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Synthesis of 2-aryl-2*H*-[1,2,4]triazoloquinolin-3-one and 2-aryl-2*H*-[1,2,4]triazoloisoquinolin-3-one derivatives from α-chloroformylarylhydrazines hydrochloride

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ABSTRACT

The reaction of α-chloroformylarylhydrazines hydrochloride with quinoline under air provided the corresponding 2-aryl-2*H*-[1,2,4]triazoloquinolin-3-ones **3a**–**3d** in 33–42% yields and unexpected isomeric 2-aryl-2*H*-[1,2,4]triazoloisoquinolin-3-ones **4a**–**4d** in 30–42% yields. These two isomers were isolated and fully characterized by spectroscopic methods including X-ray crystallography. By employing 3-methylquinoline as the starting material under the same condition, the reaction only gave compound **3e**–**3h** as sole products in 70–82% yields without the formation of isomers. A plausible mechanism was proposed through electrophilic aromatic reaction, the tandem ring cyclization and ring-opening, and oxidation for the generation of 2-aryl-2*H*-[1,2,4]triazoloisoquinolin-3-ones (**4**).

1. Introduction

Trazodone is a heterocyclic compound widely used as an antidepressant drug with clinical success.[1] It shows medium to high affinity for several serotonin receptor, in particular for $5HT_{2A}$[2] and α_1 adrenergic receptor.[3] Many molecules related to trazodone have been studied[4] and used for therapy, examples include etoperidone[5] and nefazodone.[6] As structural analogs to trazodones, 1,2,4-triazoloquinolinones were more effective and safer antiepileptic agents,[7,8] which demonstrated comparable anticonvulsant potency to that of phenobarbital in the corresponding tests.[9,10]

In our previous study, we found α-chloroformylarylhydrazines hydrochloride **1** react with pyrimidine, pyridazine, pyridine, 1,4,5,6-tetrahydropyrimidine, and 1,3,5-triazine under air to give the corresponding 1,2,4-trazodones as single products, except for pyrimidine.[11] Furthermore, treatment of compound **1** with isoquinoline under the same conditions also provides 1,2,4-trazodone compounds in 76–81% yields as the sole products.[11]

In this work, we reported the reaction of α-chloroformylarylhydrazines hydrochloride (**1**) with quinoline. In addition to providing the anticipated product 2-aryl-2*H*-[1,2,4]triazoloquinolin-3-one, the reaction gave isomeric 2-aryl-2*H*-[1,2,4]triazoloisoquinolin-3-one in nearly equal yields. The two isomers were isolated and fully characterized by spectroscopic methods including X-ray crystallography. When using 3-methylquinoline as the starting material, the reaction only provided the corresponding 2-aryl-2*H*-[1,2,4]triazoloquinolin-3-one as a single product. A plausible mechanism was proposed for the generation of the isomers.

2. Result and discussion

We reacted α-chloroformylphenylhydrazines hydrochloride **1a** with quinoline **2a** at 80 °C under air for 2.0 h, 2-phenyl-[1,2,4]triazoloquinolin-3-one **3a** and 2-phenyl-[1,2,4]triazoloisoquinolin-3-one **4a** were isolated in 42% yield and 32% yields, respectively (see Scheme 1 and Table 1). When applying the same reaction conditions to substituted α-chloroformylarylhydrazines hydrochloride **1b**–**1d**, which equipped *p*-methyl, *p*-fluoro, and *p*-chloro on the phenyl group, the reaction also provided the corresponding two isomers in 63–75% total yields (Table 1). 1,2,4-Triazoloquinolin-3-ones **3** and 1,2,4-triazoloisoquinolin-3-ones **4** were fully characterized by spectroscopic methods including single-crystal X-ray diffraction study. The ORTEP drawing of compound **3c** and **4d** was shown in Figures 1 and 2.

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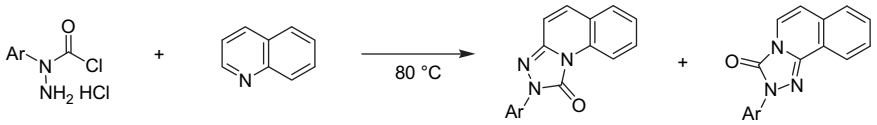


1a Ar = Ph
1b Ar = *p*-MePh
1c Ar = *p*-FPh
1d Ar = *p*-ClPh

2a **3** **4**

Scheme 1.

