A New Synthesis Method for Benzo[*f*]quinolin-3-carbonyl Urea and Thiourea Derivatives in Aqueous Media Catalyzed by TEBAC

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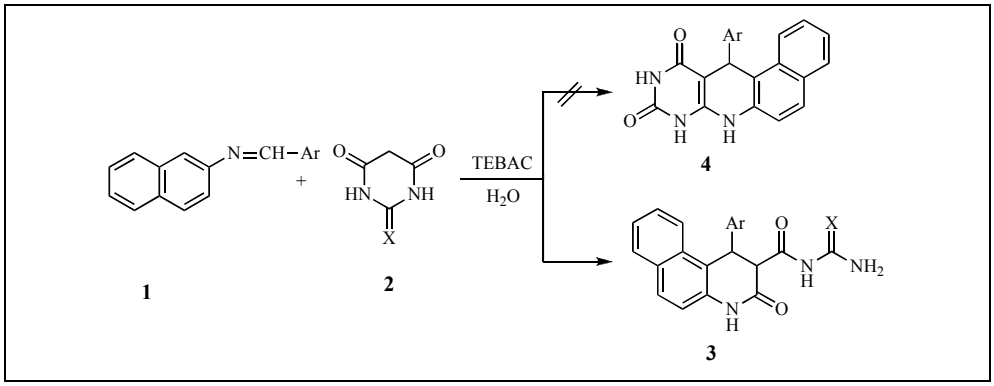
Received February 9, 2006



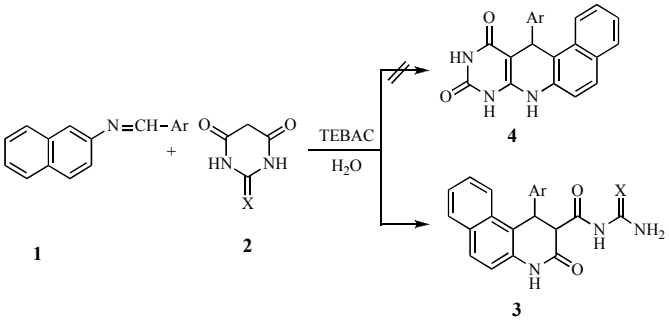
A clean and simple synthesis procedure for benzo[*f*]quinolin-3-carbonyl urea and thiourea derivatives was developed based on the reaction between *N*-arylidenenaphthalen-2-amine and barbituric acid or thiobarbituric acid in aqueous media catalyzed by triethylbenzylammonium chloride (TEBAC). It was interesting that the structures of products in solvent of DMSO-d_6 solution were different from those of the crystal states, which keep the enol form. The products were characterized by ^{1}H NMR, and ^{13}C NMR, and the crystal state was confirmed by X-ray diffraction study of **3e**. In addition, water was chosen as green solvent.

J. Heterocyclic Chem., **44**, 441 (2007).

INTRODUCTION

Benzoquinoline and its derivatives are well known compounds exhibiting a wide spectrum of pharmacological activities, such as antibacterial activity [1], vibronic activity [2], antimicrobial activity [3], antimalarial activity [4], pesticidal and growth-regulating activity [5], dopanminergic activity [6], and stimulating activity [7], or displaying postjunctional dopamine receptor against properties in the stiatum [8]. An increasing interest in this class of compounds has led to the development of new synthetic strategies. The usual methods used to synthesize these compounds is based on the reaction between Schiff base and different methyl ketones, such as acetone [9], 2-butanone [10] or methyl arylketone [11], or by irradiation of 3-amino-2-alkene imines [12], or by the reaction of unsatatured ketone with naphthylamine [13]. However, they are either tedious or have low yields, besides that organic solvents were used during all of the reactions. In order to avoid the disadvantages such as toxicity and instability that many organic solvents inherently have, we have been working to find a new procedure that will be environmentally friendly, and easy to operate for the synthesis of those above-mentioned compounds. Specifically, we focused our attention on the use of water as reaction medium. They were considered very promising and attractive substitutes for volatile organic solvents and were widely used in the Green Chemistry area. Since Breslow demonstrated hydrophobic effects could strongly enhance the rate of some organic reactions and rediscovered the use of water as solvent in organic chemistry in 1980s [14], there has been a growing recognition that water becomes an attractive medium for many organic reactions [15]. On the other hand organic reactions in water without using harmful organic solvents is one of the current focuses especially in the environmentally conscious society today.

Scheme 1



As part of our current studies on the development of new routes to synthesize heterocyclic compounds, we have reported the reactions of Schiff base with different 1,3-dicarbonyl compound using water as a medium [16]. Furthermore we think the *p*Ka of the active hydrogen in the 1,3-dicarbonyl compounds plays a critical role in this reaction, which inspired us to find some other 1,3-dicarbonyl compounds with low *p*Ka as substrates. We selected the barbituric acid or thiobarbituric acid as 1,3-dicarbonyl compounds due to their low *p*Ka [17]. When the reaction of *N*-arylidenenaphthalen-2-amine **1** was refluxed with barbituric acid or thiobarbituric acid **2** in water using TEBAC as a phase transfer catalyst, the products we obtained was not the desired pyridopyrimidine **4**, but a series of benzo[*f*]quinolin-3-carbonyl urea and thiourea derivatives **3**. (Scheme 1).

RESULTS AND DISCUSSION

We began our study of the reaction shown in Scheme 1 by optimizing the reaction conditions for the preparation of benzo[*f*]quinolin-3-carbonyl urea and thiourea derivative **3a**. A summary of the optimization experiment is provided in Table 1. It turned out that at room temperature, no reaction would be taken place even when the amount of catalyst (TEBAC) was increased to 1.84 mmol (Table 1, entries 1 and 2). The catalyst plays a crucial role in the success of the reaction in terms of the rate and the yields. From Table 1, we can see using just 0.74 mmol TEBAC at reflux in water is sufficient to make the reaction happen. Increasing the amount of the catalyst does not result in an improvement of this reaction. To find the optimum reaction time, the reaction was carried out in the presence of certain amount of TEBAC (here we used 0.74 mmol) for 3, 6, or 9 hours, resulting in the isolation of **3a** in 68%, 93% and 93% yield respectively. Thus, 0.74 mmol TEBAC and a reaction time of 6 hours were chosen. Moreover, different catalysts were further studied, from Table 1, we could conclude that the TEBAC works best for this reaction catalyst for this reaction. Moreover the catalyst can be reused for the synthesis of **3a** without significant loss of activity. The results were summarized in Table 2.

