JOC*Article*

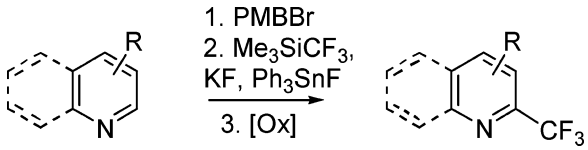
Synthesis of Trifluoromethylated Azines via Nucleophilic Oxidative Substitution of Hydrogen by Trifluoromethyl Carbanions

Rafał Loska, Monika Majcher, and Mieczysław Makosza*,†

Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw 42, Poland

icho-s@icho.edu.pl

Received March 2, 2007



A novel, three-step method of trifluoromethylation of azines via oxidative nucleophilic substitution of hydrogen in the heteroaromatic ring by a CF_3^- carbanion is presented. The key reaction of this process is the addition of the CF_3^- carbanion, generated by treatment of Me_3SiCF_3 with $KF_{(s)}$ and Ph_3SnF catalyst, to *N*-alkylazinium salts. The resulting dihydroazines containing a trifluoromethyl group are relatively stable compounds and can be isolated in a pure form. Deprotection of the *N*-*p*-methoxybenzyl substituent and aromatization of the heterocyclic ring upon treatment with CAN provides azines with a CF_3 group in the ring position originally occupied by hydrogen. The whole process can be thus considered as a nucleophilic oxidative displacement of hydrogen by a CF_3^- carbanion.

Introduction

Heteroaromatic compounds containing perfluoroalkyl, and in particular trifluoromethyl ring substituents, are currently widely applied as novel pharmaceuticals, crop protection agents, and liquid crystalline compounds.[1] Such compounds are traditionally prepared using ring-closing reactions[2] of fluorinated building blocks,[3] transformations of the corresponding trichloromethyl derivatives on treatment with fluorinated Lewis acids (SbF_3, SbF_5, etc.—the Swarts process),[1,4] or reactions of carboxylic acids and their derivatives with SF_4[5] or BrF_3.[6] Direct introduction of a CF_3 group into an aromatic ring is possible via radical[7] or electrophilic trifluoromethylation,[8] but probably the most synthetically useful method of effecting such transformation is the reaction of aryl bromides or iodides with trifluoromethylcopper reagents.[1,4,9] A useful and mild variation of this method, employing trifluoromethyltrimethylsilane (Ruppert reagent, Me_3SiCF_3) as a source of a nucleophilic CF_3 group for the generation of the reactive intermediate $CuCF_3$, has been described.[10] This reaction is quite general, but its drawback is the necessity to prepare aromatic substrates containing halogen atoms in the appropriate positions of the ring. Attempts to replace halogens or a nitro group in halodinitrobenzenes or halocyanonitrobenzenes with CF_3^-, generated from the Ruppert reagent without

† Fax : +48 226326681.

(1) (a) Chambers, R. D. *Fluorine in Organic Chemistry*; Blackwell Publishing: Oxford, U.K., 2004. (b) Kirsch, P. *Modern Fluoroorganic Chemistry*; Wiley-VCH: Weinheim, 2004. (c) Hiyama, T.; Kanie, K.; Kusumoto, T.; Morizawa, Y.; Shimizu, M. *Organofluorine Compounds: Chemistry and Applications*; Springer-Verlag: Berlin, Heidelberg 2000. (d) Langlois, B. R.; Billard, T. *Synthesis* **2003**, 185. (e) Lin, P.; Jiang, J. *Tetrahedron* **2000**, *56*, 3635.

(2) (a) Furin, G. G. *Adv. Heterocycl. Chem.* **2003**, *86*, 129. (b) Furin, G. G. *Adv. Heterocycl. Chem.* **2004**, *87*, 273. (c) Furin, G. G. *Adv. Heterocycl. Chem.* **2005**, *88*, 231.

(3) (a) Schlosser, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 5432. (b) Percy, J. M. *Top. Curr. Chem.* **1997**, *193*, 131.

(4) McClinton, M. A.; McClinton, D. A. *Tetrahedron* **1992**, *48*, 6555.

(5) Dmowski, W. in *Houben−Weyl Methods in Organic Chemistry*; Baasner, B., Hagemann, H., Tatlow, J. C., Eds.; Georg Thieme Verlag: Stuttgart, 1999, Vol. E 10a, pp 321−405.

(6) (a) Rozen, S.; Mishani, E. *J. Chem. Soc., Chem. Commun.* **1994**, 2081. (b) Rozen, S. *Acc. Chem. Res.* **2005**, *38*, 803.

(7) (a) Dolbier, W. R., Jr. *Chem. Rev.* **1996**, *96*, 1557. (b) Tiers, G. V. D. *J. Am. Chem. Soc.* **1960**, *82*, 5513. (c) Cowell, A. B.; Tamborski, C. *J. Fluorine Chem.* **1981**, *17*, 345. (d) Zhao, C.-X.; El-Taliawi, G. M.; Walling, C. *J. Org. Chem.* **1983**, *48*, 4908. (e) Sawada, H.; Yoshida, M.; Hauii, H.; Aoshima, K.; Kobayashi, M. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 215. (f) Huang, W.-Y.; Liu, J.-T.; Li, J. *J. Fluorine Chem.* **1995**, *71*, 51. (g) Zeng, Z.; Liu, C.; Jin, L.-M.; Guo, C.-C.; Chen, Q.-Y. *Eur. J. Org. Chem.* **2005**, 306.

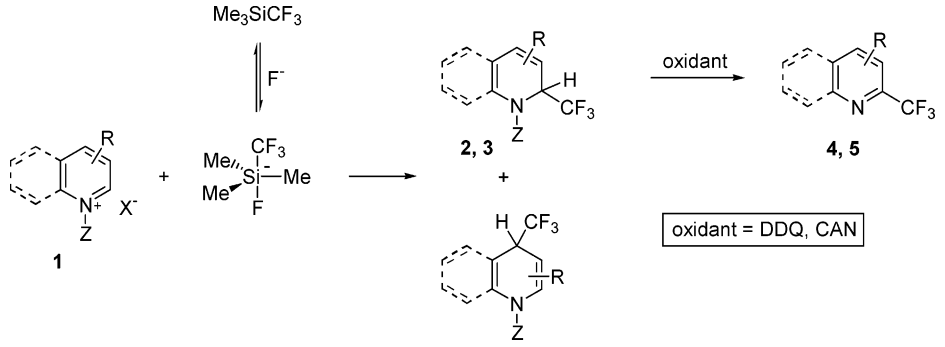
(8) (a) Umemoto, T. DE Patent 3021226, 1980; *Chem. Abstr.* **1981**, *94*, 208509. (b) Umemoto, T. *Chem. Rev.* **1996**, *96*, 1757. (c) Yagupolskii, L. M.; Maletina, I. I.; Kondratenko, N. V.; Orda, V. V. *Synthesis* **1978**, 835. (d) Yagupolskii, L. M. *J. Fluorine Chem.* **1987**, *36*, 1. (e) Eisenberger, P.; Gischig, S.; Togni, A. *Chem.—Eur. J.* **2006**, *12*, 2579. (f) Yang, J.-J.; Kirchmeier, R. L.; Shreeve, J. M. *J. Org. Chem.* **1998**, *63*, 2656. (g) Magnier, E.; Blazejewski, J.-C.; Tordeux, M.; Wakselman, C. *Angew. Chem., Int. Ed.* **2006**, *45*, 1279, 1301.

(9) McLoughlin, V. C. R.; Thrower, J. *Tetrahedron* **1969**, *25*, 5921.

