85370-38-3; **23**, 85370-39-4; **24**, 85370-40-7; **25**, 85370-41-8; **26**, 85370-42-9; **27**, 85370-43-0; **28**, 85370-44-1; **29**, 85370-45-2; **30**, 77144-30-0; **31**, 77144-38-8; **32**, 85370-46-3; **33**, 85370-47-4; **34**, 85370-48-5; **35**, 85370-49-6; **36**, 85370-50-9; **37**, 85370-51-0; **38**, 85370-52-1.

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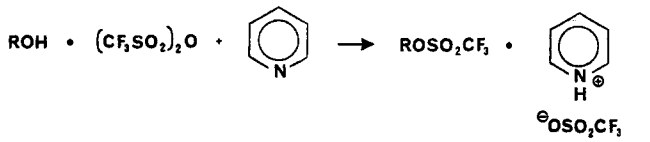
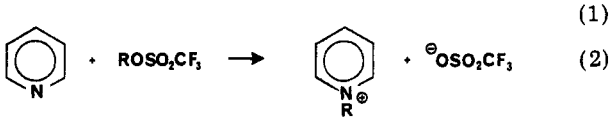
Reaction of 2,6-Dimethyl- and 2,4,6-Trimethylpyridine with Trifluoromethanesulfonic Anhydride

Summary: The reaction of trifluoromethanesulfonic anhydride with 2,6-dimethyl- and 2,4,6-trimethylpyridine produces compounds in which a methyl hydrogen is replaced by either a trifluoromethyl or a [(trifluoromethyl)sulfinyl]oxy group.

Sir: The most convenient and widely used method for preparation of esters of trifluoromethanesulfonic (triflic) acid consists of reacting the appropriate alcohol with triflic anhydride in the presence of pyridine.[1] Although pyridine is added primarily to neutralize the triflic acid formed (eq 1), its reaction with the triflate is sometimes the major pathway (eq 2).[2,3] One solution to this problem[3] is to



(1)

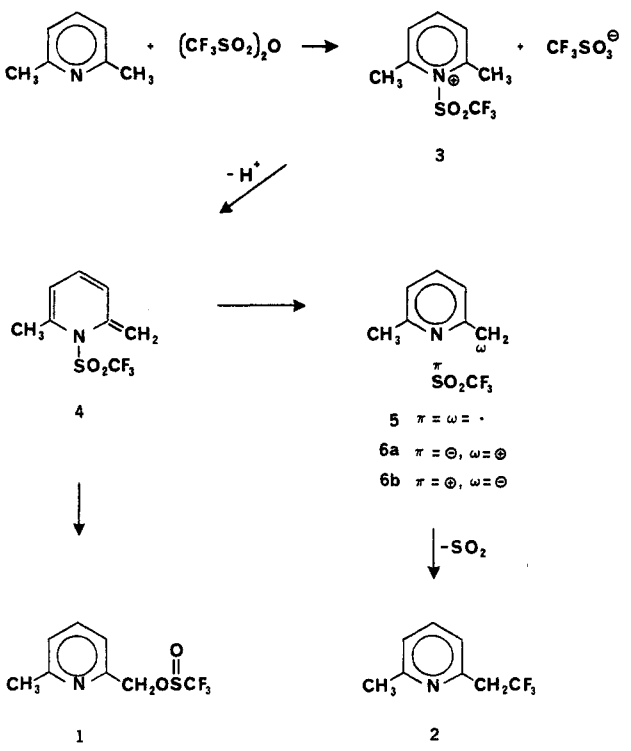


(2)

replace pyridine with one of its less nucleophilic derivatives (e.g., 2,6-dimethyl- or 2,4,6-trimethylpyridine). Although this substitution discourages displacement, new difficulties can arise. Methyl-substituted pyridines react with triflic anhydride to give products of unknown identity. These products are contained in reaction mixtures that are difficult to purify.[4] If the uncertainty about product structure could be eliminated from these reactions, the difficulty in using methyl-substituted pyridines might be overcome. With this thought in mind, we examined the reaction between triflic anhydride and 2,6-dimethylpyridine (2,6-lutidine) and found that two unusual products were formed.

Dropwise addition of triflic anhydride (3.0 mmol) to a solution of 2,6-lutidine (6.0 mmol) in carbon tetrachloride at room temperature results in an exothermic reaction that produces a dark red solution. Chromatography of the reaction mixture on silica gel removes the color and separates the mixture into three components, one of which is lutidine. The major product (48% yield, based on reacted lutidine) is 6-methyl-2-[[[(trifluoromethyl)sulfinyl]oxy]methyl]pyridine (1) and the minor product (17% yield) is 2-(2,2,2-trifluoroethyl)-6-methylpyridine (2).[5]

Scheme I



A proposed mechanism for the formation of these compounds (1 and 2) is shown in Scheme I; several observations are pertinent to this proposed process. First, pyridine derivatives are known[6] to react with triflic anhydride to form salts such as **3**. The positive charge on nitrogen in **3** should sufficiently enhance the acidity of the methyl hydrogens to permit deprotonation to give **4**.[7] The proposed rearrangement of **4** to the major product (1) can be either a concerted reaction or a stepwise process. If a nonconcerted reaction involving the radical pair **5** (Scheme I) were operative, CIDNP effects might be observable.[8] Although reaction was complete in a few seconds and measurement was made in less than 1 min, no polarized ^{1}H NMR signals were detectable. In order to gain more definitive information about the final step (**4** → 1) in this proposed mechanism (Scheme I), a second compound, 2,4,6-trimethylpyridine (*s*-collidine) was investigated.

