JOC The Journal of Organic Chemistry

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Approaches to the Construction of Substituted 4-Amino-1*H*-pyrrol-2(5*H*)-ones

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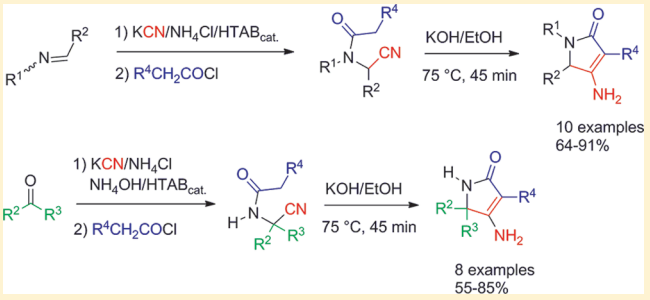
Supporting Information

ABSTRACT: Fully substituted 4-aminopyrrolones are easily accessed via simple routes starting from imines, ketones, or α-bromophenyl acetonitriles. Imines were reacted with KCN/NH_4Cl in aqueous ethanol to produce α-arylamino benzyl cyanides. On the other hand, ketones were transformed to the desired α-amino nitriles using a modified Strecker reaction. Then, α-amino nitrile precursors were allowed to react with a suitable acyl halide to produce the corresponding amides. Further treatment of these amides with ethanolic KOH converted them to highly substituted 4-amino-1*H*-pyrrol-2(5*H*)-one derivatives in moderate to excellent yields.



Pyrrolones are well-known compounds because of their existence in natural products,[1−3] vast number of biological activities,[4−6] and potential for applications in drug development[7−10] and the agricultural industry.[11,12] In one approach to synthesize pyrrolone derivatives, α,β-diketones react smoothly in aqueous solutions at room temperature with a variety of acetamides possessing a strong electron-withdrawing group in the α-position to give 3-substituted 5-hydroxy-1*H*-pyrrol-2(5*H*)-ones.[13] Another approach utilizes cycloisomerization reaction of alkylidenecarbene derivative of amides intermediate to the corresponding pyrrolones.[14] In a similar route, substituted cyclohepta[*b*]pyrrol-2-ones have been prepared via the base-promoted reaction between diethyl diazomethy1 phosphonates and 2-oxopropanamide derivatives.[15] In addition, it has been shown that benzoylformanilide undergoes a condensation reaction with acetophenones to yield aldol-type products which after subsequent treatment with HCl convert to the desired pyrrolones.[16] Another method benefits from ruthenium-catalyzed reaction of α,β-unsaturated imines with carbon monoxide and ethylene for synthesizing 1,3-dihydro-pyrrol-2-one ring systems.[17]

More recently, a super acid-catalyzed aza-Nazarov-type cyclization has been reported for the synthesis of a fused multiring pyrrolone system.[18] In addition, flash vacuum pyrolysis at 600 °C of methylaminomethylene derivatives of Meldrum's acid provides *N*-unsubstituted 3-hydroxypyrroles and/or 1*H*-pyrrol-3(2*H*)-ones in good yields.[19]

Despite simple pyrrolones having no functional groups, 4-aminopyrrolone derivatives are little known compounds, and there are few reports about their synthesis in the literature. The only reported examples of 4-amino-substituted pyrrolone have been prepared by the reaction of pyrrolidin-2,4-diones with primary amine derivatives.[20]

Although the aforesaid protocols provide rather efficient access to some pyrrolones, they work only with more acidic methylene compounds such as β-keto esters and suffer from the use of corrosive reagents, harsh reaction conditions, expensive catalysts or reagents, and environmentally pollutant organic solvents. Therefore, developing a simple and versatile method for the preparation of 4-aminopyrrolones can be an important goal in synthetic organic chemistry. Herein, we report simple and efficient routes for the synthesis of highly substituted 4-aminopyrrolones from readily available starting materials.

