The *o*-Amino–Trifluoromethyl Functionality as a Novel Synthon for 4-Fluoroquinolines

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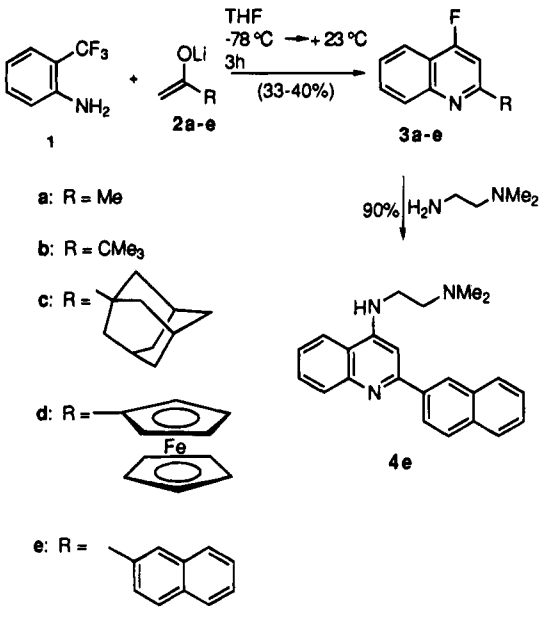
2-Substituted 4-fluoroquinolines **3** are obtained by the reaction of 2-(trifluoromethyl)aniline (**1**) with lithium enolates **2** derived from methyl ketones. A similar reaction of **1** with lithium enolate of acetaldehyde produces 4-fluoroquinoline. 1-Fluoro-3-phenyl-4,6-phenanthroline (**18**) is obtained by treatment of lithium enolate of acetophenone with 4-(trifluoromethyl)quinolin-3-amine (**17**). By contrast, (*Z*)-*N*-[2-(1-fluoroalkenyl)phenyl]carboxamides **10** and **12** are the products of the reaction of **1** with the respective enolate ions derived from 3-pentanone and isobutyl phenyl ketone. A unified mechanism for the formation of quinolines and carboxamides is proposed.

The trifluoromethyl group in 2-(trifluoromethy)aniline (**1**), its para isomer, and heteroaromatic analogs exhibits unusual reactivity under basic conditions that cause ionization of the amino function.[1,2] The CF_3 group in such substrates is easily hydrolyzed to a carboxylate group in the presence of hydroxide base and transformed into a carbonitrile function in an amide ion mediated reaction.[1,2] Recently, the anionically activated CF_3 group has emerged as a valuable synthon for substituted dihydro-1*H*-imidazoles,[3] 1,4,5,6-tetrahydropyrimidines,[3–5] acyclic amidines,[4] benzothiazoles,[6] benzoxazoles,[6] and alkenes.[7] Ketimines derived from **1** are efficiently cyclized to quinolines in base-mediated reactions.[4,5,8–10] The quinolines obtained in the presence of lithium alkylamide or dialkylamide reagents contain an amino function in the C-4 position. A similar approach has been used in a novel synthesis of quinazolin-4-amines[11] from **1**. This chemistry permits a facile preparation of amino-substituted heterobiaryls which, depending on structure, bind selectively to different types of nucleic acids.[10,12–15] Several RNA binding agents of this class of compounds show promise for development as anti-HIV-1 drugs.[9,10,15] Some cationic heterobiaryls are DNA triple-helix specific intercalators, and they are currently being developed as antigene enhancers in a novel approach to selectively target the AIDS virus.[13,14]

Scheme 1



In this paper we report the first synthesis of 4-fluoroquinolines by the reaction of **1** with enolate ions. We also show that the heterocyclization reaction with the involvement of the CF_3 group can be extended on other substrates containing the ortho NH_2/CF_3 moiety. Besides the intrinsic interest in the unconventional preparation of organofluorine compounds,[16] the 4-fluoroquinolines and analogs are valuable precursors to amino-substituted derivatives that are of immense interest in the biophysical chemistry of nucleic acids, as discussed.

