Further Studies on the Cyclization of Aromatic Azomethines Ortho-Substituted with a Trifluoromethyl Group: Synthesis of 2,4-Di- or 2,3,4-Trisubstituted Quinolines

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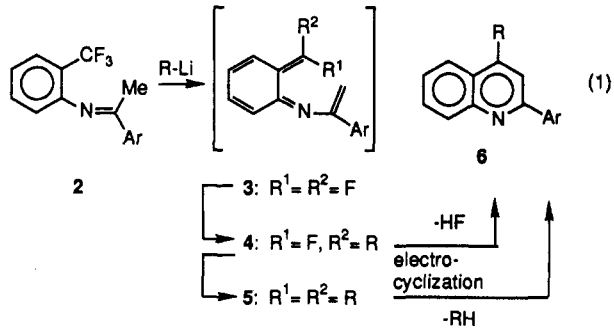
Received August 5, 1991

The scope and limitations of the novel synthetic route to quinolines (Strekowski et al. *J. Org. Chem.* **1990**, *55*, 4777) have been studied. A direct condensation of 2-(trifluoromethyl)aniline (1) with methyl aryl ketones, methyl heteroaryl ketones, ethyl aryl ketones, methyl vinyl ketones, 1-indanone, 1-tetralone, camphor, and cyclohexanone provides an easy access to the corresponding ketimines. An indirect one-pot preparation of dialkyl ketimines and *C*-alkyl-substituted amidines derived from 1, but inaccessible by the direct condensation method, is also presented. All these ketimines and amidines are cyclized in the presence of alkylamide, dialkylamide, or alkoxide bases to give a quinoline containing the base function at C-4. Analysis of byproducts of the base-mediated reactions provides strong support for the originally proposed mechanism of the quinoline formation.

Recently, we described in detail a base-mediated cyclization of ketimine **2** (eq 1, Ar = Ph) derived from 2-(trifluoromethyl)aniline (1) and acetophenone.[1] In the



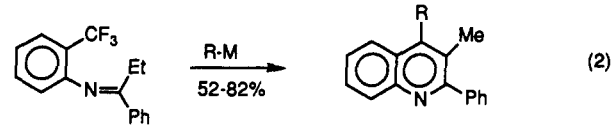
R = alkylamino or dialkylamino
Ar = aryl or heteroaryl

presence of a lithium alkylamide or dialkylamide reagent the reaction produces a 2-phenylquinoline (**6**) containing the amino function in the C-4 position. The results of mechanistic studies[1,2] are consistent with the intermediacy of **3** formed by ionization of **2** at the methyl group and then elimination of fluoride. It was proposed that a subsequent fast addition reaction of an amide anion with **3** is also followed by elimination of fluoride to give **4**. A similar sequence of reactions with **4** then produces **5**. Both **4** and **5** may undergo electrocyclization to give the corresponding 3,4-dihydroquinolines, the precursors to quinoline **6**. Due to the apparent fast addition reaction of the amide anion with **3**, the electrocyclization of **3** is less likely to occur.[3] Few mechanistically related processes are known.[4]

Following the discovery that several of the initially synthesized 4-aminoquinolines were active against HIV-1, a large number of 2-aryl- and 2-heteroaryl-substituted derivatives **6** were prepared in a similar fashion.[5] After additional examples of active compounds were found, systematic studies were conducted to determine whether or not quinolines with other substituent types can be synthesized by using the discussed approach. The scope and limitations of the method are presented in this paper.[6]

Results and Discussion

Direct Synthesis of Ketimines and Their Cyclization. Condensation of **1** with propiophenone furnished a single *E* diastereomer[7] of ketimine **7** in a 75% yield, the treatment of which with LDA and *t*-BuOK gave the respective quinolines **8** and **9** (eq 2). The facility of the synthesis of these sterically congested 2,3,4-trisubstituted quinolines is consistent with the intramolecular nature of the cyclization reaction.



Aniline **1** was also reacted with 4-methyl-3-penten-2-one and 4-phenyl-3(*E*)-buten-2-one to give rather unstable vinyl imines **10** and **12**, respectively, which could not be obtained in an analytically pure form (eq 3). Nevertheless, a simple prepurification of these imines by a Kugelrohr distillation followed by treatments with lithium amide reagents gave the corresponding 2-vinylquinolines **11** and **13** in quite respectable yields.

Several cycloalkanones were condensed efficiently with **1** to furnish stable ketimines. A 1-indanone-derived ketimine ((*E*)-**14**) and a 1-tetralone derivative ((*E*)-**16**) were cyclized to the respective fused quinolines **15** and **17** (eq

(1) Strekowski, L.; Wydra, R. L.; Cegla, M. T.; Czarny, A.; Harden, D. B.; Patterson, S. E.; Battiste, M. A.; Coxon, J. M. *J. Org. Chem.* **1990**, *55*, 4777.

(2) (a) Strekowski, L.; Wydra, R. L.; Harden, D. B.; Honkan, V. A. *Heterocycles* **1990**, *31*, 1565. (b) Wydra, R. L.; Patterson, S. E.; Strekowski, L. *J. Heterocycl. Chem.* **1990**, *27*, 803.

(3) Extensive experimental and some computational data presented in refs 1 and 2 are not duplicated in this paper.

(4) (a) References cited in ref 1. (b) Bunnett, J. F.; Galli, C. *J. Chem. Soc., Perkin Trans. I* **1985**, 2515.

(5) Strekowski, L.; Mokrosz, J. L.; Honkan, V. A.; Czarny, A.; Cegla, M. T.; Wydra, R. L.; Patterson, S. E.; Schinazi, R. F. *J. Med. Chem.* **1991**, *34*, 1739.

(6) For selected reviews on other methods of quinoline synthesis, see: (a) Newkome, G. R.; Paudler, W. W. *Contemporary Heterocyclic Chemistry*; Wiley: New York, 1982; p 199. (b) Katritzky, A. R. *Handbook of Heterocyclic Chemistry*; Pergamon Press: Oxford, 1985; p 457.

(7) The *E* stereochemistry of **7**, as expected for a thermodynamic product, was shown by NOE experiments. The geometry of the major thermodynamic diastereomer of a ketimine derived from **1** in a direct condensation reaction can be predicted on the basis of the relative steric bulk of the two C substituents and taking into account co-planarity of the ketimine function with the *C*-aryl or *C*-heteroaryl substituent. The *N*-aryl is approximately perpendicular to the C=N plane: Strekowski, L.; Cegla, M. T.; Harden, D. B.; Kong, S.-B. *J. Org. Chem.* **1989**, *54*, 2464 and references cited therein.