Table 1
Reaction of α-chloroformylarylhydrazine hydrochloride with quinoline

α-Chloroformylarylhydrazine hydrochloride		The yield (%) of isomers[a]		Total isolated yield (%) of **3** and **4**
1	Ar	**3a**–**3d**	**4a**–**4d**	
1a	Ph	42 (**3a**)	32 (**4a**)	74
1b	*p*-MePh	40 (**3b**)	35 (**4b**)	75
1c	*p*-FPh	33 (**3c**)	30 (**4c**)	63
1d	*p*-ClPh	39 (**3d**)	35 (**4d**)	74

[a] The isolation yield.

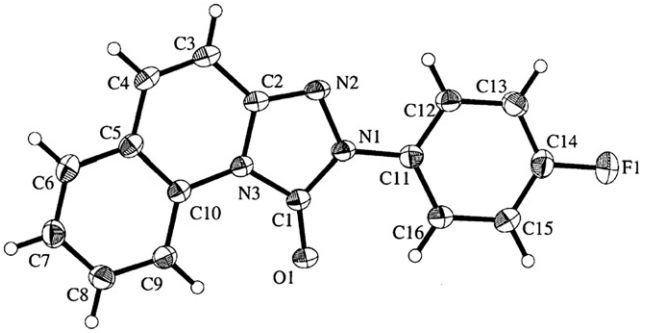


Figure 1. ORTEP diagram of 2-(*p*-fluorophenyl)-2*H*-[1,2,4]triazolo-[3,4-*a*]quinolin-3-one (**3c**).[12]

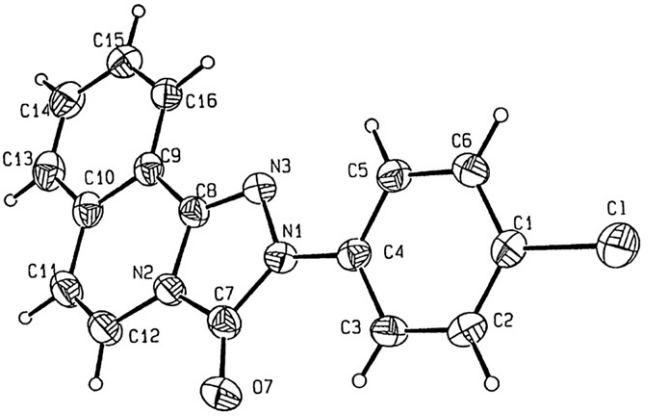


Figure 2. ORTEP diagram of 2-(*p*-chlorophenyl)-2*H*-[1,2,4]triazolo-[4,3-*a*]isoquinolin-3-one (**4d**).[13]

When using 3-methylquinoline **2b** as the substrate to react with α-chloroformylarylhydrazines hydrochloride **1a**–**1d** under the same conditions, we only obtained the corresponding 2-aryl-2*H*-[1,2,4]triazoloquinolin-3-ones **3e**–**3h** in 70–82% yields as sole products (see Scheme 2 and Table 2).

Table 2
Yields of 2-aryl-2*H*-[1,2,4]triazoloquinolin-3-one **3e**–**3h** from the reaction of α-chloroformylarylhydrazines hydrochloride **1a**–**1d** with 3-methylquinoline (**2b**)

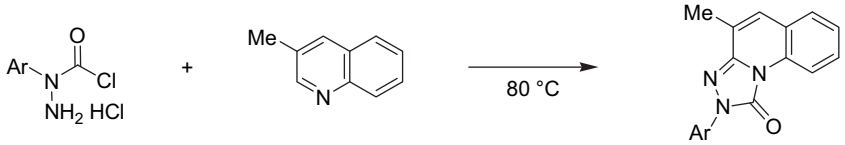
2-Aryl-2*H*-[1,2,4]triazoloquinolin-3-one **3e**–**3h**		Yield[a] (%)
3	Ar	
3e	Ph	82
3f	*p*-MePh	76
3g	*p*-FPh	72
3h	*p*-ClPh	70

[a] The isolation yield.

Scheme 3 illustrated a proposed mechanism for the generation of 1,2,4-triazoloquinolin-3-one **3** and 1,2,4-triazoloisoquinolin-3-one **4** from the reaction of α-chloroformylarylhydrazine hydrochloride **1** with quinoline **2**. For the generation of compound **3**, the electrophilic species **1** reacted with compound **2** to provide cation **5** through *N*-acylation,[11] followed by intramolecular neutralization to form intermediate **6**. In the presence of oxygen from air, oxidation reaction took place to convert **6** to compound **3** as the final product (see the path A of Scheme 3).