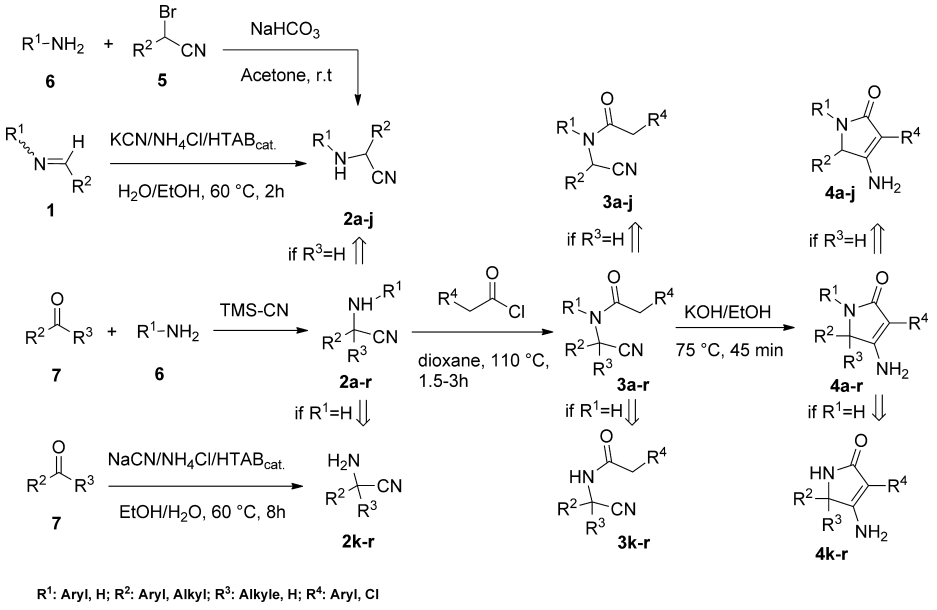
All imines used in this study were prepared by direct condensation of the benzaldehyde derivatives and anilines in ethanol. At the outset of one of approaches, a solution of aldimines **1** in EtOH was reacted with aqueous solution of KCN in the presence of equimolar amounts of NH_4Cl and catalytic amount of hexadecyltrimethylammonium bromide (HTAB) to produce α-arylamino derivatives of the corresponding aryl acetonitrile **2a−j** (Scheme 1). Secondary amines **2a−j** also could be available directly by means of the three-component reaction between aldehydes, amines, and trimethylsilyl cyanide TMS-CN (modified Strecker reaction).[21] TMS-CN works better in cyanoamination reactions, but KCN is a cheap and industrial reagent; however, its toxicity does not make it an environmentally friendly reagent. The secondary amines **2a−j** were treated with phenyl acetyl chloride in refluxing dioxane to give the corresponding amides **3a−j** which, after treatment with ethanolic KOH, transformed to the desired 4-amino-1,3,5-triaryl-1*H*-pyrrol-2(5*H*)-ones **4a−j** in rather good to excellent yields (64−91%).

In another approach, α-bromobenzyl cyanides **5** were chosen and reacted with aromatic amines **6** to produce the desired substrate **2** and then by the same route converted to the corresponding 4-aminopyrrolones **4**. In order to evaluate the

Received: March 5, 2012
Published: June 4, 2012

dx.doi.org/10.1021/jo3004309 | *J. Org. Chem.* 2012, 77, 5808−5812

Scheme 1



R^1: Aryl, H; R^2: Aryl, Alkyl; R^3: Alkyle, H; R^4: Aryl, Cl

scope and the versatility of the method, other types of imines were also investigated in the reaction course. Hence, ketimines formed as intermediates in the modified Strecker reaction of ketones **7** were directly transformed to primary amines **2k–r** with a mixture of KCN/NH_4Cl/NH_4OH/HTAB in one step, and after treatment with an acetyl chloride derivative, amides **3k–r** were produced in nearly quantitative yields. Further treatment of the amides **3k–r** with KOH/EtOH converted them to the corresponding 3,5,5-trisubstituted 4-amino-1*H*-pyrrol-2(5*H*)-ones **4k–r** in moderate to good yields (55–85%).

