Regioselective Oxyfunctionalization of Unactivated Tertiary and Secondary C–H Bonds of Alkylamines by Methyl(trifluoromethyl)dioxirane in Acid Medium

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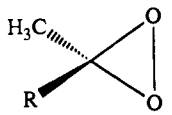
Abstract: Tetrafluoroborate salts of primary, secondary, and tertiary alkylamines are resistant toward N oxidation by methyl(trifluoromethyl)dioxirane (**1b**), which allows the selective oxidation of aliphatic tertiary and secondary C–H bonds in the alkyl side chain. The oxidations are carried out at 0 °C with a ketone-free solution of methyl(trifluoromethyl)-dioxirane (**1b**) in methylene chloride. By this procedure, within 3 h the tertiary C–H bonds of acyclic, cyclic, and polycyclic amines **2a–e** are hydroxylated to give the corresponding amino alcohols **3a–e**. In the case of the acyclic amines **2a,b** longer reaction times were necessary, and in the strong acid medium the corresponding amino acetamides **4a,b** were obtained through Ritter reaction with the solvent acetonitrile. The strong electron-withdrawing nature of the ammonium group deactivates the oxidation of even tertiary C–H bonds at the α and β positions. Secondary C–H bonds of the linear aliphatic primary amines **2f–h** were oxidized exclusively at the ϵ position to give the 2,3,4,5-tetrahydro-6-alkylpyridines **6f–h** after intramolecular condensation of the corresponding amino ketones **5f–h**.

Introduction

Oxidation of the nitrogen atom of amines and α C–H bonds of their amide derivatives can be performed by a variety of oxidants.[1] Furthermore, the efficient N-oxidation of primary and secondary amines by dimethyldioxirane (**1a**) in high yields has been recently reported.[2] However, up to now, selective oxyfunctionalization of *remote* unactivated C–H bonds in the aliphatic chain of alkylamines can only be achieved by biological systems on the corresponding amide derivatives.[3]



1a R= CH_3
1b R= CF_3

Methyl(trifluoromethyl)dioxirane (**1b**), hereafter TFDO, is a powerful O-transfer reagent, which is able to perform O atom insertion into C–H bonds of saturated hydrocarbons to afford the corresponding alcohols and/or ketones.[4] Recently we reported[5] on the isolation of TFDO (**1b**) in ketone-free chlorinated solvents and proved that **1b** is stable toward strong acids (CF_3COOH, CF_3SO_3H, H_2SO_4). These findings prompted us to explore the synthetic value of the oxidation reactions by TFDO in acid media. In this context, alkylamines constitute suitable substrates for oxyfunctionalization in the side chain, provided that protonation protects the amino functionality toward oxidation.

Although ammonium chlorides undergo N-oxidation by dimethyldioxirane (**1a**),[2a,b] we presently report that ammonium tetrafluoroborates do not with TFDO (**1b**). This allows us to perform the selective O atom insertion into remote tertiary C–H bonds of the alkyl side chains to give the corresponding tertiary amino alcohols after neutralization. In the case of linear primary aliphatic ammonium salts, secondary C–H bonds are oxidized exclusively at the ϵ position to afford, after intramolecular condensation of the corresponding amino ketones, 2,3,4,5-tetrahydro-6-alkylpyridines.

Results and Discussion

Oxidations were carried out at 0 °C by simply adding a stoichiometric amount of a 0.2–0.4 M ketone-free solution of TFDO in methylene chloride, prepared as described previously,[5] to a solution of the ammonium tetrafluoroborate in acetonitrile (initial concentration ranging between 0.1 and 1 M). The use of ketone-free solutions of TFDO is required for the success of the reaction under our conditions, because the presence of trifluoroacetone leads to high-molecular-weight materials, which encumbers the isolation of the reaction products. Acetonitrile was found to be the solvent of choice for carrying out these oxidations because, on the one hand, it is a fairly good solvent for the ammonium salts and, on the other, mixed with methylene chloride it gives a homogeneous reaction medium. Ammonium salt solutions were prepared *in situ* by adding aqueous tetrafluoroboric acid to an acetonitrile solution of the amine to pH 2–3. Alternatively, identical results were obtained when ammonium tetrafluoroborate salts were previously isolated and used in oxidations in the absence of an excess of tetrafluoroboric acid. The workup procedure consists of evaporation of the solvent under