For compound **4**, the reaction followed electrophilic aromatic reaction to form anion **6**.[14] Then, the intramolecular bond-rotation occurred to generate intermediate **8** (see the path B of Scheme 3). The tandem ring cyclization and ring-opening proceeded to give the nitrogen atom migration intermediate **9**. After the further oxidation by oxygen from air, compound **9** was successfully converted to the final product **4**. By using 3-methylquinoline as the starting material, the similar reaction shown in the path B of Scheme 3 did not take place, possibly due to the steric hindrance at C-3 position. This would account for the sole product produced from the reaction of α-chloroformylarylhydrazine hydrochloride **1** with 3-methylquinoline.

In conclusion, the reaction of α-chloroformylarylhydrazines hydrochloride **1** with quinoline provided two isomers of 2-aryl-2*H*-[1,2,4]triazoloquinolin-3-ones **3a**–**3d** and 2-aryl-2*H*-[1,2,4]triazoloisoquinolin-3-ones **4a**–**4d**. Their structures were characterized by spectroscopic methods including X-ray crystallography.

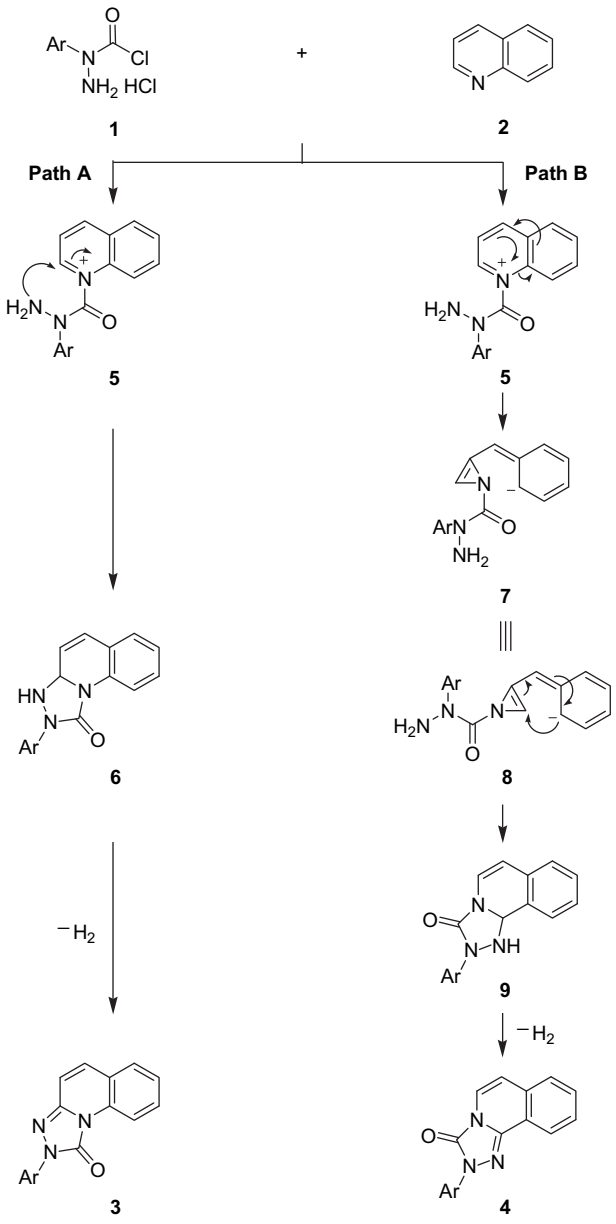


1a Ar = Ph
1b Ar = *p*-MePh
1c Ar = *p*-FPh
1d Ar = *p*-ClPh

2b

3e Ar = Ph
3f Ar = *p*-MePh
3g Ar = *p*-FPh
3h Ar = *p*-ClPh

Scheme 2.



Scheme 3.

We proposed a plausible mechanism for the generation of compound **4** starting from *N*-substitution, the tandem ring cyclization and ring-opening, and oxidation. The formation of sole product from compound **1** with 3-methylquinoline would rationalize the possible existence of the mechanism shown in Scheme 3.

