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FACILE AND CONVENIENT SYNTHESES FOR FLUORINE-CONTAINING PYRAZOLO[4,3-*c*]QUINOLINES, ISOXAZOLO-QUINOLINES, AND 1,4-DIAZEPINO[6,5-*c*]QUINOLINES

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Abstract – *N*,*N*-Dimethyl-3-trifluoroacetyl-4-quinolylamine underwent an aromatic nucleophilic *N*-*N* exchange reaction with hydrazines followed by cyclocondensation to afford the corresponding novel fluorine-containing 1*H*- and 2*H*-pyrazolo[4,3-*c*]quinolines in good to high yields. This reaction could be extended to the synthesis of novel CF_3-containing isoxazoloquinolines using hydroxylamine. Furthermore, the use of 1,2-ethylenediamine and 1,2-phenylenediamines gave the corresponding fluorine-containing 1,4-diazepino[6,5-*c*]quinoline derivatives in high yields.

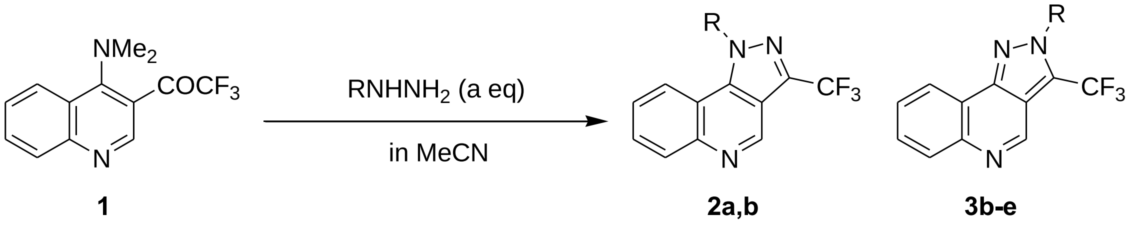
INTRODUCTION

Pyrazolo[4,3-*c*]quinolines have attracted much attention because of their pharmacological properties. For example, they have demonstrated potential applications as antiproliferative,[1,2] antitumor,[1,3] allergy inhibit,[2] anti-inflammatory,[2] antiparkinsonian,[4] analgesic,[5] and antipyretic activities.[5] Isoxazoloquinoline and the related derivatives show interesting biological activities such as antioxidant,[6] analgesic,[7] anticonvulsant,[7] antiepileptic,[7] anxiolytic,[7] antidepressant,[7,8] antimalarial,[9] and antibacterial activities.[10] 1,4-Diazepino[6,5-*c*]quinoline derivatives are also important heterocyclic systems having interesting biological properties such as anti-alzheimer,[11] antiproliferative,[11] antitumor,[11] antiviral,[11] antibacterial,[12] and HIV-1 reverse transcriptase inhibit activities.[13] Besides, considerable attention in recent years has been paid to the development of new methodologies for the syntheses of many kinds of fluorine-containing heterocycles, since these compounds are now widely recognized as important organic materials showing interesting biological activities for their potential use in medicinal and agricultural scientific fields.[14] Thus, it would be very important to develop facile and convenient synthetic methods for novel fluorine-containing pyrazolo[4,3-*c*]quinolines, isoxazoloquinolines, and 1,4-diazepino[6,5-*c*]quinolines, which would be strongly expected to present new bioactivities or functionalities.