Results and Discussion

The treatment of **1** with methyl ketone enolates **2a–e** furnished the corresponding 2-substituted 4-fluoroquinolines **3a–e** as the major low molecular weight products derived from **1** (Scheme 1). A modest efficiency of the reaction was greatly offset by a high reproducibility of the synthesis and the ease of isolation of the relatively nonpolar fluoroquinolines **3** by chromatography on silica gel with hexanes as an eluent. In all cases studied the fluoroquinolines were eluted in the first fractions. The enolates are conveniently generated *in situ* from ketones

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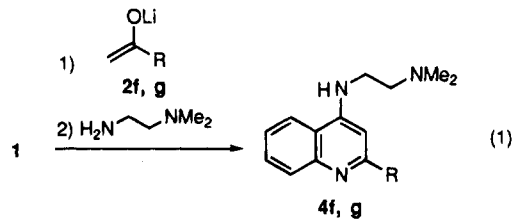
and LDA, and the optimized molar ratio of 1/ketone/LDA is 1:4:6. The excess of lithium enolate and the presence of LDA in the mixture are necessary to suppress self-condensation of a ketone. This side reaction became a major process with the ratio of 1/enolate ion greater than 1:4. Both increasing the amount of lithium enolate in the absence of LDA and decreasing the amount of the enolate while increasing the amount of LDA in the mixture gave rise to additional products. GC–MS analyses, with EI and CI modes, consistently suggested that these additional components were the corresponding products of nucleophilic substitution of fluoride in **3** by enolate and diisopropylamide ions. Under the given optimized ratio of the reagents all low molecular weight byproducts are formed in individual yields smaller than 5%, as estimated by GC–MS analyses, and the yield of fluoroquinoline **3** is maximized. Tar is the remaining major component of the material balance.

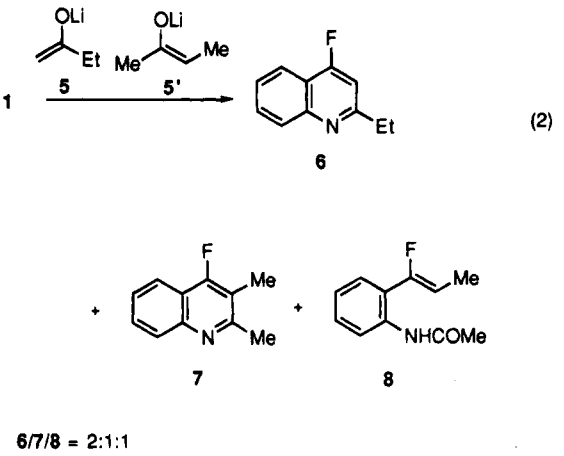
4-Fluoro-2-methylquinoline (**3a**) thus obtained was virtually identical with the authentic sample prepared from 4-amino-2-methylquinoline by the Balz–Schiemann reaction.[17] A coupling contant $J = 11.5 \pm 0.5$ Hz between C3–H and C4–F was observed in both the ^1H and ^{19}F NMR spectra of all products **3a–e**. An additional structural proof was obtained by the synthesis of known amino derivative[10] **4e** from **3e**, as shown in Scheme 1.

Synthesis of 4-aminoquinolines by this approach does not require isolation of pure 4-fluoroquinolines. This is illustrated in eq 1 by the preparation of a known

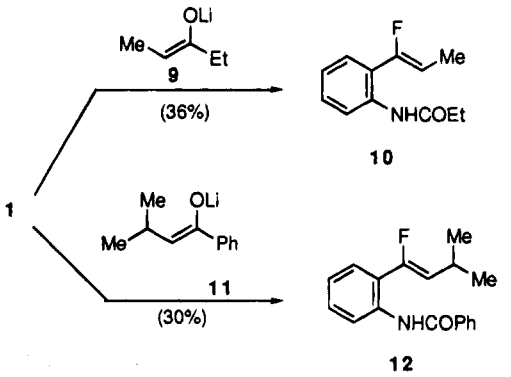


compound[9] **4f** and a new 1-naphthyl derivative **4g**. It is important to note that the conformationally restricted 2-(1-naphthyl)quinoline **4g** could not be obtained by the previously reported method that involves condensation of **1** with a ketone followed by amide base mediated cyclization of the resultant ketimine.[4,5] All attempts to condense **1** with 1-acetylnaphthalene failed to produce the desired ketimine under a variety of experimental conditions.