Table 1

Synthesis of **3a** in water under different reaction conditions[a]

Entry	Temp. /°C	Amount /mmol	Catalyst	Time/ h	Yield [b]/%
1	r.t.	0.74	TEBAC	3	0
2	r.t.	1.84	TEBAC	6	0
3	100	0.74	TEBAC	3	68
4	100	0.74	TEBAC	6	93
5	100	0.74	TEBAC	9	93
6	100	0.37	TEBAC	6	86
7	100	1.10	TEBAC	6	92
8	100	0.74	$CH_3(CH_2)_{15}NMe_3Br$	6	90
9	100	0.74	$CH_3(CH_2)_{11}SO_3Na$	6	88

[a]Reaction condition: 10 mL water, 2 mmol **1a** and 2 mmol barbituric acid. [b] Isolated yields

In order to apply this reaction to a library synthesis, various kinds of *N*-arylidenenaphthalen-2-amine and **2** were subjected to give the corresponding benzo[*f*]quinolin-3-carbonyl urea and thiourea derivatives **3**, and representative examples are shown in Table 3. All of the *N*-arylidenenaphthalen-2-amine gave expected products with high yields, either bearing electron-withdrawing groups (such as halide, nitro) or electron-donating groups (such as alkyl group, alkoxyl group) under same reaction conditions. Therefore we concluded that the electronic nature of the substituents has no significant effects on this reaction.

Table 2

Reuse of the Catalyst for Synthesis of **3a** [a]

Round	1	2	3	4
Yield [b]	93	94	94	92

[a]Reaction condition: 10 mL water, 2 mmol **1a** and 2 mmol barbituric acid. [b] Isolated yields.

Table 3

The reaction time and yields of the products **3**

Entry	Ar	X	Time/ h	Yields /%
3a	$4\text{-}ClC_6H_4$	O	6	93
3b	$4\text{-}CH_3OC_6H_4$	O	8	90
3c	$2,4\text{-}Cl_2C_6H_3$	O	6	95
3d	$3,4\text{-}Cl_2C_6H_3$	O	6	95
3e	$4\text{-}FC_6H_4$	O	6	92
3f	$3\text{-}NO_2C_6H_4$	O	6	89
3g	$4\text{-}BrC_6H_4$	O	8	88
3h	$2\text{-}ClC_6H_4$	O	6	90
3i	$3,4\text{-}(CH_3)_2C_6H_3$	S	10	92
3j	C_6H_5	S	10	90
3k	$3\text{-}ClC_6H_4$	S	6	97
3l	$4\text{-}CH_3OC_6H_4$	S	8	94
3m	$2\text{-}ClC_6H_4$	S	6	94
3n	$4\text{-}ClC_6H_4$	S	6	95
3o	$2,4\text{-}Cl_2C_6H_3$	S	6	98
3p	$4\text{-}FC_6H_4$	S	6	94
3q	$3,4\text{-}Cl_2C_6H_3$	S	6	95
3r	$4\text{-}BrC_6H_4$	S	6	93
3s	$3,4\text{-}(CH_3O)_2C_6H_3$	S	10	88
3t	$2\text{-}NO_2C_6H_4$	S	6	90

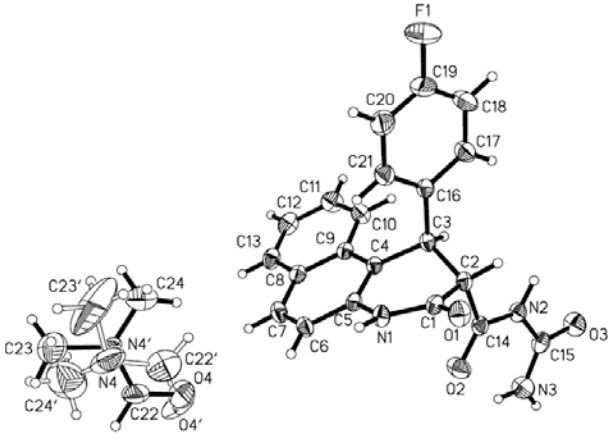
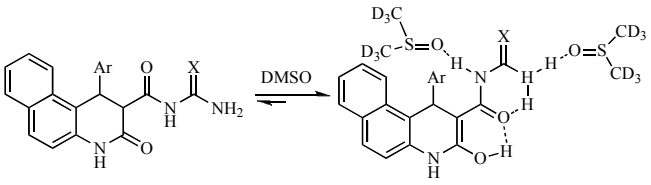
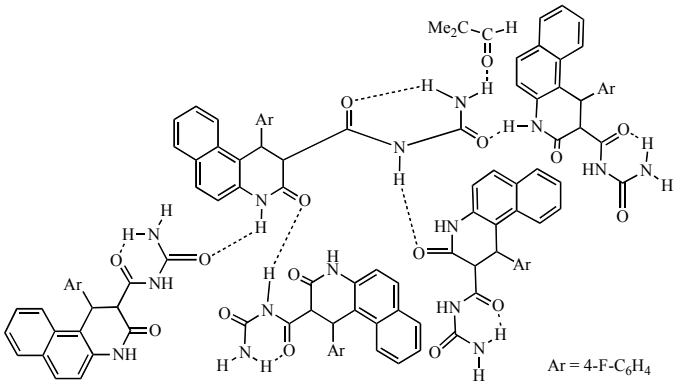


Figure 1. The structure of **3e** DMF solvate showing 50% probability displacement ellipsoids.

The structure of the products **3e** was confirmed by X-ray diffraction analysis [18], as shown in Figure 1. The analyses were in good agreement with their structures. The IR spectrum of **3e** exhibited sharp bands at 3407, 3239, 3174 cm^{-1} (NH), 1718, 1666 cm^{-1} (C=O). It was interesting that the double peak of the vicinal methine (CH) in the structure was not observed in the ^1H NMR spectrum of **3**. We think in the solvent of DMSO-d_6 solution (here used as solvent for ^1H NMR analyses), the structure of **3** could turn into in the enol form (Scheme 2), due to existence of the intramolecular hydrogen bonds and intermolecular hydrogen bonds. On the other hand, the C=C double bond in the enol form further expands the conjugative system, which also stabilizes the structure. The enol form was also confirmed by the ^{13}C NMR spectrum, where only a methine (CH) was observed at 56.1 ppm, there were corresponding to a total of sixteen C=C double carbon bond atoms except for two carbonyl groups at 165.8 and 170.0 ppm in **3e**.