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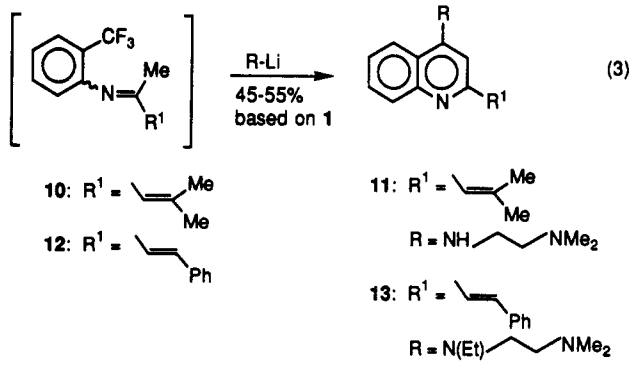
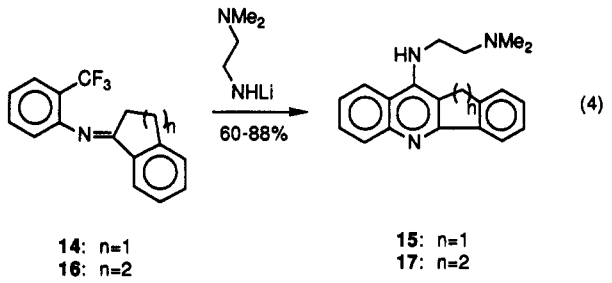


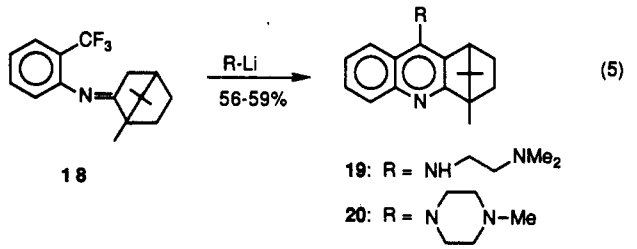
(3)

4). A stable ketimine ((*E*)-18) derived from camphor was



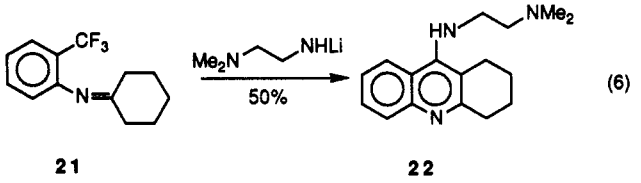
(4)

cyclized to bornane-fused quinolines **19** and **20** in high yields (eq 5). With enantiomerically pure camphor the absolute values of specific rotations were virtually identical for all pairs of enantiomers of **18**–**20** and were not affected by changes in conditions of the reactions. These results strongly suggest that both the condensation and cyclization reactions occur without any racemization.



(5)

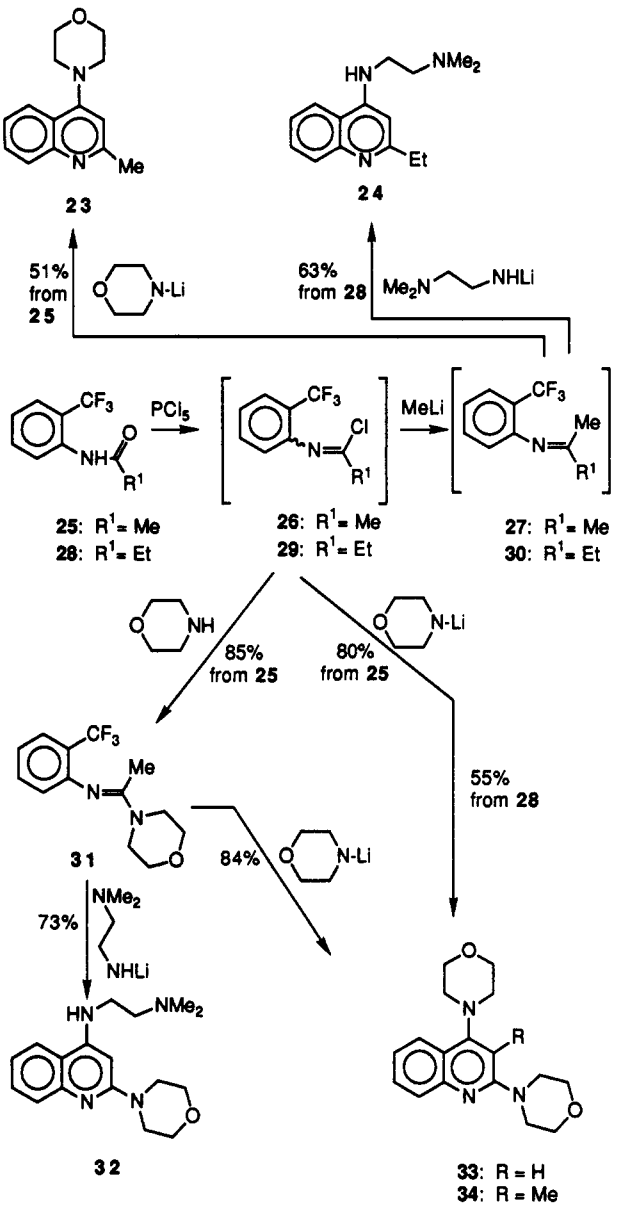
In sharp contrast to the highly successful condensation reactions discussed above, a cyclohexanone derivative (**21**), the precursor to a tetrahydroacridine (**22**, eq 6), was obtained in a 10% yield only under optimized conditions. Attempted condensation reactions of **1** with 2-indanone or aliphatic acyclic ketones failed to produce ketimines.[8]



(6)

Indirect Method. The inaccessibility of aliphatic ketimines severely limited the scope of this novel synthetic route to quinolines. A solution to this problem is illustrated in Scheme I by the successful preparation of 2-alkylquinolines **23** and **24** starting with the respective amides **25** and **28**. The ketimine **27** required for the synthesis of **23** was obtained by treatment of **25** with PCl_5 followed by reaction of the resultant chloro imine **26**, without purification, with MeLi.[9] A lithium morpholide mediated cyclization of crude ketimine **27** was accomplished in the same reaction flask. 2-Ethylquinoline **24** was synthesized in a similar fashion. Interestingly, the crude 2-ethylquinoline **24** was not contaminated with an isomeric 2,3-dimethylquinoline which could have been originated from ionization of the ethyl group in ketimine **30** and/or intermediate products derived from **30**. The exclusive ionization of the methyl group may reflect the formation of the more thermodynamically stable anion.

Scheme I

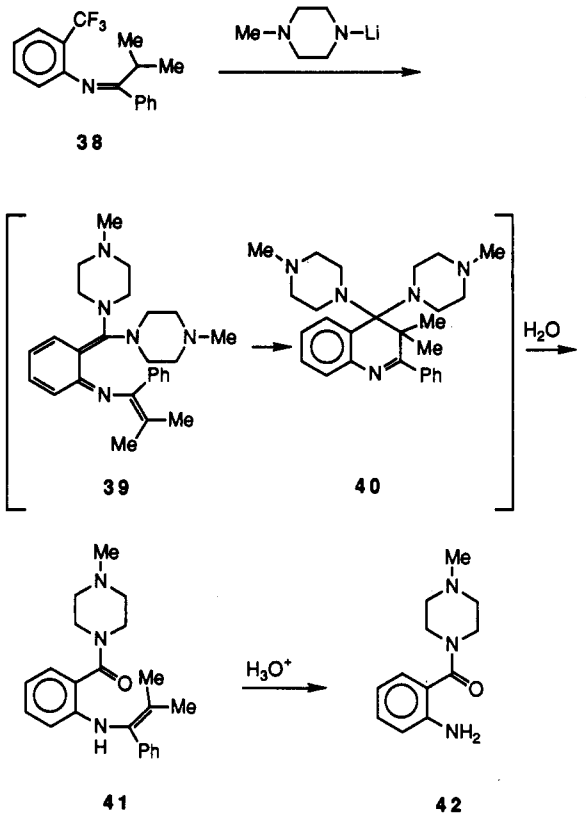


A successful extension of this approach to synthesis of 2,4-diaminoquinoline derivatives containing two different amino functions, such as **32**, or the same amino groups, such as **33** and **34**, is also given in Scheme I. Thus, chloro imine **26** was reacted with morpholine[9] and the resultant amidine **31** upon treatment with lithium 2-(dimethylamino)ethylamide or lithium morpholide was cyclized to the respective quinolines **32** and **33**. The direct treatment of chloro imine **26** with lithium morpholide furnished **33**,

(8) Analysis (chromatography and ^1H NMR) of products obtained both in protic acid and Lewis acid catalyzed reactions suggested self-condensation of the initially formed ketimine and/or its condensation with a ketone.