The reactions of Scheme 1 and eq 1 were conducted with single ketone enolates. By contrast, two enolate ions, **5** and **5′**, are generated from 2-butanone upon treatment with LDA (eq 2). The presence of neither



Scheme 2



enolate ion is expected to be favored substantially under the conditions of the reaction with **1** that cause equilibration of the enolates. Two 4-fluoroquinolines, major **6** derived from **5** and minor **7** derived from **5′**, were obtained. A fluoro olefin **8** was also a minor product, and it was obtained as a single geometrical isomer. A coupling constant[18] $J = 38$ Hz between the fluorine atom and the olefinic hydrogen, observed in both the ^1H and the ^{19}F NMR spectra, strongly suggests the *Z*-stereochemistry of **8**. Again, as for the previously discussed synthesis of **3**, the maximized total yield of **6–8** corresponds to the molar ratio 1:2-butanone:LDA of 1:4:6.

On the basis of the ratio of **6**:**7**:**8** = 2:1:1 it can be hypothesized that the sterically congested quinoline **7** and the alkene **8** are formed from the same intermediate product in which steric features provide an additional mechanistic pathway leading to **8**. Consistent with this hypothesis are the results of the reactions of **1** with enolate ions **9** and **11** (Scheme 2). The respective fluoro olefins (*Z*)-**10** and (*Z*)-**12** were obtained, and the corresponding 4-fluoroquinolines could only be detected as minor products (<2%) in crude mixtures by GC–MS analyses.

Attempts were made to conduct reactions of **1** with enolate ions derived from other carbonyl compounds. A complicated mixture of products was obtained with the enolate ion of cyclohexanone generated by treatment of cyclohexanone with LDA. Although the GC–MS analysis

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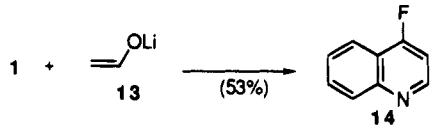
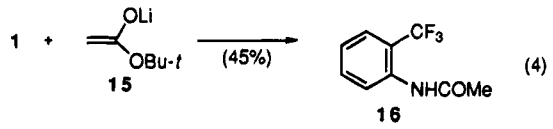
was consistent with the presence of the expected 1,2,3,4-tetrahydroacridine and cyclic olefin products (structures not shown), this crude mixture resisted chromatographic separation under a variety of conditions. On the other hand, the reaction was successful with acetaldehyde enolate **13** generated by lithiation of THF with *n*-BuLi and followed by thermal fragmentation of the resultant 2,3,4,5-tetrahydrofuryllithium.[19] A single major product was readily purified by flash chromatography and shown to be 4-fluoroquinoline (**14**) by direct comparison with an authentic sample[20,21] (eq 3). The treatment of **1** with the



(3)

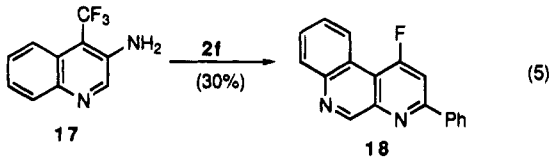
lithium enolate of *tert*-butyl acetate furnished known acetamide derivative[5] **16** as the major product (eq 4).



(4)

Finally, anions derived from β-dicarbonyl compounds including acetylacetone, ethyl acetoacetate, and diethyl malonate, as well as anions derived from ethyl cycanoacetate and malononitrile, all were inert toward **1**. It can be concluded that these stabilized anions are not basic enough (pK_a < 15) to cause ionization of the amino group in **1**.