To obtain the best results, influencing factors such as the solvent and the base type were changed, and the screening results are summarized in Table 1.

Table 1. Solvent and Base Screening in the Synthesis of Pyrrolone 4a

entry	solvent	base	yield (%)
1	DMF	K_2CO_3	37
2	DMF	Et_3N	41
3	DMF	DBU	59
4	DMF	KOH	67
5	NMP	KOH	68
6	MeOH	MeONa	31
7	EtOH	KOH	91[a]
8	solvent-free[b]	KOH	34

[a]amide **3a** (1 mmol), KOH (1.2 mmol, 0.2 mL, 6 M), EtOH (4 mL), 45 min. [b]At 100 °C or at the melting point of the mixture, 60 min.

It is notable that increasing the reaction time and temperature higher does not increase the yield of pyrrolones, and our examinations demonstrated that in these situations the reaction mixture was contaminated with some colored or tarry materials. We were also surprised to find that MeONa/MeOH showed little conversion to the desired product **4a** and mainly the formation of decomposition products were observed. This is probably attributed to the higher basicity of MeONa/MeOH compared to KOH, favoring the elimination of HCN from cyanomethylamides.

Using the optimized conditions, we next showed the generality of the reaction by successful synthesis of eighteen new 4-amino-1*H*-pyrrol-2(5*H*)-ones in moderate to excellent yields (55–91%, Table 2).

Feasibility of the method for the preparative synthesis of the pyrrolone product was also investigated. Hence, starting from compound **1a** on a 25 mmol scale, compound **4a** was obtained in 72% overall yield in three steps.

In summary, efficient and novel approaches for the synthesis of highly substituted 4-amino-1*H*-pyrrol-2(5*H*)-one derivatives from readily available starting materials have been developed. In addition to the simplicity of the methods, high yields, and easy workup, the salient futures of the methodologies lie in the fact that the reactions are carried out using cheap starting materials and in aqueous alcohols as safe and rather green solvent. Additionally, purification of the products achieves with a simple recrystallization in EtOH (95%). Moreover, the method is compatible with a wide range of substituents such as halogen, alkoxy, alkylthio, bulky aryl groups, etc. in the substrates.

EXPERIMENTAL SECTION

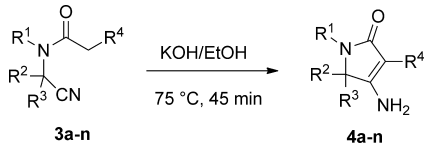
Caution! Potssium cyanide is highly toxic. Care should be taken to avoid direct contact of the chemical or its solutions with the skin, and impervious gloves should be worn to handle the reagent. All discarded aqueous extracts should be neutralized with bleach before disposal.

General procedure for the preparation of amines **2a–j**: A solution of KCN (4M, 5.2 mL, 20.8 mmol) and HTAB (40 mg) was added with vigorous stirring to a solution of aldimines **1a–j** (20 mmol) in EtOH (30 mL) at ambient temperature. Thereafter, the reaction mixture was heated at 60 °C, and a solution of NH_4Cl (4 M, 6 mL, 24 mmol) was added dropwise during 2 min. After heating and stirring for a further two hours, the reaction mixture was poured in a mixture of ice–water and the crude product was filtered. Final purification was achieved by crystallization from EtOH (95%) to afford amines **2a–j** as white or off-white materials.