Previously, we have found that *N*,*N*-dimethyl-2,4-bis(trifluoroacetyl)-1-naphthylamine[15] and *N*,*N*-dimethyl-5,7-bis(trifluoroacetyl)-8-quinolylamine[16] undergoes *N-N* exchange reaction and the subsequent cyclization with various bifunctional *N*-nucleophiles to achieve the facile syntheses of naphthalene[15] and quinoline[16] fused heterocycles bearing trifluoromethyl groups. Recently, we have reported the synthesis of *N*,*N*-dimethyl-3-trifluoroacetyl-4-quinolylamine (**1**) and its aromatic nucleophilic *N-N* exchange reactions with amines to give the corresponding 3-trifluoroacetyl-4-quinolylamines in high yields.[17,18] Later, we succeeded in applying this type of aromatic nucleophilic *N-N* exchange reaction to the simple synthesis of CF_3-containing heterocycles having a quinoline skeleton such as dibenzo[*b*,*h*][1,6]naphthyridines by the combination of *N-N* exchange and acid catalyzed cyclization.[19] In connection with this work, we wish to report the facile and convenient syntheses of novel fluorine-containing pyrazolo[4,3-*c*]quinolines (**2**, **3**), isoxazolo[4,3-*c*]quinolines (**5**), and 1,4-diazepino[6,5-*c*]quinolines (**8**, **9**) through the *N-N* exchange reaction and cyclization of **1** with bifunctional *N*-nucleophiles such as hydrazines, hydroxylamine, and 1,2-diamines. Furthermore, we also report the synthetic method for isoxazolo[4,5-*c*]quinoline derivative (**7**), the regioisomer of **5**, from 3-trifluoroacetyl-4-quinolylamine (**6**) with hydroxylamine hydrochloride.

RESULTS AND DISCUSSION

Firstly, we examined the reaction of **1** with hydrazines (Scheme 1 and Table 1). Reaction of **1** with hydrazine monohydrate proceeded easily at room temperature for 4 h in acetonitrile to afford the *N*-unsubstituted 1*H*-pyrazolo[4,3-*c*]quinoline (**2a**) in almost quantitative yield. A treatment of methylhydrazine at room temperature gave a mixture of the two regioisomers **2b**/**3b** in a ratio of about 5:1. Interestingly, when the reaction was carried out in refluxing acetonitrile, the ratio changed to about 1:3 (yield: 87%). Separation of a mixture of 1*H*-isomer (**2b**) and 2*H*-isomer (**3b**) was easily effected by chromatography on a silica gel column. *tert*-Butylhydrazine hydrochloride reacted readily with **1** in the presence of triethylamine to provide solely the 2*H*-isomer (**3c**) in 95% yield. Likewise, phenylhydrazine gave the corresponding 2-phenyl-2*H*-pyrazoloquinolines (**3d**) regioselectively in 97% yield. In the case of *p*-nitrophenylhydrazine hydrochloride, the reaction required more forced conditions (3 equiv of hydrazine and the prolonged time to 24 h) to afford the corresponding 2-*p*-nitrophenyl-2*H*-pyrazoroquinoline derivative (**3e**) in good yield.



Scheme 1

Table 1. Reaction of **1** with Hydrazines

Entry	R	a (eq)	Temp. (℃)	Time (h)	Product	Yield (%)[a]
1	H	1	rt	4	**2a**	99
2	Me	3	rt	72	**2b** / **3b**	83 / 17
3	Me	1.2	reflux	1	**2b** / **3b**	20 / 67
4	*t*-Bu[b]	3	reflux	1	**3c**	95
5	Ph	1.2	reflux	24	**3d**	97
6	*p*-$O_2NC_6H_4$[c]	3	reflux	24	**3e**	71

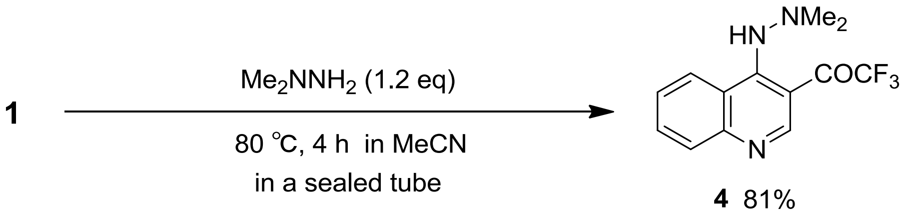
[a] Isolated yields.

[b] *tert*-Butylhydrazine hydrochloride was used in the presence of Et_3N (3 equiv).