(10) (a) Urata, H.; Fuchikami, T. *Tetrahedron Lett.* **1991**, *32*, 91. (b) Cottet, F.; Schlosser, M. *Eur. J. Org. Chem.* **2002**, 327. (c) Cottet, F.; Marull, M.; Lefebvre, L.; Schlosser, M. *Eur. J. Org. Chem.* **2003**, 1559.

10.1021/jo0703552 CCC: $37.00
Published on Web 06/22/2007

SCHEME 1. General Concept of Oxidative Nucleophilic Substitution of Hydrogen in *N*-alkylazinium Salts by Trifluoromethyl Carbanions Generated from Me_3SiCF_3



a metal catalyst, gave mixtures of the expected trifluoromethylnitroarenes in low yields.[11]

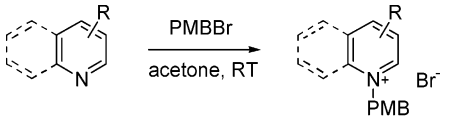
Me_3SiCF_3 in the presence of fluoride anion sources is widely used in nucleophilic trifluoromethylation of various electrophiles.[12] We thus started to explore its reactions with electrophilic arenes in the hope to find new ways of introducing a CF_3 group selectively into an aromatic ring via nucleophilic substitution of hydrogen. We have already described a reaction of oxidative nucleophilic substitution of hydrogen in nitroarenes containing additional electron withdrawing substituents by a trifluoromethyl carbanion generated from Me_3SiCF_3 in the presence of $(Me_2N)_3S^+Me_2SiF_3^-$ (TASF).[13] Oxidation of the intermediary σ^H adducts with dimethyldioxirane (DMD) afforded trifluoromethylated phenols. Oxidative nucleophilic replacement of hydrogen in trinitrobenzene by CF_3^- carbanion was reported earlier by Stahly.[14]

Recently, we described a new reaction of nucleophilic substitution of hydrogen in azines by perfluoroisopropyl carbanions, which were generated in situ by addition of fluoride anions (from solid KF) to hexafluoropropene.[15] The reaction consists of three steps: (i) conversion of the azine into its *N*-benzyl or *N*-*p*-methoxybenzyl (PMB) salt, (ii) addition of the perfluorocarbanion to form perfluoroalkylated dihydroazines, and (iii) oxidative N-deprotection and aromatization of the dihydroazines to provide the respective azines containing a $(CF_3)_2CF$ group in the heteroaromatic ring. The addition step proceeded in high yields in spite of considerable steric bulk of $(CF_3)_2CF^-$ and strong delocalization of negative charge by its two CF_3 groups. We thus expected that azinium salts might be appropriate substrates for the reaction of nucleophilic trifluoromethylation with $Me_3Si(F)CF_3^-$. By analogy to the process described above, oxidation of the resulting dihydroazine adducts should afford the desired trifluoromethylated azines, that is, products of nucleophilic replacement of hydrogen by a CF_3^- carbanion in the heteroaromatic ring (Scheme 1).

Results and Discussion

Preparation of the Azinium Salts (1). *N*-Alkylazinium salts are well-known compounds and are usually prepared simply by heating an equimolar mixture of the azine and the alkylating agent.[16] Salt **1c** (*N*-benzhydrylisoquinolinium chloride) was prepared in this way in 87% yield. We found that the most convenient way to obtain other salts used in this study (the *N*-*p*-methoxybenzyl (PMB) salts) was to mix equimolar amounts of the appropriate azine and PMBBr in acetone at room temperature (Scheme 2). After a few hours or days the crystalline salt was collected, washed, and dried under vacuum. The idenity and purity of each salt was confirmed by its melting point, elemental analysis, and ^1H NMR spectrum. They were all obtained in nearly quantitative yields.

SCHEME 2. Preparation of the *N*-PMB Azinium Salts



1a quinolinium
1b R = 3-Me
1d R = 3-CO_2Me
1e R = 3-CN
1f R = 3-COPh
1g 5-methoxyquinolinium
1h phenantrolinium

Initial Studies on the Nucleophilic Trifluoromethylation. In the preliminary experiment *N*-*p*-methoxybenzylquinolinium bromide **1a** was treated with an excess of Me_3SiCF_3 and $KF_{(s)}$ in dry CH_2Cl_2 at room temperature (Scheme 3). After 2.5 h of vigorous stirring of the heterogeneous reaction mixture, we observed the formation of the addition product, dihydroquinoline **2a**, which was isolated in 25% yield after column chromatography.

The low rate of formation and yield of **2a** were probably due to slow formation of the hypervalent silicate anions $Me_3Si(F)CF_3^-$, because of low accessibility of fluoride anions in the solid−liquid two-phase system.

Use of $Ph_3SnF_2^-$ Anions for Promoting the Nucleophilic Trifluoromethylation by Me_3SiCF_3. In order to increase the efficiency of activation of Me_3SiCF_3, we decided to employ a catalytic solid−liquid phase-transfer system based on the use of hypervalent triphenyltin fluorides (Scheme 4). Triphenyltin fluoride was found to be an efficient cocatalyst in the PTC

(11) (a) Adams, D. J.; Clark, J. H.; Hansen, L. B.; Sanders, V. C.; Stewart, J. T. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3081. (b) Adams, D. J.; Clark, J. H.; Heath, P. A.; Hansen, L. B.; Sanders, V. C.; Tavener, S. J. *J. Fluorine Chem.* **2000**, *101*, 187.

(12) (a) Prakash, G. K. S.; Yudin, A. K. *Chem. Rev.* **1997**, *97*, 757. (b) Prakash, G. K. S.; Mandal, M. *J. Fluorine Chem.* **2001**, *112*, 123. (c) Singh, R. P.; Shreeve, J. M. *Tetrahedron* **2000**, *56*, 7613.

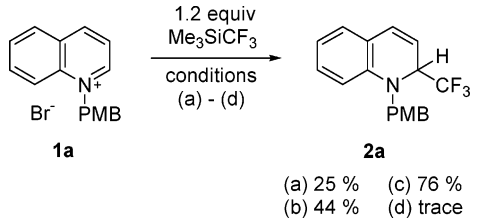
(13) Surowiec, M.; Makosza, M. *Tetrahedron* **2004**, *60*, 5019.

(14) Stahly, G. P. *J. Fluorine Chem.* **1989**, *45*, 431.

(15) Loska, R.; Makosza, M. *J. Org. Chem.* **2007**, *72*, 1354.

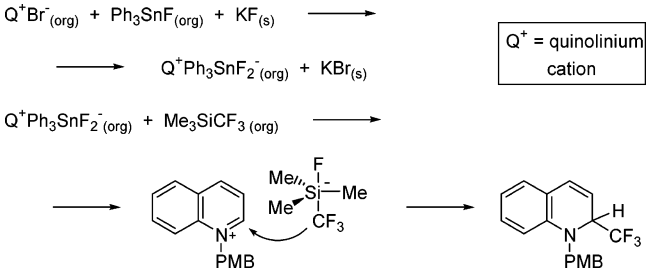
(16) See for example: (a) Cymerman, Craig J.; Garnett, J. L.; Temple, D. M. *J. Chem. Soc.* **1964**, 4057. (b) Bunting, J. W.; Sindhuatmadja, S. *J. Org. Chem.* **1981**, *46*, 4211. (c) Fukuzumi, S.; Kommitsu, S.; Hironaka, K.; Tanaka, T. *J. Am. Chem. Soc.* **1987**, *109*, 305. (d) MacTavish, J.; Proctor, G. R.; Redpath, J. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2545. (e) Lo, H. C.; Buriez, O.; Kerr, J. B.; Fish, R. H. *Angew. Chem., Int. Ed.* **1999**, *38*, 1429.