(9) For a review on the preparation of chloro imines and their additive reaction with nucleophilic reagents, see: Bonnet, R. In *The Chemistry of the Carbon-Nitrogen Double Bond*; Patai, S., Ed.; Interscience: London, 1970, p 597.

Scheme II

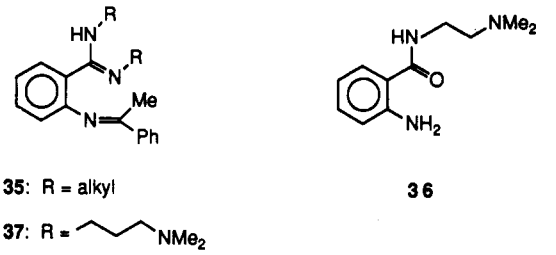


apparently through intermediacy of **31**. The simplicity and efficiency of the preparation of 3-methylquinoline **34** indicates again that the method is highly suitable for the synthesis of sterically congested 2,3,4-trisubstituted quinolines.

This approach, thus, permits a facile preparation of substituted imines and amidines that can be cyclized to quinolines. With the exception of imines derived from cyclic ketones, this approach also provides a useful alternative in the synthesis of imines, such as **2**, **10**, and **12**, obtained normally by condensation of **1** with acyclic ketones. Several acyl chlorides were reacted with **1** followed by treatment with PCl_5 and then MeLi, as outlined in Scheme I, to give imines in yields comparable to those of the direct condensation reaction of **1** with the corresponding methyl ketones. Other alkyl aryl ketimines, such as **7**, can be prepared in a similar manner.[10]

Structural Effects in the Base and Side Reactions. 2-Substituted quinolin-4-amines with a primary amino group, such as **6** (R = NH_2), could not be obtained in attempted cyclization reactions of ketimines **2** with lithium, sodium, or potassium amide in ether, which is apparently due to insolubility of these amide reagents. The experiments were not pursued further because the quinolin-4-amines are easily accessible through LDA-mediated cyclization of ketimines derived from 2-aminobenzonitrile.[11]

The formation of 4-(alkylamino)quinolines on treatment of ketimines with primary alkylamides is accompanied by varying amounts of amidines,[1] such as **35**. These highly polar compounds are separated easily from much less polar quinolines by using a rapid flash chromatography method.



35: R = alkyl

37: R =

The ratio of quinoline/amidine decreases with decreasing steric bulk of the alkyl group in the lithium reagent and in the presence of an excess of the amine used for the preparation of the lithium reagent. A cyclic amidine is the major low molecular weight product for the reaction conducted in the presence of lithium 3-aminopropylamide.[12] These effects were accounted for in the proposed unified mechanism of the quinoline and amidine formation.[1,2]

The cyclization reactions conducted in the presence of a lithium reagent derived from 2-(dimethylamino)ethylamine are a notable exception because they give quinolines with high efficiency, even in the presence of an excess of the amine. For example, a quinoline **6** (Ar = Ph, R = $NHCH_2CH_2NMe_2$) was obtained in a 93% yield[5] upon treatment of **2** with lithium 2-(dimethylamino)ethylamide, and this yield was not affected by the excess of the amine used for the generation of the lithium amide reagent. No additional products could be isolated from the mixture quenched with 1 equiv of water. A chromatographic separation of the mixture treated with excess of an aqueous acid gave amide **36** in a 2% yield.

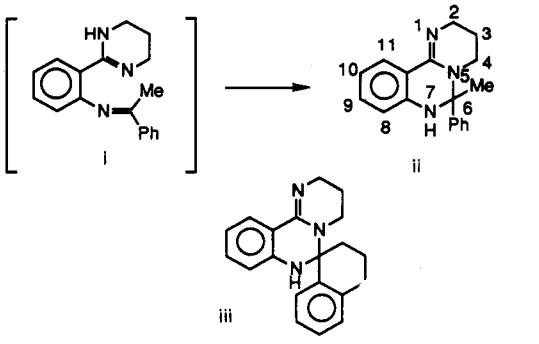
The effect of 2-(dimethylamino)ethylamine thus resembles that of a highly sterically hindered amine, such as *tert*-butylamine.[1] The results with the former amine can be explained in terms of the formation of stable molecular aggregates[13] by lithium derivatives of the intermediate product **5** (eq 1, R = $NHCH_2CH_2NMe_2$). The structure of such aggregates is apparently of unfavorable stereochemistry for amidine formation but permits the electrocyclization reaction within the aggregate.

The hypothesis of specific aggregate formation is strongly supported by experiments with a lithium reagent derived from 3-(dimethylamino)propylamine. In sharp contrast to the results discussed above, the treatment of

(10) Benzyllithium (generated from benzyl methyl ether: Gilman, H.; McNinch, H. A. *J. Org. Chem.* **1961**, *26*, 3723) was also reacted with **26** to give the corresponding benzyl methyl ketimine identified by ^1H NMR. Unfortunately, treatment of this crude ketimine with lithium 4-methylpiperazide gave mainly polymeric materials.

(11) Strekowski, L.; Kong, S.-B.; Cegla, M. T.; Harden, D. B. *Heterocycles* **1989**, *29*, 539.

(12) It escaped our attention (ref 1) that the chemical shifts for the methyl group in acyclic amidines **35** (δ 2.25 ± 0.02) differs from that for the corresponding cyclic amidine derived from lithium 3-aminopropylamine (δ 1.84). The initially formed amidine i undergoes ring closure to give ii. NOE experiments (400 MHz) gave the following interactions for ii: Me···N7H, Me···C4H, N7H···C8H. In a similar way it was shown that the corresponding amidine derived from **16** has the structure iii. This amidine does not exist in an open form as stated erroneously in ref 2a. The structural differences are reflected by conditions for hydrolysis in 1 N HCl to give an aniline and a ketone without affecting the amidine portion: **35**, 23 °C; ii and iii, 80 °C.



(13) For excellent reviews on aggregation of lithium compounds, see: (a) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1624. (b) Gregory, K.; Schleyer, P. v. R.; Snaith, R. *Adv. Organomet. Chem.* In press.

ketimine 2 (Ar = Ph) with this reagent furnished amidine 37 as the major low molecular weight product. Analysis of the ^{1}H NMR spectrum of a crude mixture revealed the absence of proton signals characteristic for a 2-substituted quinolin-4-amine,[1,5] such as the lowest field doublets for H5 and H8 and a high-field singlet for H3.

The quinoline syntheses conducted in the presence of lithium reagents derived from secondary amines were all efficient. Occasionally, a small quantity (<5%) of an amide, such as 42 (Scheme II), was isolated from a mixture after acidic workup. It was suggested that the amides might result from hydrolysis of the intermediate products 5 and/or its cyclized derivatives. In order to test this hypothesis the reaction of isopropyl-substituted ketimine 38 with lithium 4-methylpiperazide was investigated in detail. This reaction can follow the mechanistic pathway of eq 1 with the formation of an aza triene (39) and its subsequent cyclization to a dihydroquinoline (40), but the latter product cannot undergo aromatization to a quinoline. Hydrolysis of 39/40 was expected to give an amide. Indeed, the enamine-substituted[14] amide 41 was isolated in 65% yield after quenching the mixture with 1 molar equiv of water. Acid hydrolysis of 41 furnished known amide 42.[15] These results not only suggest the origin of an amide byproduct in the quinoline synthesis but also strongly support the proposed mechanism for quinoline formation, which was elucidated previously by using an independent approach.[1,2]

The effect of steric hindrance in the alkoxide base on the formation of a 4-alkoxyquinoline was investigated in the cyclization reactions of ketimine 2 (Ar = Ph) in the presence of *t*-BuOK and EtOK. 4-*tert*-Butoxy-2-phenylquinoline[1] and 4-ethoxy-2-phenylquinoline (43) were obtained in 83% and 25% yields, respectively, under optimized conditions. The steric hindrance effect, thus, is similar to that observed with amines. The increased efficiency of quinoline formation in the presence of sterically hindered bases may reflect a decreased ability of the sterically congested intermediate products 5 to undergo intermolecular reactions, including polymerization, which compete with the intramolecular electrocyclization reaction.