The results presented so far clearly indicate the greatest synthetic utility of this novel chemistry for the preparation of 4-fluoroquinoline and its 2-substituted analogs. An extension of this approach to the synthesis of other fused derivatives of 2-substituted 4-fluoropyridines is illustrated in eq 5 by the successful preparation

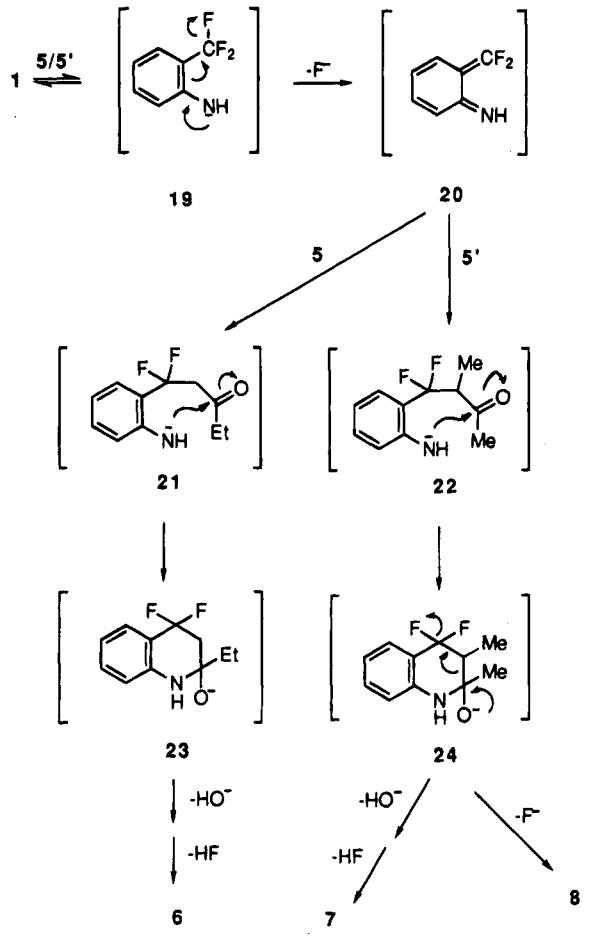


(5)

of a phenanthroline **18**. The synthetic potential of this chemistry is further enhanced by a facile preparation of starting materials, such as **17**,[6] by trifluoromethylation of aromatic amines.[22]

A unified mechanism for the discussed chemistry is given in Scheme 3. For the sake of clarity, the suggested transformations are presented for the particular reactions of eq 2. Elimination of fluoride ion from anion **19** to give intermediate 6-(difluoromethylene)-2,4-cyclohexadien-1-

Scheme 3



imine (**20**) is strongly supported by other studies.[1-8] The intermediate product **20** may undergo aromatization by the addition reactions of enolate ions **5** and **5'** to give the respective adducts **21** and **22**, and these processes are expected to be followed by intramolecular cyclizations. The resultant tetrahydroquinolines **23** and **24** can be aromatized to the respective 4-fluoroquinolines **6** and **7**, the observed products.[23] Due to a steric strain in **24**, an additional mechanistic pathway is operative for this intermediate product. Thus, ring opening of **24**, as indicated, is suggested to produce the observed fluoro olefin **8**. The exclusive *Z*-stereochemistry of **8** is fully consistent with the intermediacy of the cyclic product **24**. Similar analyses of the results of Schemes 1 and 2 and eqs 1, 3, and 5 provide rationalization for other discussed reactions.

In summary, it can be concluded that the particular mechanistic pathways are governed by steric features in the intermediate products such as **23** and **24**. Aromatization is the major pathway for relatively unstrained fused tetrahydropyridines. A ring-opening reaction becomes an important feature for the intermediate fused

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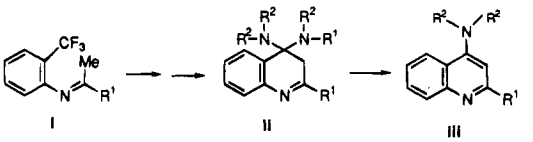
(21) Complicated mixtures of products, none of them major, were obtained in attempted reactions of **1** with lithium or potassium enolates derived from higher aliphatic aldehydes.