SCHEME 3. Addition of Trifluoromethyl Carbanions to Quinolinium Salt 1a under Various Conditions[a]



[a] Conditions: (a) 1.7 equiv of $KF_{(s)}$, CH_2Cl_2, rt, 2.5 h (b) 1.7 equiv of $KF_{(s)}$, 0.33 equiv of Ph_3SnF, CH_2Cl_2, rt, 2.5 h (c) 1.7 equiv of $KF_{(s)}$, 0.33 equiv of Ph_3SnF, CH_2Cl_2, rt, 24 h (d) 1.7 equiv of $KF_{(s)}$, 0.33 equiv of Ph_3SnF, DME, rt, 24 h.

SCHEME 4. Operation of the Catalytic Phase-Transfer System Which Allows Facile Transport of F^- Anions from the Solid to the Organic Phase in the Form of Hypervalent Tin Fluoride Anions



nucleophilic fluorination of alkyl sulfonates and bromides.[17] This system was applied by us previously in the reaction of nucleophilic trifluoromethylation of aromatic aldehydes and ketones with Me_3SiCF_3 in the presence of catalytic amounts of $KF_{(s)}$, Ph_3SnF, and n-$Bu_3MeN^+HSO_4^-$ as a phase-transfer catalyst.[18] In the reaction described herein, the azinium salt **1a** can behave as a PT catalyst by itself. According to the mechanism depicted in Scheme 4, lipophilic hypervalent $Ph_3SnF_2^-$ anions can be generated on the surface of the solid KF and then form highly lipophilic ion pairs with azinium cations (Q^+). After migration of these pairs into the bulk of the apolar organic phase, $Ph_3SnF_2^-$ ions can act as efficient donors of fluoride anions and react with Me_3SiCF_3 to form new ionic pairs $Q^+Me_3Si(F)CF_3^-$. Subsequent transfer of the CF_3^- carbanion from silicon to the positively charged aromatic ring should occur to provide the final product of the type **2a**.

Indeed, the reaction of **1a** performed in CH_2Cl_2 in the presence of 0.33 equiv of Ph_3SnF proceeded much faster to provide **2a** in 44% yield under otherwise identical conditions (Scheme 3). A longer reaction time (24 h) allowed us to obtain **2a** in even better yield (76%). On the other hand, the reaction performed in 1,2-dimethoxyethane led to a complex mixture of products containing only traces of **2a** by TLC analysis (Scheme 3, conditions d).

Synthesis of Trifluoromethyl-Substituted Dihydroazines. Using the optimized conditions c from Scheme 3, we then performed a series of reactions of various azinium salts with Me_3SiCF_3 (Table 1). In most of these examples we used azinium salts containing electron withdrawing substituents in the aromatic ring. Such substituents are known to render the respective dihydroazines reasonably stable.[19] Nevertheless, the reaction proceeds efficiently with the picoline derivative **1b** as well, although the product **2b** was unstable and could not be fully characterized. The reaction of 3-benzoylpyridinium salt **1f** (entry 5) is particularly notable—we have not observed any products resulting from nucleophilic addition of CF_3^- to the highly electrophilic carbonyl group.

Most of the examples of nucleophilic trifluoromethylation reactions shown in Table 1 were performed at 2 mmol scale. In order to test the scalability, the reaction of the salt **1d** was successfully performed at 10 mmol scale according to the identical protocol.

In all cases, with the possible exception of **1h**, the CF_3^- carbanion adds exclusively in the 2-/6-positions of the aromatic azinium ring. Such regioselectivity of addition to azinium salts is typical for hard nucleophiles.[19] This observation is in agreement with the fact that nucleophilic trifluoromethylation with Me_3SiCF_3 of α,β-unsaturated carbonyl compounds proceeds exclusively as 1,2-addition.[20]

In addition to standard NMR techniques (^1H, ^{13}C, and ^{19}F 1D spectra), the structure of selected addition products (**2a**, **2d**, and **3d**) was confirmed using COSY, DEPT, $^1H-^{13}C$ HMQC, and HMBC NMR experiments. In all cases the ^{13}C NMR chemical shift of the sp^3 carbon of the dihydroazine ring (q, $^3J_{CF}$ ca. 30 Hz) confirms that the products have the structure of a 1,2- or 1,6-dihydroazine and not of a 1,4-dihydroazine.[15,21]

From a practical point of view, the formation of mixtures of regioisomeric 1,2- and 1,6-dihydroadducts (**2** and **3**) in the pyridine series is an obvious drawback of the method presented herein. However, these regioisomers can be readily separated by column chromatography.

Oxidative Deprotection/Aromatization of Trifluoromethylated Dihydroazines. An *N*-*p*-methoxybenzyl substituent can be readily cleaved by oxidizing agents such as DDQ or CAN.[22] On the other hand, N-alkylated dihydroazines are generally known to give azinium salts under oxidizing conditions.[19] By analogy with the 1,2-dihydroazines bearing a $(CF_3)_2CF$ group described by us earlier,[15] we expected that treatment of the products **2** and **3** with DDQ or CAN might lead first to N-deprotection of the PMB group and then to aromatization of the heterocyclic ring. The CF_3 group would be located in the

(17) (a) Makosza, M.; Bujok, R. *Tetrahedron Lett.* **2002**, *43*, 2761. (b) Bujok R.; Makosza M. *Synlett* **2002**, 1285. (c) Makosza, M.; Bujok, R. *Tetrahedron Lett.* **2004**, *45*, 1385. (d) Bujok R.; Makosza M. *Synlett* **2004**, 371.

(18) Borkin, D.; Loska, R.; Makosza, M. *Pol. J. Chem.* **2005**, *79*, 1187.

(19) (a) Lavilla, R. *J. Chem. Soc., Perkin Trans.* **2002**, *1*, 1141. (b) Eisner, U.; Kuthan, J. *Chem. Rev.* **1972**, *72*, 1. (c) Kuthan, J.; Kurfürst, A. *Ind. Eng. Chem. Prod. Res. Dev.* **1982**, *21*, 191. (d) Stout, D. M.; Meyers, A. I. *Chem. Rev.* **1982**, *82*, 223. (e) Comins, D. L.; O'Connor, S. *Adv. Heterocycl. Chem.* **1988**, *44*, 199. (f) Sausinš, A.; Duburs, G. *Heterocycles* **1988**, *27*, 291. (g) Bennasar, M.-L.; Roca, T.; Monerris, M.; Juan, C.; Bosch, J. *Tetrahedron* **2002**, *58*, 8099.

(20) (a) Wiedemann, J.; Heiner, T.; Mlostoń, G.; Prakash, G. K. S.; Olah, G. A. *Angew. Chem., Int. Ed.* **1998**, *37*, 820. (b) Singh, R. P.; Kirchmeier, R. L.; Shreeve, J. M. *Org. Lett.* **1999**, *1*, 1047.

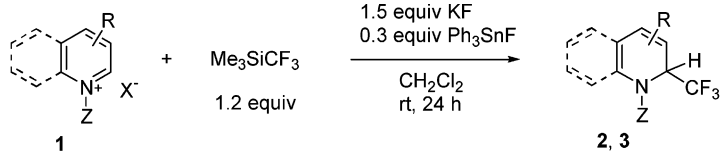
(21) Lavilla, R.; Gotsens, T.; Guerrero, M.; Masdeu, C.; Santano, M. C.; Minguillón, C.; Bosch, J. *Tetrahedron* **1997**, *53*, 13959.