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(2) (a) Crandall, J. K.; Reix, T. *J. Org. Chem.* **1992**, *57*, 6759. (b) Murray, R. W.; Rajadhyaksha, S. N.; Mohan, L. *J. Org. Chem.* **1989**, *54*, 5783. (c) Murray, R. W.; Singh, M. *Tetrahedron Lett.* **1988**, *29*, 4677. (d) Murray R. W.; Mohan, L.; Jeyaraman, R. *Tetrahedron Lett.* **1986**, *27*, 2335.
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(4) Mello, R.; Fiorentino, M.; Fusco, C.; Curci, R. *J. Am. Chem. Soc.* **1989**, *111*, 6749.
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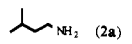
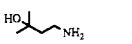
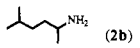
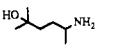
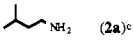
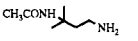
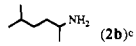
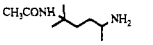
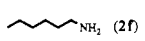
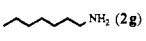
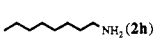
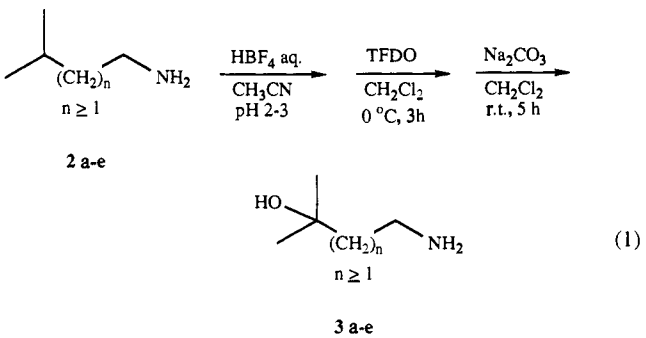
Table I. Selective C–H Bond Oxyfunctionalization of Aliphatic Ammonium Tetrafluoroborates by TFDO (**1b**)[a]

Entry	Amine	Molar ratio RNH_3^+: 1b	Reaction time (h)	Conversion[b] (%)	Product	Yield[b] (%)
1	 (2a)	1:1.1	3	95	 (3a)	95
2	 (2b)	1:1.1	3	99	 (3b)	98
3	 (2c)	1:1.1	15	60	 (3c)	99
4	 (2d)	1:1.1	5	98	 (3d)	98
5	 (2e)	1:1.1	3	99	 (3e)	98
6	 (2a)[c]	1:1.1	10	97	 (4a)	96
7	 (2b)[c]	1:1.1	10	99	 (4b)	97
8	 (2f)	1:2.2	8	98	 (6f)	90[d]
9	 (2g)	1:2.2	8	99	 (6g)	95[d]
10	 (2h)	1:2.2	8	96	 (6h)	92[d]

[a] Reactions were carried out either *in situ* or by using the previously prepared and isolated ammonium salt. [b] As determined by capillary GC analysis. [c] The *in situ* method was employed (pH 2–3). Reaction temperature was allowed to rise from 0 °C up to room temperature. [d] Products were identified by comparison with authentic samples prepared as described.[12,13]

vacuum followed by treatment of the residue with solid sodium carbonate in methylene chloride. The results are shown in Table I.

Tertiary C–H bonds, separated by at least two carbons atoms from the ammonium group, were readily oxidized by TFDO (entries 1–3, Table I) to afford the corresponding amino alcohols in excellent yields (eq 1). The α and β C–H bonds were found to be unreactive toward **1b**. Thus, 2-methyl-1-butylamine,

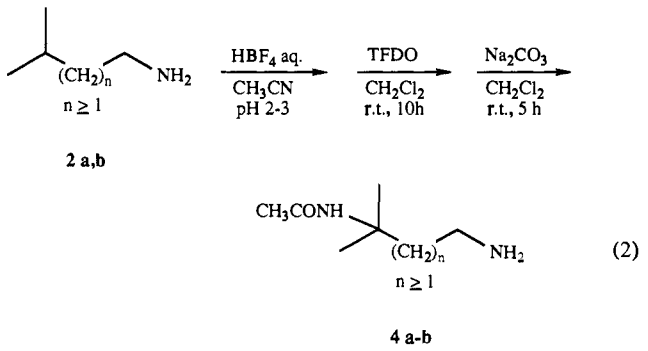


(1)

cyclohexylamine, and (aminomethyl)cyclohexane did not react with TFDO even after 20 h under our oxidation conditions. Conversely, bridgehead C–H bonds of polycyclic saturated amines (entries 4 and 5 Table I) were readily oxidized by TFDO under these conditions to give the corresponding amino alcohols in nearly quantitiative yields. Our results reflect quite well the trend of reactivity exhibited in the oxidation by TFDO of bridgehead tertiary C–H bonds of acyclic, bicyclic, and policyclic alkanes.[4]

