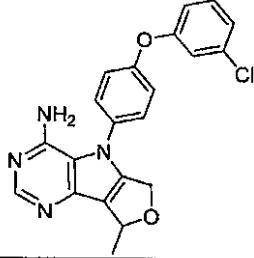
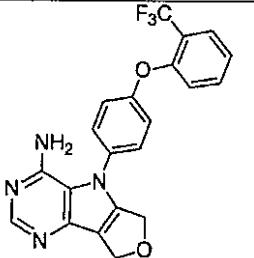
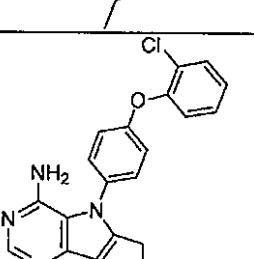
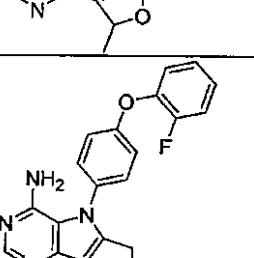
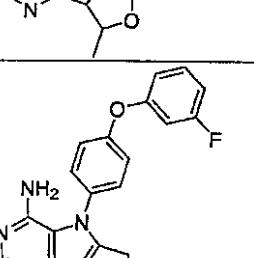
| | | |
|----|---|---------------------------|
| 10 |  | [M+H] ⁺ =434.2 |
| 11 |  | [M+H] ⁺ =448.2 |
| 12 |  | [M+H] ⁺ =498.1 |
| 13 |  | [M+H] ⁺ =357.2 |

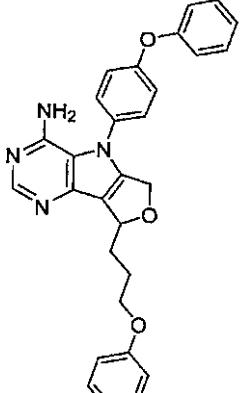
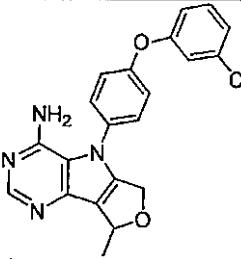
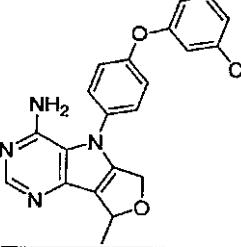
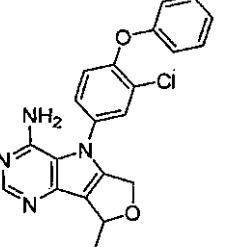
| | | |
|----|---|---------------------------|
| 14 |  | [M+H] ⁺ =372.2 |
| 15 |  | [M+H] ⁺ =386.3 |
| 16 |  | [M+H] ⁺ =462.1 |
| 17 |  | [M+H] ⁺ =415.1 |

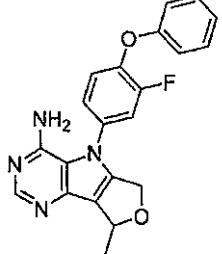
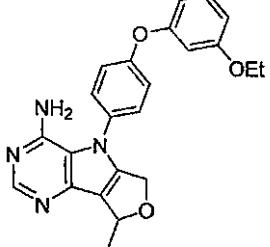
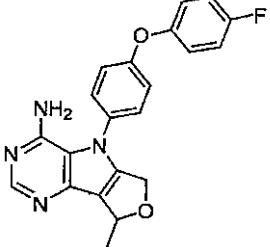
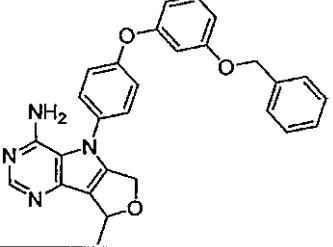
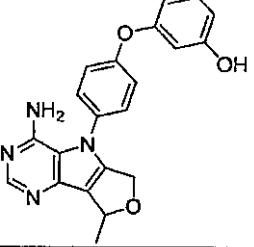
| | | |
|-----------|---|--------------------------------|
| 18 |  | [M+H] ⁺ =448.3 |
| 19 |  | [M+H] ⁺ =401.2 |
| 20 |  | [M+H] ⁺ =359.2 |
| 21 |  | [M+H] ⁺ =345.2 |
| <u>22</u> |  | <u>[M+H]⁺=341.3</u> |