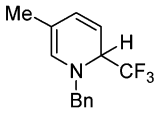
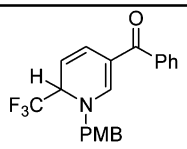
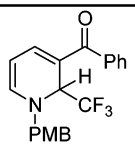
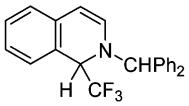
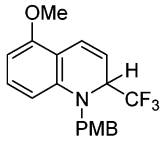
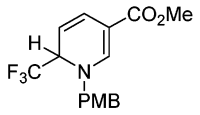
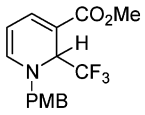
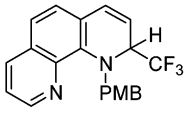
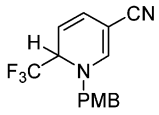
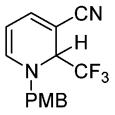
(22) (a) Fukuyama, T.; Laird, A. A.; Hotchkiss, L. M. *Tetrahedron Lett.* **1985**, *26*, 6291. (b) Oikawa, Y.; Yoshioka, T.; Yonemitsu, O. *Tetrahedron Lett.* **1982**, *23*, 885. (c) Murakata, C.; Ogawa, T. *Carbohydr. Res.* **1992**, *234*, 75. (d) Bull, S. D.; Davies, S. G.; Fenton, G. A.; Mulvaney, W.; Prasad, R. S.; Smith, A. D. *Chem. Commun.* **2000**, 337. (e) Bull, S. D.; Davies, S. G.; Kelly, P. M.; Gianotti, M.; Smith, A. D. *J. Chem. Soc., Perkin Trans. 1* **2001**, 3106. (f) Nair, V.; Deepthi, A. *Chem. Rev.* **2007**, *107*, 1862.

(23) (a) Raasch, M. S. *J. Org. Chem.* **1962**, *27*, 1406. (b) Keller, H.; Schlosser, M. *Tetrahedron* **1996**, *52*, 4637. (c) Marull, M.; Schlosser, M. *Eur. J. Org. Chem.* **2003**, 1576.

(24) Cooke, J. W. B.; Coleman, M. J.; Caine, D. M.; Jenkins, K. P. *Tetrahedron Lett.* **1998**, *39*, 7965.

TABLE 1. Trifluoromethylation of Azinium Salts with $TMSCF_3$



	Products		Products	
1	 **2b** (41 %)		5	 **2f** (44 %)
				 **3f** (36 %)
2	 **2c** (85 %)		6	 **2g** (76 %)
3	 **2d** (40 %)	 **3d** (30 %)	7	 **2h** (88 %)[a]
4	 **2e** (29 %)	 **3e** (20 %)		

[a] Small amounts (ca. 5%) of another product were also formed; based on its MS and HRMS spectra and on NMR spectra of the mixture with **2h,** it is probably the 1,4-dihydro isomer of **2h**.

position previously occupied by hydrogen. This was indeed the case, as demonstrated by the examples listed in Table 2.

Products **3** and **4** were formed almost instantly upon dropwise addition of aqueous solution of CAN to a vigorously stirred solution of the dihydroazine in MeOH. After extraction with diethyl ether, they could be isolated by evaporation and chromatography in good yields. A lower yield of compounds **5d** and **4e** (Table 2, entries 3 and 4) resulted from losses due to their volatility. The reaction proceeded efficiently in both the pyridine and the quinoline series. DDQ was also an effective oxidant for this reaction as exemplified by the synthesis of pyridine **4e** (Table 2, entry 4), but its use is less convenient than CAN.

The two reactions, nucleophilic trifluoromethylation of the azinium salt and deprotection/aromatization, can be performed as a one-pot process without isolating the intermediate dihydroazine. For example, after the reaction of 5-methoxyquinolinium salt **1g** with KF, Ph_3SnF, and Me_3SiCF_3 under standard conditions, we evaporated the solvent (CH_2Cl_2), dissolved the residue in MeOH, and treated the resulting mixture with aqueous solution of CAN to obtain product **4g** in 87% overall yield.

Summary and Conclusions

In conclusion, we have elaborated a new type of nucleophilic trifluoromethylation of aromatic azines using *N*-alkylazinium salts as substrates for the fluoride-induced reaction with the Ruppert reagent, Me_3SiCF_3, as the key step. Nucleophilic addition of CF_3^- carbanions to these salts affords the respective dihydroazines. The reaction is initiated with the readily available source of fluoride anions—solid potassium fluoride. High efficiency of the process is ensured by employing Ph_3SnF as a phase-transfer catalyst, which transports F^- anions to the apolar organic phase. In the quinoline series, the reaction proceeds with complete regioselectivity.

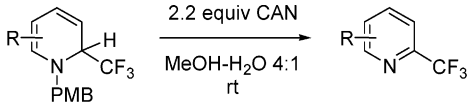
The trifluoromethyl-substituted dihydroazines can be N-deprotected and aromatized with CAN to provide products of oxidative nucleophilic substitution of hydrogen in the original azine ring by a CF_3^- carbanion. The whole two-step process constitutes a new, mild synthetic method of trifluoromethylation of the heteroaromatic ring. It allows us to introduce the CF_3 substitutent directly into the position originally occupied by hydrogen, and thus it provides an alternative to the existing methods. However, the overall yields in some cases are only moderate, and the reaction with pyridine derivatives is additionally hampered by the necessity of separating two regioizomers. Owing to the relatively high cost of Me_3SiCF_3, the reaction is better suited for small laboratory scale syntheses.

The intermediate dihydroazines are interesting by themselves, since they can be used potentially in the synthesis of various heterocyclic systems containing a CF_3 group.[19]

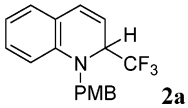
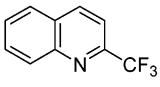
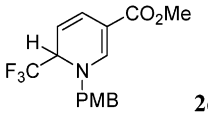
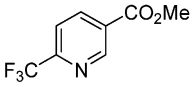
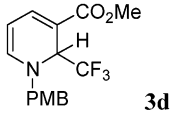
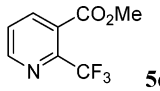
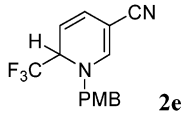
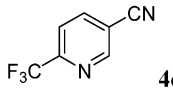
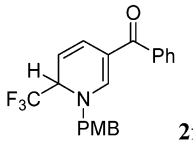
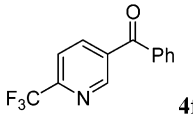
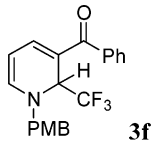
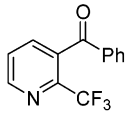
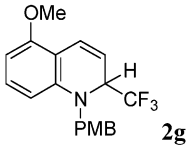
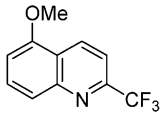
Experimental Section

General Information. The ^1H, ^{13}C, and ^{19}F NMR spectra were recorded using a 400 MHz spectrometer in $CDCl_3$ unless otherwise stated. Chemical shifts are given in ppm relative to TMS for ^1H

TABLE 2. Aromatization of 2-Trifluoromethyl-1,2-dihydroazines 2 and 3



2, **3** **4**, **5**

	Substrate	Product (yield)	Overall yield for 3 steps	Total overall yield of two isomers
1	 **2a**	 **4a**[23] (77 %)	59 %	
2	 **2d**	 **4d**[10(c)] (79 %)	32 %	46 %
3	 **3d**	 **5d**[10(c)] (47%)	14 %	
4	 **2e**	 **4e**[24] (62 %) [a]	18 %	
5	 **2f**	 **4f** (91 %)	40 %	62 %
6	 **3f**	 **5f** (60 %)	22 %	
7	 **2g**	 **4g** (90 %)	68 %	

