JOC The Journal of Organic Chemistry

Article

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Construction of Multifunctional 3-Amino-2-carbamimidoylacrylamides and Their Crystalline Channel-Type Inclusion Complexes

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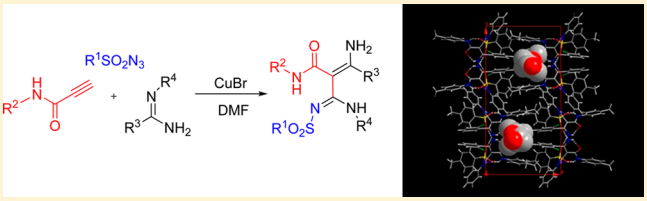
Supporting Information

ABSTRACT: 3-Amino-2-carbamimidoylacrylamides were efficiently prepared via a copper(I)-catalyzed three-component reaction of sulfonylazides, propriolamides, and amidines. The synthesized compounds provided three kinds of crystalline structures based on the position of halogen. Two of them presented channel-type inclusion complexes with ethyl acetate through intermolecular hydrogen bonding, intermolecular C−H···π and π−π interactions, and van der Waals forces.



INTRODUCTION

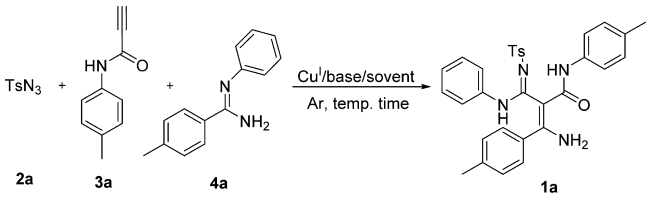
Crystalline channel-type inclusion complexes based on intermolecular hydrogen bonding, C−H···π and π−π interactions, and van der Waal interactions have attracted much attention recently.[1] They possess potentials in broad applications such as molecular recognition,[2] resolution of enantiomers,[3] storage and separation of small molecules,[4] and drug delivery systems.[5] On the other hand, their architectures might be used for better understanding a number of disciplines including crystal engineering,[6] biochemistry, and catalysis.[7,8] Molecules with multifunctional groups that prefer to form hydrogen bonding, such as hydroxyl, amino, carbonyl, amide, etc., are generally considered to be used in the design of the host architecture.[9−14]

On the other hand, copper-catalyzed azide−alkyne cycloaddition (CuAAC) has immerged as a powerful tool to form ketenimines,[15,16] which shine light on the development of multicomponent approaches to a variety of principal nitrogen-containing compounds.[17,18] As a continuation of our work on ketenimine chemistry,[17,18] we recently synthesized a series of 3-amino-2-carbamimidoylacrylamides containing amino, amide, and carbamimidoyl groups from sulfonylazides, propriolamides, and amidines and unexpectedly obtained their crystalline channel-type inclusion complexes with the guest ethyl acetate. Herein we report the details of this effort.

RESULTS AND DISCUSSION

3-Amino-2-carbamimidoylacrylamides **1** were prepared from the copper-catalyzed cascade reactions of sulfonylazides **2**, propriolamides **3**, and amidines **4**. At the beginning, the reaction of tosylazide (**2a**), *N*-(*p*-tolyl)propiolamide (**3a**), and 4-methyl-*N*′-phenylbenzimidamide (**4a**) in the presence of CuOTf and pyridine was tested. After the mixture reacted in acetonitrile at 50 °C for 18 h, **1a** was obtained in 44% isolated yield (Table 1, entry 1). The structure of **1a** was established based on its single crystal analysis. Either extension or shortening of the reaction time led to a decrease of the yield (Table 1, entries 2 and 3). A slightly higher yield was obtained by using CuBr as the catalyst in comparison with other catalysts, such as CuI and CuCl (Table 1, entries 4−6). When different bases were used, such as triethylamine, or potassium carbonate, the isolated yields were apparently decreased (Table 1, entries 7 and 8). It was noticeable

Table 1. Screening of the Reaction Conditions[a]



entry	catalyst	base[b]	solvent	temp (°C)	time (h)	yield (%)[c]
1	CuOTf	pyridine	MeCN	50	18	44
2	CuOTf	pyridine	MeCN	50	14	43
3	CuOTf	pyridine	MeCN	50	24	42
4	CuI	pyridine	MeCN	50	18	33
5	CuCl	pyridine	MeCN	50	18	36
6	CuBr	pyridine	MeCN	50	18	45
7	CuBr	TEA	MeCN	50	18	40
8	CuBr	K_2CO_3	MeCN	50	18	22
9	CuBr	–	MeCN	50	18	49
10	CuBr	–	DMF	50	18	86
11	CuBr	–	toluene	50	18	33
12	CuBr	–	DCE	50	18	31
13	CuBr	–	DMF	25	18	90
14	CuBr	–	DMF	0	18	90

[a]Reaction conditions: **2a** (0.5 mmol), **3a** (0.5 mmol), **4a** (0.5 mmol), catalyst (0.1 equiv), solvent (2 mL). [b]2 equiv. [c]Isolated yield.

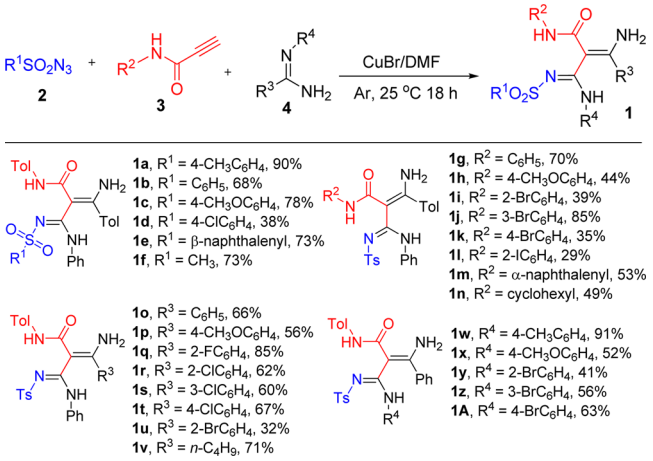
Received: April 14, 2015
Published: May 14, 2015

DOI: 10.1021/acs.joc.5b00827
J. Org. Chem. 2015, 80, 5842−5850

that a slightly higher yield was observed without base. Further changing of solvent to DMF, **1a** was isolated in 86% yield (Table 1, entries 9−12). The yield was improved when the reaction temperature decreased to 25 °C. In this case, the isolated yield of **1a** approached 90% (Table 1, entry 13). Further lowering the reaction temperature to 0 °C did not improve the result (Table 1, entry 14). Thus, the optimal reaction conditions for the formation of **1a** were established (Table 1, entry 13).

With the optimal reaction conditions in hand, we investigated the substrate diversity. First, various sulfonyl azides **2** were tested (Table 2). In comparison with tosyl azide (**2a**), other sulfonyl azides worked for this transformation to give 3-amino-2-carbamimidoylacrylamides **1b−f** in relatively lower yields (38%−78%). Arenesulfonyl azides with an electron-donating group (CH_3, OCH_3) on the arene ring gave better yields (90%, 78%) than those with an electron-withdrawing group (Cl, 38%) on the arene ring. Methanesulfonyl azide furnished **1f** in 73% yield. Second, we investigated the diversity of *N*-arylpropiolamides **3**. Substituent and steric effects of aromatic ring on the yields were apparent. By altering the bromine atom from ortho, to meta, and to para position, **1i**, **1j**, and **1k** were isolated in yields of 39%, 85%, and 35%, respectively. Moreover, *N*-alkylpropiolamide also worked for the reaction. For instance, *N*-cyclohexylpropiolamide provided **1n** in 49% yield. Finally, we moved our attention to the third component of this reaction, the substituted *N*′-aryllbenzimidamides **4**. By changing the substituted group on benzimidamide, the corresponding products **1o−v** were obtained in yields that varied from 32% to 85%. Substituents could either be electron-donating (OCH_3) or electron-withdrawing (F, Cl, Br). By altering the chlorine atom from ortho, to meta, and to para, **1r**, **1s**, and **1t** were obtained in yields of 62%, 60%, and 67%, respectively. By changing fluorine, to chlorine, and to bromine, **1q**, **1r**, and **1u** were prepared in 85%, 62%, and 32% yields, respectively. It was noticeable that alkanimidamide could also be used as the substrate. Thus, *N*′-phenylpentanimidamide provided the desired product **1v** in 71% yield. A series of *N*′-arylbenzimidamides were also examined for this transformation. The desired products **1w−1A** were prepared in 41−91% yields. Substituents with either electron-donating (OCH_3) or electron-withdrawing (Br) on the arene of *N*′-aryllbenzimidamides tolerated the reaction conditions and afforded the corresponding products. By changing the bromine from ortho position to meta and para position, **1y**, **1z**, and **1A** were obtained in yields of 41%, 56%, and 63%, respectively.