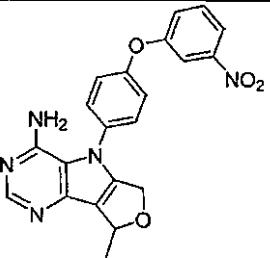
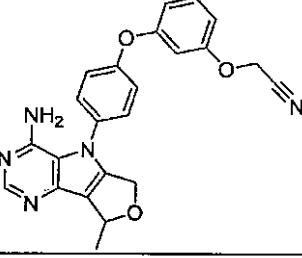
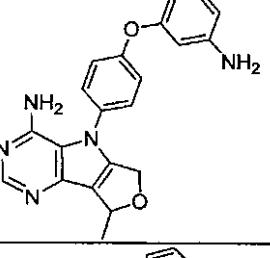
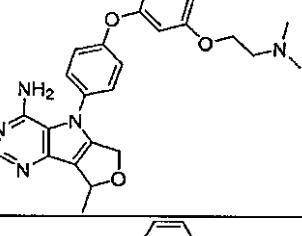
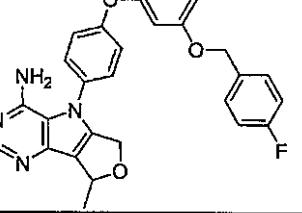
| | | |
|----|--|---------------------------|
| 23 | | [M+H] ⁺ =373.2 |
| 24 | | [M+H] ⁺ =373.3 |
| 25 | | [M+H] ⁺ =389.2 |
| 26 | | [M+H] ⁺ =493.3 |

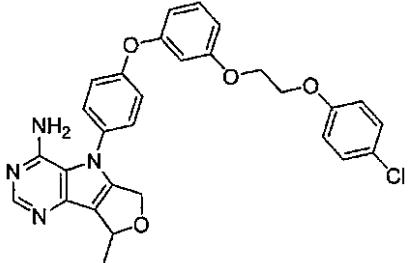
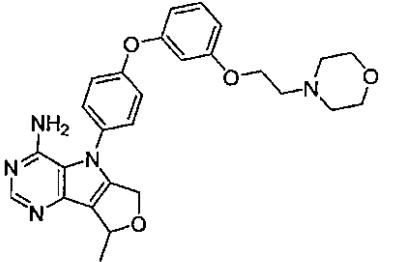
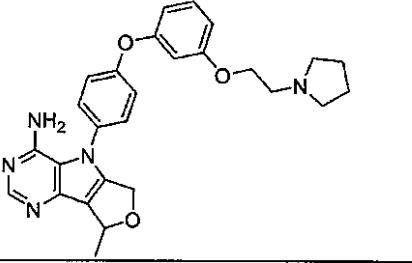
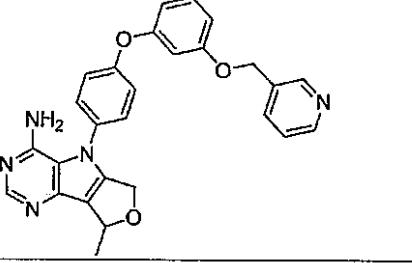
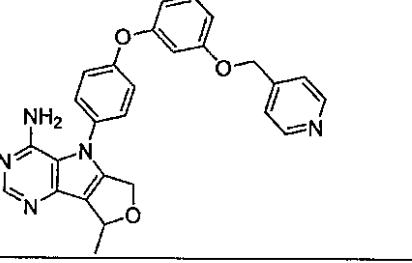
| | | |
|----|---|-----------------|
| 27 |  | $[M+H]^+=403.3$ |
| 28 |  | $[M+H]^+=389.3$ |
| 29 |  | $[M+H]^+=427.2$ |
| 30 |  | $[M+H]^+=421.2$ |

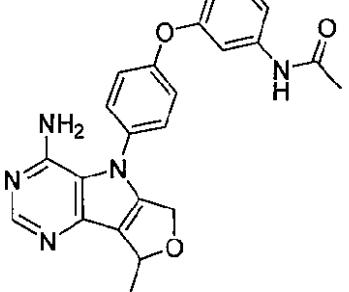
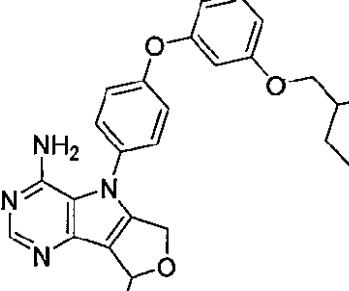
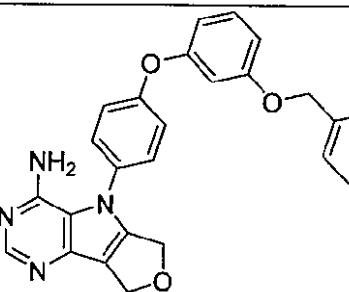
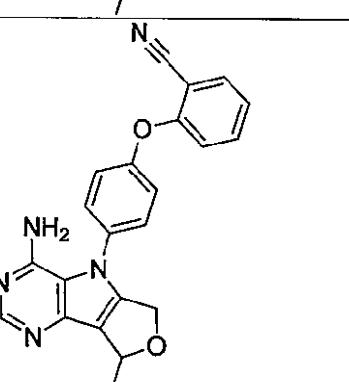
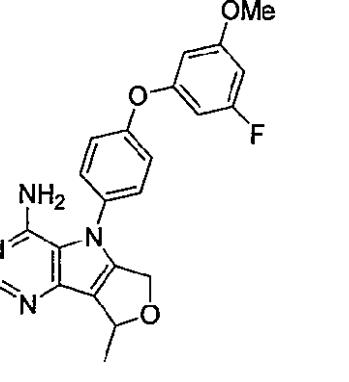
| | | |
|----|---|-----------------|
| 31 |  | $[M+H]^+=393.4$ |
| 32 |  | $[M+H]^+=427.2$ |
| 33 |  | $[M+H]^+=393.4$ |
| 34 |  | $[M+H]^+=377.2$ |
| 35 |  | $[M+H]^+=377.4$ |