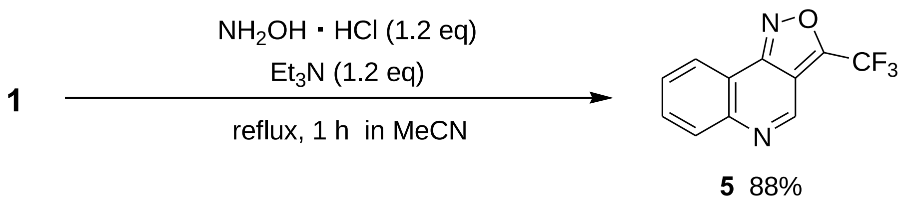
[c] *p*-Nitrophenylhydrazine hydrochloride was used in the presence of Et_3N (3 equiv).

The structural discrimination between these two regioisomers **2** and **3**, was definitely made by comparison of ^{13}C-NMR spectral data with those of 1*H*- and 2*H*-isomers of benz[*g*]indazoles[15] and pyrazolo[4,3-*h*]quinolines[16] having trifluoromethyl group at the 3-position.

The possibility that the reaction proceeds via the prior formation of a hydrazone at the 2-trifluoroacetyl group followed by an intramolecular *N-N* exchange to give the cyclized product seems unlikely, since the reaction of **1** with *N*,*N*-dimethylhydrazine gave the exchange product **4** and the corresponding hydrazone could not be detected (Scheme 2).



Scheme 2

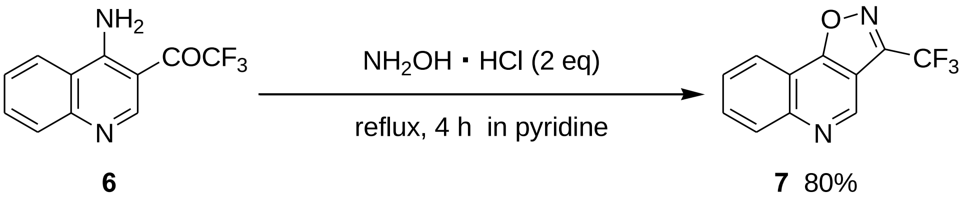


Scheme 3

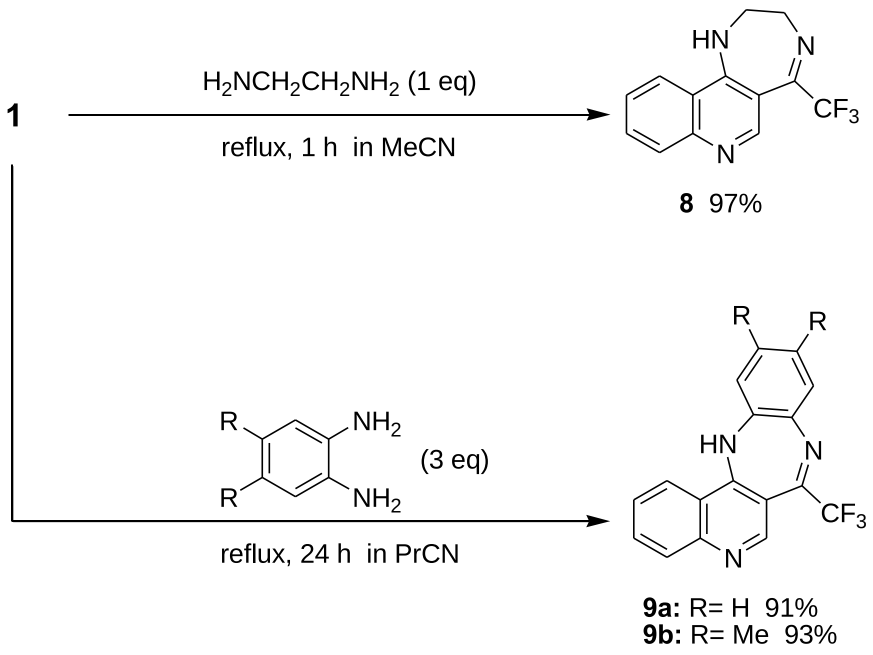
Hydroxylamine hydrochloride was also successfully used as a nucleophile in reaction with **1** to give 3-trifluoromethylisoxazolo[4,3-*c*]quinoline (**5**) in high yield (Scheme 3). Its possible structural isomer, the isoxazolo[4,5-*c*]quinoline derivative (**7**) was prepared from 3-trifluoroacetyl-4-quinolylamine (**6**)[17,18] with hydroxylamine hydrochloride in refluxing pyridine for 4 h (Scheme 4). ^{13}C-NMR spectrometry enabled discrimination between these two isomer. The trifluoromethyl-substituted carbon (at the 3-position) of **5** appeared at $\delta = 154.0$, while the trifluoromethyl-substituted carbon (at the 3-position) of **7** gave a signal at $\delta = 149.9$.