Scheme 2. The possible hydrogen bonds in solvent of DMSO-d_6 solution.



Scheme 3. The hydrogen bonds in the crystals of **3e** DMF solvate.

However, in the crystal form, one molecule of **3e** links four vicinal molecules and forms four intermolecular hydrogen bonds of C-H…O, forming polymers along *a* axis, except for the intramolecular hydrogen bond N-H…O. In addition, **3e** links a solvent molecule of DMF *via* intermolecular hydrogen bond N-H…O. The chemical scheme of hydrogen bonds, the packing arrangements in a unit cell of **3e** along *a*, the hydrogen bonds data and the selected bond lengths, and the selected bond angles for **3e** are shown in Scheme 3, Figure 2, Table 4 and Table 5, respectively.

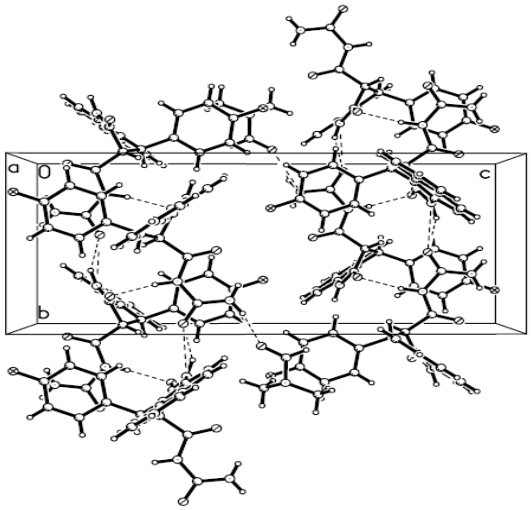


Figure 2. The packing arrangement in a unit cell of **3e** along *a*.

Table 4.
The hydrogen bonds data in **3e**

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(3)-H(3A)...O(4)[a]	0.86	2.10	2.921(7)	160.7
N(3)-H(3A)...O(4') [a]	0.86	2.00	2.816(16)	156.9
N(2)-H(2A)...O(1) [b]	0.94(3)	2.04(4)	2.967(3)	169(3)
N(1)-H(1)...O(3) [c]	0.92(3)	1.97(3)	2.784(3)	147(2)
N(3)-H(3B)...O(2)	0.86	2.05	2.699(3)	131.3

[a] -x+1,-y+2,-z, [b] -x+3/2,y+1/2,-z+1/2, [c] x,y-1,z

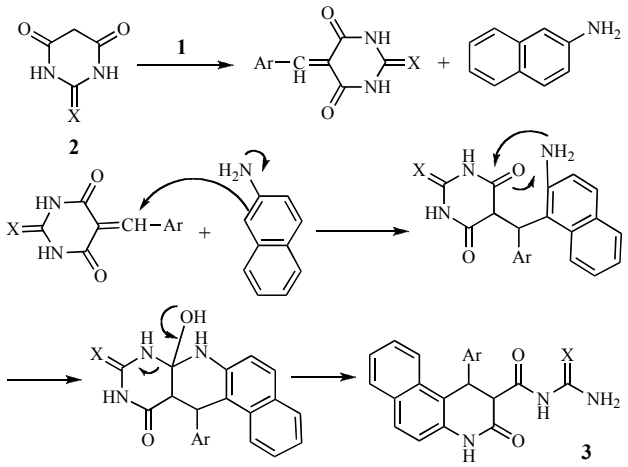
Table 5
Selected Bond Lengths (Å) and Selected Bond Angles (°) for **3e**

C(1)-C(2)	1.512(3)	C(2)-C(3)	1.559(3)
N(1)-C(1)	1.333(3)	C(3)-C(4)	1.514(3)
N(1)-C(5)	1.402(3)	C(4)-C(5)	1.369(3)
C(1)-N(1)-C(5)	124.3(2)	C(4)-C(3)-C(2)	109.6(2)
N(1)-C(1)-C(2)	115.8(2)	C(5)-C(4)-C(3)	118.8(2)
C(1)-C(2)-C(3)	110.67(18)	C(4)-C(5)-N(1)	120.3(2)

Although the detailed mechanism of above reaction has not been clarified yet, the formation of benzo[*f*]quinolin-3-carbonyl urea and thiourea derivatives **3** can be explained by a possible mechanism presented in Scheme 4.

In a further study, we found that the product **3a** can be obtained at 78% yield by the three-component reaction of 4-chlorobenzaldehyde, 2-aminonaphthalene and barbituric acid in water at 100 °C in the presence of TEBAC. This result possibly indicates that the cleavage of the C=N bond may take place in the mechanism mentioned above.

Scheme 4



But it should be noted that in this three-component reaction the starting material of solid 4-chlorobenzaldehyde always stays at the bottom of the condenser when the reaction temperature is controlled above 80 °C, which reduces the reaction yield badly, meanwhile the reaction time is long (18 h).

In conclusion, an efficient green chemistry method for the synthesis of benzo[*f*]quinolin-3-carbonyl urea and thiourea derivatives by condensation reaction of barbituric acid or thiobarbituric acid and *N*-arylidenenaphthalen-2-amine was successfully developed. This new method has the advantages of good yields, mild reaction conditions, easy work-up, inexpensive reagents and environmentally friendly procedure. In addition, the water was chosen as green solvent.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a TENSOR 27 spectrometer in KBr. ^{1}H NMR spectra were obtained in DMSO-d_6 with Me_4Si as internal standard using a Bruker-400 spectrometer. Elemental analyses were carried out using Carlo Erba 1110 analyzer. X-ray diffraction was measured on a CCD area detector diffractometer.

General procedure. A suspension of the mixture of *N*-arylidenenaphthalen-2-amine **1** (2 mmol), barbituric acid or thiobarbituric acid **2** (2 mmol) and TEBAC (0.74 mmol) was stirred in water (10 mL) at 100 ℃ for 6-10 h. The crystalline powder formed was collected by filtration, washed with water and recrystallized from DMF and water, followed by keeping at 100 °C for 5 hours under vacuum to give pure benzo[*f*]quinolin-3-carbonyl urea and thiourea derivatives **3**.