| | | |
|----|---|---------------------------|
| 36 |  | [M+H] ⁺ =479.3 |
| 37 |  | [M+H] ⁺ =384.3 |
| 38 |  | [M+H] ⁺ =402.2 |
| 39 |  | [M+H] ⁺ =393.6 |

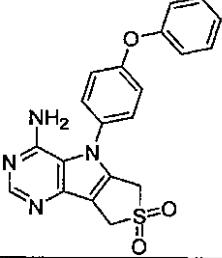
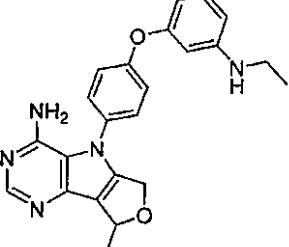
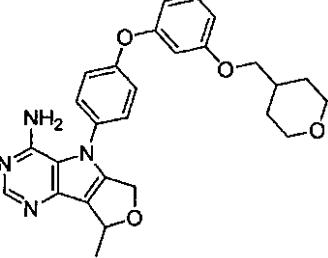
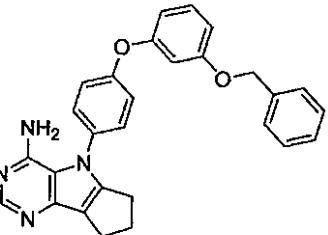
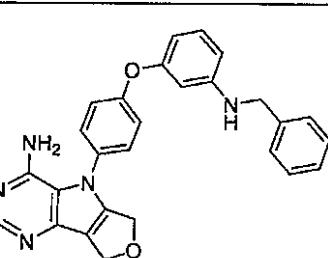
| | | |
|----|---|---------------------------|
| 40 |  | [M+H] ⁺ =377.2 |
| 41 |  | [M+H] ⁺ =403.3 |
| 42 |  | [M+H] ⁺ =377.2 |
| 43 |  | [M+H] ⁺ =465.2 |
| 44 |  | [M+H] ⁺ =375.2 |

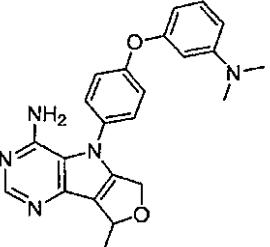
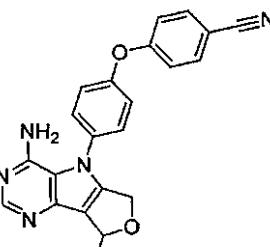
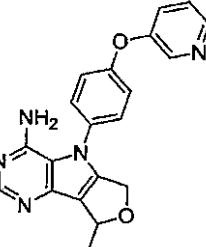
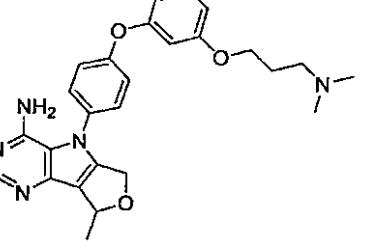
| | | |
|----|---|---------------------------|
| 45 |  | [M+H] ⁺ =404.2 |
| 46 |  | [M+H] ⁺ =414.2 |
| 47 |  | [M+H] ⁺ =374.2 |
| 48 |  | [M+H] ⁺ =446.4 |
| 49 |  | [M+H] ⁺ =483.2 |

| | | |
|----|---|-----------------|
| 50 |  | $[M+H]^+=529.3$ |
| 51 |  | $[M+H]^+=488.2$ |
| 52 |  | $[M+H]^+=472.3$ |
| 53 |  | $[M+H]^+=466.2$ |
| 54 |  | $[M+H]^+=466.2$ |