Table 2. Substrate Scope of the Azides[a]



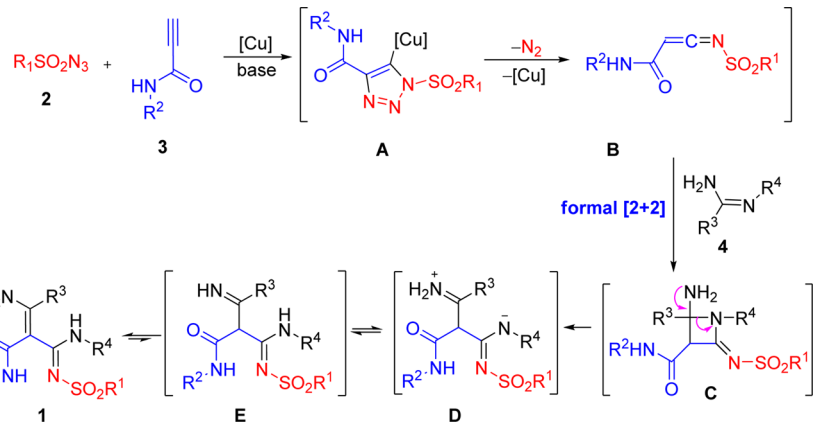
[a]Reaction conditions: **2** (0.5 mmol), **3** (0.5 mmol), **4** (0.5 mmol), CuBr (0.05 mmol), DMF (2 mL). [b]Isolated yield.

On the bases of the work of Chang's group[15,16] and our previous studies on ketenimine chemistry[17,18] and the outcome of the reaction, we proposed a possible mechanism for this three-component reaction (Scheme 1). First, 1,4-disubstituted triazole **A** is formed from **2** and **3** via copper-catalyzed alkyne−azide cycloaddition (CuAAC).[19−21] Because the N1−N2 bond of triazole **A** is weakened by the electron-withdrawing sulfonyl group,[22,23] the fragile triazole undergoes ring-opening, followed by Dimroth rearrangement to form ketenimine intermediate **B** with the exclusion of nitrogen.[16−18] Then a formal [2 + 2] cycloaddition[24] of benzimidine **4** and ketenimine forms the active azetidine intermediate **C**. Through a sequential ring opening, proton transfer, and tautoumerism, **1** is finally achieved.

Fortunately, we obtained the single crystals of compounds **1a**, **1y**, **1l**, **1r**, and **1u.** Their structures are presented in Scheme 2, and their crystallographic data are listed in Table 3. The results indicate that the changes of the crystal system as well as the space group take place when the halogen atom is substituted on different aromatic rings of these compounds.

Figure 1a presents the single crystal structure of **1a**. It is clear that the molecule is composed of two planar structures. One is the chain skeleton of 3-aminoacrylamide (O1−C8−C9−C10−N2), and the other is the carbamimidoyl group (N3−C18−N4). The dihedral angle is 58° (C8−C9−C18−N3). The tolyl group on C10 is slight twisted, and a $\pi-\pi$ stacking exists between two

Scheme 1. Proposed Mechanism for the Formation of 1



DOI: 10.1021/acs.joc.5b00827
J. Org. Chem. 2015, 80, 5842−5850

Scheme 2. Structures of 1a, 1y, 1l, 1r, and 1u

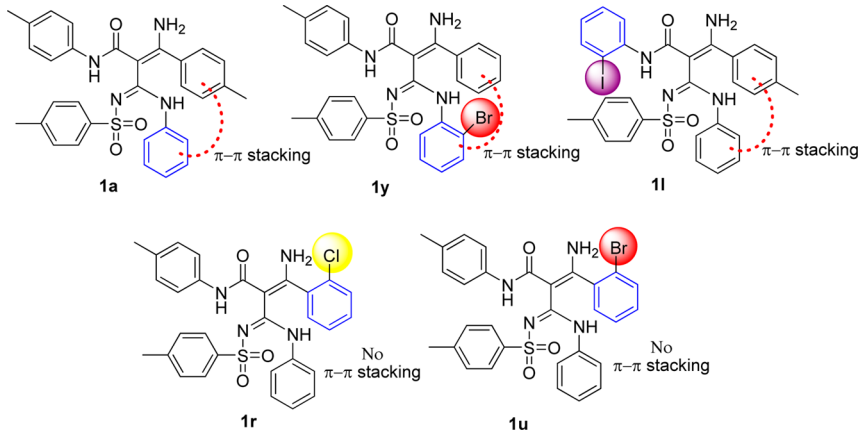


Table 3. Crystal Data of 1a, 1y, 1l, 1r, and 1u

	1a	1y	1l	1r	1u
formula	$C_{31}H_{30}N_4O_3S$	$C_{30}H_{27}BrN_4O_3S$	$C_{30}H_{27}IN_4O_3S$	$C_{124}H_{108}Cl_4N_{16}O_{14}S_4$	$C_{124}H_{108}Br_4N_{16}O_{14}S_4$
CCDC no.	989236	989083	989238	989239	989237
system	triclinic	triclinic	monoclinic	monoclinic	monoclinic
space group	*P*1	*P*1	*P*21/*c*	*P*21/*c*	*P*21/*c*
a (Å)	10.0980(8)	9.6424(6)	14.5464(7)	12.6036(5)	12.6036(7)
b (Å)	10.4098(8)	10.3792(9)	13.4795(7)	24.3794(8)	24.4452(12)
c (Å)	14.2493(13)	15.5817(10)	18.7867(12)	10.3073(3)	10.3548(4)
α	81.816(7)	101.835(6)	90	90	90
β	71.450(7)	99.157(6)	128.458(3)	100.851(3)	100.952(5)
γ	80.408(6)	110.433(7)	90	90	90
volume (Å^3)	1393.78(19)	1384.25(17)	2884.5(3)	3110.48(18)	3132.2(3)
Z	2	2	4	4	4
D_{calcd} (g·cm^{-3})	1.283	1.448	1.498	1.194	1.280
T (K)	293	293	293	293	293
*R*1, *wR*2 [$I \geq 2\sigma(I)$]	0.0511, 0.0825	0.0433, 0.0685	0.0425, 0.0635	0.0584, 0.0797	0.0590, 0.0925
*R*1, *wR*2 (all data)	0.1162, 0.1377	0.0945, 0.1073	0.0926, 0.1053	0.1619, 0.1815	0.1621, 0.1852
S	1.037	1.046	1.040	1.071	1.016

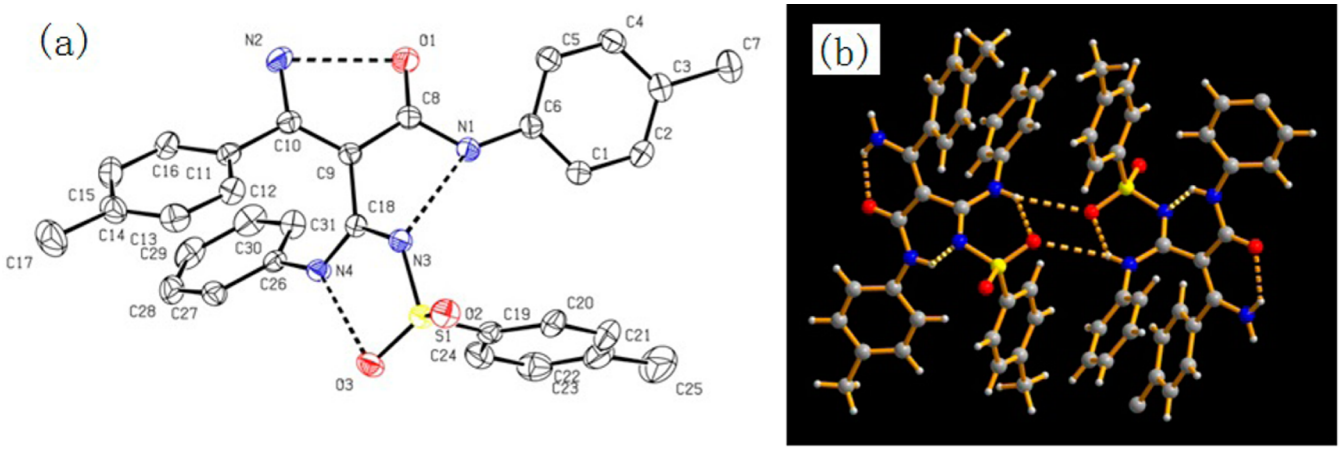


Figure 1. ORTEP view of **1a** with 30% ellipsoid probability showing intramolecular hydrogen bonds (a) and self-assembled dimer through hydrogen bonds (b). The hydrogen bonds are the dotted lines.

aromatic rings with a distance of 4.2077 Å as illustrated in Figure 1a and Scheme 2. Three intramolecular hydrogen bonds are observed. The distances of N2–H···O1, N4–H···O3, and N1–H···N3 are 2.598 Å, 2.750 Å, and 2.861 Å, respectively. **1a** self-assembles to form an anti-head-to-tail dimer via two intermolecular hydrogen bonds as shown in Figure 1b. The distance of intermolecular hydrogen bonding is determined to be 3.331 Å. Further aggregation of dimers leads to the formation of the three-dimensional architecture which adopts a triclinic system with space group of *P*1 (Figure S1, Supporting Information).