3. Experimental section

3.1. General procedure

Analytical thin-layer chromatography (TLC) was performed on precoated plates (silica gel 60 F-254), purchased from Merck Inc. Purification by gravity column chromatography was carried out by use of Merck Reagents Silica Gel 60 (particle size 0.063–0.200 mm, 70–230 mesh ASTM). Infrared (IR) spectra were measured on a Bomem Michelson Series FT-IR spectrometer. The wavenumbers reported are referenced to the polystyrene absorption at 1601 cm^{-1}. Absorption intensities are recorded by the following abbreviations: s, strong; m, medium; w, weak. Proton NMR spectra were obtained on a Bruker (500 MHz) spectrometer by use of DMSO-d_6 as solvent. Carbon-13 NMR spectra were obtained on a Bruker (125 MHz) spectrometer by using DMSO-d_6 as solvent. Multiplicities are recorded by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; *J*, coupling constant (hertz). Elemental analyses were carried out on a Heraeus CHN–O RAPID element analyzer.

3.2. Standard procedure for the synthesis of 2-aryl-2*H*-[1,2,4]triazoloquinolin-3-one 3a–3h and 2-aryl-2*H*-[1,2,4]triazoloisoquinolin-3-one 4a–4d

To 10 mL of neat quinoline (**2a**) or 3-methylquinoline (**2b**) was added α-chloroformylphenylhydrazines hydrochloride (**1a**–**1d**, 0.60 g, 2.9 mmol). The reaction mixture was heated at 80 °C under air for 2.0 h. After the reaction was completed, the reaction mixture was poured into a 1.0 N HCl aqueous solution (100 mL). The resultant precipitate was filtered, purified by column chromatography on silica gel (30% EtOAc in *n*-hexane), and recrystallized from THF/EtOAc to give 2-phenyl-2*H*-[1,2,4]triazolo-[3,4-*a*]isoquinoline-3-ones **3a**–**3h** and 2-phenyl-2*H*-[1,2,4]triazolo-[4,3-*a*]quinoline-3-ones **4a**–**4d**.

*3.2.1. 2-Phenyl-2H-[1,2,4]triazolo-[3,4-a]isoquinolin-3-one (**3a**).* Colorless needles; mp 139–140 °C; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.98 (d, *J*=8.3 Hz, 1H), 8.06 (d, *J*=8.2 Hz, 2H), 7.84 (d, *J*=7.7 Hz, 1H), 7.65–7.73 (m, 2H), 7.47–7.58 (m, 3H), 7.25–7.34 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.3, 140.9, 137.5, 132.8, 130.8, 129.8, 129.1, 128.7, 125.8, 125.5, 122.8, 119.0, 114.9, 114.0; IR (KBr) 1703 cm^{-1}; MS *m*/*z* (relative intensity) 261 (M^+, 40), 204 (23), 190 (12), 111 (25), 91 (100), 77 (69); Anal. Calcd for $C_{16}H_{11}N_3O$: C, 73.56; H, 4.21; N, 16.09. Found: C, 73.50; H, 4.23; N, 16.01.

*3.2.2. 2-(p-Methylphenyl)-2H-[1,2,4]triazolo-[3,4-a]isoquinolin-3-one (**3b**).* Colorless needles; mp 152–154 °C; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.93 (d, *J*=8.3 Hz, 1H), 7.89 (d, *J*=8.4 Hz, 2H), 7.80 (d, *J*=7.4 Hz, 1H), 7.62–7.79 (m, 2H), 7.45–7.50 (m, 1H), 7.31 (d, *J*=8.3 Hz, 2H), 7.22 (d, *J*=9.7 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.2, 142.9, 134.1, 132.7, 130.5, 129.7, 129.1, 128.6, 124.8, 124.5, 122.8, 119.5, 114.7, 113.7, 15.1; IR (KBr) 1706, 1705 cm^{-1}; MS *m*/*z* (relative intensity) 275 (M^+, 100), 218 (20), 204 (10), 128 (23), 91 (42); Anal. Calcd for $C_{17}H_{13}N_3O$: C, 74.18; H, 4.76; N, 15.26. Found: C, 74.15; H, 4.70; N, 15.31.