3-(4-Chlorophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]quinolin-3-carbonyl urea (3a). This compound was obtained as pale yellow powder, m.p. 228~230 °C; ir (KBr): ν_{max} 3402, 3241, 3175, 2932, 1717, 1662, 1626, 1601, 1586, 1521, 1489, 1473, 1380, 1298, 1244, 1195, 1174, 1102, 833, 802, 789, 761; ^{1}H nmr (DMSO-d_6): δ 3.86 (s, 1H, OH), 5.28 (s, 1H, CH), 7.22 (d, J = 8.4 Hz, 2H, ArH), 7.27 (s, 1H, NH), 7.29 (s, 1H, NH), 7.33~7.39 (m, 4H, ArH), 7.42~7.46 (m, 1H, ArH), 7.78 (d, J = 8.4 Hz, 1H, ArH), 7.86~7.90 (m, 2H, ArH), 10.69 (s, 1H, NH), 10.82 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 55.9, 115.2, 117.2, 122.5, 124.3, 127.4, 128.5, 128.86, 128.89, 129.2, 129.5, 130.2, 131.0, 132.0, 135.8, 140.0, 153.6, 165.2, 169.9. *Anal.* calcd for $C_{21}H_{16}ClN_3O_3$: C 64.05, H 4.09, N 10.67; found C 63.90, H 4.11, N 10.52.

3-(4-Methyoxylphenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]-quinolin-3-carbonyl urea (3b). This compound was obtained as pale yellow powder, m.p. 245~246 °C; ir (KBr): ν_{max} 3429, 3326, 3253, 3062, 2934, 2891, 1695, 1626, 1606, 1569, 1510, 1460, 1429, 1391, 1319, 1288, 1252, 1176, 1113, 1026, 820, 773, 752; ^{1}H nmr (DMSO-d_6): δ 3.67 (s, 3H, CH_3O), 3.84 (s, 1H, OH), 5.18 (s, 1H, CH), 6.82 (d, J = 8.8 Hz, 2H, ArH), 7.12 (d, J = 8.8 Hz, 2H, ArH), 7.26 (s, 1H, NH), 7.28 (s, 1H, NH), 7.33~7.44 (m, 3H, ArH), 7.79 (d, J = 8.4 Hz, 1H, ArH), 7.86 (d, J = 8.4 Hz, 2H, ArH), 10.69 (s, 1H, NH), 10.76 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 55.2, 56.3, 114.2, 116.0, 117.1, 122.6, 124.3, 127.3, 128.6, 128.8, 128.9, 129.3, 130.2, 131.1, 132.8, 135.6, 153.6, 158.4, 165.5, 170.2. *Anal.* calcd for $C_{22}H_{19}N_3O_4$: C 67.86, H 4.92, N 10.79; found C 67.78, H 5.02, N 10.87.

3-(2,4-Dichlorophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]-quinolin-3-carbonyl urea (3c). This compound was obtained as pale yellow powder, m.p. 250~252 °C; ir (KBr): ν_{max} 3441, 3329, 3056, 2887, 1691, 1628, 1607, 1565, 1520, 1504, 1466, 1430, 1399, 1344, 1324, 1236, 1198, 1100, 867, 820, 797, 744; ^{1}H nmr (DMSO-d_6): δ 3.83 (s, 1H, OH), 5.40 (s, 1H, CH), 6.65 (d, J = 8.4 Hz, 1H, ArH), 7.26 (dd, J = 8.4 Hz, J' = 2.0 Hz, 1H, ArH), 7.29~ 7.42 (m, 4H, ArH), 7.46 (s, 1H, NH), 7.47 (s, 1H, NH), 7.82 (d, J = 2.0 Hz, 1H, ArH), 7.89 (d, J = 8.4 Hz, 1H, ArH), 7.92 (d, J = 8.4 Hz, 1H, ArH), 10.24 (s, 1H, NH), 10.98 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 53.7, 114.4, 117.1, 121.8, 124.5, 127.8, 128.4, 129.1, 129.6, 129.7, 129.8, 130.4, 130.5, 130.7, 133.1, 133.2, 135.6, 137.6, 153.2, 164.1, 169.2. *Anal.* calcd for $C_{21}H_{15}Cl_2N_3O_3$: C 58.89, H 3.53, N 9.81; found C 58.72, H 3.66, N 9.94.

3-(3,4-Dichlorophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]-quinolin-3-carbonyl urea (3d). This compound was obtained as pale yellow powder, m.p. 239~241 °C; ir (KBr): ν_{max} 3408, 3314, 3257, 3120, 2963, 1698, 1652, 1631, 1578, 1522, 1504, 1472, 1399, 1374, 1290, 1262, 1224, 1195, 1033, 817, 808, 749; ^{1}H nmr (DMSO-d_6): δ 3.86 (s, 1H, OH), 5.33 (s, 1H, CH), 6.91 (dd, J = 8.4 Hz, J' = 2.0 Hz, 1H, ArH), 7.28 (s, 1H, NH), 7.30 (s, 1H, NH), 7.36~7.40 (m, 2H, ArH), 7.45~ 7.49 (m, 1H, ArH), 7.52 (d, J = 8.0 Hz, 1H, ArH), 7.73 (d, J = 2.0 Hz, 1H, ArH), 7.80 (d, J = 8.4 Hz, 1H, ArH), 7.89 (d, J = 8.4 Hz, 1H, ArH), 7.92 (d, J = 8.8 Hz, 1H, ArH), 10.72 (s, 1H, NH), 10.88 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 55.8, 115.1, 117.2, 120.6, 122.5, 124.3, 127.5, 128.9, 129.3, 129.4, 129.8, 130.2, 130.5, 131.0, 131.5, 131.8, 135.8, 140.4, 153.6, 165.2, 169.9. *Anal.* calcd for $C_{21}H_{15}Cl_2N_3O_3$: C 58.89, H 3.53, N 9.81; found C 58.70, H 3.62, N 9.78.