[a] DDQ was used instead of CAN (2.2 equiv of DDQ, CH_2Cl_2, 0 °C to rt).

and ^{13}C NMR spectra and $CFCl_3$ for ^{19}F NMR spectra. IR spectra were obtained using a FT-IR spectrometer. Mass spectra were obtained using electron impact (EI) ionization. Flash chromatography was performed using silica gel 60 (0.040−0.063 mm) or neutral aluminum oxide. Thin layer chromatography was performed on pre-coated silica gel plates and visualized under a UV lamp. All solvents were distilled before use. Dry CH_2Cl_2 and DME were obtained by distillation from CaH_2.[25] Commercially available spray-dried KF was used as obtained without any further drying. Ph_3SnF was obtained from commercially available Ph_3SnCl, and KF by stirring in a two phase-system, water−AcOEt, in nearly quantitative

(25) Armarego, W. F. L.; Perrin, D. D. *Purification of Laboratory Chemicals*; Butterworth-Heinemann: Oxford, U.K.,1996.

yield.[26] *p*-Methoxybenzyl bromide was prepared according to a literature procedure.[27]

General Procedure for Trifluoromethylation of Azinium Salts. A flame-dried 10 mL round-bottom flask was charged with dry CH_2Cl_2 (4.0 mL), azinium salt (2.00 mmol), $TMSCF_3$ (341 mg, 356 μL, 2.4 mmol), Ph_3SnF (221 mg, 0.6 mmol), and spray-dried KF (174 mg, 3.0 mmol). After 24 h of vigorous stirring in an argon atmosphere at room temperature, the reaction mixture was poured on water (10 mL), diluted with CH_2Cl_2 (ca. 5 mL), and the phases were separated. The organic phase was dried over anhydrous Na_2SO_4 and evaporated, and the products purified by column chromatography on silica gel using 5:1 or 10:1 hexanes−AcOEt or 5:1 hexanes−Et_2O.

1-(*p*-Methoxybenzyl)-2-trifluoromethyl-1,2-dihydroquinoline (2a). Colorless oil: IR (film, ν_{max}, cm^{-1}) 3037, 2957, 2838, 1646, 1612, 1600, 1513, 1493, 1456, 1400, 1304, 1248, 1159, 1119, 1035, 955, 837, 819, 772, 748; ^1H NMR δ 3.78 (3H, s, OCH_3), 4.38 (1H, d, $^2J_{HH}$ = 15.3 Hz, NCH_2), 4.44 (1H, m, ^3J = 6.9 Hz, $CHCF_3$), 4.82 (1H, d, $^2J_{HH}$ = 15.4 Hz, NCH_2), 5.60 (1H, dd, $^3J_{HH}$ = 9.5 Hz, 5.9 Hz, C*H*CHCF$_3$), 6.68 (1H, d, $^3J_{HH}$ = 8.4 Hz, C*H*═CHCH), 6.71 (2H, m, H_{arom}), 6.85 (2H, dm, $^3J_{HH}$ = 8.8 Hz, PMB), 7.02 (1H, dd, $^3J_{HH}$ = 7.4 Hz, $^4J_{HH}$ = 1.5 Hz, H_{arom}), 7.09 (1H, m, H_{arom}), 7.19 (2H, dm, $^3J_{HH}$ = 8.8 Hz, PMB); ^{13}C NMR δ 53.8, 55.2, 58.1 (q, $^2J_{CF}$ = 30.2 Hz), 112.7, 114.1, 114.5, 118.1, 121.6, 125.2 (q, $^1J_{CF}$ = 290.5 Hz), 127.6, 128.6, 128.7, 129.5, 131.0, 143.2, 159.0; ^{19}F NMR δ −77.48 (d, $^3J_{FH}$ = 6.7 Hz, CF_3); MS (EI 70 eV) *m*/*z* (%) 319 (M^+, 5), 250 (20), 121(100); HRMS (EI) calcd for $C_{18}H_{16}NOF_3$ (M^+), 319.1184; found, 319.1174. Anal. Calcd for $C_{18}H_{16}NOF_3$: C, 67.70; H, 5.05; N, 4.39. Found: C, 67.37; H, 4.96; N, 4.20.

1-Benzyl-5-methyl-2-trifluoromethyl-1,2-dihydropyridine (2b). Yellow oil, decomposes after a few hours at RT: ^1H NMR (200 MHz, $CDCl_3$) δ 1.81 (3H, s, Me), 4.25 (1H, q, $^3J_{HF}$ = 7.3 Hz, $CHCF_3$), 4.43 (2H, s, NCH_2), 4.96 (1H, t, $^3J_{HH}$ = 6.2 Hz, C*H*═CHN), 6.04 (1H, d, $^3J_{HH}$ = 5.0 Hz, C*H*CH═CH), 6.16 (1H, d, $^3J_{HH}$ = 7.1 Hz, C*H*CH═CH), 7.15−7.60 (5H, m, Ph); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.5 (d, $^4J_{CF}$ = 2.2 Hz), 58.5, 62.1 (q, $^2J_{CF}$ = 29.3 Hz), 96.9, 112.5, 124.1, 126.4 (q, $^4J_{CF}$ = 293.3 Hz), 127.0, 127.6, 128.7, 133.6, 137.8.

2-Benzhydryl-1-trifluoromethyl-1,2-dihydroisoquinoline (2c). White solid: mp 109−111 °C; IR (KBr, ν_{max}, cm^{-1}) 3030, 1622, 1597, 1563, 1491, 1454, 1249, 1217, 1162, 1116, 953, 768, 748, 729, 699, 686; ^1H NMR δ 5.00 (1H, q, $^3J_{HF}$ = 7.3 Hz, $CHCF_3$), 5.39 (d, $^3J_{HH}$ = 7.5 Hz, NCH═C*H*), 5.87 (1H, s, $CHPh_2$), 6.01 (1H, dm, $^3J_{HH}$ = 7.5, $^5J_{HF}$ = 1.3 Hz, NC*H*═CH), 6.96 (1H, d, $^3J_{HH}$ = 7.5 Hz, H_{arom}), 7.01 (1H, dd, $^3J_{HH}$ = 7.7 Hz, $^4J_{HH}$ = 1.1 Hz, H_{arom}), 7.07 (1H, td, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.3 Hz, H_{arom}), 7.16−7.37 (11H, m, H_{arom}, Ph); ^{13}C NMR δ 62.3 (q, $^2J_{CF}$ = 29.3 Hz), 70.8, 98.9, 119.7, 123.5, 125.2, 125.7 (q, $^1J_{CF}$ = 289.7 Hz), 127.4, 127.8, 128.1, 128.1, 128.6, 128.7, 129.1, 129.9, 131.7, 133.9, 139.0, 140.6; ^{19}F NMR δ −77.55 (dd, $^3J_{FH}$ = 7.7 Hz, $^5J_{FH}$ = 1.1 Hz, CF_3); MS (EI 70 eV) *m*/*z* (%) 365 (M^+, 8), 296 (13), 167 (100), 152 (15); HRMS (EI) calcd for $C_{23}H_{18}NF_3$ (M^+), 365.1391; found, 365.1395. Anal. Calcd for $C_{23}H_{18}NF_3$: C, 75.60; H, 4.97; N, 3.83; F, 15.60. Found: C, 75.75; H, 5.07; N, 3.82; F, 15.69.