*3.2.3. 2-(p-Fluorophenyl)-2H-[1,2,4]triazolo-[3,4-a]isoquinolin-3-one (**3c**).* Colorless needles; mp 168–170 °C; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.96 (d, *J*=8.3 Hz, 1H), 8.04–8.11 (m, 2H), 7.84 (d, *J*=7.4 Hz, 1H), 7.65–7.73 (m, 2H), 7.47–7.53 (m, 1H), 7.35–7.42 (m, 2H), 7.27 (d, *J*=9.7 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 160.6, 148.2, 145.8, 133.8, 132.7, 130.2, 129.7, 128.5, 125.5, 122.9, 121.1, 116.1, 115.6, 113.6; IR (KBr) 1715 cm^{-1}; MS *m*/*z* (relative intensity) 279 (M^+, 100), 222 (26), 128 (29), 95 (43); Anal. Calcd for $C_{16}H_{10}N_3OF$: C, 68.82; H, 3.58; N, 15.05. Found: C, 68.80; H, 3.55; N, 15.09.

*3.2.4. 2-(p-Chlorophenyl)-2H-[1,2,4]triazolo-[3,4-a]isoquinolin-3-one (**3d**).* Colorless needles; mp 183–185 °C; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.95 (d, *J*=8.4 Hz, 1H), 8.23 (d, *J*=8.4 Hz, 2H), 7.85 (d, *J*=7.4 Hz, 1H), 7.52–7.85 (m, 5H), 7.25 (d, *J*=9.7 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.5, 143.9, 134.2, 133.7, 131.4, 130.2, 129.1, 128.4, 125.3, 123.9, 120.1, 116.1, 114.9, 113.7; IR (KBr) 1708 cm^{-1}; MS *m*/*z* (relative intensity) 297 (M+2, 31), 295 (M^+, 100), 240 (6), 238 (18), 128 (37), 111 (35); Anal. Calcd for $C_{16}H_{10}ClN_3O$: C, 64.98; H, 3.41; Cl, 11.90; N, 14.21. Found: C, 65.04; H, 3.37; Cl, 11.92; N, 14.24.

*3.2.5. 2-Phenyl-4-methyl-2H-[1,2,4]triazolo-[4,3-a]quinolin-3-one (**3e**).* Mp 159–160 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 8.95 (d, *J*=8.3 Hz, 1H), 8.08 (d, *J*=7.8 Hz, 2H), 7.75 (d, *J*=7.4 Hz, 1H), 7.61–7.68

(m, 1H), 7.49–7.58 (m, 3H), 7.43–7.48 (m, 1H), 7.30–7.36 (m, 1H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.5, 141.3, 137.4, 131.7, 129.6, 128.8, 128.5, 127.6, 125.6, 125.2, 122.9, 122.8, 119.0, 114.4, 14.6; IR (KBr) 3011 (s), 1716 (m, C=O) cm^{-1}; MS *m*/*z* (relative intensity) 275 (M$^+$, 100), 218 (24), 91 (22), 77 (29); Anal. Calcd for $C_{17}H_{13}N_3O$: C, 74.18; H, 4.73; N, 15.27. Found: C. 74.20; H, 4.72; N, 15.32.

*3.2.6. 2-(p-Methylphenyl)-4-methyl-2H-[1,2,4]triazolo-[4,3-a]quinolin-3-one (**3f**).* Mp 178–180 °C; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.88 (d, *J*=8.3 Hz, 1H), 7.90 (d, *J*=8.4 Hz, 2H), 7.69 (d, *J*=7.7 Hz, 1H), 7.52–7.59 (m, 1H), 7.37–7.45 (m, 2H), 7.29 (d, *J*=8.4 Hz, 2H), 2.34 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 147.5, 140.7, 136.9, 130.7, 129.0, 128.4, 128.1, 127.2, 125.8, 125.1, 123.6, 122.4, 119.2, 114.7, 17.6, 14.5; IR (KBr) 2931 (s), 1715 (m, C=O) cm^{-1}; MS *m*/*z* (relative intensity) 289 (M$^+$, 100), 232 (18), 91 (36); Anal. Calcd for $C_{18}H_{15}N_3O$: C, 74.74; H, 5.19; N, 14.53. Found: C, 74.68; H, 5.18; N, 14.55.