(22) A convenient method involves treatment of an aromatic amine in DMF with CF_3Br, SO_2, and Zn: Tordeux, M.; Langlois, B.; Wakselman, C. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2293 and references cited therein. The reaction apparently involves the intermediary of a strongly electrophilic trifluoromethyl radical. We have shown (manuscript in preparation) that the trifluoromethylation of aromatic amines, often highly ortho-regioselective, takes place at the site with the highest HOMO electron density, as obtained by AMPAC computations. Also, see ref 6.

(23) 4-Fluoroquinolines are not intermediates in the lithium dialkylamide mediated cyclizations of ketimines i to quinolines iii. These reactions proceed via the intermediacy of ii:



see ref 4 and 5.

tetrahydropyridines that contain substituents at the 2- and 3-position. In general, the formation of either a fused pyridine or a fluoro olefin as the major product can be predicted from the structure of a carbonyl substrate.

The suggested unified mechanism is fully consistent wtih the required excess of enolate ion. As can be seen from Scheme 3, 2 equiv of the enolate are needed as a base and the third equivalent acts as a nucleophile in an overall transformation of 1 equiv of **1**. This theoretical ratio of **1**/enolate of 1:3 is increased in practice to 1:4, and a slight excess of LDA is present in the mixture to minimize self-condensation of a carbonyl substrate.

Experimental Section

General. THF was distilled from sodium benzophenone ketyl immediately before use. Lithium enolates **2a–g**, **5/5′**, **9**, **11**, and **15** were generated by a slow addition of a solution of the corresponding carbonyl compound (5 mmol) in THF (3 mL) to a solution of LDA (7.5 mmol) in THF (20 mL) at −50 °C. Lithium enolate **13** of acetaldehyde was generated by the following modification of the published procedure.[19] *n*-BuLi (2 M in hexanes, 2.5 mL, 5 mmol) was added to THF (15 mL) at 23 °C under a nitrogen atmosphere, and the solution was heated under reflux for 1 h, cooled to −78 °C, and used immediately for a reaction with **1**. Crude mixtures were analyzed, and mass spectra of pure components were obtained on a GC–MS instrument equipped with an on-column injector, a poly(dimethylsiloxane)-coated capillary column, and a mass selective detector operating at 70 eV. Melting points (Pyrex capillary) are uncorrected. ^{1}H NMR (400 MHz) and ^{19}F NMR (377.4 MHz) spectra were taken in $CDCl_3$ solutions with TMS and $CFCl_3$ as the respective internal references. Coupling constants smaller than 2 Hz are not reported.

Reactions of Lithium Enolates 2a–g, 9, 11, 13, and 15 with 1 and Lithium Enolate 2f with 17: General Procedure. A stirred solution of the enolate (5 mmol) in THF (23 mL) was treated dropwise at −78 °C under a nitrogen atmosphere with a solution of **1** (200 mg, 1.25 mmol) in THF (2 mL). The resultant yellow mixture was stirred at −78 °C for 1 h and then allowed to reach 23 °C within the next 1 h, and stirred at 23 °C for 1–2 h until TLC and GC–MS analyses showed the absence of **1**. Quenching with water (1 mL) was followed by concentration on a rotary evaporator, extraction of the residue with ether (3 × 25 mL), and drying of the extract with Na_2SO_4. Products were purified on a chromatotron with a silica gel coated rotor. Quinolines **3a–e** and **14**, and a phenanthroline **18** were eluted with hexanes. Carboxamides **10**, **12**, and **16** were eluted with hexanes/ether (19:1). Solid products **3c–e**, **10**, **16**, and **18** were crystallized from cyclohexane.

4-Fluoro-2-methylquinoline[17] (**3a**, from **1** and **2a**): yield 41%; an oil; ^{19}F NMR δ −115 (d, J_{HF} = 11 Hz).