1-(*p*-Methoxybenzyl)-2-trifluoromethyl-5-methoxycarbonyl-1,2-dihydropyridine (2d). Pale yellow oil: IR (film, ν_{max}, cm^{-1}) 2952, 1693, 1640, 1573, 1514, 1436, 1296, 1252, 1171, 1123, 1025, 850, 736; ^1H NMR δ 3.71 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 4.47 (1H, m, $CHCF_3$), 4.49 (2H, s, NCH_2), 4.94 (1H, dd, $^3J_{HH}$ = 9.6 Hz, 5.5 Hz, CH═C*H*CHCF$_3$), 6.74 (1H, d, $^3J_{HH}$ = 9.6 Hz, C*H*═CHCHCF$_3$), 6.90 (2H, d, $^3J_{HH}$ = 8.7 Hz, PMB), 7.16 (2H, d, $^3J_{HH}$ = 8.7 Hz, PMB), 7.52 (1H, d, $^4J_{HH}$ = 0.7 Hz, NC*H*═C(CO_2Me)); ^{13}C NMR δ 50.9, 55.2, 57.1 (q, $^2J_{CF}$ = 31.0 Hz), 59.0, 100.0, 103.2, 114.4, 124.6 (q, $^1J_{CF}$ = 288.8 Hz), 126.7, 126.9, 129.0, 146.4, 159.7, 166.3; ^{19}F NMR δ −78.20 (d, $^3J_{FH}$ = 6.6 Hz, CF_3); MS (EI 70 eV) *m*/*z* (%) 327 (M^+, 4), 296 (1), 258 (12), 121 (100); HRMS (EI) calcd for $C_{16}H_{16}NO_3F_3$ (M^+), 327.1082; found, 327.1079. Anal. Calcd for $C_{16}H_{16}NO_3F_3$: C, 58.72; H, 4.93; N, 4.28; F, 17.41. Found: C, 58.79; H, 4.94; N, 4.31; F, 17.37.

1-(*p*-Methoxybenzyl)-2-trifluoromethyl-3-methoxycarbonyl-1,2-dihydropyridine (3d). Pale yellow oil: IR (film, ν_{max}, cm^{-1}) 2953, 2840, 1694, 1612, 1515, 1438, 1290, 1257, 1175, 1125, 1091, 995, 844, 742, 709; ^1H NMR (500 MHz, $CDCl_3$) δ 3.70 (3H, s, OCH_3), 3.77 (3H, s, OCH_3), 4.47 (2H, AB, $^2J_{HH}$ = 15.5 Hz, NCH_2), 5.08 (1H, t, $^3J_{HH}$ = 6.7 Hz, C*H*═CHN), 5.16 (1H, qd, $^3J_{HF}$ = 7.2 Hz, $^3J_{HH}$ = 0.9 Hz, $CHCF_3$), 6.58 (1H, d, $^3J_{HH}$ = 6.9 Hz, CH═C*H*N), 6.86 (2H, d, $^3J_{HH}$ = 8.7 Hz, PMB), 7.11 (2H, d, $^3J_{HH}$ = 8.6 Hz, PMB), 7.36 (1H, d, $^3J_{HH}$ = 6.5 Hz, C*H*═C(CO_2Me)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 51.4, 55.1, 56.8 (q, $^2J_{CF}$ = 31.4 Hz), 58.7, 96.3, 101.4, 114.3, 125.6 (q, $^1J_{CF}$ = 291.6 Hz), 127.7, 128.8, 138.0, 142.3, 159.5, 166.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −78.27 (d, $^3J_{FH}$ = 7.5 Hz, CF_3); MS (EI 70 eV) *m*/*z* (%) 327 (M^+, 2), 258 (13), 121 (100); HRMS (EI) calcd for $C_{16}H_{16}NO_3F_3$ (M^+), 327.1082; found, 327.1092. Anal. Calcd for $C_{16}H_{16}NO_3F_3$: C, 58.72; H, 4.93; N, 4.28; F, 17.41. Found: C, 58.94; H, 4.96; N, 4.27; F, 17.45.

5-Cyano-1-(*p*-methoxybenzyl)-2-trifluoromethyl-1,2-dihydropyridine (2e). Pale yellow oil: IR (film, ν_{max}, cm^{-1}) 2938, 2206, 1643, 1612, 1572, 1514, 1303, 1252, 1175, 1132, 1027, 851; ^1H NMR δ 3.82 (3H, s, OCH_3), 4.45 (2H, AB, $^2J_{HH}$ = 15.1 Hz, NCH_2), 4.52 (1H, m, ^3J = 6.4 Hz, $CHCF_3$), 4.99 (1H, dd, $^3J_{HH}$ = 9.6 Hz, 5.6 Hz, C*H*CHCF$_3$), 6.24 (1H, d, $^3J_{HH}$ = 9.5 Hz, C*H*═CHCHCF$_3$), 6.93 (2H, d, $^3J_{HH}$ = 8.7 Hz, PMB), 7.00 (1H, d, $^4J_{HH}$ = 0.9 Hz, CH═CCN), 7.16 (2H, d, $^3J_{HH}$ = 8.8 Hz, PMB); ^{13}C NMR δ 55.3, 56.9 (q, $^2J_{CF}$ = 31.9 Hz), 59.0 (q, $^4J_{CF}$ = 1.7 Hz), 80.5, 104.9, 114.6, 119.7, 124.3 (q, $^1J_{CF}$ = 288.8 Hz), 125.8, 126.3, 129.3, 147.3, 160.0; ^{19}F NMR δ −78.19 (d, $^3J_{FH}$ = 6.4 Hz, CF_3); MS (EI 70 eV) *m*/*z* (%) 294 (M^+, 4), 121 (100); HRMS (EI) calcd for $C_{15}H_{13}N_2OF_3$ (M^+), 294.0980; found, 294.0984. Anal. Calcd for $C_{15}H_{13}N_2OF_3$: C, 61.22; H, 4.45; N, 9.52; F, 19.37. Found: C, 61.72; H, 4.41; N, 9.46; F, 17.55.

3-Cyano-1-(*p*-methoxybenzyl)-2-trifluoromethyl-1,2-dihydropyridine (3e). Pale yellow oil: IR (film, ν_{max}, cm^{-1}) 2937, 2201, 1613, 1515, 1465, 1252, 1175, 1124, 1033, 709; ^1H NMR δ 3.83 (3H, s, OCH_3), 4.46 (2H, AB, $^2J_{HH}$ = 15.0 Hz, NCH_2), 4.60 (1H, qd, $^3J_{HF}$ = 6.7 Hz, $^4J_{HH}$ = 1.1 Hz, $CHCF_3$), 5.08 (1H, t, $^3J_{HH}$ = 6.9 Hz, NCH═C*H*), 6.64 (1H, d, $^3J_{HH}$ = 7.0 Hz, NC*H*═CH), 6.92 (2H, d, $^3J_{HH}$ = 8.7 Hz, PMB), 6.95 (1H, d, $^3J_{HH}$ = 6.6 Hz, CH═CCN), 7.16 (2H, d, $^3J_{HH}$ = 8.8 Hz, PMB); ^{13}C NMR δ 55.3, 57.5 (q, $^2J_{CF}$ = 32.0 Hz), 58.9, 81.4, 96.3, 114.6, 118.9, 125.0 (q, $^1J_{CF}$ = 291.4 Hz), 126.6, 129.0, 142.4, 142.6, 159.9; ^{19}F NMR δ −78.46 (d, $^3J_{FH}$ = 7.0 Hz, CF_3); MS (EI 70 eV) *m*/*z* (%) 294 (M^+, 9), 225 (4), 188 (9), 121 (100); HRMS (EI) calcd for $C_{15}H_{13}N_2OF_3$ (M^+), 294.0980; found, 294.0982; Anal. Calcd for $C_{15}H_{13}N_2OF_3$: C, 61.22; H, 4.45; N, 9.52; F, 19.37. Found: C, 61.71; H, 4.71; N, 9.48; F, 17.35.