3-(4-Fluorophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]quinolin-3-carbonyl urea (3e). This compound was obtained as pale yellow crystals, m.p. 235~236 °C; ir (KBr): ν_{max} 3407, 3239, 3174, 2937, 1718, 1666, 1625, 1602, 1521, 1508, 1473, 1390, 1293, 1247, 1230, 1176, 1161, 1101, 868, 844, 831, 803, 784, 760; ^{1}H nmr (DMSO-d_6): δ 3.86 (s, 1H, OH), 5.27 (s, 1H, CH), 7.10 (t, J = 8.4 Hz, 2H, ArH), 7.22 ~7.29 (m, 5H, ArH + 2NH), 7.34~7.38 (m, 1H, ArH), 7.43~7.46 (m, 1H, ArH), 7.79 (d, J = 8.4 Hz, 1H, ArH), 7.80 (d, J = 8.0 Hz, 1H, ArH), 7.88 (d, J = 8.8 Hz, 1H, ArH), 10.64 (s, 1H, NH), 10.78(s, 1H, NH). ^{13}C nmr

(DMSO-d_6): δ 56.1, 115.6, 115.8, 117.2, 122.5, 124.3, 127.4, 128.8, 129.2, 129.46, 129.54, 130.2, 131.0, 135.7, 137.1, 153.4, 160.5, 165.3, 170.1. *Anal.* calcd for $C_{21}H_{16}FN_3O_3$: C 66.84, H 4.27, N 11.14; found C 66.80, H 4.35, N 11.08.

3-(3-Nitrophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]quinolin-3-carbonyl urea (3f). This compound was obtained as yellow powder, m.p. 231~233 °C; ir (KBr): ν_{max} 3445, 3327, 3068, 2887, 1685, 1628, 1566, 1524, 1474, 1401, 1348, 1274, 1236, 1200, 1179, 1098, 974, 850, 820, 796, 776, 748, 700; ^{1}H nmr (DMSO-d_6): δ 3.91 (s, 1H, OH), 5.50 (s, 1H, CH), 7.29~7.40 (m, 3H, ArH), 7.44~7.49 (m, 3H, ArH + 2NH), 7.54~7.58 (m, 1H, ArH), 7.83 (d, J = 8.8 Hz, 1H, ArH), 7.89 (d, J = 8.0 Hz, 1H, ArH), 7.94 (d, J = 8.0 Hz, 1H, ArH), 8.09 (d, J = 8.4 Hz, 1H, ArH), 8.33 (s, 1H, ArH), 10.73 (s, 1H, NH), 10.92(s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 55.7, 114.3, 117.2, 122.1, 122.6, 122.7, 122.9, 124.4, 127.7, 128.9, 130.0, 130.3, 130.5, 131.0, 134.0, 136.1, 143.1, 148.3, 153.6, 165.0, 169.7. *Anal.* calcd for $C_{21}H_{16}N_4O_5$: C 62.37, H 3.99, N 13.86; found C 62.21, H 4.12, N 13.91.

3-(4-Bromophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]quinolin-3-carbonyl urea (3g). This compound was obtained as pale yellow powder, m.p. 239~240 °C; ir (KBr): ν_{max} 3401, 3245, 3180, 2930, 1717, 1703, 1664, 1626, 1586, 1520, 1486, 1474, 1378, 1298, 1244, 1229, 1170, 1101, 1010, 833, 801, 789, 761; ^{1}H nmr (DMSO-d_6): δ 3.87 (s, 1H, OH), 5.27 (s, 1H, CH), 7.16 (d, J = 8.4 Hz, 2H, ArH), 7.27 (s, 1H, NH), 7.29 (s, 1H, NH), 7.35~7.49 (m, 5H, ArH), 7.78 (d, J = 8.4 Hz, 1H, ArH), 7.86~7.90 (m, 2H, ArH), 10.70 (s, 1H, NH), 10.82 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 55.7, 114.3, 117.2, 122.4, 124.4, 127.4, 128.9, 129.6, 130.1, 130.2, 131.0, 131.1, 131.5, 135.9, 142.0, 153.5, 165.0, 169.7. *Anal.* calcd for $C_{21}H_{16}BrN_3O_3$: C 57.55, H 3.68, N 9.59; found C 57.34, H 3.75, N 9.50.

3-(2-Chlorophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]quinolin-3-carbonyl urea (3h). This compound was obtained as pale yellow powder, m.p. 250~251 °C; ir (KBr): ν_{max} 3441, 3325, 3064, 2933, 2890, 1691, 1627, 1608, 1567, 1523, 1472, 1431, 1401, 1322, 1272, 1235, 1200, 1183, 1038, 819, 775, 752; ^{1}H nmr (DMSO-d_6): δ 3.84 (s, 1H, OH), 5.44 (s, 1H, CH), 6.67 (dd, J = 8.0 Hz, J' = 1.6 Hz, 1H, ArH), 7.13~7.17 (m, 1H, ArH), 7.26~7.51 (m, 7H, ArH + 2NH), 7.62 (d, J = 8.0 Hz, 1H, ArH), 7.88 (d, J = 8.4 Hz, 1H, ArH), 7.91 (d, J = 8.8 Hz, 1H, ArH), 10.24 (s, 1H, NH), 10.95(s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 53.9, 115.0, 117.0, 121.9, 124.4, 127.7, 127.8, 128.2, 128.5, 129.0, 129.4, 130.2, 130.3, 130.5, 130.8, 132.2, 135.6, 138.5, 153.2, 164.2, 169.4. *Anal.* calcd for $C_{21}H_{16}ClN_3O_3$: C 64.05, H 4.09, N 10.67; found C 63.94, H 4.18, N 10.50.

3-(3,4-Dimethylphenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]-quinolin-3-carbonyl thiourea (3i). This compound was obtained as pale yellow powder, m.p. 229~231 °C; ir (KBr): ν_{max} 3341, 3221, 3160, 3050, 2816, 1702, 1654, 1605, 1540, 1510, 1472,1430, 1368, 1339, 1299, 1271, 1253, 1219, 1047, 825, 814, 772, 750, 670 ; ^{1}H nmr (DMSO-d_6): δ 2.12 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 4.00 (s, 1H, OH), 5.14 (s, 1H, CH), 6.76 (d, J = 7.6 Hz, 1H, ArH), 6.97(d, J = 8.0 Hz, 1H, ArH), 7.12 (s, 1H, ArH), 7.26 (d, J = 8.8 Hz, 1H, ArH), 7.33~ 7.37 (m, 1H, ArH), 7.41~ 7.44 (m, 1H, ArH), 7.78 (d, J = 8.4 Hz, 1H, ArH), 7.85~ 7.87 (m, 2H, ArH), 9.26 (s, 1H, NH), 9.42 (s, 1H, NH), 10.80 (s, 1H, NH), 11.59 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 19.1, 19.8, 55.9, 115.8, 117.1, 122.7, 124.2, 124.5, 124.7, 127.3, 128.8, 128.9, 129.2, 129.8, 130.3, 131.1, 135.3, 135.6, 136.5, 138.3, 165.3, 169.4, 181.5. *Anal.* calcd for $C_{23}H_{21}N_3O_2S$: C 68.46, H 5.25, N 10.41; found C 68.33, H 5.36, N 10.52.