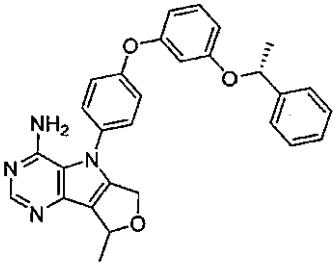
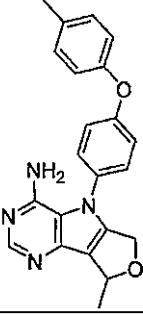
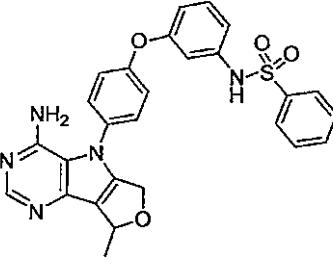
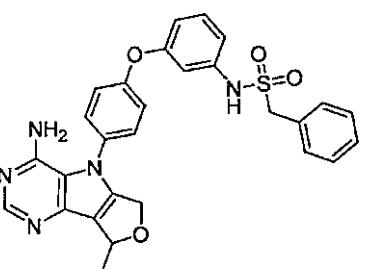
| | | |
|----|---|-----------------------------------|
| 55 |  | $[M+H]^+=416.3$ |
| 56 |  | $[M+H]^+=471.3$ |
| 57 |  | $[M+H]^+=533.1$ |
| 58 |  | $[M+H]^+=384.4$ |
| 59 |  | <u>$[M+H]^+=407.4$</u> |

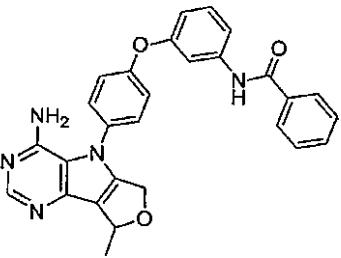
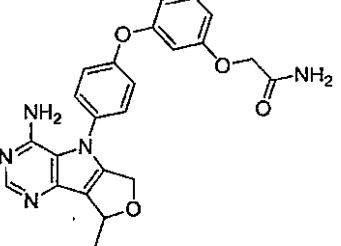
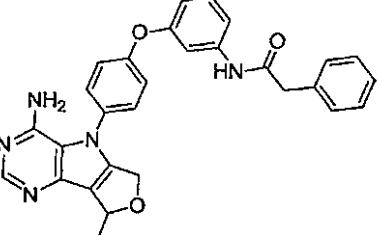
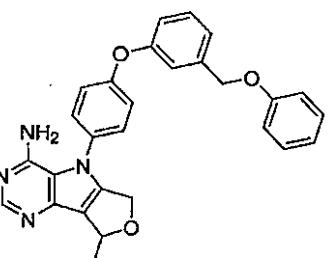
| | | |
|----|--|--------------------------|
| 60 | | $[M+H]^{\ddagger}=402.2$ |
| 61 | | $[M+H]^{\ddagger}=359.2$ |
| 62 | | $[M+H]^{\ddagger}=450.2$ |
| 63 | | $[M+H]^{\ddagger}=361.2$ |
| 64 | | $[M+H]^{\ddagger}=490.2$ |

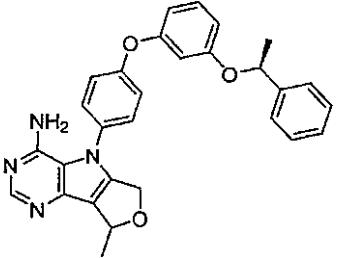
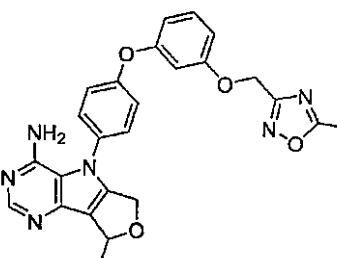
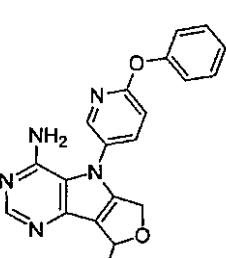
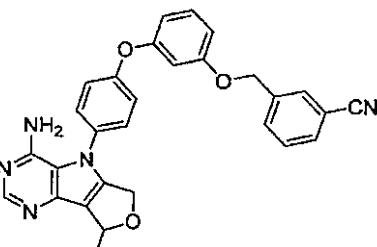
| | | |
|----|---|-----------------|
| 65 |  | $[M+H]^+=393.2$ |
| 66 |  | $[M+H]^+=402.2$ |
| 67 |  | $[M+H]^+=473.3$ |
| 68 |  | $[M+H]^+=449.2$ |
| 69 |  | $[M+H]^+=464.2$ |

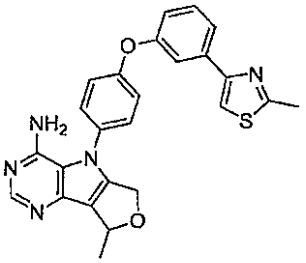
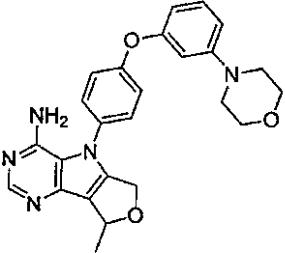
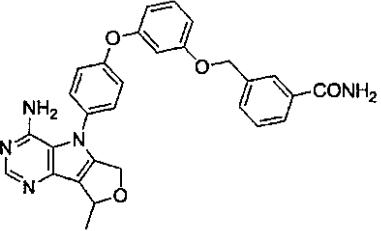
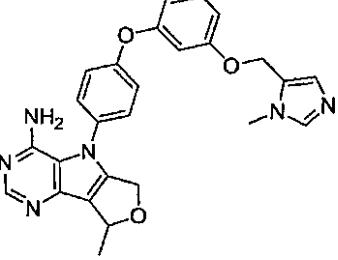
| | | |
|----|---|---------------------------|
| 70 |  | [M+H] ⁺ =402.3 |
| 71 |  | [M+H] ⁺ =384.2 |
| 72 |  | [M+H] ⁺ =360.2 |
| 73 |  | [M+H] ⁺ =460.2 |