Complete hydroxylation of tertiary C–H bonds was achieved within reaction times of 3–15 h, which are significantly longer than those necessary for the hydroxylation of alkanes. These results confirm the strongly deactivating inductive effect of the ammonium group, which presumably is responsible for the regioselective C–H hydroxylations, as controlled by the distance from the ammonium moiety.

Interestingly, in the case of oxidation of tertiary C–H bonds of acyclic amines (entries 6 and 7, Table I) longer reaction times led to amino acetamides (eq 2). This result is rationalized in

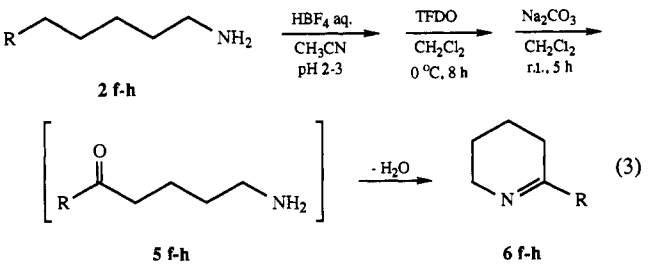


(2)

terms of a carbocation intermediate produced from the tertiary alcohols in the strong acid medium, which is trapped by acetonitrile (Ritter reaction). Thus, the overall process constitutes a selective *in situ* N-functionalization of unactivated C–H bonds mediated through O transfer by TFDO. The direct preparation of 1,*n*-diamines, in which one of the amino groups is selectively protected as amide, is of an unquestionable synthetic interest.

Ammonium tetrafluoroborates derived from aromatic amines were found to be only sparingly soluble under our experimental oxidation conditions but also served as substrates for the oxidation and gave rise in this case to the corresponding nitro compounds, e.g. 30% yield in the oxidation of isopropylanilinium tetrafluoroborate, when equimolar amounts of TFDO and amine were employed. The lower basicity of the aromatic amino group may be responsible in this case for the different behavior.

Also secondary C–H bonds of linear aliphatic amines (entries 8–10, Table I) were oxidized by TFDO in excellent yields either in acid medium or by employing the isolated ammonium salts. 2,3,4,5-Tetrahydro-6-alkylpyridines **6f–h** were obtained by intramolecular, acid-promoted condensation of the resulting amino ketones **5f–h**, which are produced by subsequent oxidation of the secondary alcohols (eq 3). This constitutes a remarkable unprecedented transformation, in which simple aliphatic amines **2f–h** are regioselectively functionalized into the synthetically valuable tetrahydropyridines **6f–h** in high yields through the one-pot oxidation by TFDO.



(3)

As presently witnessed, in spite of its high reactivity, TFDO is a very selective O-transfer reagent[6] and the oxidations of the remarkably simple molecules **2f–h** are unprecedented. The strong electron-withdrawing effect of the ammonium group would be expected to direct the oxidation to the most remote and consequently less deactivated methylene group present in these substrates. We propose that the high regioselectivity of the O atom insertion (*exclusively* at the ϵ-methylene group) is achieved by the cooperative effect of the deactivating effect of the