Finally, we attempted to carry out the reaction of **1** with 1,2-diamines (Scheme 5). Reaction of **1** with 1,2-ethylenediamine proceeded successfully for 1 h in refluxing acetonitrile to give the desired 5-(trifluoromethyl)-2,3-dihydro-1*H*-[1,4]diazepino[6,5-*c*]quinoline (**8**) almost quantitatively without the formation of the intermediate cyclic hemiaminal. Aromatic diamines such as 1,2-phenylenediamine and its 4,5-dimethyl-substituted derivative also reacted with **1** under forced conditions (24 h in refluxing butyronitrile) to afford solely the corresponding diazepinoquinolines (**9a** and **9b**) in high yields.

In summary, we succeeded in the reactions of **1** with various bifunctional *N*-nucleophiles and demonstrated a facile and convenient approach for the syntheses of 1*H*- and 2*H*-pyrazolo[4,3-*c*]quinolines (**2**, **3**), isoxazolo[4,3-*c*]quinolines (**5**), and 1,4-diazepino[6,5-*c*]quinolines (**8**, **9**) which are not easily



Scheme 4



Scheme 5

accessible by other methods. Furthermore, we also found that isoxazolo[4,5-*c*]quinolone derivative (**7**), structural isomer of **5**, was easily prepared from 3-trifluoroacetyl-4-quinolylamine (**6**) with hydroxylamine hydrochloride. Evaluation of biological activities for all new compounds **2**, **3**, **5**, and **7-9** is now under way.

EXPERIMENTAL

All reagents and solvents were purchased as reagent grade and used without further purification. Melting points were determined on an electrothermal digital melting point apparatus and are uncorrected. ^{1}H NMR spectra were obtained with JEOL PMX 60SI (60 MHz) and Bruker Avance 500 (500 MHz) spectrometers and ^{13}C NMR spectra were obtained with JEOL FX-90Q (22.5 MHz) and Bruker Avance 500 (125 MHz) spectrometers; TMS was used as an internal standard. IR spectra were recorded on Hitachi EPI-G3 and PerkinElmer Spectrum ONE spectrophotometers. Microanalyses were taken with a Yanaco CHN-Coder MT-5 analyzer.

1*H*- and 2*H*-Pyrazolo[4,3-c]quinolines 2 and 3; General Procedure

Using Hydrazine monohydrate, Methyl- and Phenylhydrazines; To a solution of **1**[17,18] (268 mg, 1 mmol) in MeCN (7 mL) was added the appropriate hydrazines (1-3 mmol) and the mixture was stirred at room temperature-reflux temperature for 4-72 h. The solvent was evaporated in vacuo to give the practically pure product **2a**. In the case of **2b**, **3b**, **d**, the crude product was chromatographed using *n*-hexane:EtOAc, 5:1 for **2b** and *n*-hexane:EtOAc, 10:1 for **3b**, **d**, as eluents.