2-*tert*-Butyl-4-fluoroquinoline (**3b**, from **1** and **2b**): yield 39%; an oil; ^{1}H NMR δ 1.44 (s, 9 H), 7.20 (d, J_{HF} = 12 Hz, 1 H), 7.51 (t, J = 8 Hz, 1 H), 7.71 (t, J = 8 Hz, 1 H), 8.02 (d, J = 8 Hz, 1 H), 8.07 (d, J = 8 Hz, 1 H); ^{19}F NMR δ −116 (d, J_{HF} = 12 Hz); MS *m/z* 188 (100), 203 (25, M$^+$). Anal. Calcd for $C_{13}H_{14}FN$: C, 76.82; H, 6.94; N, 6.89. Found: C, 77.08; H, 7.12; N, 6.85.

2-(1-Adamantyl)-4-fluoroquinoline (**3c**, from **1** and **2c**): yield 35%; mp 121–121.5 °C; ^{1}H NMR δ 1.82 (m, 6 H), 2.09 (m, 6 H), 2.16 (m, 3 H), 7.17 (d, J_{HF} = 12 Hz, 1 H), 7.51 (t, J = 8 Hz, 1 H), 7.71 (t, J = 8 Hz, 1 H), 8.02 (d, J = 8 Hz, 1 H), 8.07 (d, J = 8 Hz, 1 H); ^{19}F NMR δ −116 (d, J_{HF} = 12 Hz); MS *m/z* 224 (43), 281 (100, M$^+$). Anal. Calcd for $C_{19}H_{20}FN$: C, 81.10; H, 7.17 N, 4.98. Found: C, 81.03; H, 7.23; N, 4.91.

2-Ferrocenyl-4-fluoroquinoline (**3d**, from **1** and **2d**): yield 39%; mp 116–117 °C; ^{1}H NMR δ 4.11 (s, 5 H), 4.52 (s, 2 H), 5.07 (s, 2 H), 7.25 (d, J_{HF} = 12 Hz, 1 H), 7.53 (t, J = 8 Hz, 1 H), 7.73 (t, J = 8 Hz, 1 H), 8.03 (d, J = 8 Hz, 1 H), 8.06 (d, J = 8 Hz, 1 H); ^{19}F NMR δ −117 (d, J_{HF} = 12 Hz); MS *m/z* 266 (37), 331 (100, M$^+$). Anal. Calcd for $C_{19}H_{14}FFeN$: C, 68.91; H, 4.26; N, 4.23. Found: C, 68.77; H, 4.27; N, 4.15.

4-Fluoro-2-(2-naphthyl)quinoline (**3e**, from **1** and **2e**): yield 33%; mp 122–123 °C; ^{1}H NMR δ 7.45–7.61 (m, 3 H), 7.73 (d, J_{HF} = 11 Hz, 1 H), 7.77–7.93 (m, 2 H), 7.99 (m, 2 H), 8.11 (d, J = 8 Hz, 1 H), 8.23 (d, J = 8 Hz, 1 H), 8.34 (d, J = 8 Hz, 1 H), 8.58 (s, 1 H); ^{19}F NMR δ −102 (d, J_{HF} = 11 Hz); MS *m/z* 136 (18), 272 (60), 273 (100, M$^+$). Anal. Calcd for $C_{19}H_{12}FN$: C, 83.49; H, 4.43; N, 5.12. Found: C, 83.32; H, 4.54; N, 5.20.

(*Z*)-*N*-[2-(1-Fluoropropenyl)phenyl]propionamide (**10**, from **1** and **9**): yield 36%; mp 51–52 °C; ^{1}H NMR δ 1.18 (t, J = 7.6 Hz, 3 H), 1.75 (dd, J = 7 Hz, J_{HF} = 2.4 Hz, 3 H), 2.33 (q, J = 7.6 Hz, 2 H), 5.10 (dq, J_{HF} = 38 Hz, J = 7 Hz, 1 H), 6.99 (t, J = 8 Hz, 1 H), 7.21 (d, J = 8 Hz, 1 H), 7.27 (t, J = 8 Hz, 1 H), 7.62 (br s, exchangeable with D_2O, 1 H), 8.18 (d, J = 8 Hz, 1 H); ^{19}F NMR δ −109 (dq, J_{HF} = 38 and 2.4 Hz); MS *m/z* 130 (100), 150 (95), 151 (100), 207 (50, M$^+$); HRMS exact mass calcd for $C_{12}H_{14}FNO$ 207.1059, found 207.1060. Anal. Calcd for $C_{12}H_{14}FNO$: C, 69.54; H, 6.81; N, 6.76. Found: C, 69.61; H, 6.86; N, 6.69.