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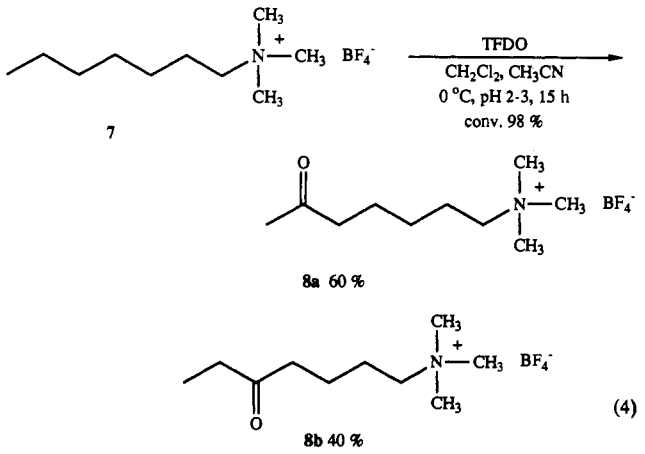
ammonium group, the hydrogen bonding between the dioxirane and the ammonium ion moiety, and the conformational flexibility of the aliphatic chain, which brings the ϵ-methylene group near to the free and activated oxygen atom of TFDO. The oxidation of *n*-heptyltrimethylammonium tetrafluoroborate with TFDO under our standard conditions (eq 4) corroborates this proposal in that the ζ methylene of the *n*-heptyl chain was now oxidized preferably (ζ/ϵ = 60/40). Thus, on permethylation of the



(4)

ammonium nitrogen center, as in $RNMe_3^+$, hydrogen bonding is not feasible with TFDO, the extent to which ϵ oxidation occurs is substantially diminished, and ζ oxidation becomes competitive.

Additional support for the directing effect of the ammonium group was found in the oxidation of cyclic amines with TFDO in acid medium. Thus, cyclooctylamine and cyclohexylmethylamine ammonium tetrafluoroborates, both containing ϵ-methylene groups, were found to be unreactive toward TFDO. Generally, cyclic methylene groups are more prone to undergo oxygen atom insertion by TFDO than their alicyclic counterparts;[4] however, these cyclic ammonium salts cannot adopt a conformation in which their ϵ-methylene groups are proximate to the ammonium-coordinated TFDO. Consequently, deactivation by the electron-withdrawing effect of the ammonium group predominates, which renders these substrates unreactive.

Conclusions

In summary, we have demonstrated the synthetic potential of TFDO as oxygen atom insertion reagent into remote C–H bonds of aliphatic amines in strong acid medium. In this medium the alkylamines are protected through protonation toward N-oxidation by TFDO. Thus, tertiary C–H bonds of cyclic and alicyclic aliphatic amines can be efficiently hydroxylated to give the corresponding amino alcohols in excellent yields. Upon prolonged standing under these acid conditions, the amino alcohols are converted into amino acetamides by the Ritter reaction with acetonitrile. Particularly valuable from the synthetic viewpoint is the direct, highly regioselective, oxidative cyclization of linear primary alkylamines into tetrahydropyridines through intramolecular condensation of the intermediary amino ketones.

Experimental Section

General Aspects. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC 200 spectrometer. IR spectra were run on a Perkin-Elmer 843 spectrometer. GLC analyses were performed on a KNK 3000-HRGC (Konik) instrument equipped with a DB-1 capillary column (25 m, film thickness 1 μm, i.d. 0.25 mm). High-resolution mass spectra were conducted on a VG AUTOSPEC instrument. GCMS measurements were made on a Hewlett-Packard Model 5970 mass-selective detector connected to a Model 5890 gas chromatograph. All solvents and reagents were purified by standard procedures and freshly distilled prior to use. Methyl(trifluoromethyl)dioxirane (**1b**) or TFDO solutions in trifluoroacetone and ketone-free solutions in methylene chloride were obtained by the previously reported methods.[4,5] Trifluoroacetone, the Caroate triple salt $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, and HBF_4 (ca. 8 M aqueous solution or 54% ethereal solution) were purchased from Fluka. The amines were all commercially available (Fluka or Aldrich). Alkylammonium tetrafluoroborates were prepared by treating the corresponding alkylamines, dissolved in ether, with an equimolar amount of a ca. 54% HBF_4 ethereal solution at –15 °C. The precipitate was collected by filtration, washed with cold ether, and dried under vacuum.

Reaction of Alkylamines with TFDO in Acid Medium. (A) *In Situ* Method. To a stirred solution of 44.0 mg (0.520 mmol) of isopentylamine (**2a**) in 1.0 mL of CH_3CN was added a ca. 8 M aqueous solution of HBF_4 at 0 °C until pH 2–3 (ca. 60 μL), followed by 2.3 mL of a 0.25 M (0.570 mmol) ketone-free solution of TFDO in CH_2Cl_2, which was added at once. The resulting reaction mixture was kept under stirring at 0 °C until a KI–starch paper test showed that the TFDO was consumed (3 h). The solvent was evaporated under vacuum, and the residue was treated with 0.120 g (1.16 mmol) of solid Na_2CO_3 in CH_2Cl_2 at room temperature under vigorous stirring for 5 h. The solid was removed by filtration and the resulting solution analyzed by GC and GCMS. The solvent was evaporated under vacuum to afford 56.0 mg (95% yield) of 4-amino-2-methyl-2-butanol (**3a**) as a colorless oil, which was fully characterized by the standard spectral methods (see below).