General procedure for the preparation of amines[1] **2k–n**: To a solution of KCN (50 mmol, 3.25 g) in water (5 mL), NH_4Cl (3.24 g, 60 mmol) in warm water (45 °C, 6 mL), and HTAB[2] (70 mg) were added. The solution was smoothly stirred and a solution of acetophenone derivatives (49 mmol) in EtOH (16 mL) was added. Then, the reaction mixture was stirred at 60 °C for a further 8 h. After cooling to 5 °C a semisolid or an oily crude product was obtained.

dx.doi.org/10.1021/jo3004309 | J. Org. Chem. 2012, 77, 5808–5812

Table 2. Construction of Highly Substituted 4-Amino-1*H*-pyrrol-2(5*H*)-ones



3a-n **4a-n**

entry	R^1	R^2	R^3	R^4	product[a]	yield[b] (%)
1	4-MePh	Ph	H	Ph	**4a**	91
2	Ph	4-MePh	H	Ph	**4b**	81
3	4-MePh	4-MePh	H	Ph	**4c**	83
4	Ph	4-ClPh	H	Ph	**4d**	87
5	4-MePh	4-ClPh	H	Ph	**4e**	89
6	4-MePh	4-MeSPh	H	Ph	**4f**	79
7	Ph	3,4-di-MeOPh	H	Ph	**4g**	80
8	4-MePh	3,4-di-MeOPh	H	Ph	**4h**	82
9	4-MePh	2-thienyl	H	Ph	**4i**	77
10	4-MePh	9-anthracenyl	H	Ph	**4j**	64
11	H	Me	Ph	Ph	**4k**	78
12	H	Me	4-MePh	Ph	**4l**	76
13	H	Me	4-ClPh	Ph	**4m**	85
14	H	CN	Ph	Cl	**4n**	70
15	H	Et	Et	Ph	**4o**	68
16	H	Et	Me	Ph	**4p**	66
17	H	Bn	Bn	Ph	**4q**	58
18	H		$-CH_2(CH_2)_3CH_2-$	Ph	**4r**	55

[a]All products were characterized by IR, ^{1}H NMR, ^{13}C NMR, and elemental analysis. [b]All yields refer to pure isolated products.

Further purification was achieved with flash chromatography on silica gel using a mixture of EtOAc–hexane (1:4) as eluent.

General procedure for the preparation of amides **3a–n** in dioxane: In a round-bottomed flask, an acetyl chloride derivative (11 mmol) was added dropwise at ambient temperature to a solution of amines **2a–n** (10 mmol) in dioxane (10 mL) with good stirring. The reaction mixture was heated at reflux conditions for further 3 h. Then, the reaction mixture was cooled and poured into a mixture of ice–water. The precipitated crude product was filtered and recrystallized in EtOH (95%) to afford the corresponding amides as white solids.

General procedure for the conversion of amides **3a–n** to 4-amino-1*H*-pyrrol-2(5*H*)-ones **4a–n**: In a round-bottom flask, amide **3** (2 mmol) was dissolved in EtOH (95%, 5 mL) by heating the mixture at 75 °C. Then KOH solution (5 M, 0.5 mL) was added, and the reaction mixture was vigorously stirred and heated at the same temperature for further 45 min. After the reaction mixture was cooled to room temperature, water (10 mL) was added and the crude precipitated product filtered. Thereafter, the crude off-white solid compound was recrystallized from EtOH (95%) to afford pure 4-amino-1*H*-pyrrol-2(5*H*)-one **4** as a white and odorless solid.

4-Amino-3,5-diphenyl-1-*p*-tolyl-1*H*-pyrrol-2(5*H*)-one (compound **4a**): white solid (619 mg, 91%); mp 219–220 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.18–7.58 (m, 12 H), 6.98 (d, J = 5.6 Hz, 2 H), 6.51 (s, 2 H), 5.72 (s, 1 H), 2.15 (s, 3H); ^{13}CNMR (100 MHz, DMSO-d_6) δ 170.7, 160.3, 138.1, 136.3, 133.3, 131.9, 129.3, 129.1, 128.6, 128.3, 128.1, 128.0, 125.8, 121.0, 98.3, 62.9, 21.0. Anal. Calcd for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.27. Found: C, 81.20; H, 5.95; N, 8.24.