5-Benzoyl-1-(*p*-methoxybenzyl)-2-trifluoromethyl-1,2-dihydropyridine (2f). Pale yellow oil: IR (CH_2Cl_2, ν_{max}, cm^{-1}) 3061, 2937, 1642, 1612, 1564, 1514, 1417, 1327, 1303, 1253, 1214, 1167, 1130, 1111, 1024, 723, 705; ^1H NMR δ 3.78 (3H, s, OMe), 4.43 (1H, $^2J_{HH}$ = 15.0 Hz, NCH_2), 4.49−4.60 (2H, m, $CHCF_3$, NCH_2), 5.12 (1H, dd, $^3J_{HH}$ = 9.7 Hz, 5.5 Hz, CH═C*H*CHCF$_3$), 6.87 (2H, d, $^3J_{HH}$ = 8.6 Hz, PMB), 7.04 (1H, d, $^3J_{HH}$ = 9.7 Hz, C*H*═CHCHCF$_3$), 7.10 (2H, d, $^3J_{HH}$ = 8.6 Hz, PMB), 7.24 (1H, s, NC*H*═CCOPh), 7.35−7.42 (2H, m, Ph), 7.42−7.49 (1H, m, Ph), 7.52−7.58 (2H, m, Ph); ^{13}C NMR δ 55.2, 57.4 (q, $^2J_{CF}$ = 31.5 Hz), 59.3 (d, J_{CF} = 1.3 Hz), 104.7, 110.2, 114.5, 124.6 (q, $^1J_{CF}$ = 288.8 Hz), 126.1, 127.1, 128.1, 128.6, 129.0, 130.6, 139.3, 150.1, 159.8, 190.9; ^{19}F NMR δ −77.62 (d, $^3J_{FH}$ = 6.5 Hz, CF_3); MS (EI 70 eV) *m*/*z* (%) 373 (M^+, 4), 304 (14), 251 (8), 121 (100), 105 (24), 77 (22); HRMS (EI) calcd for $C_{21}H_{18}NO_2F_3$ (M^+), 373.1290; found, 373.1276. Anal. Calcd for $C_{21}H_{18}NO_2F_3$: C, 67.55; H, 4.86; N, 3.75; F, 15.26. Found: C, 67.18; H, 5.16; N, 3.63; F, 15.31.

3-Benzoyl-1-(*p*-methoxybenzyl)-2-trifluoromethyl-1,2-dihydropyridine (3f). Yellow oil: IR (CH_2Cl_2, ν_{max}, cm^{-1}) 3060, 2936, 1627, 1513, 1251, 1207, 1176, 1113, 1064, 1029, 719, 643; ^1H

(26) Gingras, M. *Tetrahedron Lett.* **1991**, *32*, 7381.
(27) Ruder, S. M.; Ronald, R. C. *Tetrahedron Lett.* **1987**, *28*, 135.

NMR δ 3.81 (3H, s, OMe), 4.56 (2H, AB, $^2J_{HH}$ = 15.0 Hz, NCH_2), 5.08 (1H, t, $^3J_{HH}$ = 6.7 Hz, NCH=C*H*), 5.70 (1H, qd, $^3J_{HF}$ = 7.4 Hz, $^4J_{HH}$ = 1.2 Hz, $CHCF_3$), 6.65 (1H, d, $^3J_{HH}$ = 6.9 Hz, NC*H*=CH), 6.90 (2H, dm, $^3J_{HH}$ = 8.7 Hz, PMB), 7.04 (1H, d, $^3J_{HH}$ = 6.6 Hz, C*H*=CCOPh), 7.16 (2H, dm, $^3J_{HH}$ = 8.7 Hz, PMB), 7.38−7.44 (2H, m, Ph), 7.45 (1H, m, Ph), 7.57−7.62 (2H, m, Ph); ^{13}C NMR δ 55.3, 56.7 (q, $^2J_{CF}$ = 31.9 Hz), 59.1, 96.5, 111.6, 114.4, 125.7 (q, $^1J_{CF}$ = 290.5 Hz), 127.3, 128.1, 128.5, 129.1, 130.9, 139.1, 141.4, 143.2, 159.6, 194.0; ^{19}F NMR δ −78.20 (d, $^3J_{FH}$ = 7.5 Hz, CF_3); MS (EI 70 eV) *m*/*z* (%) 373 (M^+, 3), 304 (14), 121 (100), 105 (27), 77 (18); HRMS (EI) calcd for $C_{21}H_{18}NO_2F_3$ (M^+), 373.1290; found, 373.1304. Anal. Calcd for $C_{21}H_{18}NO_2F_3$: C, 67.55; H, 4.86; N, 3.75; F, 15.26. Found: C, 67.74; H, 4.91; N, 3.65; F, 15.01.

5-Methoxy-1-(*p*-methoxybenzyl)-2-trifluoromethyl-1,2-dihydroquinoline (2g). Colorless oil: IR (film, ν_{max}, cm^{-1}) 2937, 2839, 1612, 1643, 1597, 1575, 1513, 1478, 1387, 1250, 1165, 1119, 1036, 838, 748; ^{1}H NMR δ 3.77 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 4.37 (1H, d, $^2J_{HH}$ = 15.2 Hz, NCH_2), 4.41 (1H, m, ^3J = 7.0 Hz, $CHCF_3$), 4.84 (1H, d, $^2J_{HH}$ = 15.4 Hz, NCH_2), 5.52 (1H, dd, $^3J_{HH}$ = 9.7 Hz, 6.0 Hz, C*H*CHCF), 6.29 (1H, dd, $^3J_{HH}$ = 8.3 Hz, $^4J_{HH}$ = 0.6 Hz, H_{arom}), 6.37 (1H, dd, $^3J_{HH}$ = 8.2 Hz, $^4J_{HH}$ = 0.6 Hz, Hz, C*H*=CHCHCF$_3$), 6.84 (2H, dm, $^3J_{HH}$ = 8.6 Hz, PMB), 7.03 (1H, t, $^3J_{HH}$ = 8.4 Hz, H_{arom}), 7.14 (1H, d, $^3J_{HH}$ = 9.3 Hz, H_{arom}), 7.17 (2H, dm, $^3J_{HH}$ = 8.8 Hz, PMB); ^{13}C NMR δ 54.1, 55.2, 55.4, 57.8 (q, $^2J_{CF}$ = 30.2 Hz), 100.6, 106.2, 110.5, 112.3, 114.1, 125.0, 125.3 (q, $^1J_{CF}$ = 290.5 Hz), 128.6, 128.8, 129.5, 144.1, 155.7, 158.9; ^{19}F NMR δ −77.62 (d, $^3J_{FH}$ = 7.0 Hz, CF_3); MS (EI 70 eV) *m*/*z* (%) 349 (M^+, 6), 280 (22), 121 (100); HRMS (EI) calcd for $C_{19}H_{18}NO_2F_3$ (M^+), 349.1290; found, 349.1302. Anal. Calcd for $C_{19}H_{18}NO_2F_3$: C, 65.32; H, 5.19; N, 4.01; F, 16.31. Found: C, 65.34; H, 5.40; N, 3.86; F, 16.32.