Using tert-Butyl- and p-Nitrophenylhydrazine Hydrochlorides; To a solution of **1** (268 mg, 1 mmol) in MeCN (7 mL) was added hydrazine hydrochlorides (3 mmol) and Et_3N (304 mg, 3 mmol) and the mixture was stirred at reflux temperature for 1-24 h. The solvent was evaporated under reduced pressure, and CH_2Cl_2 (50 mL) was added to the residue. The solution was washed with H_2O (50 mL), and the organic layer was separated and dried (Na_2SO_4). The solvent was evaporated in vacuo and the crude product was chromatographed using *n*-hexane:EtOAc, 20:1 for **3c** and *n*-hexane:EtOAc, 6:1 for **3e**, as eluents.

3-(Trifluoromethyl)-1*H*-pyrazolo[4,3-*c*]quinoline (2a): mp 246 °C (dec.) (*n*-hexane/EtOAc); IR (KBr): 3064, 1172, 1143, 1109 cm^{-1}; ^1H NMR (DMSO-d_6-$CDCl_3$): δ 14.89-14.26 (br, 1H, NH), 9.28 (s, 1H, H-4), 8.44 (d, J = 7.4 Hz, 1H), 8.25 (d, J = 7.4 Hz, 1H), 7.79 (t, J = 7.4 Hz, 1H), 7.69 (t, J = 7.4 Hz, 1H); ^{13}C NMR (DMSO-d_6-$CDCl_3$): 143.6, 142.6, 140.6, 134.9 (q, J_{CF} = 38.7 Hz), 128.6, 128.3, 126.3, 121.1, 120.6 (q, J_{CF} = 268.5 Hz), 114.2, 112.0. Anal. Calcd for $C_{11}H_6F_3N_3$: C, 55.70; H, 2.55; N, 17.72. Found: C, 55.49; H, 2.78; N, 17.84.

3-(Trifluoromethyl)-1-methyl-1*H*-pyrazolo[4,3-*c*]quinoline (2b): mp 137-138 °C (*n*-hexane/EtOAc); IR (KBr): 1180, 1133, 1098 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.25 (s, 1H, H-4), 8.37 (d, J = 7.5 Hz, 1H), 8.30 (d, J = 7.5 Hz, 1H), 7.82 (t, J = 7.5 Hz, 1H), 7.73 (t, J = 7.5 Hz, 1H), 4.57 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): 145.4, 141.1, 139.7, 134.6 (q, J_{CF} = 39.1 Hz), 130.6, 129.2, 127.4, 121.4 (q, J_{CF} = 269.8 Hz), 120.9, 115.7, 114.5, 40.7. Anal. Calcd for $C_{12}H_8F_3N_3$: C, 57.37; H, 3.21; N, 16.73. Found: C, 57.19; H, 3.24; N, 16.88.

3-(Trifluoromethyl)-2-methyl-2*H*-pyrazolo[4,3-*c*]quinoline (3b): mp 116-117 °C (*n*-hexane/EtOAc); IR (KBr): 1184, 1121, 1109 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.24 (s, 1H, H-4), 8.50 (d, J = 7.7 Hz, 1H), 8.18 (d, J = 7.7 Hz, 1H), 7.75 (t, J = 7.7 Hz, 1H), 7.68 (t, J = 7.7 Hz, 1H), 4.38 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): 146.2, 144.5, 144.3, 130.0, 128.9, 127.6, 125.3 (q, J_{CF} = 40.3 Hz), 121.8, 120.6 (q, J_{CF} = 269.8 Hz), 119.2, 115.0, 39.4. Anal. Calcd for $C_{12}H_8F_3N_3$: C, 57.37; H, 3.21; N, 16.73. Found: C, 57.35; H, 3.39; N, 16.43.