4-Amino-1,3-diphenyl-5-*p*-tolyl-1*H*-pyrrol-2(5*H*)-one (compound **4b**): white solid (551 mg, 81%); mp 226–227 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.54–7.59 (m, 4 H), 7.36 (t, J = 7.6 Hz, 2 H), 7.27 (d, J = 7.6 Hz, 2 H), 7.18–7.20 (m, 3 H), 7.11 (d, J = 7.6 Hz, 2 H), 6.89 (t, J = 7.2 Hz, 1 H), 6.52 (s, 2 H), 5.71 (s, 1 H), 2.23 (s, 3 H); ^{13}CNMR (100 MHz, DMSO-d_6) δ 170.8, 160.6, 139.0, 137.8, 135.1, 133.3, 129.7, 128.8, 128.5, 128.3, 127.8, 125.7, 122.6, 120.6, 98.0, 62.5, 21.2. Anal. Calcd for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23. Found: C, 81.12; H, 5.96; N, 8.25.

4-Amino-3-phenyl-1,5-di-*p*-tolyl-1*H*-pyrrol-2(5*H*)-one (compound **4c**): white solid (588 mg, 83%); mp 224–228 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.58 (d, J = 7.6 Hz, 2 H), 7.41 (d, J = 8.4 Hz, 2 H), 7.35 (t, J = 7.2 Hz, 2 H), 7.24 (d, J = 7.6 Hz, 2 H), 7.19 (t, J = 6.4 Hz, 1 H), 7.10 (d, J = 6.4 Hz, 2 H), 6.98 (d, J = 7.6 Hz, 2 H), 6.46 (s, 2 H), 5.66 (s, 1 H), 2.22 (s, 3 H), 2.15 (s, 3 H); ^{13}CNMR (100 MHz, DMSO-d_6) δ 170.6, 160.4, 137.8, 136.4, 135.1, 133.4, 131.6, 129.7, 129.3, 128.5, 128.3, 127.9, 125.7, 121.0, 98.1, 62.7, 21.2, 20.8. Anal. Calcd for $C_{24}H_{22}N_2O$: C, 81.33; H, 6.26; N, 7.90. Found: C, 81.35; H, 6.30; N, 7.85.

4-Amino-5-(4-chlorophenyl)-1,3-diphenyl-1*H*-pyrrol-2(5*H*)-one (compound **4d**): white solid (628 mg, 87%); mp 254–257 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.54–7.59 (m, 4 H), 7.35–7.43 (m, 6 H), 7.18–7.21 (m, 3 H), 6.91 (t, J = 7.2 Hz, 1 H), 6.63 (s, 2 H), 5.81 (s, 1 H); ^{13}CNMR (100 MHz, DMSO-d_6) δ 170.7, 160.2, 138.7, 137.2, 133.2, 133.1, 130.0, 129.2, 128.9, 128.5, 128.3, 125.8, 122.9, 120.8, 98.3, 62.0. Anal. Calcd for $C_{22}H_{17}ClN_2O$: C, 73.23; H, 4.75; Cl, 9.83; N, 7.76. Found: C, 73.18; H, 4.72; Cl, 9.80; N, 7.79.

4-Amino-5-(4-chlorophenyl)-3-phenyl-1-*p*-tolyl-1*H*-pyrrol-2(5*H*)-one (compound **4e**): white solid (667 mg, 89%); mp 256–257 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.57 (d, J = 7.6 Hz, 2 H), 7.34–7.42 (m, 8 H), 7.18 (t, J = 8 Hz, 1 H), 6.99 (d, J = 8 Hz, 2 H), 6.57 (s, 2 H), 5.76 (s, 1 H), 2.16 (s, 3 H); ^{13}CNMR (100 MHz, DMSO-d_6) δ 170.5, 160.0, 137.2, 136.2, 133.2, 133.1, 131.9, 130.0, 129.3, 129.1, 128.5, 128.3, 125.8, 121.0, 98.2, 62.1, 20.8. Anal. Calcd for $C_{23}H_{19}ClN_2O$: C, 73.69; H, 5.11; Cl, 9.46; N, 7.47. Found: C, 73.65; H, 5.15; Cl, 9.40; N, 7.50.