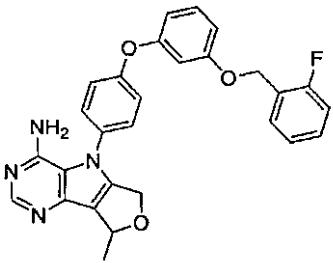
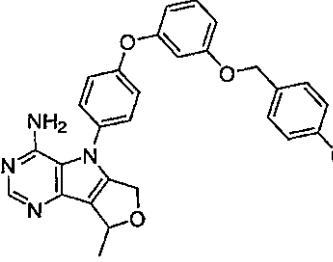
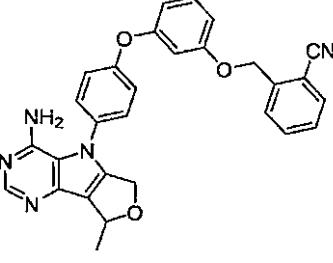
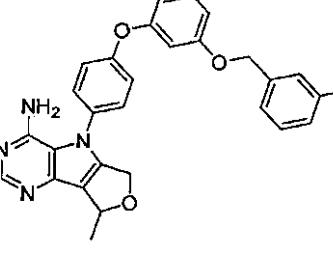
| | | |
|----|--|---------------------------|
| 74 | | [M+H] ⁺ =360.3 |
| 75 | | [M+H] ⁺ =466.2 |
| 76 | | [M+H] ⁺ =452.2 |
| 77 | | [M+H] ⁺ =479.2 |

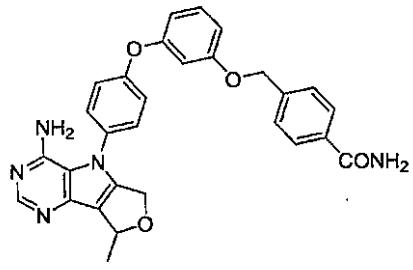
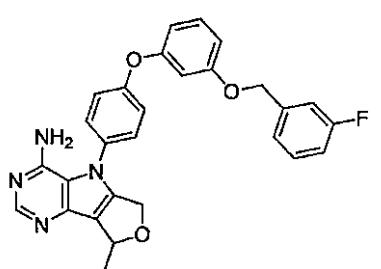
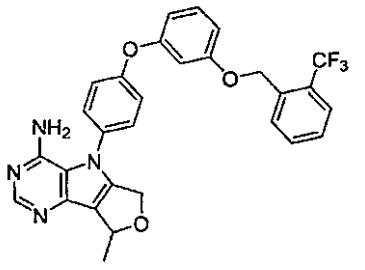
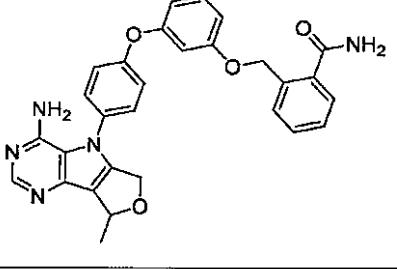
| | | |
|----|---|---------------------------|
| 78 |  | [M+H] ^t =479.2 |
| 79 |  | [M+H] ^t =373.3 |
| 80 |  | [M+H] ^t =514.1 |
| 81 |  | [M+H] ^t =528.1 |

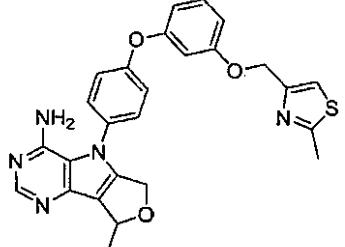
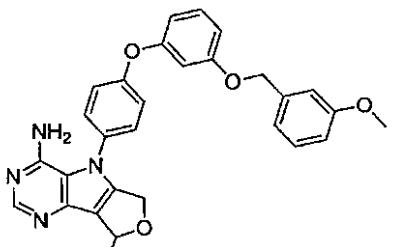
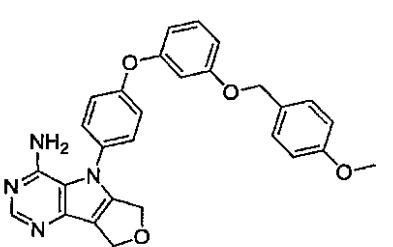
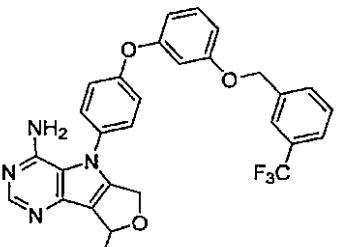
| | | |
|----|---|---------------------------|
| 82 |  | [M+H] ⁺ =478.2 |
| 83 |  | [M+H] ⁺ =432.2 |
| 84 |  | [M+H] ⁺ =492.2 |
| 85 |  | [M+H] ⁺ =465.2 |