(B) Reaction of Isolated Alkylammonium Tetrafluoroborates with TFDO. To a stirred solution of 50.0 mg (0.290 mmol) of isopentylammonium tetrafluoroborate in 1.0 mL of CH_3CN at 0 °C was added with stirring 1.4 mL of a 0.25 M (0.320 mmol) ketone-free solution of TFDO in CH_2Cl_2. The reaction mixture was kept at 0 °C until a KI–starch paper test showed total consumption of TFDO (3 h). The solvent was evaporated under vacuum and the residue treated with 60.0 mg (0.580 mmol) of solid Na_2CO_3 in CH_2Cl_2 at room temperature with vigorous stirring for 5 h. The solid was removed by filtration and the resulting solution analyzed by GC, GCMS, and NMR, which gave essentially the same results as the *in situ* method.

4-Amino-2-methyl-2-butanol (3a): colorless oil, 95% yield, bp 72–73 °C/10 Torr (lit.[7] bp 75–80 °C/13 Torr, lit.[8] bp 71.5 °C/10 Torr). ^{1}H NMR ($DCCl_3$, 200 MHz): δ 1.16 (s, 6H), 1.58 (t, J = 6.5 Hz, 2H), 2.94 (t, J = 6.4 Hz, 2H), 3.97 (bs, 1H). ^{13}C NMR ($DCCl_3$, 50 MHz): δ 29.30, 37.48, 42.24, 70.54. IR (CCl_4): 3353, 2968, 2926, 2867, 1549, 1461, 1378, 1363, 1260, 1214, 1155, 1095, 1012 cm^{-1}. MS (EI, 70 eV): m/z 88.08 ($M^+ - CH_3$, 10.5), 70.07 (84.0), 69.07 (11.1), 59.05 (36.4), 58.07 (100.0), 56.06 (14.6).

5-Amino-2-methyl-2-hexanol[9] (3b): colorless oil, 98% yield. ^{1}H NMR ($DCCl_3$, 200 MHz): δ 1.01 (d, J = 6.3 Hz, 3H), 1.10 (s, 6H), 1.25–1.49 (m, 4H), 2.50 (bs, 1H), 2.79 (m, 1H). ^{13}C NMR ($DCCl_3$, 50 MHz): δ 24.40, 29.00, 29.61, 33.94, 40.55, 47.32, 69.47. IR (CCl_4): 3373, 3211, 2966, 2924, 2867, 1580, 1548, 1455, 1376, 1214, 1156, 1100, 1079 cm^{-1}. MS (EI, 70 eV): m/z 116.11 ($M^+ - CH_3$, 28.3), 100.08 (10.2), 99.08 (100.0), 98.10 (42.2), 81.07 (78.7), 59.05 (86.3), 57.06 (59.5), 55.05 (57.1).

4-Hydroxy-4-methylpiperidine[10] (3c): pale yellow oil, 99% yield. ^{1}H NMR ($DCCl_3$, 200 MHz): δ 1.19 (s, 3H), 1.49–1.55 (m, 4H), 2.76–2.93 (m, 4H). ^{13}C NMR ($DCCl_3$, 50 MHz): δ 29.89, 39.43, 42.48, 67.69.

4-Hydroxy-1-azabicyclo[2.2.2]octane (3d): white solid, mp 157–159 °C (lit.[11] mp 155–160 °C), 98% yield. ^{1}H NMR (D_2CCl_2, 200 MHz): δ 2.02 (m, 6H), 3.51 (m, 6H). ^{13}C NMR (D_2CCl_2, 50 MHz): δ 23.76, 54.25, 68.70. MS (EI, 70 eV): m/z 127.10 (M^+, 7.8), 113.00 (27.6), 111.10 (100.0), 110.10 (86.4), 101.00 (12.8), 96.08 (59.9), 83.07 (40.1), 82.07 (99.2), 70.0 (12.6), 69.06 (40.3), 68.05 (18.4), 57.06 (34.2), 56.05 (23.0), 55.05 (74.5), 54.04 (25.2).