4-Amino-5-(4-(methylthio)phenyl)-3-phenyl-1-*p*-tolyl-1*H*-pyrrol-2(5*H*)-one (compound **4f**): white solid (610 mg, 79%); mp 228–229 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.59 (d, d, J = 8.2 Hz, J = 1.2 Hz, 2 H), 7.43 (d, J = 8.4 Hz, 2 H), 7.37 (t, J = 7.6 Hz, 2 H), 7.31 (d, J = 8.4 Hz, 2 H), 7.17–7.21 (m, 3 H), 7.00 (d, J = 8.4 Hz, 2 H), 6.50 (s, 2 H), 5.70 (s, 1 H), 2.42 (s, 3 H), 2.18 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.1, 159.7, 138.0, 135.8, 134.1, 132.8, 131.2, 128.8, 128.1, 128.0, 127.7, 125.8, 125.2, 120.5, 97.7, 61.9, 20.3, 14.3. Anal. Calcd for $C_{24}H_{22}N_2OS$: C, 74.58; H, 5.74; N, 7.25; S, 8.30. Found: C, 74.60; H, 5.71; N, 7.30; S, 8.28.

4-Amino-5-(3,4-dimethoxyphenyl)-1,3-diphenyl-1*H*-pyrrol-2(5*H*)-one (compound **4g**): white solid (618 mg, 80%); mp 192–195 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.56–7.58 (m, 4 H), 7.36 (t, J = 7.6 Hz, 2 H), 7.17–7.21 (m, 3 H), 7.02 (s, 1 H), 6.82–6.92 (m, 3 H), 6.52

dx.doi.org/10.1021/jo3004309 | J. Org. Chem. 2012, 77, 5808–5812

(s, 2 H), 5.67 (s, 1 H), 3.73 (s, 3 H), 3.68 (s, 3 H); ^{13}CNMR (100 MHz, DMSO-d_6) δ 170.7, 160.7, 149.1, 148.9, 139.1, 133.4, 130.1, 128.8, 128.5, 128.3, 125.7, 122.7, 120.7, 119.6, 112.3, 111.9, 97.8, 62.6, 55.9, 55.9. Anal. Calcd for $C_{24}H_{22}N_2O_3$: C, 74.59; H, 5.74; N, 7.25. Found: C, 74.64; H, 5.70; N, 7.28.

4-Amino-5-(3,4-dimethoxyphenyl)-3-phenyl-1-*p*-tolyl-1*H*-pyrrol-2(5*H*)-one (compound **4h**): yellow solid (656 mg, 82%); mp 155−160 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.59 (d, J = 7.2 Hz, 2 H), 7.44 (d, J = 8 Hz, 2 H), 7.36 (t, J = 7.2 Hz, 2 H), 7.18 (t, J = 7.2 Hz, 1H), 6.99−7.00 (m, 3H), 6.81−6.88 (m, 2 H), 6.48 (s, 2 H), 5.63 (s, 1 H), 3.72 (s, 3 H), 3.68 (s, 3 H), 2.17 (s, 3 H); ^{13}CNMR (100 MHz, DMSO-d_6) 170.6, 160.5,149.1, 148.9, 136.5, 133.5, 130.2, 129.3, 128.9, 128.5, 128.3, 125.6, 121.0, 119.7, 112.3, 111.8, 97.8, 62.7, 55.9, 55.8, 20.8. Anal. Calcd for $C_{25}H_{24}N_2O_3$: C, 74.98; H, 6.04; N, 7.00. Found: C, 74.95; H, 6.08; N, 7.04.