| | | |
|----|---|---------------------------|
| 86 |  | [M+H] ^t =479.2 |
| 87 |  | [M+H] ^t =471.2 |
| 88 |  | [M+H] ^t =360.2 |
| 89 |  | [M+H] ^t =490.1 |

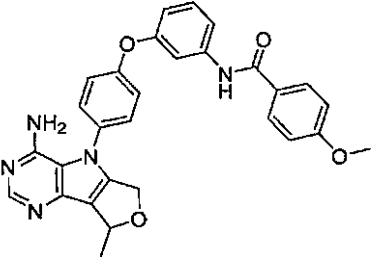
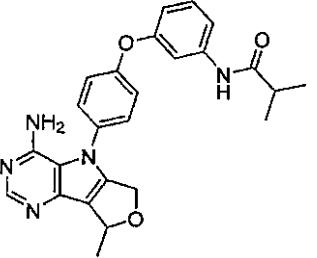
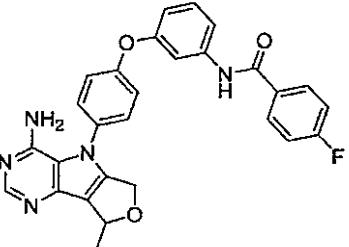
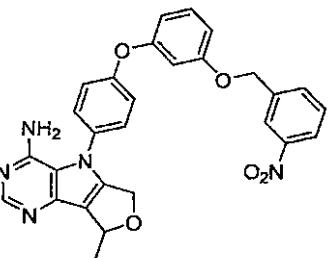
| | | |
|----|---|---------------------------|
| 90 |  | [M+H] ⁺ =456.2 |
| 91 |  | [M+H] ⁺ =444.2 |
| 92 |  | [M+H] ⁺ =508.1 |
| 93 |  | [M+H] ⁺ =469.3 |

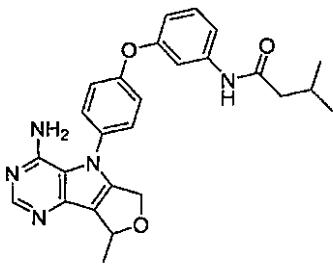
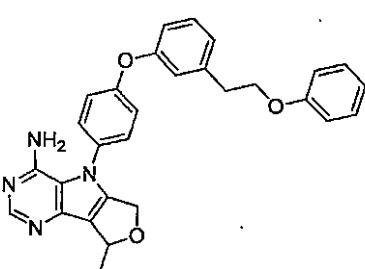
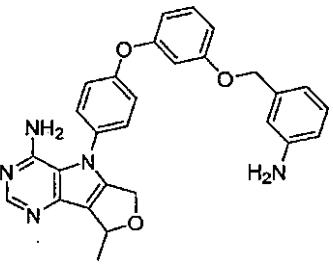
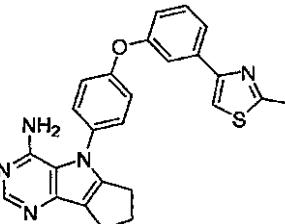
| | | |
|----|---|---------------------------|
| 94 |  | [M+H] ⁺ =483.1 |
| 95 |  | [M+H] ⁺ =499.3 |
| 96 |  | [M+H] ⁺ =490.2 |
| 97 |  | [M+H] ⁺ =499.3 |

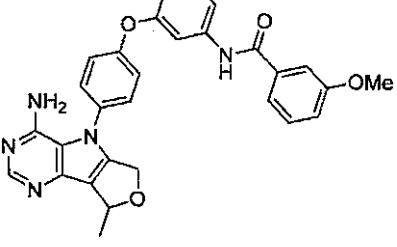
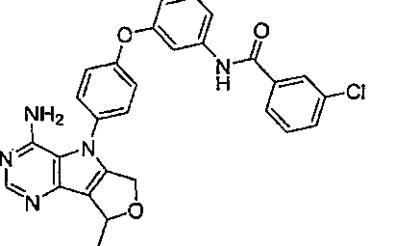
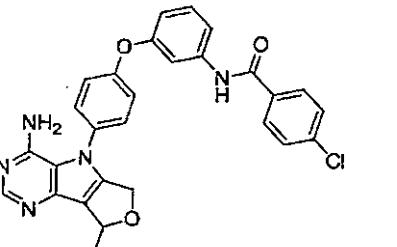
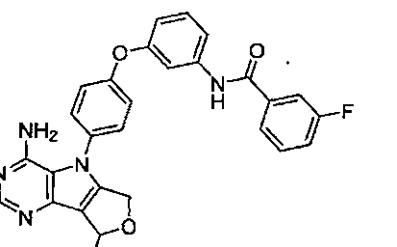
| | | |
|-----|---|--------------------------|
| 98 |  | $[M+H]^{\ddagger}=508.2$ |
| 99 |  | $[M+H]^{\ddagger}=483.1$ |
| 100 |  | $[M+H]^{\ddagger}=533.1$ |
| 101 |  | $[M+H]^{\ddagger}=508.1$ |