2-Oxo-3-phenyl-1,2,3,4-tetrahydrobezo[*f*]quinolin-3-carbonyl thiourea (3j). This compound was obtained as pale yellow powder, m.p. 230~231 °C; ir (KBr): ν_{max} 3345, 3228, 3155, 3063, 2815, 1702, 1665, 1604, 1542, 1510, 1473, 1395, 1342, 1300, 1272, 1252, 1226, 1179, 1044, 815, 749, 697; ^{1}H nmr (DMSO-d_6): δ 4.06 (s, 1H, OH), 5.25 (s, 1H, CH), 7.18~7.30 (m, 6H, ArH), 7.34~7.37 (m, 1H, ArH), 7.41~7.45 (m, 1H, ArH), 7.82 (d, J = 8.4 Hz, 1H, ArH), 7.86 (d, J = 8.0 Hz, 1H, ArH), 7.87 (d, J = 8.4 Hz, 1H, ArH), 9.27 (s, 1H, NH), 9.43 (s, 1H, NH), 10.84 (s, 1H, NH), 11.61 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 55.7, 115.7, 117.1, 119.7, 122.7, 124.2, 127.3, 127.6, 128.2, 128.80, 128.84, 129.0, 130.0, 131.1, 135.6, 141.0, 165.2, 169.4, 181.5. *Anal.* calcd for $C_{21}H_{17}N_3O_2S$: C 67.18, H 4.56, N 11.19; found C 67.02, H 4.70, N 11.18.

3-(3-Chlorophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]quinolin-3-carbonyl thiourea (3k). This compound was obtained as pale yellow powder, m.p. 215~216 °C; ir (KBr): ν_{max} 3355, 3291, 3119, 2971, 1703, 1650, 1621, 1570, 1538, 1474, 1399, 1284, 1230, 1169, 1082, 1034, 853, 811, 785, 747, 701; ^{1}H nmr (DMSO-d_6): δ 4.04 (s, 1H, OH), 5.35 (s, 1H, CH), 6.95 (d, J = 7.2 Hz, 1H, ArH), 7.24~7.30 (m, 3H, ArH), 7.36~7.39 (m, 1H, ArH), 7.44~7.47 (m, 1H, ArH), 7.51 (s, 1H, ArH), 7.82 (d, J = 8.4 Hz, 1H, ArH), 7.87~7.91 (m, 2H, ArH), 9.25 (s, 1H, NH), 9.44 (s, 1H, NH), 10.88 (s, 1H, NH), 11.65 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 55.5, 114.8, 117.1, 122.6, 124.4, 125.9, 127.45, 127.53, 127.9, 128.9, 129.4, 130.3, 130.8, 131.0, 133.5, 135.8, 143.3, 165.0, 169.1, 181.4. *Anal.* calcd for $C_{21}H_{16}ClN_3O_2S$: C 61.53, H 3.93, N 10.25; found C 61.28, H 3.99, N 10.17.

3-(4-Methoxylphenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]-quinolin-3-carbonyl thiourea (3l). This compound was obtained as pale yellow powder, m.p. 228~229 °C; ir (KBr): ν_{max} 3345, 3301, 3154, 2934, 2836, 1686, 1654, 1623, 1601, 1540, 1509, 1459, 1427, 1392, 1318, 1252, 1226, 1176, 1162, 1094, 1026, 830, 796, 770, 677; ^{1}H nmr (DMSO-d_6): δ 3.67 (s, 3H, CH_3O), 4.02 (s, 1H, OH), 5.18 (s, 1H, CH), 6.82 (d, J = 8.8 Hz, 2H, ArH), 7.27 (d, J = 8.8 Hz, 2H, ArH), 7.33~7.37 (m, 1H, ArH), 7.41~7.45 (m, 1H, ArH), 7.79 (d, J = 8.8 Hz, 1H, ArH), 7.85~7.87 (m, 2H, ArH), 9.26 (s, 1H, NH), 9.41 (s, 1H, NH), 11.06 (s, 1H, NH), 11.61 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 55.2, 56.0, 114.2, 116.0, 117.1, 122.7, 124.9, 127.3, 128.7, 128.8, 128.9, 129.3, 130.3, 131.1, 132.7, 135.5, 158.5, 165.3, 169.4, 181.0. *Anal.* calcd for $C_{22}H_{19}N_3O_3S$: C 65.17, H 4.72, N 10.36; found C 65.10, H 4.85, N 10.20.

3-(2-Chlorophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]quinolin-3-carbonyl thiourea (3m). This compound was obtained as pale yellow powder, m.p. 229~231 °C; ir (KBr): ν_{max} 3364, 3318, 3266, 3171, 3026, 2941, 2902, 1704, 1670, 1615, 1521, 1467, 1427, 1373, 1342, 1310, 1271, 1220, 1198, 1166, 1038, 1012, 966, 816, 765, 750, 714, 674; ^{1}H nmr (DMSO-d_6): δ 4.07 (s, 1H, OH), 5.46 (s, 1H, CH), 6.89 (dd, J = 8.0 Hz, J' = 2.4 Hz, 1H, ArH), 7.13~7.17 (m, 1H, ArH), 7.26~7.38 (m, 3H, ArH), 7.43~7.52 (m, 2H, ArH), 7.63 (d, J = 8.0 Hz, 1H, ArH), 7.88 (d, J = 8.4 Hz, 1H, ArH), 7.91 (d, J = 8.8 Hz, 1H, ArH), 9.27 (s, 1H, NH), 9.52 (s, 1H, NH), 11.02 (s, 1H, NH), 11.08 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 53.7, 114.9, 117.1, 121.9, 124.4, 127.7, 127.8, 128.2, 128.5, 129.0, 129.46, 129.49, 130.2, 130.5, 130.8, 132.2, 135.5, 138.5, 164.1, 168.5, 181.0. *Anal.* calcd for $C_{21}H_{16}ClN_3O_2S$: C 61.53, H 3.93, N 10.25; found C 61.33, H 4.12, N 10.10.