4-Amino-3-phenyl-5-(thiophen-2-yl)-1-*p*-tolyl-1*H*-pyrrol-2(5*H*)-one (compound **4i**): white solid (533 mg, 77%); mp 223−224 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.57 (d, J = 8.0 Hz, 2 H), 7.41−7.43 (m, 3 H), 7.36 (m, 3 H), 7.18 (t, J = 7.6 Hz, 1 H), 7.03 (d, J = 8.0 Hz, 2H), 6.94 (t, J = 4.4 Hz, 1 H), 6.64 (s, 2 H), 6.11 (s, 1 H), 2.19 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.0, 159.8, 136.1, 133.2, 129.7, 129.3,129.1, 128.5, 128.2, 128.0, 127.1, 126.7, 125.7, 121.5, 97.5, 59.1, 20.8. Anal. Calcd for $C_{21}H_{18}N_2OS$: C, 72.80; H, 5.24; N, 8.09; S, 9.26. Found: C, 72.75; H, 5.30; N, 8.05; S, 9.32.

4-Amino-5-(anthracen-10-yl)-3-phenyl-1-*p*-tolyl-1*H*-pyrrol-2(5*H*)-one (compound **4j**): white solid (564 mg, 64%); mp 296 °C dec; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (d, J = 8 Hz, 1 H), 8.60 (s, 1 H), 8.31 (d, J = 8 Hz, 1 H), 8.09, (d, J = 8 Hz, 1 H), 8.02 (d, J = 8 Hz, 1 H), 7.65−7.71 (m, 3 H), 7.52−7.56 (t, J = 8 Hz, 1 H), 7.40−7.47 (m, 5 H), 7.21 (t, J = 8 Hz, 1 H), 7.13 (d, J = 8 Hz, 2 H), 6.74 (d, J = 8 Hz, 2 H), 6.35 (s, 2 H), 1.98 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.6,161.9, 136.0, 133.7, 129.9, 129.8, 129.7, 128.9, 128.6, 128.3, 127.7, 126.7, 125.7, 125.5, 125.5, 124.2, 123.8, 123.3, 98.0, 62.5, 20.6. Anal. Calcd For $C_{31}H_{24}N_2O$: C, 84.52; H, 5.49; N, 6.36 Found: C, 84.43; H, 5.56; N, 6.21.

4-Amino-5-methyl-3,5-diphenyl-1*H*-pyrrol-2(5*H*)-one (compound **4k**): white solid (412 mg, 78%); mp 113−114 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.71 (s, 1 H), 7.58 (d, J = 7.2 Hz, 2 H), 7.45 (d, J = 7.6 Hz, 2 H), 7.27−7.38 (m, 5 H), 7.12 (t, J = 7.2 Hz, 1 H), 6.32 (s, 2 H), 1.75 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.6, 164.6, 142.8, 133.7, 128.1, 127.8, 127.4, 127.1, 126.0, 124.6, 96.5, 60.7, 23.6. Anal. Calcd for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60 Found: C, 77.30; H, 6.13; N, 10.58.

4-Amino-5-methyl-3-phenyl-5-*p*-tolyl-1*H*-pyrrol-2(5*H*)-one (compound **4l**): white solid (423 mg, 76%); mp 182−184 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.66 (s, 1 H), 7.57 (d, J = 7.2 Hz, 2 H), 7.33−7.29 (m, 4 H), 7.10−7.17 (m, 3 H), 6.27 (s, 2 H), 2.29 (s, 3 H), 1.72 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.6, 164.7, 139.8, 136.2, 133.7, 128.7, 127.8, 127.4, 125.9, 124.5, 96.4, 60.5, 23.7, 20.5. Anal. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.06 Found: C, 77.70; H, 6.55; N, 9.98.

4-Amino-5-(4-chlorophenyl)-5-methyl-3-phenyl-1*H*-pyrrol-2(5*H*)-one (compound **4m**): white solid (507 mg, 85%); mp 190−193 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.75 (s, 1 H), 7.57 (s, 2 H), 7.44 (s, 5 H), 7.32 (s, 2 H), 7.13 (s, 1 H), 6.36 (s, 2 H), 1.74 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.5, 164.3, 141.9, 133.5, 131.8, 128.1, 128.1, 127.8, 127.4, 124.7, 96.6, 60.3, 23.4. Anal. Calcd for $C_{17}H_{15}ClN_2O$: C, 68.34; H, 5.06; Cl, 11.87; N, 9.38 Found: C, 68.30; H, 5.10; Cl, 11.85; N, 9.35.