*3.2.7. 2-(p-Fluorophenyl)-2H-[1,2,4]triazolo[4,3-a]quinolin-3-one (**3g**).* Mp 183–185 °C; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.93 (d, *J*=8.3 Hz, 1H), 8.05–8.12 (m, 2H), 7.74 (d, *J*=7.6 Hz, 1H), 7.61–7.67 (m, 1H), 7.51 (s, 1H), 7.42–7.48 (m, 1H), 7.35–7.41 (m, 2H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.6, 145.8, 141.4, 133.8, 131.7, 130.4, 129.8, 128.6, 127.7, 125.3, 122.9, 121.1, 115.6, 114.4, 14.6; IR (KBr) 3058 (s), 2826 (s), 1718 (m, C=O) cm^{-1}; MS *m*/*z* (relative intensity) 293 (M$^+$, 100), 236 (30), 142 (18), 115 (17), 95 (22); Anal. Calcd for $C_{17}H_{12}N_3OF$: C, 69.62; H, 4.10; N, 14.33. Found: C, 69.60; H, 4.16; N, 14.31.

*3.2.8. 2-(p-Chlorophenyl)-2H-[1,2,4]triazolo[4,3-a]quinolin-3-one (**3h**).* Mp 207–209 °C; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.94 (d, *J*=8.3 Hz, 1H), 8.20 (d, *J*=8.3 Hz, 2H), 7.84 (d, *J*=7.4 Hz, 1H), 7.54–7.87 (m, 5H), 7.23 (d, *J*=9.6 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.3, 142.5, 134.1, 133.6, 132.0, 130.4, 129.5, 128.3, 125.8, 124.9, 121.1, 115.9, 114.3, 113.7, 15.1; IR (KBr) 3018 (s), 1716 (m, C=O) cm^{-1}; MS *m*/*z* (relative intensity) 309 (M+2, 100), 252 (26), 142 (21), 111 (24); Anal. Calcd for $C_{17}H_{12}ClN_3O$: C, 65.91; H, 3.88; N, 13.57. Found: C, 65.77; H, 3.82; N; 13.56.

*3.2.9. 2-Phenyl-2H-[1,2,4]triazolo-[4,3-a]quinolin-3-one (**4a**).* Colorless needles; mp 132–133 °C; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.30 (d, *J*=7.8 Hz, 1H), 8.11 (d, *J*=7.8 Hz, 2H), 7.84 (d, *J*=7.8 Hz, 1H), 7.72–7.78 (m, 2H), 7.65–7.71 (m, 1H), 7.52–7.58 (m, 2H), 7.30–7.35 (m, 1H), 7.03 (d, *J*=7.4 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 147.3, 140.2, 137.7, 131.7, 131.4, 129.2, 128.9, 127.8, 125.7, 122.7, 120.1, 119.9, 118.8, 112.0; IR (KBr) 1714 cm^{-1}; MS *m*/*z* (relative intensity) 261 (M$^+$, 100), 206 (10), 204 (30), 128 (29), 105 (8), 77 (41); Anal. Calcd for $C_{16}H_{11}N_3O$: C, 73.56; H, 4.21; N, 16.09. Found: C, 73.58; H, 4.21; N, 16.13.

*3.2.10. 2-(p-Methylphenyl)-2H-[1,2,4]triazolo-[4,3-a]quinolin-3-one (**4b**).* Colorless needles; mp 143–145 °C; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.25 (d, *J*=7.8 Hz, 1H), 7.94 (d, *J*=8.5 Hz, 1H), 7.79 (d, *J*=7.7 Hz, 1H), 7.62–7.73 (m, 3H), 7.33 (d, *J*=8.3 Hz, 2H), 7.00 (d, *J*=7.4 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.2, 141.2, 137.4, 131.6, 131.2, 128.3, 127.9, 127.1, 125.8, 123.7, 121.2, 119.8, 118.9, 113.3, 14.6; IR (KBr) 1706, 1724 cm^{-1}; MS *m*/*z* (relative intensity) 275 (M$^+$, 100), 233 (4), 218 (17), 138 (4), 128 (37), 105 (74), 91 (64); Anal. Calcd for $C_{17}H_{13}N_3O$: C, 74.18; H, 4.76; N, 15.26. Found: C, 74.11; H, 4.80; N, 15.31.

*3.2.11. 2-(p-Fluorophenyl)-2H-[1,2,4]triazolo-[4,3-a]quinolin-3-one (**4c**).* colorless needles; mp 193–194 °C; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.28 (d, *J*=7.8 Hz, 1H), 8.08–8.15 (m, 2H), 7.83 (d, *J*=7.8 Hz, 1H), 7.65–7.78 (m, 3H), 7.35–7.42 (m, 2H), 7.03 (d, *J*=7.4 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 158.7, 147.2, 140.2, 134.1, 131.7, 130.4, 128.9, 127.8, 122.6, 121.0, 120.9, 119.9, 116.1, 112.6; IR (KBr) 1703 cm^{-1}; MS *m*/*z* (relative intensity) 279 (M$^+$, 100), 222 (28), 128 (40), 95 (62); Anal. Calcd for $C_{16}H_{10}N_3OF$: C, 68.82; H, 3.58; N, 15.05. Found: C, 68.88; H, 3.49; N, 15.00.