DOI: 10.1021/acs.joc.5b00827
J. Org. Chem. 2015, 80, 5842–5850

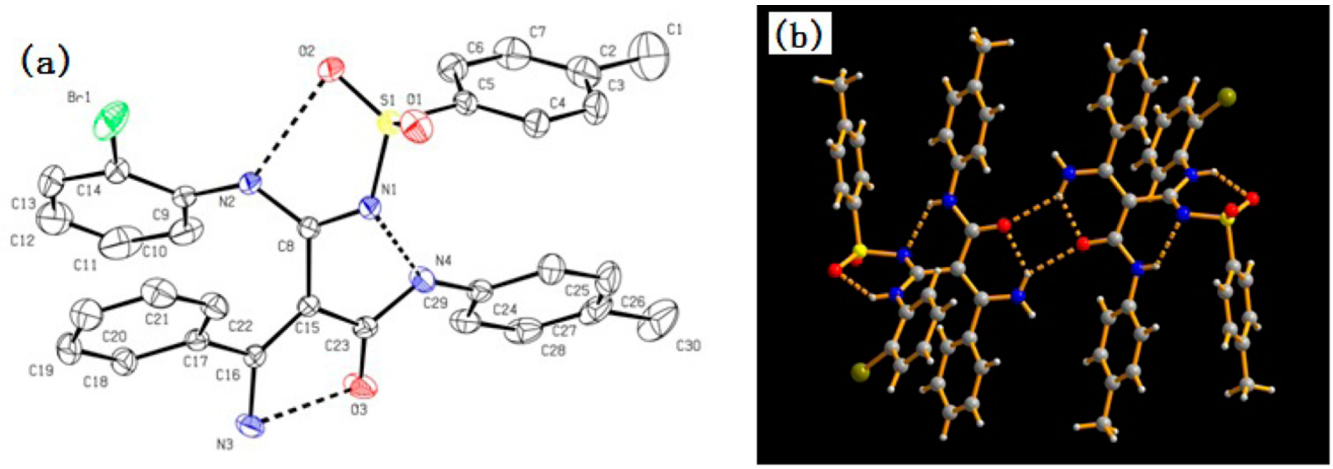


Figure 2. ORTEP view of **1y** with 30% ellipsoid probability showing intramolecular hydrogen bonds (a) and self-assembled dimer complex through two intermolecular hydrogen bonds (b). The hydrogen bonds are the dotted lines.

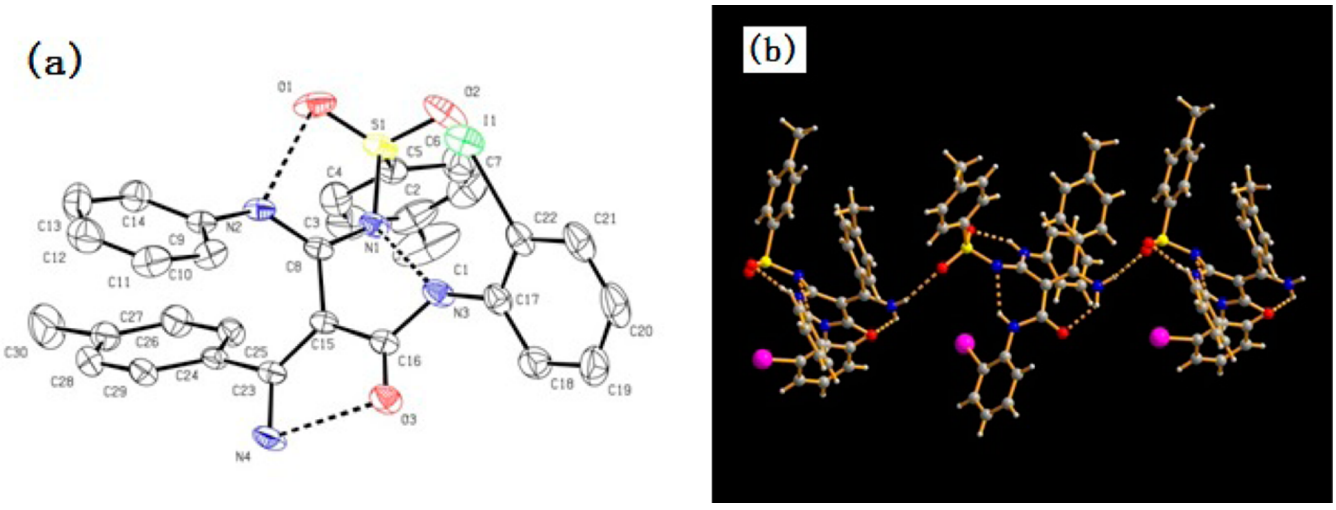


Figure 3. ORTEP view of **1l** with 30% ellipsoid probability showing intramolecular hydrogen bonds (a) and its linear formation through an intermolecular hydrogen bond (b). The hydrogen bonds are the dotted lines.

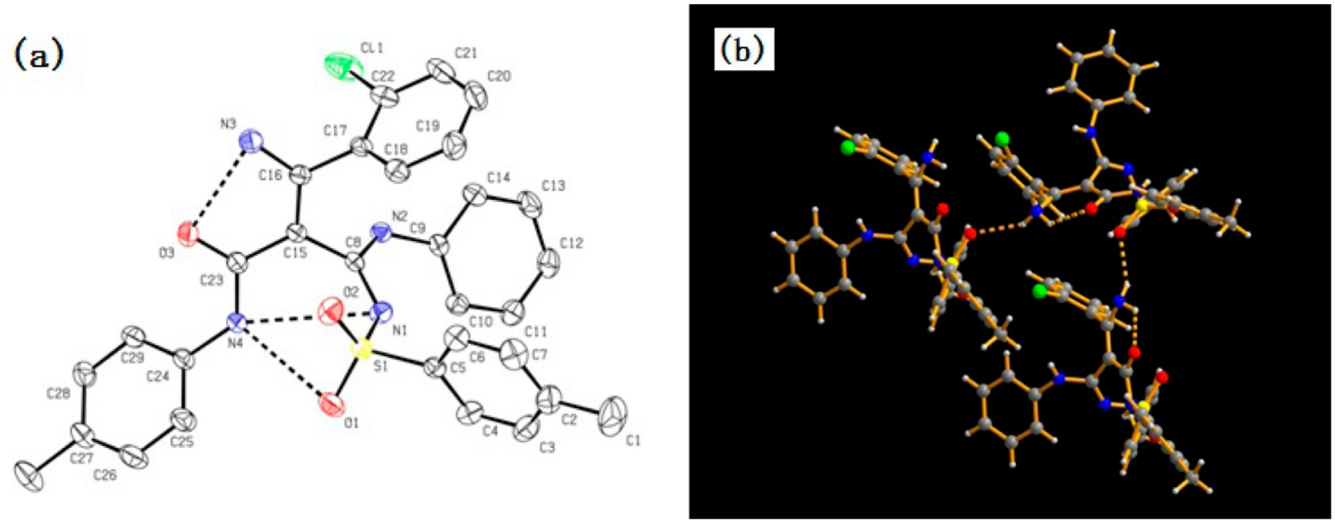


Figure 4. ORTEP view of **1r** with 30% ellipsoid probability showing intramolecular hydrogen bonds (a) and its linear formation through intermolecular hydrogen bonds (b). The hydrogen bonds are the dotted lines.