Conclusions

A synthetic route to 4-(substituted amino)- and 4-alkoxy-2-substituted quinolines has been described. The method is especially efficient in the preparation of derivatives with bulky amino and alkoxy groups. Sterically congested 2,3,4-trisubstituted quinolines are also easily accessible. The method uses commercially available starting materials. All results are consistent with the mechanism of quinoline formation as originally proposed.[1]

Experimental Section

All reagents were obtained from Aldrich. Amines were stored over pellets of sodium hydroxide. Ether and THF was distilled from sodium benzophenone ketyl immediately before use. For air-sensitive reactions the glassware was dried at 140 °C, assembled hot, and cooled in a stream of nitrogen. The liquids were transferred with syringes.

Unless stated otherwise the procedures published previously[5] for a direct condensation of 1 with ketones to give ketimines, generation of lithium amide reagents from amines and *n*-butyllithium, the amide reagent-mediated reactions of ketimines, and the preparation of hydrobromide salts from oily amine products were used without modification. With the exception of optically active ketimines 18 the remaining ketimines were distilled on a Kugelrohr (100–150 °C/0.1–0.5 mmHg) apparatus. All chromatographic separations were conducted on a chromatotron with silica gel coated rotors. Unless stated otherwise solid compounds were additionally crystallized from toluene/hexanes (ketimines, amidines, and quinolines) or EtOH/H_2O (salts). The reported yields correspond to analytically pure products.

Melting points (Pyrex capillary) are uncorrected. Unless stated otherwise, ^{1}H NMR spectra were obtained on a Varian VXR-400 (400 MHz) instrument at 25 °C in $CDCl_3$ solutions with Me_4Si as an internal standard. Coupling constants smaller than 1.2 Hz are not reported.

(*E*)-*N*-(1-Phenylpropylidene)-2-(trifluoromethyl)aniline (7): 80%; mp 39–41 °C; ^{1}H NMR (60 MHz) δ 1.08 (t, J = 7 Hz, 3 H), 2.65 (q, J = 7 Hz, 2 H), 6.6–8.0 (m, 9 H); MS m/z 145 (83), 248 (100), 277 (M^+, 76). Anal. Calcd for $C_{16}H_{14}F_3N$: C, 69.30; H, 5.09; N, 5.05. Found: C, 69.40; H, 5.09; N, 5.01.

***N*,*N*-Diisopropyl-3-methyl-2-phenylquinolin-4-amine (8)**: 82%; an oil; ^{1}H NMR δ 1.10 and 1.13 (2 d, J = 6.5 Hz, 12 H), 2.35 (s, 3 H), 3.86 (sept, J = 6.5 Hz, 2 H), 7.39–7.44 (m, 1 H), 7.45–7.50 (m, 3 H), 7.53–7.56 (m, 2 H), 7.60 (t, J = 8 Hz, 1 H), 8.08 (d, J = 8 Hz, 1 H), 8.20 (d, J = 8 Hz, 1 H); MS m/z 261 (89), 303 (100), 318 (M^+, 12); HRMS calcd for $C_{22}H_{26}N_2$ m/z 318.2096, found 318.2087.

4-*tert*-Butoxy-3-methyl-2-phenylquinoline (9). A solution of *t*-BuOK (0.56 g, 5 mmol) and ketimine 7 (0.3 g, 1.08 mmol) in THF (25 mL) was heated under reflux for 1.5 h, then cooled to 23 °C, and quenched with water. Chromatography (hexanes/Et_3N, 19:1) followed by crystallization (hexanes) gave 0.163 g (52%) of 9: mp 64–66 °C; ^{1}H NMR δ 1.50 (s, 9 H), 2.35 (s, 3 H), 7.40–7.51 (m, 4 H), 7.55–7.60 (m, 2 H), 7.63 (t, J = 8 Hz, 1 H), 8.09 (d, J = 8 Hz, 1 H), 8.16 (d, J = 8 Hz, 1 H). Anal. Calcd for $C_{20}H_{21}NO$: C, 82.44; H, 7.26; N, 4.80. Found: C, 82.40; H, 7.27; N, 4.75.

***N*-[2-(Dimethylamino)ethyl]-2-(2-methylpropen-1-yl)-quinolin-4-amine (11).** A solution of 1 (3.44 g, 21.4 mmol), 4-methyl-3-penten-2-one (2.1 g, 21.4 mmol), and *p*-TsOH (50 mg) in benzene (50 mL) was heated under reflux for 6 h with azeotropic removal of water. Concentration under reduced pressure was followed by fractionation of the residue on a Kugelrohr apparatus. A portion (1 g) of the major fraction (2.8 g) containing ketimine 10 [^{1}H NMR δ 1.82 (s, 3 H), 1.91 (s, 3 H), 2.14 (s, 3 H), 5.93 (s, 1 H), 6.69 (d, J = 8 Hz, 1 H), 7.08 (t, J = 8 Hz, 1 H), 7.43 (t, J = 8 Hz, 1 H), 7.60 (d, J = 8 Hz, 1 H)] was treated with a lithium reagent prepared from 2-(dimethylamino)ethylamine.[5] The resultant quinoline 11 was purified by chromatography (hexanes/Et_3N/EtOH, 7:2:1) to give 0.92 g (45% based on 1) of an oil: ^{1}H NMR δ 1.97 (s, 3 H), 2.12 (s, 3 H), 2.31 (s, 3 H), 2.69 (t, J = 6.5 Hz, 2 H), 3.30 (m, 2 H; t, J = 6.5 Hz, 2 H after treatment with D_2O), 5.76 (br s, 1 H, exchangeable with D_2O), 6.37 (s, 1 H), 6.43 (br s, 1 H), 7.37 (t, J = 8 Hz, 1 H), 7.59 (t, J = 8 Hz, 1 H), 7.74 (d, J = 8 Hz, 1 H), 7.93 (d, J = 8 Hz, 1 H); MS m/z 58 (100), 269 (M^+, 73); mp for 11·2HBr·$^1/_2H_2O$ 278–280 °C. Anal. Calcd for $C_{17}H_{23}N_3$·2HBr·$^1/_2H_2O$: C, 46.38; H, 5.95; N, 9.55. Found: C, 46.32; H, 5.93; N, 9.50.