3-Aminoadamantan-1-ol (3e): white solid, mp 269 °C (lit.[12] mp 269 °C, lit.[13] mp 267 °C), 98% yield. ^{1}H NMR (DMSO-d_6, 200 MHz): δ 1.33–1.51 (m, 12H), 2.07 (bs, 2H), 3.20 (bs, 3H). ^{13}C NMR (DMSO-d_6, 50 MHz): δ 30.45, 34.79, 44.14, 44.30, 50.15, 53.40, 67.76. IR (KBr): 3314, 2886, 1457, 1354, 1034, 944 cm^{-1}. MS (EI, 70 eV): m/z 167.13 (M^+, 10.4), 126.06 (18.4), 110.06 (100.0), 94.07 (22.1), 57.05 (10.1).

***N*-(2-(4-Amino-2-methylbutyl))acetamide (4a)**: pale yellow oil, 96% yield. ^{1}H NMR ($DCCl_3$, 200 MHz): δ 1.07 (s, 6H), 1.49 (t, J = 7.0

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(11) Grob, C. A.; Brenneisen, P. *Helv. Chim. Acta* **1958**, *41*, 1184.
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Hz, 2H), 1.87 (s, 3H), 3.24 (m, 2H). ^{13}C NMR ($DCCl_3$, 50 MHz): δ 29.33, 30.40, 36.07, 41.39, 49.38, 169.88. IR (CCl_4): 1665 cm^{-1} (C=O). MS (EI, 70 eV): *m/z* 129.10 ($M^+ - CH_3$, 3.5), 70.07 (40.7), 59.07 (15.6), 58.07 (100.0). Exact mass calcd for $C_7H_{17}N_2O$ (M + H^+, LSIMS): 145.1341. Found: 145.1348.

***N*-(2-(5-Amino-2-methylhexyl))acetamide (4b)**: pale yellow oil, 97% yield. ^{1}H NMR ($DCCl_3$, 200 MHz): δ 1.04 (d, *J* = 6.3 Hz, 3H), 1.26 (s, 3H), 1.22–1.36 (m, 2H), 1.63–1.73 (m, 2H), 1.87 (s, 3H), 2.83 (m, 1H). ^{13}C NMR ($DCCl_3$, 50 MHz): δ 24.01, 24.34, 26.86, 33.95, 36.73, 47.07, 53.36, 169.60. MS (EI, 70 eV): *m/z* 172.16 (M^+, 2.0), 144.13 (11.9), 130.12 (21.9), 129.12 (29.6), 114.10 (12.2), 101.08 (48.7), 100.08 (50.9), 98.10 (65.5), 86.06 (15.8), 81.07 (18.4), 70.07 (11.1), 60.05 (40.1), 58.07 (100.0), 57.06 (46.6), 55.06 (20.2). Exact mass calcd for $C_9H_{20}N_2O$: 172.1576. Found: 172.1588.

2,3,4,5-Tetrahydro-6-methylpyridine (6f): yellow oil, bp 132–133 °C/760 Torr, 90% yield, identified by comparison with an authentic sample prepared by reaction of 1-chloro-2-methylpiperidine (obtained[14] by reaction of 2-methylpiperidine with *N*-chlorosuccinimide in ether) with KOH in CH_3OH, as described in the literature.[15] ^{1}H NMR ($DCCl_3$, 200 MHz): δ 1.30–1.44 (m, 4H), 1.67 (s, 3H), 1.89 (m, 2H), 3.26 (m, 2H). ^{13}C NMR ($DCCl_3$, 50 MHz): δ 19.14, 21.18, 26.93, 29.80, 48.60, 167.69. MS (EI, 70 eV): *m/z* 97.2 (M^+, 99), 96.2 (15), 69.0 (77), 68.0 (23), 56.0 (25), 55.6 (17), 54.0 (14), 42.0 (100), 41.0 (57).