*3.2.12. 2-(p-Chloroprene)-2H-[1,2,4]triazolo-[4,3-a]quinolin-3-one (**4d**).* Colorless needles; mp 149–151 °C; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.26 (d, *J*=7.8 Hz, 1H), 8.24 (d, *J*=8.5 Hz, 1H), 7.78 (d, *J*=7.7 Hz, 2H), 7.65–7.77 (m, 3H), 7.53 (d, *J*=8.3 Hz, 2H), 7.02 (d, *J*=7.4 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 146.6, 141.3, 135.1, 133.5, 132.6, 129.5, 128.7, 126.9, 122.7, 121.3, 120.8, 119.8, 116.2, 112.6; IR (KBr) 1714 cm^{-1}; MS *m*/*z* (relative intensity) 297 (M+2, 32), 295 (M$^+$, 100), 128 (19), 113 (6), 111 (18); Anal. Calcd for $C_{16}H_{10}ClN_3O$: C, 64.98; H, 3.41; Cl, 11.90; N, 14.21. Found: C, 64.73; H, 3.42; Cl, 11.88; N, 14.20.

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Supplementary data

Supplementary data associated with this article can be found in the online version at, doi:10.1016/j.tet.2009.11.095.

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12. Bond lengths (Å) and angles (°) of 2-(*p*-Fluorophenyl)-2*H*-[1,2,4]triazolo-[4,3-*a*]quinolin-3-one (**3c**): F(1)–C(14), 1.364(2); C(14)–C(15), 1.366(2); C(14)–C(13), 1.364(2); C(15)–C(16), 1.382(2); C(11)–C(16), 1.388(2); N(1)–C(11), 1.424(2); C(11)–C(12), 1.388(2); C(12)–C(13), 1.383(2); N(1)–N(2), 1.388(2); N(1)–C(1), 1.376(2); O(1)–C(1), 1.219(2); N(3)–C(1), 1.395(2); N(3)–C(2), 1.378(2); N(2)–C(2), 1.300(2); N(3)–C(10), 1.413(2); C(2)–C(3), 1.433(2); C(5)–C(10), 1.404(2); C(9)–C(10), 1.391(2); C(8)–C(9), 1.379(2); C(7)–C(8), 1.388(2); C(6)–C(7), 1.371(2); C(5)–C(6), 1.401(2); C(4)–C(5), 1.441(2); C(3)–C(4), 1.339(2); C(3)–H(1), 0.95; C(4)–H(2), 0.95; C(6)–H(3), 0.95; C(7)–H(4), 0.95; C(8)–H(5), 0.95; C(9)–H(6), 0.95; C(12)–H(7), 0.95; C(13)–H(8), 0.95; C(15)–H(9), 0.95; C(16)–H(10), 0.95; N(2)–N(1)–C(1), 112.8(1); N(2)–N(1)–C(11), 119.1(1); C(1)–N(1)–C(11), 128.1(1); N(1)–N(2)–C(2), 104.2(1); C(1)–N(3)-C(2), 107.8(1); C(1)––N(3)–C(10), 129.1(1); C(2)–N(3)–C(10), 123.2(1); O(1)–C(1)–N(1), 129.2(1); O(1)–C(1)–N(3), 127.9(1); N(1)–C(1)–N(3), 102.8(1); N(2)–C(2)–N(3), 112.4(1); N(2)–C(2)–C(3), 128.1(1); N(3)–C(2)–C(3), 119.5(1); C(2)–C(3)–C(4), 118.5(1); C(3)–C(4)–C(5), 122.3(1); C(4)–C(5)–C(6), 121.8(1); C(4)–C(5)–C(10), 119.9(1); C(6)–C(5)–C(10), 118.3(1); C(5)–C(6)–C(7), 120.7(1); C(6)–C(7)–C(8), 120.1(2); C(7)–C(8)–C(9), 120.9(2); C(8)–C(9)–C(10), 119.1(1); N(3)–C(10)–C(5), 116.5(1); N(3)–C(10)–C(9), 122.6(1); C(5)–C(10)–C(9), 120.9(1); N(1)–C(11)–C(12), 118.7(1); N(1)–C(11)–C(16), 121.0(1); C(12)–C(11)–C(16), 120.2(1); C(11)–C(12)–C(13), 120.2(1); C(12)–C(13)–C(14), 118.4(2); F(1)–C(14)–C(13), 118.8(2); F(1)–C(14)–C(15), 118.5(2); C(13)–C(14)–C(15), 122.7(2); C(14)–C(15)–C(16), 119.3(2); C(11)–C(16)–C(15), 119.1(1); C(4)–C(3)–H(1), 120.8; C(2)–C(3)–H(1), 120.7; C(5)–C(4)–H(2), 118.8; C(3)–C(4)–H(2), 118.9; C(7)–C(6)–H(3), 119.7; C(5)–C(6)–H(3), 119.6; C(8)–C(7)–H(4), 119.9; C(6)–C(7)–H(4), 120.0; C(9)–C(8)–H(5), 119.6; C(7)–C(8)–H(5), 119.5; C(10)–C(9)–H(6), 120.4; C(8)–C(9)–H(6), 120.5; C(13)–C(12)–H(7), 119.9; C(11)–C(12)–H(7), 119.8; C(14)–C(13)–H(8), 120.8; C(12)–C(13)–H(8), 120.8;