DOI: 10.1021/acs.joc.5b00827
J. Org. Chem. 2015, 80, 5842−5850

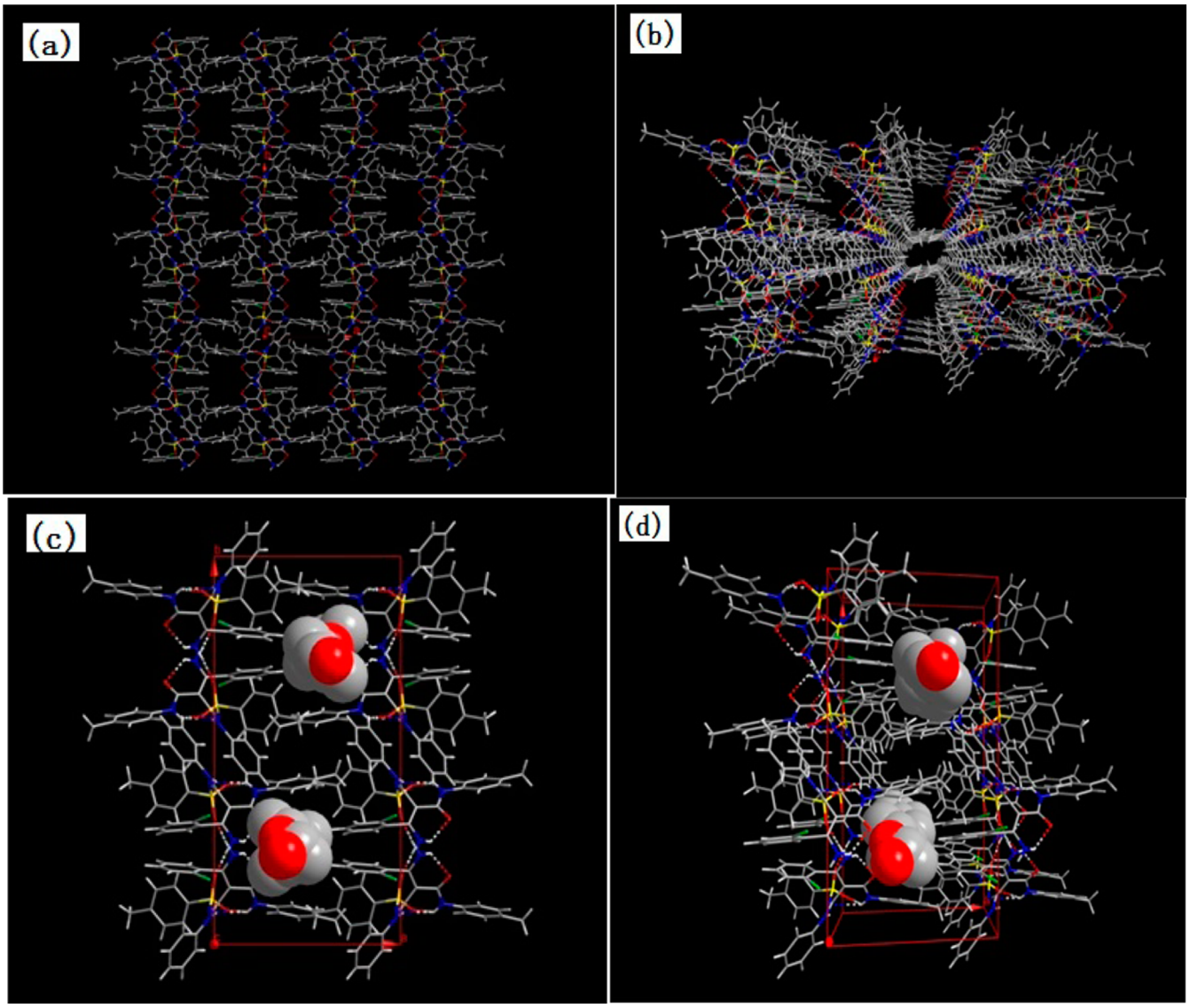


Figure 5. Crystal structures of **1r**·CH_3COOEt: (a) 2D structure of **1r** along the *c* axis; (b) channel structure of **1r**; (c) 2D structure of **1r**·CH_3COOEt along the *c* axis; (d) channel inclusion of **1r**·CH_3COOEt.

Similar architecture is observed for **1y** as shown in Figure 2. The structure comprises two planes. One is the plane of N1−C8−N2, and the other is O3−C23−C15−C16−N3. The dihedral angle is 61°. Two benzene rings stack in a distance of 4.1544 Å as indicated in Figure 2a and Scheme 2. Three intramolecular hydrogen bonds are detected. Distances of N2−H···O2, N4−H···N1, and N3−H···O3 are 2.297 Å, 2.876 Å, and 2.589 Å, respectively. Despite these common intramolecular hydrogen bonds resulting from nitrogen and oxygen, a weak intramolecular hydrogen bonding through N2−H···Br (3.059 Å) is observed. Similar to **1a**, **1y** exists in its anti-head-to-tail dimer form through two intermolecular hydrogen bonds (Figure 2b) and assembles to three-dimensional structure (Figure S2, Supporting Information) which is quite similar to that of **1a**.

When the aryl of *N*-arylpropiolamide is changed from phenyl to 2-iodophenyl, the corresponding **1l** is obtained (Scheme 2). Similar to **1a** and **1y**, the skeleton of **1l** comprises two planars: one is the plane of N1−C8−N2, and the other is the plane of O3−C16−C15−C23−N4 (Figure 3a). The dihedral angle (N1−C8−C15−C16) is 57°. An intramolecular $\pi-\pi$ stacking still exists between tolyl (on C23) and phenyl (on N2). The distance between them is calculated to be 4.3199 Å. There are three intramolecular hydrogen bonds. Distances of N2−H···O1, N3−H···N1, and N4−H···O3 are 2.690 Å, 2.854 Å, and 2.618 Å, respectively. Despite these, a weak hydrogen bonding through N3−H···I (3.197 Å) exists. Overall, the skeleton of a single molecule is quite similar to those of **1a** and **1y**. However, as the single molecule aggregates, a linear structure is assembled through intermolecular hydrogen bonding (Figure 3b). The distance of this intermolecular hydrogen bond is determined to be 3.055 Å. Further aggregation leads to three-dimensional crystalline structure in a monoclinic system with the space group of *P*21/*c* (Figure S3, Supporting Information).

The situation changes when we change phenyl to 2-chlorophenyl (Figure 4a). Although the structure of **1r** still comprises two planes, one is N3−C16−C15−C23-O3 and the other is N2−C8−N1, the dihedral angle (N1−C8−C15-C23) becomes larger (68°). There is no $\pi-\pi$ stacking between two aryl rings, which exists in the crystal structures of **1a**, **1y**, and **1l**. The reason might be the hindrance raised from the ortho chlorine on the aryl ring and the lack of hydrogen bonding between the amidine nitrogen and sulfonyl oxygen which exists in the crystal

DOI: 10.1021/acs.joc.5b00827
J. Org. Chem. 2015, 80, 5842−5850

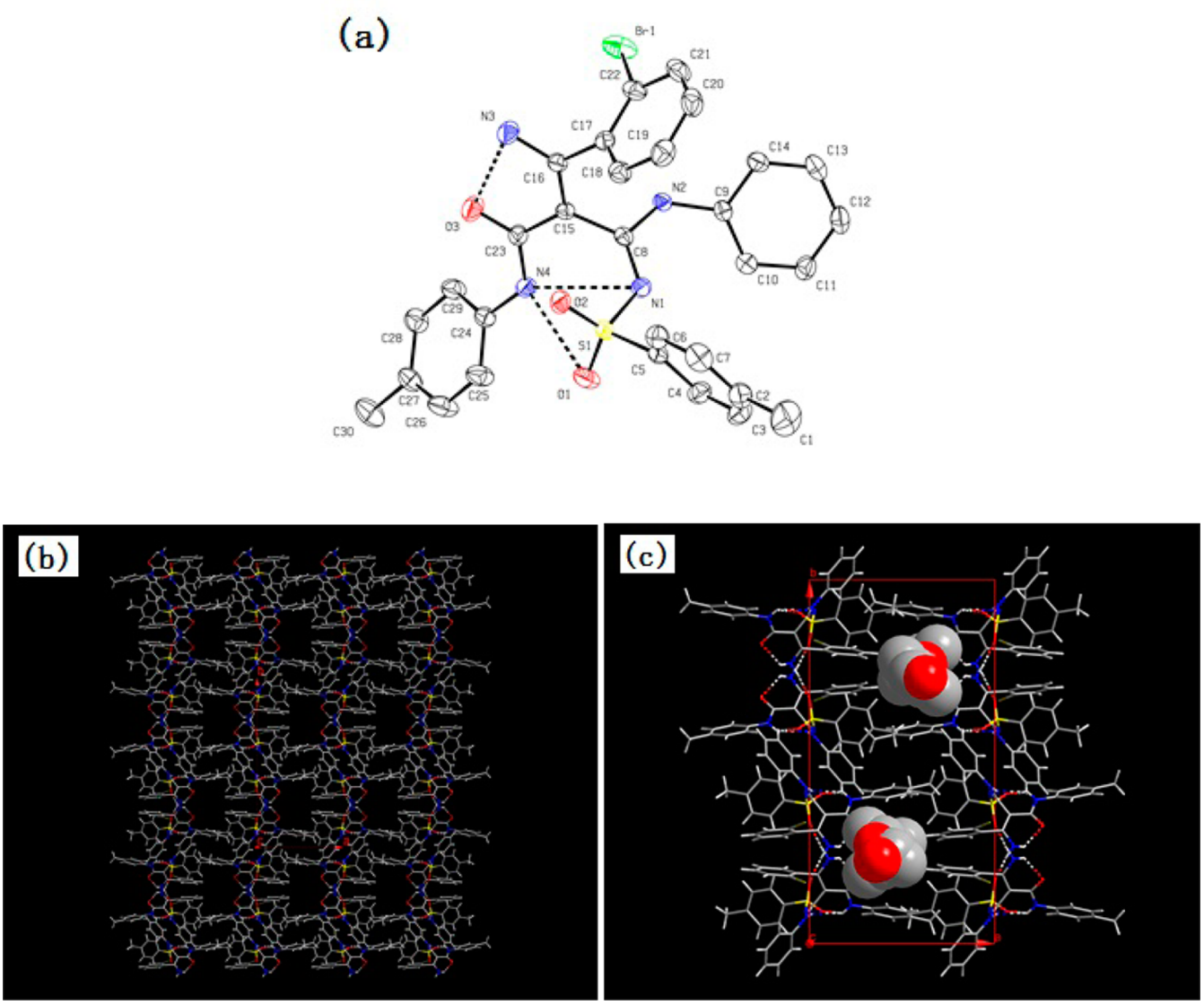


Figure 6. ORTEP view of **1u** with 30% ellipsoid probability (a), two channels in **1u** (b), and inclusion with ethyl acetate (c).

structures of **1a**, **1y**, and **1l**. Three intramolecular hydrogen bonds still exist. Distances of N3−H···O3, N4−H···N1, and N4−H···O1 are 2.644 Å, 3.177 Å, and 3.110 Å, respectively. As the molecule aggregates, a linear structure forms through intermolecular hydrogen bonds as shown in Figure 4b. The distance of the intermolecular hydrogen bonding was determined to be 2.915 Å.

As the molecules of **1r** further aggregate into a two-dimensional structure (Figure 5a), and into a three-dimensional structure (Figure 5b), one channel appears with cross-sectional areas of 5 × 3 $Å^2$. This architecture is stabilized by multiple intermolecular hydrogen bonds: C−H···π and π−π interactions with distances of 3.482[C3−H···Cg(C24 > C29)], 3.571[C30−H···Cg(C2 > C6)], 3.572[C30−H···Cg(C9 > C14)], and 3.368[Cg(C9 > C14)···Cg(C9 > C14), and further strengthened by the existence of internal disorder from ethyl acetate via van der Waals interactions. Although **1r** possesses the same crystal system (monoclinic) and the same space group ($P21/c$) as those of **1l**, a, b, and c values are totally different (Table 3).