(*Z*)-*N*-[2-(1-Fluoro-3-methyl-1-butenyl)phenyl]benzamide (**12**, from **1** and **11**): yield 30%; an oil; ^{1}H NMR δ 1.11 (d, J = 7 Hz, 6 H), 2.98 (m, 1 H), 5.07 (dd, J_{HF} = 38 Hz, J = 9 Hz, 1 H), 7.13 (t, J = 7 Hz, 1 H), 7.35–7.59 (m, 5 H), 7.89 (d, J = 7 Hz, 2 H), 8.46 (d, J = 8 Hz, 1 H), 8.56 (d, J = 8 Hz, 1 H); ^{19}F NMR δ −108 (dd, J_{HF} = 38 and 7 Hz); MS *m/z* 105 (100), 178 (30), 283 (10, M$^+$); HRMS exact mass for $C_{18}H_{18}FNO$ 283.1372, found 283.1372.

4-Fluoroquinoline[20] (**14**, from **1** and **13**): yield 53%; an oil; ^{19}F NMR δ −114 (t, J_{H2F} = J_{H3F} = 11 Hz).

***N*-[2-(Trifluoromethyl)phenyl]acetamide** (**16**, from **1** and **15**): yield 45%; mp 94–95 °C (lit.[5] mp 94–95 °C); ^{19}F NMR δ −60.7 (s).

1-Fluoro-3-phenyl-4,6-phenanthroline (**18**, from **17** and **2f**): yield 30%; mp 186–187 °C; ^{1}H NMR δ 7.55 (m, 3 H), 7.76 (t, J = 8 Hz, 1 H), 7.83 (t, J = 8 Hz, 1 H), 7.92 (d, J_{HF} = 13 Hz, 1 H), 8.23 (d, J = 8 Hz, 2 H), 8.28 (d, J = 8 Hz, 1 H), 8.87 (d, J = 8 Hz, 1 H), 9.59 (s, 1 H); ^{19}F NMR δ −103 (d, J_{HF} = 13 Hz); MS *m/z* 273 (50), 274 (100, M$^+$). Anal. Calcd for $C_{18}H_{11}FN_2$: C, 78.81; H, 4.04; N, 10.21. Found: C, 78.51; H, 4.07; N, 10.31.

Compounds 6–8. Lithium enolates **5/5′** derived from ethyl methyl ketone were allowed to react with **1** by using the general procedure described above. A short-path column chromatography on silica gel slurry packed in hexanes and with hexanes/ether (19:1) as an eluent gave a mixture of **6–8**. This mixture was separated on a chromatotron with a silica gel coated rotor. Elution with hexanes gave **6** and then **7**. Compound **8** was eluted with hexanes/ether (19:1).

2-Ethyl-4-fluoroquinoline (6): yield 34%; an oil; ^{1}H NMR δ 1.37 (t, J = 7.6 Hz, 3 H), 2.97 (q, J = 7.6 Hz, 2 H), 6.98 (d, J_{HF} = 11 Hz, 1 H), 7.50 (t, J = 8 Hz, 1 H), 7.70 (t, J = 8 Hz, 1 H), 8.00–8.05 (m, 2 H); ^{19}F NMR δ −115 (d, J_{HF} = 11 Hz); MS *m/z* 147 (25), 174 (100), 175 (59, M$^+$); HRMS (CI, isobutane) exact mass calcd for $C_{11}H_{11}FN$ 176.0876 (MH$^+$), found 176.0877.