2-*tert*-Butyl-3-(trifluoromethyl)-2*H*-pyrazolo[4,3-*c*]quinoline (3c): mp 83-84 °C (*n*-hexane/EtOAc); IR (KBr): 1180, 1155, 1122 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.28 (s, 1H, H-4), 8.55 (d, J = 7.5 Hz, 1H), 8.14 (d, J = 7.5 Hz, 1H), 7.72 (t, J = 7.5 Hz, 1H), 7.65 (t, J = 7.5 Hz, 1H), 1.88 (s, 9H, CH_3); ^{13}C NMR ($CDCl_3$): 145.7 (q, J_{CF} = 4.9 Hz), 144.4, 144.2, 130.0, 128.8, 127.5, 124.8 (q, J_{CF} = 41.5 Hz), 121.9, 121.2 (q, J_{CF} = 268.6 Hz), 119.8, 117.3, 66.1, 30.0. Anal. Calcd for $C_{15}H_{14}F_3N_3$: C, 61.43; H, 4.81; N, 14.33. Found: C, 61.43; H, 4.91; N, 14.23.

3-(Trifluoromethyl)-2-phenyl-2*H*-pyrazolo[4,3-*c*]quinoline (3d): mp 162-163 °C (*n*-hexane/EtOAc); IR (KBr): 1182, 1128, 1109 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.34 (s, 1H, H-4), 8.57 (d, J = 7.7 Hz, 1H), 8.20 (d, *J* = 7.7 Hz, 1H), 7.78 (t, *J* = 7.7 Hz, 1H), 7.68 (t, *J* = 7.7 Hz, 1H), 7.65-7.54 (m, 5H, C_6H_5); ^{13}C NMR ($CDCl_3$): 147.2, 145.2, 144.5, 138.9, 130.4, 130.1, 129.5, 129.3, 127.9, 126.5 (q, J_{CF} = 41.0 Hz), 126.2, 122.1, 120.1 (q, J_{CF} = 270.4 Hz), 119.2, 115.6. Anal. Calcd for $C_{17}H_{10}F_3N_3$: C, 65.18; H, 3.22; N, 13.41. Found: C, 65.25; H, 3.49; N, 13.18.

3-(Trifluoromethyl)-2-(4-nitrophenyl)-2*H*-pyrazolo[4,3-*c*]quinoline (3e): mp 165-166 °C (*n*-hexane/EtOAc); IR (KBr): 1530, 1351, 1194, 1137, 1111 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.35 (s, 1H, H-4), 8.56 (d, *J* = 7.5 Hz, 1H), 8.50 (d, *J* = 8.7 Hz, 2H), 8.22 (d, *J* = 7.5 Hz, 1H), 7.90 (d, *J* = 8.7 Hz, 1H), 7.82 (t, *J* = 7.5 Hz, 1H), 7.72 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$): 148.5, 147.9, 145.0, 144.5, 143.5, 130.2, 130.0, 128.3, 127.0, 126.6 (q, J_{CF} = 41.5 Hz), 122.1, 119.9 (q, J_{CF} = 270.8 Hz), 118.8, 116.1. Anal. Calcd for $C_{17}H_9F_3N_4O_2$: C, 56.99; H, 2.53; N, 15.64. Found: C, 57.02; H, 2.71; N, 15.43.

2,2,2-Trifluoro-1-(4-[(dimethylamino)amino]quinolin-3-yl)ethanone (4)

To a solution of **1** (268 mg, 1 mmol) in MeCN (7 mL) was added *N*,*N*-dimethylhydrazine (72 mg, 1.2 mmol) and the mixture was heated in a sealed tube at 80 °C for 4 h. The solvent was evaporated in vacuo and the crude product was chromatographed using EtOAc as an eluent to give **4**. **4:** mp 178-179 °C (*n*-hexane/EtOAc); IR (KBr): 2845, 1689, 1191, 1120, 1060 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.15 (s, 1H, H-2), 7.90 (d, *J* = 7.7 Hz, 1H), 7.82 (d, *J* = 7.7 Hz, 1H), 7.71 (t, *J* = 7.7 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 1H), 7.35 (br s, 1H, NH), 2.65 (s, 6H, $N(CH_3)_2$); ^{13}C NMR ($CDCl_3$): 182.0 (q, J_{CF} = 41.0 Hz), 152.4, 146.7, 144.9, 130.9, 126.7, 125.3, 122.9, 117.7 (q, J_{CF} = 285.9 Hz), 116.5, 108.7, 45.2. Anal. Calcd for $C_{13}H_{12}F_3N_3O$: C, 55.12; H, 4.27; N, 14.84. Found: C, 54.93; H, 4.34; N, 14.72.