The inclusion complex of **1r** and ethyl acetate is stable up to 130 °C. From 130 °C to 144 °C, 4.65% weight loss was observed by thermogravimetric analysis. With further heating of the sample, a plateau appeared until 210 °C. Beyond 210 °C, a steady weight loss was detected (Figure S4, Supporting Information).

Analogous to **1r**, **1u** presents a very similar crystal structure to **1r** which adopts a monoclinic system with the space group $P21/c$. Moreover, values of a, b, and c are almost identical to those of **1r** (Table 3). One channel is observed in the crystalline structure of **1u** and holds ethyl acetate as well through weak intermolecular C−H···π bonding and weak van der Waals forces (Figure 6).

In conclusion, we developed a copper-catalyzed three-component synthesis of 3-amino-2-carbamimidoylacrylamides from sulfonyl azides, propriolamides, and amidines. Lots of substituents tolerated the reaction conditions and provided 3-amino-2-carbamimidoylacrylamides in moderate to good yields. The cascade process for this transformation includes a copper-catalyzed alkyne−azide cycloaddition (CuAAC), a ring-opening of *N*-tosyl-1,4-disubstituted-1,2,3-triazole, a Dimroth rearrangement, a [2 + 2] cycloaddition of ketenimine and amidine, and a subsequent ring opening of azetidine. By analyzing the crystal structures of 3-amino-2-carbamimidoylacrylamides, three crystal systems are observed. Structures of **1a** and **1y** are triclinic with the space group $P1$ and exist as dimers via intermolecular hydrogen bonding. The structure of **1l** is monoclinic with the

DOI: 10.1021/acs.joc.5b00827
J. Org. Chem. 2015, 80, 5842−5850

space group $P21/c$ and exists as a linear structure via intermolecular hydrogen bonding. Although the same space groups ($P21/c$) were observed for **1r** and **1u**, these crystal structures lost intramolecular $\pi-\pi$ stacking and created channels for complexation with the ethyl acetate guest via intermolecular hydrogen bonds, intermolecular C−H···π and $\pi-\pi$ interactions, and van der Waals forces.

EXPERIMENTAL SECTION

General Considerations. Infrared spectra were obtained on a FTIR spectrometer. ^{1}H NMR spectra were recorded on a 500 or 400 MHz spectrometer and refer to the internal solvent signals (0 ppm for TMS in $CDCl_3$ or 2.5 ppm for residual DMSO). The following abbreviations are used to describe peak patterns where appropriate: b = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants are reported in hertz (Hz). ^{13}C NMR spectra were recorded on a 125 or 100 MHz spectrometer and refer to the internal solvent signals (77.27 ppm for $CDCl_3$ or 40.0 ppm for DMSO-d_6). High resolution mass spectroscopy (HRMS) was performed on an electron ionization time-of-flight (EI-TOF) mass spectrometer. Melting points were measured with a micro melting point apparatus.

General Procedure for the Synthesis of (*Z*)-3-Amino-2-carbamimidoylacrylamide 1. To a solution of propiolamide **3** (0.5 mmol), amidine **4** (0.5 mmol), and CuBr (0.05 mmol) in DMF (1.5 mL) protected by argon was added a solution of sulfonyl azide **2** (0.5 mmol) in DMF (0.5 mL) via syringe, and the mixture was stirred at room temperature for 18 h. After filtration, the reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with water and brine, dried over anhydrous Na_2SO_4, and evaporated in vacuum. The residue was subjected to silica gel column chromatography with ethyl acetate (EA)/petroleum ether (Pet) (1:2, v/v) as eluent to give the pure product **1**.

(*Z*)-3-Amino-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-*N*,3-di-*p*-tolylacrylamide (1a). A light yellow powder (242 mg, 90% yield); mp 187.6−188.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (b, 1H), 9.62 (s, 1H), 9.54 (s, 1H), 7.91 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.15−7.01 (m, 9H), 6.87 (d, J = 7.6 Hz, 2H), 6.45 (d, J = 7.6 Hz, 2H), 4.82 (b, 1H), 2.43 (s, 3H), 2.38 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ166.3, 163.7, 163.6, 143.8, 141.6, 139.4, 137.3, 136.0, 134.2, 133.3, 130.0, 129.4, 129.4, 129.0, 127.9, 126.7, 125.7, 123.6, 120.3, 92.7, 21.8, 21.7, 21.1; IR (KBr) ν 3454, 3308, 3239, 2917, 1595, 1562, 1513,1402, 1382, 1295, 1137, 1082, 814, 766 cm^{-1}; HRMS (EI) calcd for $C_{31}H_{30}N_4O_3S$, 538.2039; found, 538.2041.

(*Z*)-3-Amino-2-((*Z*)-*N*-phenyl-*N*′-(phenylsulfonyl)-carbamimidoyl)-*N*,3-di-*p*-tolylacrylamide (1b). A light yellow powder (178 mg, 68% yield); mp 181.1−182.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (b, 1H), 9.60 (d, J = 4.0 Hz, 2H), 8.04 (d, J = 6.8 Hz, 2H), 7.62−7.51 (m, 3H), 7.18−7.02 (m, 9H), 6.86 (d, J = 7.6 Hz, 2H), 6.46 (d, J = 7.6 Hz, 2H), 4.83 (b, 1H), 2.38 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 163.9, 163.7, 142.3, 141.7, 137.3, 136.0, 134.2, 133.4, 132.9, 129.5, 129.5, 129.0, 127.9, 126.7, 125.8, 123.6, 120.3, 92.6, 21.7, 21.1; IR (neat) ν 3410, 3265, 2922, 1593, 1561, 1512, 1444, 1311, 1290, 1233, 1080, 879, 814, 748 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{28}N_4O_3S$, 524.1882; found, 524.1882.

(*Z*)-3-Amino-2-((*Z*)-*N*′-((4-methoxyphenyl)sulfonyl)-*N*-phenylcarbamimidoyl)-*N*,3-di-*p*-tolylacrylamide (1c). A light yellow powder (216 mg, 78% yield); mp 194.0−194.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (b, 1H), 9.60 (s, 1H), 9.58 (s, 1H), 7.95 (dd, J_1 = 8.8 Hz, J_2 = 1.6 Hz, 2H), 7.16−7.02 (m, 9H), 6.97 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 7.2 Hz, 2H), 6.45 (d, J = 7.6 Hz, 2H), 4.81 (b, 1H), 3.85 (s, 3H), 2.38 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 163.6, 163.4, 163.3, 141.6, 137.4, 136.0, 134.2, 134.1, 133.4, 129.5, 129.0, 128.8, 127.9, 125.7, 123.5, 120.4, 114.6, 92.7, 21.7, 21.1; IR (neat) ν 3408, 3276, 3027, 2920, 1594, 1561, 1513, 1497, 1402, 1287, 1135, 1081, 817, 751 cm^{-1}; HRMS (EI) calcd for $C_{31}H_{30}N_4O_4S$, 554.1988; found, 554.1983.

(*Z*)-3-Amino-2-((*Z*)-*N*′-((4-chlorophenyl)sulfonyl)-*N*-phenylcarbamimidoyl)-*N*,3-di-*p*-tolylacrylamide (1d). A white powder (106 mg, 38% yield); mp 189.7−190.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.92 (b, 1H), 9.55 (d, J = 9.2 Hz, 2H), 7.97 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.20−7.08 (m, 7H), 7.03 (d, J = 8.0 Hz, 2H), 6.84 (d, J = 7.2 Hz, 2H), 6.47 (d, J = 7.6 Hz, 2H), 4.86 (b, 1H), 2.38 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 164.0, 163.9, 141.8, 140.9, 139.4, 137.2, 135.9, 134.1, 133.6, 129.7, 129.6, 129.5, 129.1, 128.2, 127.8, 125.9, 123.6, 120.3, 92.6, 21.7, 21.1; IR (neat) ν 3406, 3278, 2923, 2853, 1593, 1561, 1513, 1403, 1312, 1297, 1139, 1086, 816, 748 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{27}ClN_4O_3S$, 558.1492; found, 558.1514.

(*Z*)-3-Amino-2-((*Z*)-*N*′-(naphthalen-2-ylsulfonyl)-*N*-phenylcarbamimidoyl)-*N*,3-di-*p*-tolylacrylamide (1e). A yellow powder (210 mg, 73% yield); mp 193.7−194.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (b, 1H), 9.70 (s, 1H), 9.56 (s, 1H), 8.59 (s, 1H), 8.03−7.91 (m, 4H), 7.68−7.60 (m, 2H), 7.17−7.12 (m, 3H), 7.03 (d, J = 8.0 Hz, 2H), 6.95 (d, J = 8.0 Hz, 2H), 6.89−6.83 (m, 4H), 6.48 (d, J = 7.6 Hz, 2H), 4.81 (b, 1H), 2.34 (s, 3H), 2.251 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 163.9, 163.7, 141.6, 139.1, 137.3, 135.8, 135.2, 134.1, 133.3, 132.6, 129.9, 129.6, 129.4, 129.4, 129.0, 129.0, 128.2, 127.8, 127.7, 125.8, 123.6, 122.3, 120.2, 92.7, 21.6, 21.1; IR (neat) ν 3405, 3274, 3027, 2922, 1593, 1561, 1513, 1492, 1397, 1293, 1140, 1118, 1069, 813, 754 cm^{-1}; HRMS (EI) calcd for $C_{34}H_{30}N_4O_3S$, 574.2039; found, 574.2038.