| | | |
|-----|---|---------------------------|
| 102 |  | [M+H] ⁺ =486.2 |
| 103 |  | [M+H] ⁺ =495.1 |
| 104 |  | [M+H] ⁺ =495.0 |
| 105 |  | [M+H] ⁺ =533.0 |

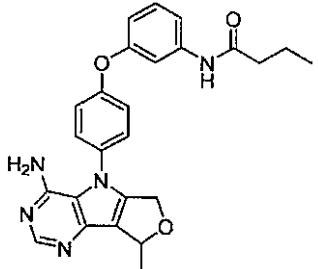
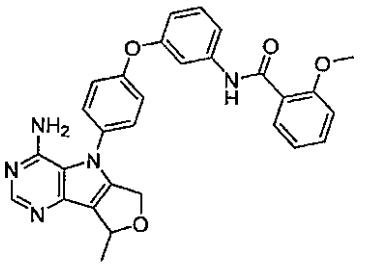
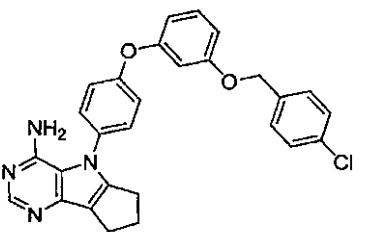
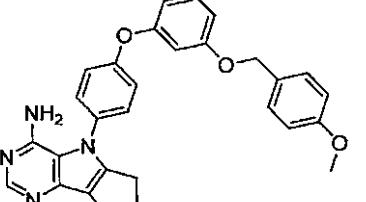
| | | |
|-----|--|---------------------------|
| 106 | | [M+H] ⁺ =522.1 |
| 107 | | [M+H] ⁺ =499.3 |
| 108 | | [M+H] ⁺ =495.1 |
| 109 | | [M+H] ⁺ =522.1 |

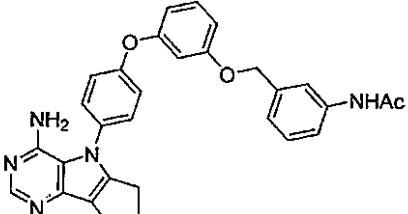
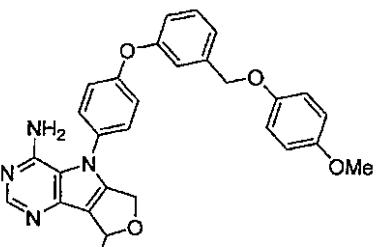
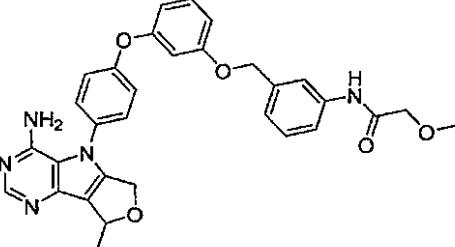
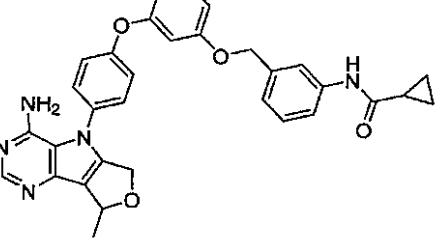
| | | |
|-----|---|---------------------------|
| 110 |  | [M+H] ⁺ =508.1 |
| 111 |  | [M+H] ⁺ =444.2 |
| 112 |  | [M+H] ⁺ =496.1 |
| 113 |  | [M+H] ⁺ =510.1 |