3-(Trifluoromethyl)isoxazolo[4,3-*c*]quinoline (5)

A solution of hydroxylamine hydrochloride (83 mg, 1.2 mmol), Et_3N (121 mg, 1.2 mmol), and **1** (268 mg, 1 mmol) in MeCN (7 mL) was stirred at reflux temperature for 1 h. The solvent was evaporated under reduced pressure, and CH_2Cl_2 (50 mL) was added to the residue. The solution was washed with H_2O (50 mL), and the organic layer was separated and dried (Na_2SO_4). The solvent was evaporated in vacuo to give the practically pure product **5**. **5:** mp 143-144 °C (*n*-hexane/EtOAc); IR (KBr): 1208, 1176, 1147 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.15 (s, 1H, H-4), 8.50 (d, *J* = 7.7 Hz, 1H), 8.14 (d, *J* = 7.7 Hz, 1H), 7.86 (t, *J* = 7.7 Hz, 1H), 7.73 (t, *J* = 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$): 155.7, 154.0 (q, J_{CF} = 43.9 Hz), 144.8, 144.0, 132.2, 130.7, 129.4, 123.8, 118.3 (q, J_{CF} = 271.0 Hz), 115.2, 111.7. Anal. Calcd for $C_{11}H_5F_3N_2O$: C, 55.47; H, 2.12; N, 11.76. Found: C, 55.23; H, 2.49; N, 11.89.

3-(Trifluoromethyl)isoxazolo[4,5-*c*]quinoline (7)

A solution of hydroxylamine hydrochloride (139 mg, 2 mmol) and **1** (268 mg, 1 mmol) in pyridine (7 mL) was stirred at reflux temperature for 4 h. The solvent was evaporated under reduced pressure, and CH_2Cl_2 (50 mL) was added to the residue. The solution was washed with H_2O (50 mL), and the organic layer was separated and dried (Na_2SO_4). The solvent was evaporated in vacuo and the crude product was chromatographed using *n*-hexane:EtOAc, 15:1 as an eluent to give **7**. **7:** mp 118-119 °C (*n*-hexane/EtOAc); IR (KBr): 1181, 1153, 1112 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 9.26 (s, 1H, H-4), 8.46 (d, *J* = 7.5 Hz, 1H), 8.35 (d, *J* = 7.5 Hz, 1H), 7.98 (t, *J* = 7.5 Hz, 1H), 7.83 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$): 167.1, 149.9 (q, J_{CF} = 40.3 Hz), 147.7, 143.1, 132.1, 130.2, 128.7, 121.3, 120.0 (q, J_{CF} = 271.0 Hz), 114.2, 110.7. Anal. Calcd for $C_{11}H_5F_3N_2O$: C, 55.47; H, 2.12; N, 11.76. Found: C, 55.45; H, 2.24; N, 11.89.

1,4-Diazepino[6,5-*c*]quinolines 8 and 9; General Procedure

Using 1,2-Ethylenediamine; To a solution of **1** (268 mg, 1 mmol) in MeCN (7 mL) was added 1,2-ethylenediamine (60 mg, 1 mmol) and the mixture was stirred at reflux temperature for 1 h. The solvent was evaporated in vacuo to give the practically pure product **8**.

Using 1,2-Phenylenediamines; To a solution of **1** (268 mg, 1 mmol) in PrCN (7 mL) was added the appropriate 1,2-phenylenediamines (3 mmol) and the mixture was stirred at reflux temperature for 24 h. The solvent was evaporated under reduced pressure, and CH_2Cl_2 (50 mL) was added to the residue. The solution was washed with 1 N HCl (50 mL) and H_2O (50 mL), and the organic layer was separated and dried (Na_2SO_4). The solvent was evaporated in vacuo and the crude product was chromatographed using *n*-hexane:EtOAc, 4:1 for **9a** and *n*-hexane:EtOAc, 5:1 for **9b**, as eluents.