(*E*)-*N*-[2-(Dimethylamino)ethyl]-*N*-ethyl-2-[α-styryl]-quinolin-4-amine (13). Crude ketimine 12 was prepared from 1 and (*E*)-4-phenyl-3-buten-2-one using the procedure described above. The ^{1}H NMR spectrum of 12 gave a complicated set of signals in the aromatic/vinyl region and two singlets, δ 2.01 and 2.48, for methyls in the ratio of 2.5:1, clearly indicating the presence of *E* and *Z* ketimine diastereomers. The major diastereomer was assigned the *E* stereochemistry for C=N on the basis of shielding effects in ketimines.[7] After the cyclization of crude 12 with a lithium reagent prepared from *N*-[2-(dimethylamino)ethyl]ethylamine[5] the resultant quinoline 13 was purified by chromatography (hexanes/Et_3N/EtOH, 10:2:1) to give an oil: 55% based on 1; ^{1}H NMR δ 1.20 (t, J = 7 Hz, 3 H), 2.27 (s, 6 H), 2.55 (t, J = 7 Hz, 2 H), 3.44 (q, J = 7 Hz, 2 H), 3.49 (t, J = 7 Hz, 2 H), 7.17 (s, 1 H), 7.29–7.45 (m, 5 H including d, J = 15.6 Hz, 1 H, at δ 7.38), 7.61–7.68 (m, 4 H including d, J = 15.6 Hz, 1 H, at δ 7.65), 8.03 (2 d, J = 8 Hz, 2 H); MS m/z 58 (100), 287 (97), 345 (M^+, 19); mp for 13·2HBr·H_2O 268–270 °C. Anal. Calcd for $C_{23}H_{27}N_3$·2HBr·H_2O: C, 52.58; H, 5.95; N, 8.00. Found: C, 52.34; H, 5.94; N, 7.93.

(14) For ketimine/enamine tautomerizations, see: Strekowski, L.; Patterson, S.; Cegla, M. T.; Wydra, R. L.; Czarny, A.; Harden, D. B. *Tetrahedron Lett.* **1989**, *30*, 5197 and references cited therein.

(15) Cervena, I.; Protiva, M. *Collect. Czech. Chem. Commun.* **1984**, *49*, 1009.

(*E*)-*N*-(Indan-1-ylidene)-2-(trifluoromethyl)aniline (14): 55%; mp 90–91 °C; ^{1}H NMR δ 2.57 (t, *J* = 6.4 Hz, 2 H), 3.08 (t, *J* = 6.4 Hz, 2 H), 6.87 (d, *J* = 8 Hz, 1 H), 7.16 (t, *J* = 8 Hz, 1 H), 7.39 (m, 2 H), 7.49 (m, 2 H), 7.65 (d, *J* = 8 Hz, 1 H), 7.96 (d, *J* = 8 Hz, 1 H); MS *m/z* 274 (87), 275 (M^+, 100). Anal. Calcd for $C_{16}H_{12}F_3N$: C, 69.81; H, 4.40; N, 5.09. Found: C, 69.74; H, 4.40; N, 5.01.

***N*-[2-(Dimethylamino)ethyl]-11*H*-indeno[1,2-*b*]quinolin-10-amine (15)**: 60%; mp 174–175 °C; ^{1}H NMR δ 2.35 (s, 6 H), 2.70 (t, *J* = 6 Hz, 2 H), 3.86 (m, 2 H; t, *J* = 6 Hz, 2 H after treatment with D_2O), 4.26 (s, 2 H), 5.97 (br s, 1 H, exchangeable with D_2O), 7.40–7.52 (m, 3 H), 7.57 (d, *J* = 8 Hz, 1 H), 7.63 (t, *J* = 8 Hz, 1 H), 7.85 (d, *J* = 8 Hz, 1 H), 8.09 (d, *J* = 8 Hz, 1 H), 8.26 (d, *J* = 8 Hz, 1 H); MS *m/z* 58 (100), 216 (23), 245 (25), 303 (M^+, 51). Anal. Calcd for $C_{20}H_{21}N_3$: C, 79.17; H, 6.98; N, 13.85. Found: C, 79.08; H, 6.99; N, 13.81.

(*E*)-*N*-(1,2,3,4-Tetrahydronaphthalen-1-ylidene)-2-(trifluoromethyl)aniline (16): 85%; mp 95–97 °C; ^{1}H NMR δ 1.93 (pent, *J* = 6 Hz, 2 H), 2.43 (t, *J* = 6 Hz, 2 H), 2.91 (t, *J* = 6 Hz, 1 H), 6.75 (d, *J* = 8 Hz, 1 H), 7.13 (t, *J* = 8 Hz, 1 H), 7.21 (d, *J* = 7.5 Hz, 1 H), 7.31 (t, *J* = 7.5 Hz, 1 H), 7.39 (t, *J* = 7.5 Hz, 1 H), 7.47 (t, *J* = 8 Hz, 1 H), 7.64 (d, *J* = 8 Hz, 1 H), 8.30 (d, *J* = 7.5 Hz, 1 H); IR (neat) ν 1638 cm^{-1}. Anal. Calcd for $C_{17}H_{14}F_3N$: C, 70.58; H, 4.88; N, 4.84. Found: C, 70.40; H, 4.91; N, 4.80.

***N*-[2-(Dimethylamino)ethyl]-5,6-dihydrobenz[*c*]acridin-7-amine (17)**: 88%; an oil; ^{1}H NMR and MS have been published;[2a] mp for 17·2HBr·$^1/_2H_2O$ 275–277 °C. Anal. Calcd for $C_{21}H_{23}N_3$·2HBr·$^1/_2H_2O$: C, 51.65; H, 5.37; N, 8.61. Found: C, 51.30; H, 5.41; N, 8.51.

(*E*)-*N*-[(1*R*)-Bornan-2-ylidene]-2-(trifluoromethyl)aniline [(*R*)-18]. A solution of 1 (2.42 g, 15 mmol), (1*R*)-(+)-camphor (6.10 g, 20 mmol), and *p*-TsOH (50 mg) in toluene (45 mL) was heated under reflux for 24 h with azeotropic removal of water. Chromatography (hexanes/CH_2Cl_2, 1:4) have 3.90 g (88%) of (*R*)-18 as an oil: $[\alpha]^{25}_D$ −12.7 (*c* 0.2, hexanes); ^{1}H NMR δ 0.89 (s, 3 H), 0.98 (s, 3 H), 1.10 (s, 3 H), 1.23 (m, 1 H), 1.55 (m, 1 H), 1.65–1.92 (m, 4 H), 2.19 (m, 1 H), 6.70 (d, *J* = 8 Hz, 1 H), 7.09 (t, *J* = 8 Hz, 1 H), 7.42 (t, *J* = 8 Hz, 1 H), 7.58 (d, *J* = 8 Hz, 1 H); MS *m/z* 212 (71), 295 (M^+, 100). Anal. Calcd for $C_{17}H_{20}F_3N$: C, 69.13; H, 6.83; N, 4.74. Found: C, 69.22; H, 6.85; N, 4.70.

(*E*)-*N*-[(1*S*)-Bornan-2-ylidene)-2-(trifluoromethyl)aniline [(*S*)-18]. This ketimine was obtained from 1 and (1*S*)-(−)-camphor: 87%; an oil; $[\alpha]^{25}_D$ +13.0 (*c* 0.2, hexanes). Anal. Calcd for $C_{17}H_{20}F_3N$: C, 69.13; H, 6.83; N, 4.74. Found: C, 69.14; H, 6.83; N, 4.71.