3-Trifluoromethyl-4-(*p*-methoxybenzyl)-3,4-dihydrophenanthroline (2h). Pale yellow solid: mp 93−94 °C; IR (film, ν_{max}, cm^{-1}) 3001, 2935, 2837, 1611, 1511, 1464, 1444, 1266, 1248, 1161, 1129, 1107, 1034, 869, 831, 808, 694; ^{1}H NMR δ 3.75 (3H, s, OCH_3), 4.48 (1H, m, ^3J = 7.2 Hz, $CHCF_3$), 4.69 (1H, d, $^2J_{HH}$ = 15.1 Hz, NCH_2), 5.60 (1H, dd, $^3J_{HH}$ = 9.5 Hz, 6.2 Hz, C*H*CHCF$_3$), 5.64 (1H, d, $^2J_{HH}$ = 15.1 Hz, NCH_2), 6.75 (1H, d, $^3J_{HH}$ = 9.6 Hz, C*H*=CHCHCF$_3$), 6.78 (2H, d, $^3J_{HH}$ = 8.8 Hz, PMB), 7.18−7.32 (6H, m, H_{arom}), 8.00 (1H, dd, $^3J_{HH}$ = 8.2 Hz, $^4J_{HH}$ = 1.8 Hz, H_{arom}), 8.86 (1H, dd, $^3J_{HH}$ = 4.1 Hz, $^4J_{HH}$ = 1.8 Hz, H_{arom}); ^{13}C NMR δ 55.1, 58.5 (q, $^2J_{CF}$ = 31.0 Hz), 59.9, 113.6, 116.0, 120.3, 120.8, 123.8, 125.0 (q, $^1J_{CF}$ = 286.2 Hz), 126.2, 129.6, 129.8, 130.6, 131.3, 136.3, 140.4, 141.6, 148.0, 158.9; ^{19}F NMR δ −79.44 (d, $^3J_{FH}$ = 7.9 Hz, CF_3); MS (EI 70 eV) *m*/*z* (%) 370 (M^+, 12), 301 (25), 121 (100); HRMS (EI) calcd for $C_{21}H_{17}N_2OF_3$ (M^+), 370.1293; found, 370.1297. Anal. Calcd for $C_{21}H_{17}N_2OF_3$: C, 68.10; H, 4.63; N, 7.56; F, 15.39. Found: C, 67.93; H, 4.54; N, 7.51; F, 15.30.

Oxidation of Trifluoromethylated Dihydroazines 2 and 3. Dihydroazine (0.40 mmol) was dissolved in MeOH (2.0 mL), and a solution of CAN (482 mg, 0.88 mmol) in water (0.5 mL) was added dropwise at room temperature with vigorous stirring. The reaction mixture was then diluted with H_2O (10 mL), and the product was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with H_2O (ca. 20 mL), dried (Na_2SO_4), and evaporated. The product was purified by column chromatography on silica gel (or neutral aluminum oxide when it was difficult to remove *p*-methoxybenzaldehyde).

5-Benzoyl-2-trifluoromethylpyridine (4f). Colorless solid: mp 64−65 °C; IR (KBr, ν_{max}, cm^{-1}) 3076, 1651, 1596, 1449, 1387, 1335, 1288, 1246, 1174, 1152, 1123, 1086, 1023, 942, 924, 860, 800, 770, 707, 691; ^{1}H NMR δ 7.52−7.58 (2H, m, Ph), 7.68 (1H, tm, $^3J_{HH}$ = 7.5 Hz, H_{arom}), 7.80−7.87 (3H, m, Ph), 8.28 (1H, dm, $^3J_{HH}$ = 8.1 Hz, H_{arom}), 9.08 (1H, m, H_{arom}); ^{13}C NMR δ 120.2 (m, $^3J_{CF}$ = 5.6 Hz), 121.1 (q, $^1J_{CF}$ = 274.6 Hz), 128.9, 130.1, 133.8, 135.6, 136.0, 138.7, 150.5 (q, $^2J_{CF}$ = 34.9 Hz), 150.7, 193.5; ^{19}F NMR δ −68.68 (s, CF_3); MS (EI 70 eV) *m*/*z* (%) 251 (M^+, 27), 232 (5), 182 (39), 174 (8), 146 (17), 105 (100), 77 (79); HRMS (EI) calcd for $C_{13}H_8NOF_3$ (M^+), 251.0558; found, 251.0550. Anal. Calcd for $C_{13}H_8NOF_3$: C, 62.16; H, 3.21; N, 5.58; F, 22.69. Found: C, 62.11; H, 2.94; N, 5.62; F, 22.68.

3-Benzoyl-2-trifluoromethylpyridine (5f). Colorless oil: IR (CH_2Cl_2, ν_{max}, cm^{-1}) 3063, 1676, 1597, 1584, 1450, 1325, 1289, 1268, 1212, 1185, 1143, 1074, 1052, 928, 792, 727, 709, 666; ^{1}H NMR δ 7.50 (2H, t, $^3J_{HH}$ = 7.3 Hz, Ph), 7.59−7.69 (2H, m, Ph, H_{arom}), 7.74−7.82 (3H, m, Ph, H_{arom}), 8.88 (1H, dm, $^3J_{HH}$ = 4.8 Hz); ^{13}C NMR δ 121.2 (q, $^1J_{CF}$ = 275.9 Hz), 125.8, 128.8, 130.0, 134.4, 134.4, 135.8, 136.5, 144.9 (q, $^2J_{CF}$ = 35.3 Hz), 150.3, 193.3; ^{19}F NMR δ −63.86 (s, CF_3); MS (EI 70 eV) *m*/*z* (%) 251 (M^+, 16), 232 (2), 174 (4), 146 (6), 105 (100), 77 (33); HRMS (EI) calcd for $C_{13}H_8NOF_3$ (M^+), 251.0558; found, 251.0550. Anal. Calcd for $C_{13}H_8NOF_3$: C, 62.16; H, 3.21; N, 5.58. Found: C, 61.26; H, 2.87; N, 5.26.

5-Methoxy-2-trifluoromethylquinoline (4g). White solid: mp 52−54 °C; IR (KBr, ν_{max}, cm^{-1}) 2942, 2845, 1618, 1596, 1577, 1513, 1477, 1339, 1296, 1263, 1216, 1175, 1113, 812, 761, 623; ^{1}H NMR δ 4.02 (3H, s, OCH_3), 6.94 (1H, d, $^3J_{HH}$ = 7.7 Hz, H_{arom}), 7.66−7.73 (2H, m, H_{arom}), 7.78 (1H, d, $^3J_{HH}$ = 8.7 Hz, H_{arom}), 8.74 (1H, dd, $^3J_{HH}$ = 8.8 Hz, $^4J_{HH}$ = 0.6 Hz, H_{arom}); ^{13}C NMR δ 55.8, 105.8, 113.7, 115.7 (m, $^3J_{CF}$ = 2.6 Hz), 121.6 (q, $^1J_{CF}$ = 275.0 Hz), 121.9, 129.3, 130.8, 133.1, 148.1 (q, $^2J_{CF}$ = 34.4 Hz), 154.9; ^{19}F NMR δ = −68.07 (d, $^4J_{FH}$ = 0.6 Hz, CF_3); MS (EI 70 eV) *m*/*z* (%) 227 (M^+, 100), 212 (24), 184 (82), 164 (12), 134 (15); HRMS (EI) calcd for $C_{11}H_8NOF_3$ (M^+), 227.0558; found, 227.0547. Anal. Calcd for $C_{11}H_8NOF_3$: C, 58.16; H, 3.55; N, 6.17; F, 25.09. Found: C, 58.48; H, 3.39; N, 5.55; F, 24.33.

Acknowledgment. This work was supported by the Polish Ministry of Science and Higher Education (grant 3 T09A 043 27). We thank Dr. Hubert Hugl (Bayer Chemical AG, Leverkusen) for the gift of the Ruppert reagent.

Supporting Information Available: Copies of NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0703552