(*Z*)-3-Amino-2-((*Z*)-*N*′-(methylsulfonyl)-*N*-phenylcarbamimidoyl)-*N*,3-di-*p*-tolylacrylamide (1f). A light yellow powder (169 mg, 73% yield); mp 180.3−181.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.95 (b, 1H), 9.80 (s, 1H), 9.27 (s, 1H), 7.52 (d, J = 8.4 Hz 2H), 7.14−7.06 (m, 7H), 6.89 (d, J = 7.2 Hz, 2H), 6.46 (d, J = 7.6 Hz, 2H), 4.90 (b, 1H), 3.18 (s, 3H), 2.38 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 164.3, 163.7, 141.7, 137.2, 136.2, 134.2, 133.5, 129.7, 129.5, 129.0, 127.7, 125.7, 123.4, 120.4, 92.4, 42.9, 21.7, 21.1; IR (neat) ν 3386, 3277, 3027, 2923, 1637, 1593, 1561, 1513, 1402, 1313, 1277, 1236, 1108, 962, 822, 751 cm^{-1}; HRMS (EI) calcd for $C_{25}H_{26}N_4O_3S$, 462.1726; found, 462.1728.

(*Z*)-3-Amino-*N*-phenyl-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-3-(*p*-tolyl)acrylamide (1g). A white powder (183 mg, 70% yield); mp 198.4−200.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (b, 1H), 9.64 (s, 2H), 7.92 (d, J = 7.6 Hz, 2H), 7.32 (d, J = 7.6 Hz, 2H), 7.26−7.25 (m, 4H), 7.18−7.02 (m, 6H), 6.87 (d, J = 7.6 Hz, 2H), 6.46 (d, J = 7.6 Hz, 2H), 4.84 (b, 1H), 2.43 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 163.8, 163.6, 143.8, 141.7, 139.4, 138.6, 137.3, 134.1, 130.1, 129.5, 129.0, 128.9, 127.9, 126.7, 125.7, 123.8, 123.6, 120.2, 92.6, 21.8, 21.7; IR (neat) ν 3409, 3267, 3060, 2923, 2852, 1592, 1561, 1529, 1496, 1390, 1280, 1136, 1078, 822, 753 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{28}N_4O_3S$, 524.1882; found, 524.1882.

(*Z*)-3-Amino-*N*-(4-methoxyphenyl)-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-3-(*p*-tolyl)acrylamide (1h). A white powder (121 mg, 44% yield); mp 147.7−148.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (b, 1H), 9.63 (s, 1H), 9.47 (s, 1H), 7.91 (d, J = 8.0 Hz, 2H),7.31 (d, J = 8.0 Hz, 2H), 7.18−7.11 (m, 5H), 7.03 (d, J = 7.6 Hz, 2H), 6.87 (d, J = 7.2 Hz, 2H), 6.80 (d, J = 8.8 Hz, 2H), 6.46 (d, J = 7.2 Hz, 2H), 4.79 (b, 1H), 3.80 (s, 3H), 2.43 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 163.7, 163.5, 156.2, 146.0, 143.8, 141.6, 139.4, 137.4, 134.2, 131.7, 130.1, 129.5, 129.0, 127.9, 126.7, 125.7, 123.6, 122.1, 114.1, 92.6, 21.8, 21.7; IR (neat) ν 3380, 3269, 3060, 2920, 1597, 1560, 1511, 1492, 1411, 1242, 1138, 1073, 843, 751 cm^{-1}; HRMS (EI) calcd for $C_{31}H_{30}N_4O_4S$, 554.1988; found, 554.1987.

(*Z*)-3-Amino-*N*-(2-bromophenyl)-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-3-(*p*-tolyl)acrylamide (1i). A white powder (118 mg, 39% yield); mp 191.5−192.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 2H), 9.59 (s, 1H), 8.04 (d, J = 8.0 Hz, 1H),7.91 (d, J = 8.0 Hz, 2H), 7.55 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 7.32−7.24 (m, 3H), 7.18−7.08 (m, 3H), 6.89−6.95 (m, 3H), 6.86 (d, J = 7.6 Hz, 2H), 6.47 (d, J = 7.6 Hz, 2H), 4.87 (b, 1H), 2.39 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 163.9, 163.5, 143.6, 141.7, 139.3, 137.4, 136.8, 134.0, 132.8, 129.8, 129.4, 129.0, 127.9, 127.8, 127.0, 125.7, 125.4, 124.1, 123.6, 116.2, 92.8, 21.8, 21.7; IR (neat) ν 3386, 3277, 3064, 2920, 1596, 1561, 1513, 1460, 1432, 1294, 1138, 1079, 823, 748 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{27}BrN_4O_3S$, 602.0987; found, 602.0996.

(*Z*)-3-Amino-*N*-(3-bromophenyl)-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-3-(*p*-tolyl)acrylamide (1j). A light yellow powder (257 mg, 85% yield); mp 179.5−180.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (b, 1H), 9.69 (s, 2H), 7.92 (d, J = 8.0 Hz, 2H), 7.48 (s,

DOI: 10.1021/acs.joc.5b00827
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1H), 7.34 (d, J = 8.0 Hz, 2H), 7.14−7.03 (m, 8H), 6.87 (d, J = 7.2 Hz, 2H), 6.45 (d, J = 7.2 Hz, 2H), 4.93 (b, 1H), 2.44 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 164.3, 163.4, 144.1, 141.9, 139.9, 139.3, 137.2, 133.9, 130.2, 130.2, 129.6, 129.0, 127.8, 126.6, 126.6, 125.8, 123.6, 122.8, 122.6, 118.7, 92.3, 21.9, 21.7; IR (neat) ν 3408, 3263, 3060, 1596, 1561, 1528, 1477, 1406, 1298, 1137, 1080, 820 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{27}BrN_4O_3S$, 602.0987; found, 602.0979.

(*Z*)-3-Amino-*N*-(4-bromophenyl)-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-3-(*p*-tolyl)acrylamide (1k). A white powder (106 mg, 35% yield); mp 180.5−180.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (b, 1H), 9.75 (s, 1H), 9.64 (s, 1H), 7.91 (d, J = 8.0 Hz, 2H), 7.36−7.32 (m, 4H), 7.18−7.08 (m, 5H), 7.03 (d, J = 8.0 Hz, 2H), 6.86 (d, J = 7.6 Hz, 2H), 6.45 (d, J = 7.2 Hz, 2H), 4.88 (b, 1H), 2.44 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 164.1, 163.5, 143.9, 141.9, 139.4, 137.8, 137.3, 134.0, 131.9, 130.1, 129.5, 129.0, 127.8, 126.7, 125.8, 123.6, 121.7, 116.1, 92.4, 21.8, 21.7; IR (neat) ν 3396, 3267, 2922, 1597, 1563, 1521, 1486, 1394, 1283, 1136, 1080, 821 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{27}BrN_4O_3S$, 602.0987; found, 602.1001.

(*Z*)-3-Amino-*N*-(2-iodophenyl)-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-3-(*p*-tolyl)acrylamide (1l). A white powder (93 mg, 29% yield); mp 169.5−170.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (b, 1H), 9.64 (s, 1H), 9.30 (s, 1H), 7.89 (d, J = 8.4 Hz, 2H), 7.81 (d, J = 7.2 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.35−7.31 (m, 1H), 7.21 (d, J = 8.0 Hz, 2H), 7.17−7.08 (m,3H), 6.99 (d, J = 7.6 Hz, 2H), 6.88−6.85 (m, 3H), 6.51 (d, J = 7.6 Hz, 2H), 4.90 (b, 1H), 2.37 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 163.8, 163.5, 143.6, 141.6, 139.5, 139.3, 139.2, 137.3, 133.9, 129.8, 129.4, 128.9, 128.7, 127.8, 126.9, 126.6, 125.7, 125.5, 123.7, 93.9, 92.5, 21.7, 21.7; IR (neat) ν 3369, 3269, 1598, 1561, 1512, 1497, 1400, 1285, 1138, 1079, 822, 752 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{27}IN_4O_3S$, 650.0849; found, 650.0842.

(*Z*)-3-Amino-*N*-(naphthalen-2-yl)-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-3-(*p*-tolyl)acrylamide (1m). A white powder (151 mg, 53% yield); mp 182.4−183.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.17 (s, 1H), 9.92 (b, 1H), 9.64 (s, 1H), 8.06−8.04 (m, 1H), 7.95 (d, J = 7.2 Hz, 1H), 7.87−7.82 (m, 3H), 7.66 (d, J = 8.4 Hz, 1H), 7.54−7.45 (m, 3H), 7.19−7.15 (m, 2H), 7.12−7.07 (m, 3H), 7.03 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 7.6 Hz, 2H), 6.51 (d, J = 7.6 Hz, 2H), 4.88 (b, 1H), 2.39 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 164.0, 163.9, 143.6, 141.7, 139.2, 137.5, 134.4, 134.2, 133.5, 129.9, 129.5, 129.1, 128.6, 127.9, 127.7, 126.6, 126.4, 126.1, 125.8, 125.7, 125.1, 123.5, 122.1, 120.1, 92.7, 21.7, 21.6; IR (KBr) ν 3352, 3273, 1597, 1565, 1477, 1389, 1140, 1081, 818, 714, 757 cm^{-1}; HRMS (EI) calcd for $C_{34}H_{30}N_4O_3S$, 574.2039; found, 574.2047.