(4*R*)-*N*-[2-(Dimethylamino)ethyl]-4-methyl-1,2,3,4-tetrahydro-1,4-(dimethylmethano)acridin-9-amine [(*R*)-19]. This compound was obtained from (*R*)-18: 59%, an oil; $[\alpha]^{25}_D$ +101.1 (*c* 0.2, hexanes); ^{1}H NMR δ 0.66 (s, 3 H), 1.02 (s, 3 H), 1.34 (m, 2 H), 1.38 (s, 3 H), 1.88 (m, 1 H), 2.17 (m, 1 H), 2.30 (s, 6 H), 2.62 (t, *J* = 6 Hz, 2 H), 3.31 (d, *J* = 4 Hz, 1 H), 3.55 (m, 2 H), 5.49 (br s, 1 H, exchangeable with D_2O), 7.37 (t, *J* = 8 Hz, 1 H), 7.53 (t, *J* = 8 Hz, 1 H), 7.76 (d, *J* = 8 Hz, 1 H), 7.98 (d, *J* = 8 Hz, 1 H); MS *m/z* 58 (100), 265 (15), 323 (M^+, 16); mp for (*R*)-19·2H_3PO_4·H_2O 232–233 °C. Anal. Calcd for $C_{21}H_{29}N_3$·2H_3PO_4·H_2O: C, 46.93; H, 6.94; N, 7.82. Found: C, 47.04; H, 6.87; N, 7.75.

(4*S*)-*N*-[2-(Dimethylamino)ethyl]-4-methyl-1,2,3,4-tetrahydro-1,4-(dimethylmethano)acridin-9-amine [(*S*)-19]. This compound was obtained from (*S*)-18: 57%, an oil; $[\alpha]^{25}_D$ −101.2 (*c* 0.2, hexanes); mp for (*S*)-19·2H_3PO_4·H_2O 232–233 °C. Anal. Calcd for $C_{21}H_{29}N_3$·2H_3PO_4·H_2O: C, 46.93; H, 6.94, N, 7.82. Found: C, 47.03; H, 6.74; N, 7.70.

(4*R*)-4-Methyl-9-(4-methylpiperazino)-1,2,3,4-tetrahydro-1,4-(dimethylmethano)acridine [(*R*)-20]. This compound was obtained from (*R*)-18: 56%, an oil; $[\alpha]^{25}_D$ +99.8 (*c* 0.2, hexanes); ^{1}H NMR δ 0.60 (s, 3 H), 1.04 (s, 3 H), 1.30 (m, 2 H), 1.40 (s, 3 H), 1.92 (m, 1 H), 2.19 (m, 1 H), 2.43 (s, 3 H), 2.69 (m, 4 H), 3.31 (m, 4 H), 3.42 (d, *J* = 4 Hz, 1 H), 7.40 (t, *J* = 8 Hz, 1 H), 7.56 (t, *J* = 8 Hz, 1 H), 8.01 (d, *J* = 8 Hz, 1 H), 8.13 (d, *J* = 8 Hz, 1 H); MS *m/z* 265 (46), 335 (M^+, 100); mp for (*R*)-18·HBr 240–242 °C. Anal. Calcd for $C_{22}H_{29}N_3$·HBr: C, 63.45; H, 7.26; N, 10.09. Found: C, 63.31; H, 7.20; N, 10.02.

(4*S*)-4-Methyl-9-(4-methylpiperazino)-1,2,3,4-tetrahydro-1,4-(dimethylmethano)acridine [(*S*)-20]. This compound was obtained from (*S*)-18: 57%; an oil; $[\alpha]^{25}_D$ −99.5 (*c* 0.2, hexanes). The use of excess HBr for the salt preparation gave (*S*)-20·2HBr·3H_2O, mp 240–242 °C. Anal. Calcd for $C_{22}H_{29}N_3$·2HBr·3H_2O: C, 47.92; H, 6.77; N, 7.62. Found: C, 47.98; H, 6.70; N, 7.57.

***N*-Cyclohexylidene-2-(trifluoromethyl)aniline (21)**. The condensation reaction of 1 with cyclohexanone was conducted in refluxing benzene for 2 h: 10%; an oil; ^{1}H NMR δ 1.65 (m, 4 H), 1.86 (m, 2 H), 2.09 (t, *J* = 6 Hz, 2 H), 2.49 (t, *J* = 6 Hz, 2 H), 6.68 (d, *J* = 8 Hz, 1 H), 7.10 (t, *J* = 8 Hz, 1 H), 7.42 (t, *J* = 8 Hz, 1 H), 7.58 (d, *J* = 8 Hz, 1 H). Anal. Calcd for $C_{13}H_{14}F_3N$: C, 64.72; H, 5.85; N, 5.81. Found: C, 64.88; H, 5.91; N, 5.74.

***N*-[2-(Dimethylamino)ethyl]-1,2,3,4-tetrahydroacridin-9-amine (22)**: 50%; mp 88–90 °C; ^{1}H NMR δ 1.91 (m, 4 H), 2.30 (s, 6 H), 2.50 (t, *J* = 6 Hz, 2 H), 2.75 (m, 2 H), 3.05 (m, 2 H), 3.51 (m, 2 H; t, *J* = 6 Hz, 2 H after treatment with D_2O), 5.17 (br s, 1 H, exchangeable with D_2O), 7.34 (t, *J* = 8 Hz, 1 H), 7.55 (t, *J* = 8 Hz, 1 H), 7.90 (d, *J* = 8 Hz, 1 H), 8.02 (d, *J* = 8 Hz, 1 H); MS *m/z* 58 (100), 211 (19), 269 (M^+, 20). Anal. Calcd for $C_{17}H_{23}N_3$: C, 75.80; H, 8.61; N, 15.60. Found: C, 75.90; H, 8.58; N, 15.52.

***N*-Acetyl-2-(trifluoromethyl)aniline (25)**. A solution of 1 (3.22 g, 20 mmol) and Et_3N (1.8 mL, 20 mmol) in $CHCl_3$ (20 mL) was stirred at −5 °C and treated dropwise with a solution of AcCl in $CHCl_3$ (10 mL). The mixture was stirred at 23 °C for 1 h and then concentrated, and the oily residue was stirred with water (10 mL) until it solidified. The solid was filtered, washed with water, dried, and crystallized from aqueous EtOH to give 3.86 g (95%) of **25**: mp 94–95 °C; ^{1}H NMR (60 MHz) δ 2.22 (s, 3 H), 7.2–7.8 (m, 4 H), 8.20 (d, *J* = 8 Hz, 1 H); MS *m/z* 161 (100), 203 (M^+, 24). Anal. Calcd for $C_9H_8F_3NO$: C, 53.21; H, 3.97; N, 6.89. Found: C, 53.10; H, 3.96; N, 6.84.

***N*-Propanoyl-2-(trifluoromethyl)aniline (28)**. A similar treatment of 1 with propanoyl chloride gave **28**: 93%; mp 85–87 °C; ^{1}H NMR (60 MHz) δ 1.22 (t, *J* = 7 Hz, 3 H), 2.43 (q, *J* = 7 Hz, 2 H), 4.30 (br s, 1 H, exchangeable with D_2O), 6.95–7.65 (m, 3 H), 8.14 (d, *J* = 8 Hz, 1 H); MS *m/z* 161 (100), 217 (M^+, 18). Anal. Calcd for $C_{10}H_{10}F_3NO$: C, 55.30; H, 4.64; N, 6.45. Found: C, 55.13; H, 4.66; N, 6.39.