4-Fluoro-2,3-dimethylquinoline (7): yield 17%; an oil; ^{1}H NMR δ 2.63 (s, 3 H), 3.77 (s, 3 H), 7.44 (t, J = 7 Hz, 1 H), 7.59 (t, J = 7 Hz, 1 H), 7.88–7.94 (m, 2 H); ^{19}F NMR δ −121; MS *m/z* 133 (27), 174 (30), 175 (100, M$^+$); HRMS exact mass calcd for $C_{11}H_{10}FN$ 175.0797, found 175.0798.

(*Z*)-*N*-[2-(1-Fluoropropenyl)phenyl]acetamide (8): yield 20%; an oil; ^{1}H NMR δ 1.74 (dd, J = 7 Hz, J_{HF} = 2.5 Hz, 3 H), 2.09 (s, 3 H), 5.12 (dq, J = 7 Hz, J_{HF} = 38 Hz, 1 H), 7.01 (t, J = 8 Hz, 1 H), 7.22 (d, J = 8 Hz, 1 H), 7.28 (t, J = 8 Hz, 1 H), 7.62 (br s, exchangeable with D_2O, 1 H), 8.11 (d, J = 8 Hz, 1 H); ^{19}F NMR δ −109 (dq, J_{HF} = 38 and 2.5 Hz); MS *m/z* 130 (100), 150 (90), 151 (50), 193 (48, M$^+$); HRMS exact mass calcd for $C_{11}H_{12}FNO$ 193.0903, found 193.0902.

***N*-[2-(Dimethylamino)ethyl]-2-(2-naphthyl)quinolin-4-amine (4e).** A solution of a fluoroquinoline **3e** (273 mg, 1 mmol) in *N*,*N*-dimethylethylenediamine (1 mL) was heated under reflux and under a nitrogen atmosphere for 2 h. Workup and purification was conducted as described for similar preparations[9] to give 307 mg (90%) of **4e**, mp 161–163 °C (from hexanes) (lit.[10] mp 161–163 °C).

***N*-[2-(Dimethylamino)ethyl]-2-phenylquinolin-4-amine (4f).** Compound **1** was allowed to react with acetophenone lithium enolate (**2f**), and the mixture was worked up by using a general procedure described above. Crude products were dissolved in hexanes (25 mL), and the solution was passed through silica gel (5 g) to remove polymeric materials. Removal of hexanes on a rotary evaporator was followed by treatment of the residue with *N*,*N*-dimethylethylenediamine and workup as described for **4e** to give 135 mg (37%) of **4f** as an oil. A hydrobromide salt **4f**·2HBr·2H_2O was obtained by using a general procedure,[9] mp 245–246 °C (lit.[9] mp 244–246 °C).

***N*-[2-(Dimethylamino)ethyl]-2-(1-naphthyl)quinolin-4-amine (4g).** A similar treatment of **1** with a lithium enolate **2g** derived from methyl 1-naphthyl ketone and followed by the procedure described for **4f** gave 128 mg (30%) of **4g** as an oil: ^{1}H NMR δ 2.60 (s, 6 H), 3.38 (t, J = 7.6 Hz, 2 H), 3.60 (t, J = 7.6 Hz, 2 H), 5.92 (br s, exchangeable with D_2O, 1 H), 7.35 (s, 1 H), 7.44–7.70 (m, 3 H), 8.02 (t, J = 8 Hz, 1 H), 8.18 (d, J = 8 Hz, 1 H), 8.22–8.34 (m, 4 H), 8.41 (d, J = 8 Hz, 1 H), 8.50 (d, J = 8 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$/TMS) δ 43.1, 44.6, 50.0, 100.1, 104.9, 105.3, 118.3, 122.4, 124.8, 125.5, 127.0, 127.6, 128.0, 128.4, 128.8, 129.0, 129.3, 132.1, 133.1, 133.9, 139.6, 151.4. A hydrobromide salt was obtained by using a general procedure[9] and crystallized from 95% EtOH, mp 273–274 °C dec. Anal. Calcd for $C_{23}H_{23}N_3$·2HBr·H_2O: C, 52.99; H, 5.22; N, 8.06. Found: C, 53.13; H, 5.23; N, 8.15.

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