(*Z*)-3-Amino-*N*-cyclohexyl-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-3-(*p*-tolyl)acrylamide (1n). A white powder (131 mg, 49% yield); mp 132.4−133.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (b, 1H), 9.62 (s, 1H), 7.88 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.28 (s, 1H), 7.16−7.06 (m, 3H), 7.01 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 7.6 Hz, 2H), 6.41 (d, J = 7.6 Hz, 2H), 4.63 (b, 1H), 3.76−3.67 (m, 1H), 2.44 (s, 3H), 2.36 (s, 3H), 1.95−1.84 (m, 1H), 1.70−1.57 (m, 4H), 1.36−1.26 (m, 2H), 1.15−1.08 (m, 1H), 1.01−0.94 (m, 1H), 0.77−0.72 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 163.9, 162.4, 143.6, 141.3, 139.6, 137.5, 134.4, 130.0, 129.4, 128.9, 127.8, 126.8, 125.6, 123.4, 92.7, 47.9, 33.2, 25.9, 25.1, 21.8, 21.6; IR (neat) ν 3399, 3266, 2925, 2853, 1597, 1561, 1513, 1400, 1278, 1162, 1137, 1079, 819 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{34}N_4O_3S$, 530.2352; found, 530.2347.

(*Z*)-3-Amino-3-phenyl-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-*N*-(*p*-tolyl)acrylamide (1o). A white powder (174 mg, 66% yield); mp 190.3−191.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (b, 1H), 9.65 (s, 2H), 9.53 (s, 2H), 7.91 (d, J = 8.0 Hz, 2H), 7.40 (dd, J_1 = J_2 = 7.6 Hz, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.21 (dd, J_1 = J_2 = 7.6 Hz, 2H), 7.17−7.09 (m, 5H), 7.05 (d, J = 8.4 Hz, 2H), 6.96 (d, J = 7.2 Hz, 2H), 6.44 (d, J = 7.2 Hz, 2H), 4.84 (b, 1H), 2.43 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 163.4, 163.3, 143.8, 139.4, 137.3, 137.0, 135.9, 133.4, 131.2, 130.1, 129.4, 129.0, 128.8, 127.9, 126.7, 125.7, 123.5, 120.3, 92.9, 21.8, 21.1; IR (KBr) ν 3368, 3325, 2928, 2851, 1626, 1593, 1561, 1483, 1383, 1272, 1137, 1078, 811, 769, 754 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{28}N_4O_3S$, 524.1882; found, 524.1879.

(*Z*)-3-Amino-3-(4-methoxyphenyl)-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-*N*-(*p*-tolyl)acrylamide (1p). A white powder (155 mg, 56% yield); mp 192.9−194.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (b, 1H), 9.63 (s, 1H), 9.61 (s, 1H), 7.90 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.16−7.03 (m, 7H), 6.91 (d, J = 8.0 Hz, 2H), 6.72 (d, J = 8.8 Hz, 2H), 6.47 (d, J = 7.6 Hz, 2H), 4.84 (b, 1H), 3.84 (s, 3H), 2.42 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 163.8, 163.4, 162.0, 143.8, 139.3, 137.3, 135.9, 133.3, 130.0, 129.5, 129.4, 129.1, 129.0, 126.7, 125.7, 123.5, 120.3, 114.1, 92.3, 55.7, 21.8, 21.1; IR (KBr) ν 3390, 3268, 2917, 1595, 1561, 1459, 1401, 1254, 1079, 823, 808 cm^{-1}; HRMS (EI) calcd for $C_{31}H_{30}N_4O_4S$, 554.1988; found, 554.1992.

(*Z*)-3-Amino-3-(2-fluorophenyl)-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-*N*-(*p*-tolyl)acrylamide (1q). A yellow powder (231 mg, 85% yield); mp 196.7−197.5 °C; ^{1}H NMR (400 MHz, DMSO) δ 10.07 (s, 1H), 8.56 (b, 2H), 8.22 (s, 1H),7.67 (d, J = 8.0 Hz, 2H), 7.59 (b, 1H), 7.37 (d, J = 7.2 Hz, 2H), 7.31 (d, J = 8.0 Hz, 3H), 7.14−6.99 (m, 9H), 2.35 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 165.9, 160.4, 158.0, 157.8 (d, $^1J_{CF}$ = 321.7 Hz), 142.1, 141.3, 138.7, 136.9, 132.3, 131.6 (d, $^3J_{CF}$ = 6.5 Hz), 130.4, 129.6, 129.1, 128.5, 126.5, 125.1, 124.9 (d, $^2J_{CF}$ = 15.3 Hz), 124.1 (d, $^4J_{CF}$ = 3.0 Hz), 122.2, 121.6, 116.2 (d, $^2J_{CF}$ = 21.4 Hz), 97.5, 21.4, 21.0; IR (KBr) ν 3417, 3289, 3188, 1586, 1531, 1484, 1442, 1283, 1135, 1080, 816, 759 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{27}FN_4O_3S$, 542.1788; found, 542.1794.

(*Z*)-3-Amino-3-(2-chlorophenyl)-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-*N*-(*p*-tolyl)acrylamide (1r) with ethyl acetate. A white powder (187 mg, 62% yield); mp 209.2−210.8 °C; ^{1}H NMR (400 MHz, DMSO) δ 9.65 (s, 1H), 8.56 (b, 2H), 8.23 (b, 1H), 7.66 (d, J = 7.6 Hz, 3H), 7.39−7.30 (m, 5H), 7.26−7.22 (m, 1H), 7.18−7.14 (m, 1H), 7.12−7.07 (m, 4H), 7.03−6.96 (m, 3H), 7.03−6.97 (m, 3H), 4.03 (q, J = 7.2 Hz, 1H), 2.36 (s, 3H), 2.26 (s, 3H), 1.99(s, 1.5H), 1.17 (t, J = 7.2 Hz, 1.5H); ^{13}C NMR (100 MHz, DMSO) δ 170.8, 165.9, 142.2, 141.1, 138.6, 137.0, 135.9, 132.3, 131.9, 130.9, 130.7, 129.8, 129.6, 129.1, 128.6, 126.9, 126.5, 125.1, 122.0, 121.4, 97.1, 60.3, 21.5, 21.3, 21.0, 14.6; IR (neat) ν 3397, 3271, 2923, 2853, 1593, 1561, 1512, 1402, 1141, 1076, 814, 751 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{27}ClN_4O_3S$ (M^+), 558.1492; found, 558.1495.

(*Z*)-3-Amino-3-(3-chlorophenyl)-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-*N*-(*p*-tolyl)acrylamide (1s). A white powder (168 mg, 60% yield); mp 190.3−191.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (b, 1H), 9.72 (s, 1H), 9.48 (s, 1H), 7.92 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.21−7.13 (m, 6H), 7.07 (d, J = 8.0 Hz, 3H), 6.65 (s, 1H), 6.50 (d, J = 7.6 Hz, 2H), 4.75 (b, 1H), 2.44 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 162.9, 161.2, 144.0, 139.2, 138.6, 137.1, 135.8, 134.8, 133.6, 131.1, 130.1, 129.5, 129.2, 127.9, 126.7, 126.2, 126.0, 123.4, 120.4, 93.6, 21.8, 21.1; IR (neat) ν 3396, 3266, 2923, 1593, 1561, 1512, 1403, 1298, 1139, 1080, 813 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{27}ClN_4O_3S$, 558.1492; found, 558.1489.

(*Z*)-3-Amino-3-(4-chlorophenyl)-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-*N*-(*p*-tolyl)acrylamide (1t). A yellow powder (157 mg, 56% yield); mp 193.8−194.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (b, 1H), 9.70 (s, 1H), 9.46 (s, 1H), 7.91 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.18−7.10 (m,7H), 7.06 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.0 Hz, 2H), 6.51 (d, J = 7.6 Hz, 2H), 4.74 (b, 1H), 2.44 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 163.1, 161.6, 144.0, 139.2, 137.4, 137.1, 135.8, 135.3, 133.6, 130.1, 129.5, 129.3, 129.2, 129.1, 126.8, 126.0, 123.5, 120.4, 93.4, 21.8, 21.1; IR (neat) ν 3411, 3262, 2923, 1593, 1561, 1512, 1402, 1271, 1138, 1081, 812 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{27}ClN_4O_3S$, 558.1492; found, 558.1497.