2,3,4,5-Tetrahydro-6-ethylpyridine (6g): yellow oil, bp 85–86 °C/80 Torr, 95% yield, identified by comparison with an authentic sample prepared by reaction of 1-chloro-2-ethylpiperidine (obtained[14] by reaction of 2-ethylpiperidine with *N*-chlorosuccinimide in ether) with KOH in methanol, as described in the literature.[15] ^{1}H NMR ($DCCl_3$, 200 MHz): δ 1.16 (t, *J* = 7.6 Hz, 3H), 1.77 (m, 4H), 2.55 (m, 2H), 2.59 (q, *J* = 7.6 Hz, 2H), 3.58 (m, 2H). ^{13}C NMR ($DCCl_3$, 50 MHz): δ 10.02, 16.99, 19.32, 28.46, 30.88, 44.20, 175.50. MS (EI, 70 eV): *m/z* 111.10 (M^+, 79.7), 110.10 (100.0), 96.08 (22.9), 83.07 (25.9), 82.07 (37.0), 56.05 (20.4).

2,3,4,5-Tetrahydro-6-propylpyridine (6h): yellow oil, bp 59–60 °C/10 Torr, 92% yield, identified by comparison with an authentic sample, prepared by the procedure[15] described for **6g**. The 2-propylpiperidine was prepared by reaction of pyridine with propyllithium[16] followed by sodium in ethanol hydrogenation.[17] ^{1}H NMR ($DCCl_3$, 200 MHz): δ 0.84 (t, *J* = 7.3 Hz, 3H), 1.41–1.60 (m, 8H), 2.05 (m, 4H), 3.44 (m, 2H). ^{13}C NMR ($DCCl_3$, 50 MHz): δ 13.42, 19.12, 19.40, 28.49, 42.50, 48.49, 56.67, 170.83. MS (EI, 70 eV): *m/z* 125.1 (M^+, 19), 124.1 (11), 110.2 (44), 97.2 (100), 96.0 (61), 82.0 (13), 70.0 (28), 69.0 (12), 55.0 (16), 54.0 (16), 41.0 (33).

***n*-Heptyltrimethylammonium Tetrafluoroborate (7)**. To a solution of 7 mL (47 mmol) of *n*-heptylamine and 37.0 g (350 mmol) of $NaHCO_3$ in 100 mL of distilled water was added dropwise at room temperature with stirring during 30 min 15.1 mL (160 mmol) of dimethyl sulfate. The reaction mixture was stirred overnight at room temperature and then refluxed for 5 h. The solvent was distilled at atmospheric pressure and the residue redissolved in 100 mL of distilled water. The sulfate/tetrafluoroborate anion exchange was carried out by treatment with a saturated aqueous solution of $Ba(BF_4)_2$ and filtration of the precipitated $BaSO_4$. The water was removed by distillation at atmospheric pressure and the white residue treated with 100 mL of acetonitrile. The insoluble salts were filtered off and the solvent evaporated under vacuum. The resulting white solid was dried under vacuum to yield 9.0 g (95% yield) of *n*-heptyltrimethylammonium tetrafluoroborate (**7**). ^{1}H NMR (CD_3CN, 200 MHz): δ 1.88 (t, 3 H), 2.31 (m, 6 H), 2.72 (m, 4 H), 4.00 (s, 9 H), 4.20 (m, 2 H). ^{13}C NMR (CD_3CN, 50 MHz): δ 13.81, 22.67, 22.91, 26.17, 28.81, 31.67, 53.20, 67.03.

Reaction of Ammonium Tetrafluoroborate 7 with TFDO (1b). To a stirred solution of 70.0 mg (0.290 mmol) of **7** in 2 mL of acetonitrile at 0 °C was added at once 1.45 mL of a 0.44 M solution (0.640 mmol) of TFDO in methylene chloride. The reaction mixture was kept at 0 °C with stirring for 10 h. The solvent was evaporated under vacuum, and the solid residue was dissolved in D_2O and analyzed by ^{1}H NMR. **8a**: ^{1}H NMR (D_2O, 200 MHz) δ 1.20 (m, 2H), 1.44 (m, 2H), 1.64 (m, 2H), 2.04 (s, 3H), 2.44 (m, 2H), 3.12 (m, 2H). **8b**: ^{1}H NMR (D_2O, 200 MHz) δ 0.84 (t, 3H), 1.40–1.66 (m, 4H), 2.45 (m, 4H), 3.12 (m, 2H). The ratio of the products was calculated from the integrals of the signals at δ 2.04 (s) and at δ 0.84 (t, *J* = 7.3 Hz) for the C-7 methyl groups of **8a** and **8b**.

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