3-Amino-4-chloro-5-oxo-2-phenyl-2,5-dihydro-1*H*-pyrrole-2-carbonitrile (compound **4n**): white solid (385 mg, 70%); mp 135−137 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.99 (s, 1H), 7.88 (d, J = 6.8 Hz, 2H), 7.52 (t, J = 6.8 Hz, 1H), 7.45 (t, J = 6.8 Hz, 2H), 7.39 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.9, 157.8, 148.1, 134.2, 131.2, 128.2, 127.4, 117.8, 114.7. Anal. Calcd for $C_{11}H_8ClN_3O$: C, 56.54; H, 3.45; Cl, 15.17; N, 17.98 Found: C, 56.44; H, 3.49; Cl, 15.11; N, 17.86.

4-Amino-5,5-diethyl-3-phenyl-1*H*-pyrrol-2(5*H*)-one (compound **4o**): white solid (313 mg, 68%); mp 115−117 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.93 (s, 1H), 7.53 (d, J = 8.4 Hz, 2H), 7.29 (t, J = 8.4 Hz, 2H), 7.10 (t, J = 7.2 Hz, 2H), 6.36 (s, 2H), 1.50−1.74 (m, 4H), 0.68−0.70 (m, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.2, 161.5, 129.0, 128.1, 127.2, 124.3, 99.2, 62.5, 29.5, 7.3. Anal. Calcd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.16. Found: C, 73.11; H, 7.82; N, 12.23.

4-Amino-5-ethyl-5-methyl-3-phenyl-1*H*-pyrrol-2(5*H*)-one (compound **4p**): white solid (285 mg, 66%); mp 105−106 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.95 (s, 1H), 7.53 (d, J = 8.0 Hz, 2H), 7.27 (t, J = 8.0 Hz, 2H), 7.10 (t, J = 7.2 Hz, 2H), 6.41 (s, 2H), 1.51−1.75 (m, 2H), 1.06 (t, J = 6.8 Hz, 3H), 0.70 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.4, 163.7, 136.4, 129.0, 127.8, 126.2, 124.3, 59.0, 30.2, 25.2, 7.6. Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.95. Found: C, 72.06; H, 7.53; N, 12.23.

4-Amino-5,5-dibenzyl-3-phenyl-1*H*-pyrrol-2(5H)-one (compound **4q**): white solid (411 mg, 58%); mp 125−127 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.00 (s, 1H), 6.97−7.52 (m, 15H), 6.61 (s, 2H), 3.18−3.25 (m, 2H), 2.88−2.91 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.2, 159.6, 131.2, 130.3, 129.0, 128.2, 127.8, 127.4, 127.2, 126.2, 100.8, 63.4, 41.8. Anal. Calcd for $C_{24}H_{22}N_2O$: C, 81.33; H, 6.26; N, 7.90. Found: C, 81.46; H, 6.53; N, 7.83.

4-Amino-3-phenyl-1-azaspiro[4.5]dec-3-en-2-one (compound **4r**): white solid (267 mg, 55%); mp 85−87 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.74 (s, 1H), 7.53 (t, J = 7.2 Hz, 2H), 6.89−7.32 (m, 3H), 6.42 (s, 2H), 1.06−1.91 (m, 10 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.3, 165.4, 133.9, 129.0, 128.1, 127.3, 124.3, 59.1, 34.5, 24.4, 21.8. Anal. Calcd for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56. Found: C, 74.41; H, 7.33; N, 11.49.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Complete copies of ^{1}H NMR and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are thankful to the University of Isfahan Research Council for financial support of this work.

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dx.doi.org/10.1021/jo3004309 | *J. Org. Chem.* 2012, 77, 5808−5812