3-(4-Chlorophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]quinolin-3-carbonyl thiourea (3n). This compound was obtained as pale yellow powder, m.p. 232~233 °C. IR (KBr, ν, cm^{-1}): 3352,

3268, 3191, 3143, 2930, 1684, 1640, 1602, 1520, 1489, 1406, 1393, 1371, 1320, 1226, 1179, 1160, 1093, 1014, 1004, 824, 766, 751, 728; ^{1}H nmr (DMSO-d_6): δ 4.03 (s, 1H, OH), 5.28 (s, 1H, CH), 7.23 (d, J = 8.8 Hz, 2H, ArH), 7.28 (d, J = 8.8 Hz, 1H, ArH), 7.33~7.39 (m, 3H, ArH), 7.43~7.46 (m, 1H, ArH), 7.79 (d, J = 8.0 Hz, 1H, ArH), 7.86~7.90 (m, 2H, ArH), 9.24 (s, 1H, NH), 9.39 (s, 1H, NH), 10.85 (s, 1H, NH), 11.59 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 55.5, 115.1, 117.1, 122.6, 124.3, 127.5, 128.7, 128.8, 129.3, 129.6, 130.1, 130.3, 131.0, 132.1, 135.7, 139.9, 165.0, 169.1, 181.4. *Anal.* calcd for $C_{21}H_{16}ClN_3O_2S$: C 61.53, H 3.93, N 10.25; found C 61.42, H 3.94, N 10.28.

3-(2,4-Dichlorophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]-quinolin-3-carbonyl thiourea (3o). This compound was obtained as pale yellow powder, m.p. 213~217 °C; ir (KBr): ν_{max} 3430, 3310, 3152, 3058, 2927, 1707, 1662, 1627, 1595, 1524, 1469, 1393, 1344, 1317, 1266, 1228, 1197, 1166, 1097, 1057, 971, 860, 817, 794, 773, 738; ^{1}H nmr (DMSO-d_6): δ 4.06 (s, 1H, OH), 5.43 (s, 1H, CH), 6.67 (d, J = 8.4 Hz, 1H, ArH), 7.26 (dd, J = 8.4 Hz, J' = 2.0 Hz, 1H, ArH), 7.30 (d, J = 8.8 Hz, 1H, ArH), 7.36~7.39 (m, 1H, ArH), 7.43~7.46 (m, 2H, ArH), 7.83 (d, J = 2.0 Hz, 1H, ArH), 7.88 (d, J = 8.4 Hz, 1H, ArH), 7.92 (d, J = 8.8 Hz, 1H, ArH), 9.25 (s, 1H, NH), 9.52 (s, 1H, NH), 11.04 (s, 1H, NH), 11.06 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 53.4, 114.4, 117.1, 117.4, 121.8, 124.5, 127.9, 128.4, 129.1, 129.7, 129.8, 130.4, 130.5, 130.7, 133.1, 133.2, 135.2, 137.7, 164.0, 168.3, 181.0. *Anal.* calcd for $C_{21}H_{15}Cl_2N_3O_2S$: C 56.76, H 3.40, N 9.46; found C 56.68, H 3.53, N 9.52.

3-(4-Fluorophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]quinolin-3-carbonyl thiourea (3p). This compound was obtained as pale yellow powder, m.p. 229~230 °C; ir (KBr): ν_{max} 3340, 3229, 3153, 2820, 1701, 1660, 1604, 1542, 1500, 1473, 1394, 1302, 1252, 1240, 1180, 1163, 1072, 1044, 835, 811, 742, 727, 702, 670; ^{1}H nmr (DMSO-d_6): δ 4.03 (s, 1H, OH), 5.28 (s, 1H, CH), 7.11 (t, J = 8.8 Hz, 2H, ArH), 7.23~7.29 (m, 3H, ArH), 7.35~7.38 (m, 1H, ArH), 7.42~7.42 (m, 1H, ArH), 7.81 (d, J = 8.8 Hz, 1H, ArH), 7.86~7.89 (m, 2H, ArH), 9.25 (s, 1H, NH), 9.42 (s, 1H, NH), 10.86 (s, 1H, NH), 11.62 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 55.7, 115.5, 115.7, 117.1, 122.6, 124.3, 127.4, 128.8, 129.2, 129.6, 129.7, 130.3, 131.0, 135.6, 137.0, 160.2, 165.1, 169.2, 181.4. *Anal.* calcd for $C_{21}H_{16}FN_3O_2S$: C 64.11, H 4.10, N 10.68; found C 64.03, H 4.25, N 10.66.

3-(3,4-Dichlorophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]-quinolin-3-carbonyl thiourea (3q). This compound was obtained as pale yellow powder, m.p. 228~229 °C; ir (KBr): ν_{max} 3345, 3230, 3153, 3016, 2819, 1701, 1664, 1605, 1541, 1503, 1471, 1429, 1394, 1339, 1301, 1274, 1250, 1226, 1075, 1029, 824, 810, 745, 709, 675; ^{1}H nmr (DMSO-d_6): δ 4.03 (s, 1H, OH), 5.34 (s, 1H, CH), 6.90 (dd, J = 8.4 Hz, J' = 2.0 Hz, 1H, ArH), 7.29 (d, J = 8.4 Hz, 1H, ArH), 7.37~7.40 (m, 1H, ArH), 7.45~7.48 (m, 1H, ArH), 7.51 (d, J = 8.4 Hz, 1H, ArH), 7.75 (d, J = 2.0 Hz, 1H, ArH), 7.82 (d, J = 8.0 Hz, 1H, ArH), 7.88 (d, J = 8.4 Hz, 1H, ArH), 7.91 (d, J = 8.8 Hz, 1H, ArH), 9.23 (s, 1H, NH), 9.44 (s, 1H, NH), 10.91 (s, 1H, NH), 11.65 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 55.3, 114.4, 117.1, 122.5, 124.4, 127.5, 127.6, 128.9, 129.6, 130.17, 130.21, 130.3, 131.0, 131.1, 131.5, 135.8, 141.9, 164.8, 168.9, 181.4. *Anal.* calcd for $C_{21}H_{15}Cl_2N_3O_2S$: C 56.76, H 3.40, N 9.46; found C 56.59, H 3.50, N 9.61.