5-(Trifluoromethyl)-2,3-dihydro-1*H*-[1,4]diazepino[6,5-*c*]quinoline (8): mp 231-232 °C (*n*-hexane/EtOAc); IR (KBr): 3234, 1183, 1154, 1120 cm^{-1}; ^{1}H NMR (DMSO-d_6-$CDCl_3$): δ 8.74 (s, 1H, H-6), 8.03 (d, *J* = 7.8 Hz, 1H), 7.94 (d, *J* = 7.8 Hz, 1H), 7.71 (t, *J* = 7.8 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.34 (br s, 1H, NH), 4.30-4.20 (m, 2H, CH_2), 3.87-3.76 (m, 2H, CH_2); ^{13}C NMR (DMSO-d_6-$CDCl_3$): 158.2 (q, J_{CF} = 33.5 Hz), 150.4, 147.5, 130.9, 129.4, 125.7, 122.0, 120.8 (q, J_{CF} = 280.7 Hz), 119.3, 116.8, 102.4, 53.4, 48.6. Anal. Calcd for $C_{13}H_{10}F_3N_3$: C, 58.87; H, 3.80; N, 15.84. Found: C, 58.77; H, 3.98; N, 15.76.

7-Trifluoromethyl-13*H*-quino[4,3-*b*][1,5]benzodiazepine (9a): mp 144-145 °C (*n*-hexane/ EtOAc); IR (KBr): 3321, 1195, 1177, 1125 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 8.74 (s, 1H, H-6), 8.06 (d, *J* = 7.7 Hz, 1H), 7.94 (d, *J* = 7.7 Hz, 1H), 7.78 (t, *J* = 7.7 Hz, 1H), 7.61 (t, *J* = 7.7 Hz, 1H), 7.28 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.18 (td, *J* = 7.7, 1.3 Hz, 1H), 7.13 (td, *J* = 7.7, 1.3 Hz, 1H), 6.77 (dd, *J* = 7.7, 1.3 Hz, 1H), 6.19 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$): 160.8, 156.3 (q, J_{CF} = 33.2 Hz), 148.8, 147.9 (q, J_{CF} = 3.7 Hz), 140.8, 139.0, 131.3, 129.5, 129.4, 129.1, 126.8, 125.1, 121.6, 120.6, 119.4 (q, J_{CF} = 280.0 Hz), 113.2. Anal. Calcd for $C_{17}H_{10}F_3N_3$: C, 65.18; H, 3.22; N, 13.41. Found: C, 65.54; H, 3.26; N, 13.41.

10,11-Dimethyl-7-trifluoromethyl-13*H*-quino[4,3-*b*][1,5]benzodiazepine (9b): mp 136-137 °C (*n*-hexane/ EtOAc); IR (KBr): 3308, 1194, 1178, 1124 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 8.72 (s, 1H, H-6), 8.06 (d, *J* = 7.9 Hz, 1H), 7.91 (d, *J* = 7.9 Hz, 1H), 7.78 (t, *J* = 7.9 Hz, 1H), 7.62 (t, *J* = 7.9 Hz, 1H), 7.07 (s, 1H, H-9), 6.53 (s, 1H, H-12), 5.98 (br s, 1H, NH), 2.19 (s, 6H, CH_3); ^{13}C NMR ($CDCl_3$): 160.3, 155.7 (q, J_{CF}

= 33.9 Hz), 149.3, 148.7 (q, J_{CF} = 3.7 Hz), 139.1, 137.9, 136.8, 134.1, 131.6, 130.9, 130.2, 127.2, 122.6, 120.2, 120.0 (q, J_{CF} = 279.5 Hz), 119.9, 113.6, 19.1, 18.6. Anal. Calcd for $C_{19}H_{14}F_3N_3$: C, 66.86; H, 4.13; N, 12.31. Found: C, 66.81; H, 4.07; N, 12.48.

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