C(16)–C(15)–H(9), 120.3; C(14)–C(15)–H(9), 120.3; C(15)–C(16)–H(10), 120.5; C(11)–C(16)–H(10), 120.5.

13. Bond lengths (Å) and angles (°) of 2-(*p*-Chlorophenyl)-2*H*-[1,2,4]triazolo-[3,4-*a*]-isoquinolin-3-one (**4d**): C(1)–C(2), 1.367(5); C(1)–C(6), 1.388(5); C(1)–Cl, 1.739(3); C(2)–C(3), 1.376(5); C(3)–C(4), 1.394(5); C(4)–C(5), 1.380(5); C(4)–N(1), 1.413(4); C(5)–C(6), 1.376(5); C(7)–N(1), 1.372(4); C(7)–N(2), 1.390(4); C(7)–O(7), 1.217(4); C(8)–C(9),1.449(4); C(8)–N(2), 1.371(4); C(8)–N(3), 1.299(4); C(9)–C(10), 1.407(4); C(9)–C(16), 1.389(5); C(10)–C(11), 1.453(5); C(10)–C(13), 1.409(5); C(11)–C(12), 1.332(6); C(12)–N(2), 1.392(4); C(13)–C(14), 1.369(7); C(14)–C(15), 1.384(6); C(15)–C(16), 1.382(5); N(1)–N(3), 1.398(3); C(2)–C(1)–C(6), 121.0(3); C(2)–C(1)–Cl, 119.2(3); C(6)–C(1)–Cl, 119.9(3); C(1)–C(2)–C(3), 120.0(3); C(2)–C(3)–C(4), 119.9(3); C(3)–C(4)-C(5), 119.3(3); C(3)–C(4)–N(1), 120.4(3); C(4)-C(5)–C(6), 120.9(3); C(1)–C(6)–C(5), 118.9(3); N(1)–C(7)–N(2), 102.5(3); N(1)–C(7)–O(7), 130.6(3); N(2)–C(7)–O(7), 126.9(3); C(9)–C(8)–N(2), 118.7(3); C(9)–C(8)–N(3), 129.2(3); N(2)–C(8)–N(3), 112.1(3); C(8)–C(9)–C(10), 117.0(3); C(8)–C(9)–C(16), 122.1(3); C(10)–C(9)–C(16), 120.9(3); C(9)-C(10)–C(11), 120.6(3); C(9)–C(10)–C(13), 117.8(3); C(11)–C(10)–C(13), 121.6(3); C(10)–C(11)–C(12), 120.6(3); C(11)–C(12)–N(2), 119.0(4); C(10)-C(13)–C(14), 120.6(4); C(14)–C(15)–C(16), 119.9(4); C(9)–C(16)–C(15), 119.9(3); C(4)–N(1)–C(7), 127.5(3); C(4)–N(1)–N(3), 119.6(2); C(7)–N(1)–N(3), 112.9(2); C(7)–N(2)–C(8), 108.6(2); C(7)–N(2)–C(12), 127.3(3); C(8)–N(2)–C(12), 124.0(3); C(8)–N(3)–N(1), 103.9(2).
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