3-(4-Bromophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]quinolin-3-carbonyl thiourea (3r). This compound was obtained as pale yellow powder, m.p. 230~232 °C; ir (KBr): ν_{max} 3340, 3255, 3170, 2820, 1685, 1642, 1623, 1520, 1487, 1427, 1394, 1341, 1320, 1296, 1227, 1161, 1095, 1072, 1008, 843, 821, 770, 749, 724, 696; ^{1}H nmr (DMSO-d_6): δ 4.03 (s, 1H, OH), 5.27 (s, 1H, CH), 7.17 (d, J = 8.4 Hz, 2H, ArH), 7.28 (d, J = 8.8 Hz, 1H, ArH), 7.35~7.39 (m, 1H, ArH), 7.41~7.46 (m, 1H, ArH), 7.48 (d, J = 8.4 Hz, 2H, ArH), 7.79 (d, J = 8.4 Hz, 1H, ArH), 7.86~7.90 (m, 2H, ArH), 9.25 (s, 1H, NH), 9.43 (s, 1H, NH), 10.87 (s, 1H, NH), 11.63 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 55.5, 115.1, 117.1, 120.6, 122.5, 124.3, 127.5, 128.8, 129.3, 129.9, 130.3, 130.5, 131.0, 131.8, 135.7, 140.3, 165.0, 169.1, 181.4. *Anal.* calcd for $C_{21}H_{16}BrN_3O_2S$: C 55.51, H 3.55, N 9.25; found C 55.42, H 3.53, N 9.12.

3-(3,4-Dimethoxylphenyl)-2-oxo-1,2,3,4-tetrahydrobezo-[*f*]quinolin-3-carbonyl thiourea (3s). This compound was obtained as pale yellow powder, m.p. 231~233 °C; ir (KBr): ν_{max} 3346, 3215, 3157, 3008, 2817, 1702, 1640, 1604, 1550, 1519, 1464, 1413, 1394, 1338, 1298, 1256, 1151, 1046, 1023, 848, 814, 774, 749, 694; ^{1}H nmr (DMSO-d_6): δ 3.64 (s, 3H, CH_3O), 3.75 (s, 3H, CH_3O), 4.06 (s, 1H, OH), 5.17 (s, 1H, CH), 6.31 (dd, J = 8.0 Hz, J' = 1.6 Hz, 1H, ArH), 6.73 (d, J = 1.6 Hz, 1H, ArH), 7.15 (d, J = 1.6 Hz, 1H, ArH), 7.27 (d, J = 8.0 Hz, 1H, ArH), 7.34~7.38 (m, 1H, ArH), 7.41~7.44 (m, 1H, ArH), 7.82 (d, J = 8.0 Hz, 1H, ArH), 7.85~7.89 (m, 2H, ArH), 9.27 (s, 1H, NH), 9.43 (s, 1H, NH), 10.80 (s, 1H, NH), 11.59 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 55.6, 55.8, 56.0, 111.9, 112.3, 116.0, 117.1, 119.1, 122.8, 124.2, 127.2, 128.8, 129.0, 130.3, 130.9, 131.2, 133.1, 135.5, 148.1, 149.0, 161.3, 169.4, 181.4. *Anal.* calcd for $C_{23}H_{21}N_3O_4S$: C 63.43, H 4.86, N 9.65; found C 63.40, H 4.98, N 9.54.

3-(2-Nitrophenyl)-2-oxo-1,2,3,4-tetrahydrobezo[*f*]quinolin-3-carbonyl thiourea (3t). This compound was obtained as yellow powder, m.p. 188~190 °C; ir (KBr): ν_{max} 3411, 3322, 3173, 2832, 1701, 1652, 1607, 1520, 1407, 1362, 1288, 1267, 1223, 1098, 1034, 980, 906, 857, 813, 783, 748, 711; ^{1}H nmr (DMSO-d_6): δ 4.18 (s, 1H, OH), 5.92 (s, 1H, CH), 6.87 (dd, J = 8.0 Hz, J' = 2.4 Hz, 1H, ArH), 7.31 (d, J = 8.8 Hz, 1H, ArH), 7.34~7.44 (m, 2H, ArH), 7.54~7.58 (m, 3H, ArH), 7.88 (d, J = 7.6 Hz, 1H, ArH), 7.92 (d, J = 8.8 Hz, 1H, ArH), 8.29 (dd, J = 8.0 Hz, J' = 2.4 Hz, 1H, ArH), 9.28 (s, 1H, NH), 9.53 (s, 1H, NH), 10.96 (s, 1H, NH), 11.05 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 54.4, 114.1, 117.0, 121.9, 124.5, 126.3, 127.9, 129.0, 129.3, 129.4, 129.9, 130.1, 130.5, 130.8, 135.0, 135.9, 136.2, 147.1, 164.0, 168.6, 181.0. *Anal.* calcd for $C_{21}H_{16}N_4O_4S$: C 59.99, H 3.84, N 13.33; found C 59.78, H 3.95, N 13.26.

X-ray Crystallography. The crystallographic measurement on compound **3e** was made using a CCD area detector diffractometer. Graphite monochromated MoKα radiation was used in all cases. The structures were solved using SHELXTL [19] and refined with SHELXL [20]. Crystallographic data for the structure of **3e** reported in this paper has been deposited at the Cambridge Crystallographic Data Centre as supplementary publication with No. CCDC-294647. Copies of available material can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

Acknowledgments. We are grateful to the Foundation (04KJB150139) of the Education Committee of Jiangsu Province for financial support.

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[18] X-ray diffraction analysis, $C_{23}H_{23}FN_4O_4$; M = 450.46, Colorless block crystals, 0.24 × 0.20 × 0.18 mm, Monoclinic, space group P 2(1)/n, a = 11.491 (5), b = 9.417(4), c = 20.617(8) Å, β = 91.187(8)°, V = 2230.5(16) Å ^{3}, Z = 4, Dc = 1.341 g.cm^{-3}. F(000) = 944, μ(MoKα) = 0.099 mm^{-1}. Intensity data were collected on CCD area detector diffractometer with graphite monochromated MoKα radiation (λ = 0.71073 Å) using phi and omega scan mode with 1.98° < θ < 26.51°. 4588 unique reflections were measured and 2637 reflections with I>2σ(I) were used in the refinement. Structure solved by direct methods and expanded using Fourier techniques. The final cycle of full-matrix least squares technique to R = 0.0536 and $_wR$ = 0.1345.

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