(*Z*)-3-Amino-3-(2-bromophenyl)-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-*N*-(*p*-tolyl)acrylamide (1u) with Ethyl Acetate. A white powder (103 mg, 32% yield); mp 203.1−203.8 °C; ^{1}H NMR (400 MHz, DMSO) δ 9.43 (s, 2H), 8.54 (b, 2H), 8.23 (b, 1H), 7.66 (d, J = 8.0 Hz, 3H), 7.50 (d, J = 7.2 Hz, 1H), 7.37 (d, J = 7.6 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.22−7.13 (m, 2H), 7.12−7.07 (m, 4H), 7.03−6.97 (m, 3H), 4.03 (q, J = 7.2 Hz, 1H), 2.36 (s, 3H), 2.26 (s, 3H), 1.99 (s, 1.5H), 1.18 (t, J = 7.2 Hz, 1.5H); ^{13}C NMR (100 MHz, DMSO) δ 170.9, 165.8, 159.2, 142.3, 141.1, 138.6, 137.9, 137.0, 133.1, 132.3, 131.0, 130.7, 129.7, 129.1, 128.6, 127.4, 126.5, 125.2, 122.0, 121.6, 121.3, 96.8, 60.3, 21.5, 21.3, 21.0, 14.6; IR (neat) ν 3387, 3366, 3280, 2923, 2846, 1591, 1546, 1510, 1467, 1437, 1271, 1142, 1083, 814, 757 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{27}BrN_4O_3S$ (M^+), 602.0987; found, 602.0996.

DOI: 10.1021/acs.joc.5b00827
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(*Z*)-3-Amino-2-((*Z*)-*N*-phenyl-*N*′-tosylcarbamimidoyl)-*N*-(*p*-tolyl)hept-2-enamide(1v). A white powder (179 mg, 71% yield); mp 181.2−181.5 °C; ^{1}H NMR (400 MHz, DMSO) δ 10.47 (s, 1H), 8.11 (b, 2H), 7.76 (s, 1H), 7.72 (d, J = 5.6 Hz, 2H), 7.64 (d, J = 8.0 Hz, 2H), 7.33 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 2H), 7.26 (dd, J_1 = 8.0 Hz, J_2 = 3.2 Hz, 4H), 7.13 (dd, J_1 = 7.6 Hz, J_2 = 7.2 Hz, 1H),7.03 (d, J = 8.4 Hz, 2H), 2.30 (s, 3H), 2.24 (s, 3H), 1.86−1.77 (m, 2H), 1.47 (m, 2H), 1.17−1.08 (m, 2H), 0.70 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO) δ 166.0, 163.6, 163.4, 144.0, 139.1, 138.6, 136.8, 135.8, 133.5, 131.5, 130.2, 130.1, 129.5, 129.0, 128.7, 127.8, 126.8, 126.4, 122.5, 122.4, 120.4, 92.7, 21.8, 21.1; IR (neat) ν 3416, 3267, 2956, 2925, 2855, 1596, 1561, 1511, 1438, 1311, 1141, 1085, 812, 758, 690 cm^{-1}; HRMS (EI) calcd for $C_{28}H_{32}N_4O_3S$, 504.2195; found, 504.2203.

(*Z*)-3-Amino-3-phenyl-*N*-(*p*-tolyl)-2-((*Z*)-*N*-(*p*-tolyl)-*N*′-tosylcarbamimidoyl)acrylamide (1w). A light yellow powder (246 mg, 91% yield); mp 112.8−114.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (b, 1H), 9.61 (s, 1H), 9.48 (s, 1H), 7.91 (d, J = 8.0 Hz, 2H), 7.41 (dd, J_1 = 7.6 Hz, J_2 = 7.6 Hz, 1H), 7.31 (d, J = 8.4 Hz, 2H),7.22 (dd, J_1 = 8.0 Hz, J_2 = 7.6 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 7.6 Hz, 2H), 6.99 (d, J = 7.2 Hz, 2H), 6.94 (d, J = 8.4 Hz, 2H), 6.32 (d, J = 8.0 Hz, 2H), 4.80 (b, 1H), 2.43 (s, 3H), 2.31 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 163.5, 163.0, 143.8, 139.4, 137.0, 135.9, 135.6, 134.7, 133.4, 131.1, 130.0, 129.5, 129.4, 128.8, 128.0, 126.7, 123.5, 120.4, 93.1, 21.8, 21.2, 21.1; IR (KBr) ν 3405, 3274, 2974, 2922, 1593, 1560, 1512, 1404, 1137, 1082, 808, 769 cm^{-1}; HRMS (EI) calcd for $C_{31}H_{30}N_4O_3S$, 538.2039; found, 538.2034.

(*Z*)-3-Amino-2-((*Z*)-*N*-(4-methoxyphenyl)-*N*′-tosylcarbamimidoyl)-3-phenyl-*N*-(*p*-tolyl)acrylamide (1x). A white powder (143 mg, 52% yield); mp 175.9−177.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (b, 1H), 9.60 (s, 1H), 9.44 (s, 1H), 7.91 (d, J = 8.0 Hz, 2H), 7.41 (dd, J_1 = 7.2 Hz, J_2 = 7.6 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.23 (dd, J_1 = 8.0 Hz, J_2 = 7.6 Hz, 2H), 7.14 (d, J = 8.4 Hz, 2H), 7.06−7.01 (m, 4H), 6.67 (d, J = 8.8 Hz, 2H), 6.34 (d, J = 8.8 Hz, 2H), 4.82 (b, 1H), 3.78 (s, 3H), 2.43 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 163.5, 162.8, 157.6, 143.7, 139.4, 137.0, 135.9, 133.3, 131.1, 130.2, 130.0, 129.4, 128.8, 128.0, 126.7, 125.0, 120.3, 114.1, 92.9, 55.7, 21.8, 21.1; IR (KBr) ν 3405, 3280, 2973, 2924, 1594, 1561, 1509, 1403, 1248, 1137, 1082, 820, 769 cm^{-1}; HRMS (EI) calcd for $C_{31}H_{30}N_4O_4S$, 554.1988; found, 554.1989.

(*Z*)-3-Amino-2-((*Z*)-*N*-(2-bromophenyl)-*N*′-tosylcarbamimidoyl)-3-phenyl-*N*-(*p*-tolyl)acrylamide (1y). A white powder (126 mg, 42% yield); mp 195.7−196.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 (b, 1H), 9.85 (s, 1H), 9.70 (s, 1H), 7.92 (d, J = 8.0 Hz, 2H), 7.45−7.42 (m, 1H), 7.33−7.30 (m, 3H), 7.26−7.19 (m, 5H), 7.08 (d, J = 8.0 Hz, 2H), 7.03 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 2H), 6.99−6.94 (m, 1H), 6.89 (d, J = 7.2 Hz, 2H), 4.86 (b, 1H), 2.43 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 163.8, 162.7, 143.9, 139.1, 136.9, 136.1, 135.9, 133.5, 132.8, 131.8, 130.0, 129.5, 129.1, 127.7, 127.6, 126.9, 126.5, 125.2, 120.3, 117.9, 92.5, 21.8, 21.1; IR (neat) ν 3390, 3253, 1590, 1557, 1513, 1394, 1290, 1139, 1081, 825, 775, 748, 796 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{27}BrN_4O_3S$,602.0987; found, 602.0996.

(*Z*)-3-Amino-2-((*Z*)-*N*-(3-bromophenyl)-*N*′-tosylcarbamimidoyl)-3-phenyl-*N*-(*p*-tolyl)acrylamide (1z). A light yellow powder (169 mg, 56% yield); mp 191.2−191.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (b, 1H), 9.58 (s, 2H), 7.90 (d, J = 8.4 Hz, 2H), 7.48−7.45 (m, 1H), 7.26−7.23 (m, 5H), 7.17 (d, J = 8.4 Hz, 2H), 7.08−7.04 (m, 3H), 6.60 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 2H), 6.32 (s, 1H), 4.93 (b, 1H), 2.44 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 163.6, 163.4, 144.0, 139.1, 138.6, 136.8, 135.8, 133.5, 131.5, 130.2, 130.1, 129.5, 129.0, 128.7, 127.8, 126.8, 126.4, 122.5, 122.4, 120.4, 92.7, 21.8, 21.1; IR (neat) ν 3409, 3271, 1590, 1560, 1512, 1474, 1418, 1290, 1139, 1081, 831, 763 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{27}BrN_4O_3S$, 602.0987; found, 602.0988.

(*Z*)-3-Amino-2-((*Z*)-*N*-(4-bromophenyl)-*N*′-tosylcarbamimidoyl)-3-phenyl-*N*-(*p*-tolyl)acrylamide (1A). A light yellow powder (191 mg, 64% yield); mp 121.4−122.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.95 (b, 1H), 9.55 (s, 2H), 7.90 (d, J = 8.0 Hz, 2H), 7.43 (m, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.28−7.24 (m, 4H), 7.15 (d, J = 8.4 Hz, 2H), 7.07−7.01 (m, 4H), 6.32 (d, J = 8.4 Hz, 2H), 4.91 (b, 1H), 2.44 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 163.4, 163.2, 144.0, 139.1, 136.8, 136.4, 135.8, 133.5, 132.1, 131.4, 130.1, 129.5, 129.0, 127.9, 126.8, 125.0, 120.3, 119.1, 92.6, 21.8, 21.1; IR (neat) ν 3405, 3267, 2923, 1592, 1561, 1512, 1401, 1296, 1138, 1082, 811, 796 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{27}BrN_4O_3S$, 602.0987; found, 602.0983.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details, copies of ^{1}H and ^{13}CNMR spectra for all new compounds, and crystallographic information (CIF file) for compounds **1a**, **1y**, **1l**, **1r**, and **1u**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00827.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the National Nature Science Foundation of China (nos. 21272204 and 21272203).

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DOI: 10.1021/acs.joc.5b00827
J. Org. Chem. 2015, 80, 5842−5850