2-Methyl-4-morpholinoquinoline (23). A mixture of amide **25** (1.015 g, 5 mmol), PCl_5 (1.052 g, 5.05 mmol), and benzene (10 mL) was heated under reflux for 15 min. Concentration on a rotary evaporator was followed by the addition of benzene and then additional concentration to remove traces of HCl and $POCl_3$. Ether (50 mL) was added to the crude chloro imine **26** [^{1}H NMR (60 MHz) δ 2.60 (s, 3 H), 6.80–7.80 (m, 4 H)], and the resultant solution was cooled to −10 °C and treated with MeLi (1.4 M, 3.6 mL, 5.05 mmol). The mixture was then stirred at 23 °C for 12 h, after which time the resultant crude ketimine **27** [^{1}H NMR (60 MHz) δ 1.78 (s, 3 H), 2.23 (s, 3 H), 6.60–7.75 (m, 4 H)] was treated in the same solution with lithium morpholide.[5] The resultant quinoline **23** was purified by chromatography (hexanes/Et_3N/EtOH, 6:2:2) to give 0.58 g (51% based on **25**) of an oil: ^{1}H NMR (60 MHz) δ 2.68 (s, 3 H), 3.17 (m, 4 H), 3.97 (m, 4 H), 6.73 (s, 1 H), 7.25–8.15 (m, 4 H); MS *m/z* 170 (94), 228 (M^+, 100); mp for **23**·HBr 278–280 °C. Anal. Calcd for $C_{14}H_{16}N_2O$·HBr: C, 54.38; H, 5.54; N, 9.06. Found: C, 54.27; H, 5.55; N, 9.01.

***N*-[2-(Dimethylamino)ethyl]-2-ethylquinolin-4-amine (24)**. A similar sequence of reactions starting with amide **28** gave chloro imine **29** [^{1}H NMR (60 MHz) δ 1.30 (t, *J* = 7 Hz, 3 H), 2.70 (q, *J* = 7 Hz, 2 H), 6.65–7.70 (m, 4 H)] and ketimine **30** [^{1}H NMR (60 MHz) δ 1.18 (t, *J* = 7 Hz, 3 H), 1.70 (s, 3 H), 2.40 (q, *J* = 7 Hz, 2 H), 6.40–7.60 (m, 4 H)], which was cyclized[5] to quinoline **24**: 63% from **28**; an oil; ^{1}H NMR (60 MHz) δ 1.35 (t, *J* = 7 Hz, 3 H), 2.23 (s, 6 H), 2.55 (t, *J* = 6.5 Hz, 2 H), 2.85 (q, *J* = 7 Hz, 2 H), 3.20 (m, 2 H; t, *J* = 6.5 Hz, 2 H after treatment with D_2O), 5.80 (br s, 1 H, exchangeable with D_2O), 6.22 (s, 1 H), 7.10–8.00 (m, 4 H); MS *m/z* 58 (100), 149 (4), 243 (M^+, 5); mp for **24**·2HBr 236–237 °C. Anal. Calcd for $C_{15}H_{21}N_3$·2HBr: C, 44.46; H, 5.72; N, 10.37. Found: C, 44.53; H, 5.73; N, 10.29.

(*E*)-*N*-(1-Morpholinoethylidene)-2-(trifluoromethyl)-aniline (31). Crude chloro imine **26**, prepared as described above from 0.508 g (2.5 mmol) of amide **25**, was dissolved in THF (10 mL) and treated dropwise with morpholine (0.55 mL, 6.25 mmol). The mixture was stirred at 23 °C for 2 h, then concentrated, treated with water (5 mL), and extracted with ether. Chromatography (hexanes/Et_3N/EtOH, 7:2:1) gave 0.57 g (85% based on **25**) of **31** as an oil: ^{1}H NMR δ 1.79 (s, 3 H), 3.53 (t, *J* = 4.8 Hz, 4 H), 3.75 (t, *J* = 4.8 Hz, 4 H), 6.70 (d, *J* = 8 Hz, 1 H), 7.02

(t, J = 8 Hz, 1 H), 7.39 (t, J = 8 Hz, 1 H), 7.55 (d, J = 8 Hz, 1 H); MS m/z 186 (100), 203 (34), 272 (M^+, 32). Anal. Calcd for $C_{13}H_{15}F_3N_2O$: C, 57.34; H, 5.55; N, 10.29. Found: C, 57.38; H, 5.58; N, 10.24.

Synthesis of Quinolines 32–34. A solution of amidine **31** (0.27 g, 1 mmol) in ether (5 mL) was added at −10 °C to a stirred solution of lithium 2-(dimethylamino)ethylamide or lithium morpholide (4 mmol) in ether (20 mL). The resultant mixture was stirred at 23 °C for 2 h, then quenched with water, and worked up as described.[5] The reactions of chloro imines **26** and **29** with lithium morpholide (5 equiv) were conducted in a similar manner. Quinolines **32–34** were purified by chromatography (hexanes/Et_3N/EtOH, 6:3:1).

***N*-[2-(Dimethylamino)ethyl]-2-morpholinoquinolin-4-amine (32):** 73%; mp 103–105 °C; ^1H NMR δ 2.30 (s, 6 H), 2.69 (t, J = 6 Hz, 2 H), 3.27 (m, 2 H; t, J = 6 Hz, 2 H after treatment with D_2O), 3.67 (t, J = 4.5 Hz, 4 H), 3.85 (t, J = 4.5 Hz, 4 H), 5.67 (br s, 1 H, exchangeable with D_2O), 5.89 (s, 1 H), 7.18 (t, J = 8 Hz, 1 H), 7.49 (t, J = 8 Hz, 1 H), 7.61 (d, J = 8 Hz, 1 H), 7.65 (d, J = 8 Hz, 1 H); MS m/z 58 (100), 300 (M^+, 35). Anal. Calcd for $C_{17}H_{24}N_4O$: C, 67.97; H, 8.05; N, 18.65. Found: C, 67.98; H, 8.01; N, 18.56.

2,4-Dimorpholinoquinoline (33): 80% from **25**, 84% from **31**; mp 168–169 °C; ^1H NMR δ 3.18 (t, J = 4.5 Hz, 4 H), 3.69 (t, J = 4.5 Hz, 4 H), 3.86 (t, J = 4.5 Hz, 4 H), 3.98 (t, J = 4.5 Hz, 4 H), 6.40 (s, 1 H), 7.21 (t, J = 8 Hz, 1 H), 7.51 (t, J = 8 Hz, 1 H), 7.70 (d, J = 8 Hz, 1 H), 7.82 (d, J = 8 Hz, 1 H); MS m/z 242 (89), 268 (100), 299 (M^+, 83). Anal. Calcd for $C_{17}H_{21}N_3O_2$: C, 68.20; H, 7.07; N, 14.04. Found: C, 68.13; H, 7.09; N, 14.10.

3-Methyl-2,4-dimorpholinoquinoline (34): 55% from **28**; mp 161–162 °C; ^1H NMR δ 2.38 (s, 3 H), 3.29 (t, J = 4.5 Hz, 4 H), 3.40 (m, 4 H), 3.89 (t, J = 4.5 Hz, 4 H), 3.94 (t, J = 4.5 Hz, 4 H), 7.34 (t, J = 8 Hz, 1 H), 7.54 (t, J = 8 Hz, 1 H), 7.83 (d, J = 8 Hz, 1 H), 8.05 (d, J = 8 Hz, 1 H); MS m/z 280 (100), 313 (M^+, 50). Anal. Calcd for $C_{18}H_{23}N_3O_2$: C, 68.98; H, 7.40; N, 13.41. Found: C, 69.09; H, 7.36; N, 13.45.