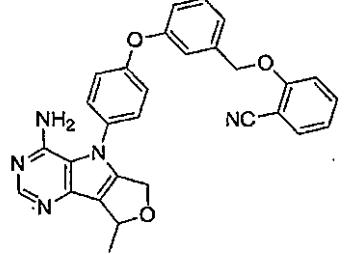
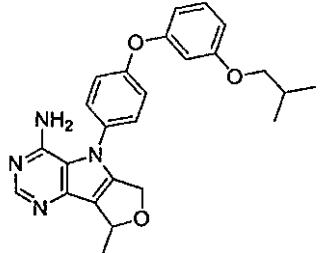
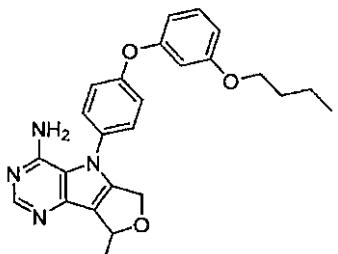
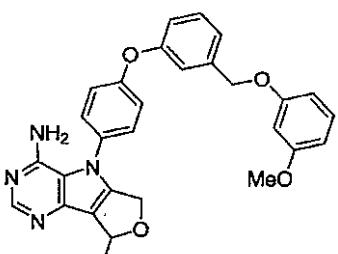
| | | |
|-----|---|---------------------------|
| 114 |  | [M+H] ⁺ =458.1 |
| 115 |  | [M+H] ⁺ =479.1 |
| 116 |  | [M+H] ⁺ =480.3 |
| 117 |  | [M+H] ⁺ =440.1 |

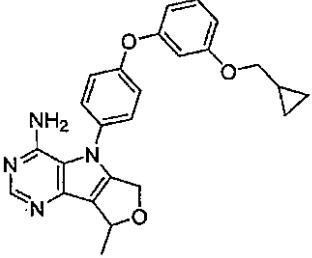
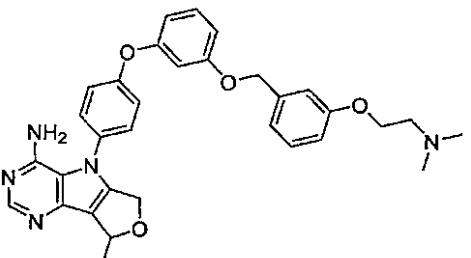
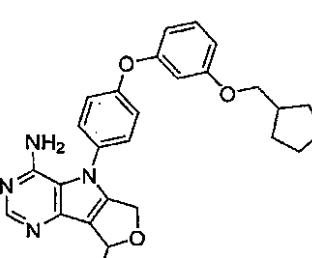
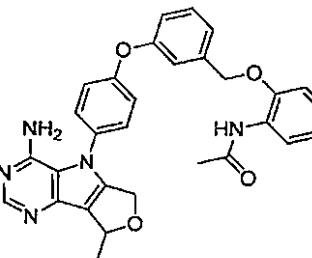
| | | |
|-----|---|---------------------------|
| 118 |  | [M+H] ⁺ =508.1 |
| 119 |  | [M+H] ⁺ =512.3 |
| 120 |  | [M+H] ⁺ =512.3 |
| 121 |  | [M+H] ⁺ =496.1 |

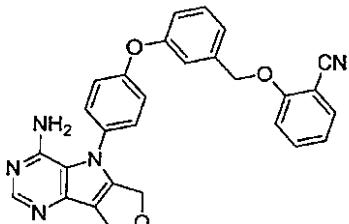
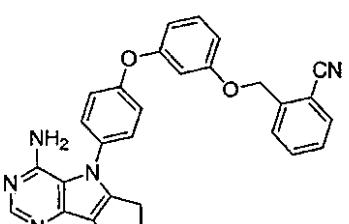
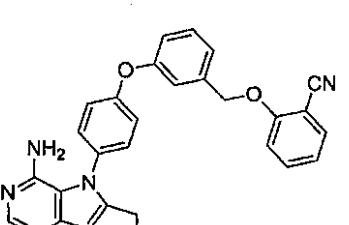
| | | |
|-----|--|-----------------|
| 122 | | $[M+H]^*=474.2$ |
| 123 | | $[M+H]^*=479.1$ |
| 124 | | $[M+H]^*=485.2$ |
| 125 | | $[M+H]^*=496.1$ |

| | | |
|-----|---|---------------------------|
| 126 |  | [M+H] ⁺ =444.2 |
| 127 |  | [M+H] ⁺ =508.1 |
| 128 |  | [M+H] ⁺ =483.3 |
| 129 |  | [M+H] ⁺ =479.1 |

| | | |
|-----|---|-----------------|
| 130 |  | $[M+H]^+=506.3$ |
| 131 |  | $[M+H]^+=495.1$ |
| 132 |  | $[M+H]^+=552.1$ |
| 133 |  | $[M+H]^+=548.1$ |

| | | |
|-----|---|---------------------------|
| 134 |  | [M+H] ⁺ =490.1 |
| 135 |  | [M+H] ⁺ =431.2 |
| 136 |  | [M+H] ⁺ =431.2 |
| 137 |  | [M+H] ⁺ =495.1 |

| | | |
|-----|---|---------------------------|
| 138 |  | [M+H] ⁺ =429.2 |
| 139 |  | [M+H] ⁺ =552.1 |
| 140 |  | [M+H] ⁺ =457.2 |
| 141 |  | [M+H] ⁺ =522.1 |

| | | |
|-----|--|---------------------------|
| 142 |  | [M+H] ⁺ =476.1 |
| 143 |  | [M+H] ⁺ =476.2 |
| 144 |  | [M+H] ⁺ =474.2 |