2-Amino-*N*-[2-(dimethylamino)ethyl]benzamide (36). In the preparation of *N*-[2-(dimethylamino)ethyl]-2-phenylquinoline[5] the mixture was made acidic with 1 N HCl, stirred at 23 °C for 10 min, and then neutralized with aqueous NaOH. Usual workup was followed by chromatography (hexanes/Et_3N/EtOH, 6:2:2) to give the quinoline (93%), which was eluted first, and then **36** (2%) identified by spectral comparison with an authentic sample.[16]

***N*,*N*′-Bis[3-(dimethylamino)propyl]-2-[(1-phenylethylidene)amino]benzamidine (37).** The reaction of *N*-(1-phenylethylidene)-2-(trifluoromethyl)aniline[5,17] with a lithium reagent prepared from 3-(dimethylamino)propylamine was conducted under standard conditions[5] and then quenched with 1 equiv of water with respect to the lithium reagent. Chromatography (hexanes/Et_3N/EtOH, 6:2:2) gave **37** (75%) as an oil: ^1H NMR δ 1.64 (m, 4 H), 2.11 (s, 12 H), 2.23 (s + m, 7 H), 3.15 (m, 4 H), 6.75 (d, J = 8 Hz, 1 H), 7.12 (t, J = 8 Hz, 1 H), 7.2–7.5 (m, 6 H), 7.90 (d, J = 8 Hz, 2 H); IR (neat) ν 1631, 3300 cm^{-1}. Anal. Calcd for $C_{25}H_{37}N_5$: C, 73.66; H, 9.15; N, 17.18. Found: C, 73.28; H, 9.03; N, 16.95.

(*E*)-*N*-(2-Methyl-1-phenylpropylidene)-2-(trifluoromethyl)aniline (38). The condensation of **1** with isobutyrophenone was conducted in xylenes under reflux for 10 h under otherwise identical conditions and workup, as described for the preparation of other ketimines:[5] 55%; an oil; ^1H NMR (60 MHz) δ 1.24 (d, J = 7 Hz, 6 H), 3.03 (sept, J = 7 Hz, 1 H), 6.3–7.6 (m, 9 H); MS m/z 248 (100), 291 (M^+, 31). Anal. Calcd for $C_{17}H_{16}F_3N$: C, 70.09; H, 5.54; N, 4.81. Found: C, 69.98; H, 5.59; N, 4.73.

4-Methyl-1-[2-[(2-methyl-1-phenylpropen-1-yl)amino]benzoyl]piperazine (41). Ketimine **38** was reacted with lithium 4-methylpiperazide in ether and the mixture was worked up using a standard procedure:[5] 65%; mp 148–149 °C; ^1H NMR δ 1.83 (s, 3 H), 1.86 (s, 3 H), 2.32 (s, 3 H), 2.42 (m, 4 H), 3.65 (m, 4 H), 6.53 (d, J = 8 Hz, 1 H), 6.56 (br s, 1 H, exchangeable with D_2O), 6.63 (t, J = 8 Hz, 1 H), 7.05 (d, J = 8 Hz, 1 H), 7.06 (t, J = 8 Hz, 1 H), 7.17–7.37 (m, 5 H); ^{13}C NMR δ 20.42, 20.87, 45.87, 45.91, 55.07, 114.82, 116.46, 119.73, 123.82, 126.83, 127.43, 127.76, 129.19, 130.21, 131.58, 138.70, 144.50, 170.01; ^{17}O NMR (MeCN, H_2O external reference) δ 342; MS m/z 250 (95), 349 (M^+, 100); HRMS calcd for $C_{22}H_{27}N_3O$ m/z 349.2154, found 349.2153. Anal. Calcd for $C_{22}H_{27}N_3O$: C, 75.61; H, 7.79; N, 12.02. Found: C, 75.39; H, 7.77; N, 12.05.

1-(2-Aminobenzoyl)-4-methylpiperazine (42). A solution consisting of **41** (100 mg, 0.28 mmol), EtOH (10 mL), and 1 N HCl (10 mL) was heated at 50 °C for 1 h, cooled, and made alkaline with aqueous NaOH. Extraction with ether was followed by chromatography (hexanes/Et_3N/EtOH, 6:2:2) to give an oil (43 mg, 70%) identified as **42** by comparison of the IR and ^1H NMR spectra with those published.[15]

4-Ethoxy-2-phenylquinoline (43). A mixture of EtONa [prepared from NaH (130 mg, 5.4 mmol) and EtOH (0.32 mL, 5.4 mmol)] and *N*-(1-phenylethylidene)-2-(trifluoromethyl)-aniline[5,17] (290 mg, 1.1 mmol) in anhydrous THF (25 mL) was refluxed for 20 h. Chromatography (hexanes/Et_3N, 4:1) gave 68 mg (25%) of **43**: mp 97–99 °C (from hexanes); ^1H NMR δ 1.61 (t, J = 7 Hz, 3 H), 4.35 (q, J = 7 Hz, 2 H), 7.16 (s, 1 H), 7.43–7.54 (m, 4 H), 7.70 (t, J = 8 Hz, 1 H), 8.10 (d, J = 8 Hz, 1 H, and m, 2 H), 8.22 (d, J = 8 Hz, 1 H); MS m/z 221 (73), 249 (M^+, 100). Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.07; N, 5.62. Found: C, 81.96; H, 6.14; N, 5.54.

The use of EtOK (prepared from KH and EtOH) gave similar results.

Acknowledgment. We thank NIH NIAID (grant AI27196) for support of this research. Use of a high-field NMR spectrometer was made possible through an NSF equipment grant (CHEM-8409599).

Registry No. **1**, 88-17-5; **2**, 75040-61-8; **7**, 137434-30-1; **8**, 137434-31-2; **9**, 137434-32-3; **10**, 137434-33-4; **11**, 137434-33-4; **11**·2HBr·$^1/_2H_2O$, 137434-58-3; (*E*)-**12**, 137434-35-6; (*Z*)-**12**, 137434-56-1; **13**, 137434-36-7; **13**·2HBr·H_2O, 137434-57-2; **14**, 137434-37-8; **15**, 137434-38-9; **16**, 137434-39-0; **17**, 137434-40-3; (*R*)-**18**, 137434-41-4; (*R*)-**18**·HBr, 137566-48-4; (*S*)-**18**, 137492-73-0; (*R*)-**19**, 137434-42-5; (*R*)-**19**·2H_3PO_4·H_2O, 137492-75-2; (*S*)-**19**, 137492-74-1; (*S*)-**19**·2H_3PO_4·H_2O, 137566-41-7; (*R*)-**20**, 137434-43-6; (*S*)-**20**, 137492-76-3; (*S*)-**20**·2HBr·3H_2O, 137566-42-8; **21**, 137434-44-7; **22**, 137434-45-8; **23**, 82607-87-2; **23**·HBr, 137434-59-4; **24**, 137434-46-9; **24**·2HBr, 137434-60-7; **25**, 344-62-7; **26**, 137434-47-0; **27**, 137434-48-1; **28**, 2924-94-9; **29**, 64321-72-8; **30**, 137434-49-2; **31**, 137434-50-5; **32**, 137434-51-6; **33**, 122914-29-8; **34**, 137434-52-7; **36**, 6725-13-9; **37**, 137434-53-8; **38**, 137434-54-9; **41**, 137434-55-0; **42**, 93288-86-9; LDA, 4111-54-0; *t*-BuOK, 865-47-4; 4-ethoxy-2-phenylquinoline, 22680-63-3; propiophenone, 93-55-0; 4-methyl-3-penten-2-one, 141-79-7; (*E*)-4-phenyl-3-buten-2-one, 1896-62-4; 1-indanone, 83-33-0; 1-tetralone, 529-34-0; lithium *N*-[2-(dimethylamino)ethyl]amide, 132608-39-0; (1*R*)-(+)-camphor, 464-49-3; (1*S*)-(−)-camphor, 464-48-2; lithium 4-methylpiperazide, 105563-31-3; cyclohexanone, 108-94-1; propanoyl chloride, 79-03-8; lithium *N*-[3-(dimethylamino)propyl]amide, 134099-07-3; isobutyrophenone, 611-70-1; morpholine, 110-91-8.

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