If a mechanism similar to that shown in Scheme I is assumed for reaction between *s*-collidine and triflic anhydride, then any substitution on the 4-methyl group, must arise from a nonconcerted process. Triflic anhydride and *s*-collidine react readily to give 2-[[[(trifluoromethyl)-

(1) Stang, P. J.; Hanack, M.; Subramanian, L. R. *Synthesis* **1982**, 85.
(2) Hall, L. D.; Miller, D. C. *Carbohydr. Res.* **1976**, *47*, 299.
(3) (a) Leroux, J.; Perlin, A. S. *Carbohydr. Res.* **1976**, *47*, C8. (b) Leroux, J.; Perlin, A. S. *Ibid.* **1978**, *67*, 163.
(4) Reference 1, p 107.

(5) Characterizing data for compound 1: bp 100–102 °C (2 torr); ^{1}H NMR ($CDCl_3$) δ 7.74–6.95 (m, H-3, H-4, H-5), 5.39, 5.12 (CH_2, J = 12.6 Hz), 2.52 (s, CH_3); ^{13}C NMR ($CDCl_3$) δ 158.75 (C_6), 153.19 (C_2), 137.40 (C_4), 123.46 (C_5), 123.10 (q, CF_3, $^1J_{CF}$ = 338 Hz), 119.23 (C_3), 70.36 (CH_2), 24.28 (CH_3) (off-resonance decoupling produced the expected multiplicity for each signal); mass spectrum (CI, methane), m/z (rel intensity) 240 (18), 170 (15), 106 (100). Compound 1 was homogenous by TLC and VPC but decomposed upon standing overnight as a neat liquid. Characterizing data for compound 2: ^{1}H NMR (CD_3COCD_3) δ 7.83–6.92 (m, H-3, H-4, H-5), 3.56 (q, CH_2, $^3J_{HF}$ = 10.6 Hz), 2.47 (s, CH_3); ^{13}C NMR (CD_3COCD_3) δ 158.67 (C_6), 150.12 (C_2), 136.96 (C_4), 125.00 (q, CF_3), 122.42, 121.48 (C_3, C_5), 42.94 (q, CH_2, $^2J_{CF}$ = 28.79 Hz), 23.79 (CH_3) (off-resonance decoupling produced the expected multiplicity for each signal); mass spectrum (CI, methane), m/z (rel intensity) 176 (45), 156 (100). Compound 2 also was homogenous by TLC and VPC. Anal. Calcd for $C_8H_8F_3N$: C, 54.86; H, 4.60; N, 8.00. Found: C, 54.64; H, 4.61; N, 7.89.
(6) Stang, P. J.; Treptow, W. *Synthesis* **1980**, 283.
(7) Phillips, A. P. *J. Org. Chem.* **1947**, *12*, 333.
(8) CIDNP effects clearly were observable in a reaction that involved radicals similar to **5**. Bleeker, P. I.; Engberts, J. B. F. N. *J. Org. Chem.* **1981**, *46*, 1012.

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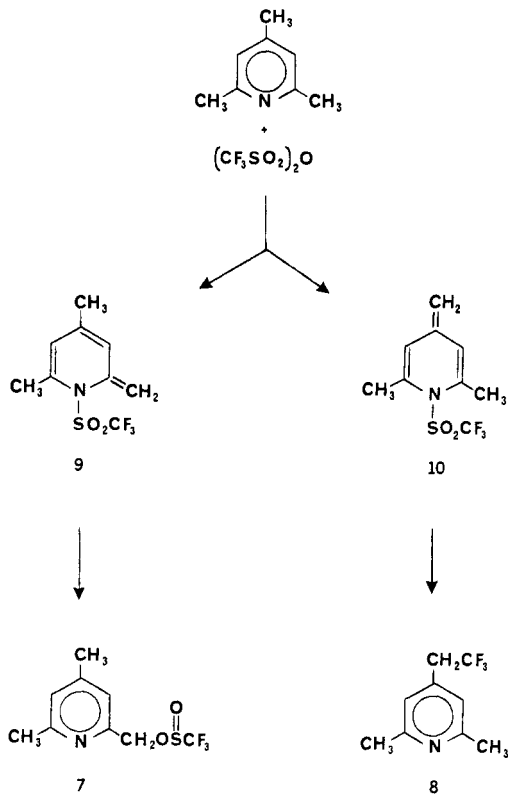
Scheme II



sulfinyl]oxy]methyl]-4,6-dimethylpyridine (**7**, 5%) and 4-(2,2,2-trifluoroethyl)-2,6-dimethylpyridine[9] (**8**, 62%) but no 4-[[(trifluoromethyl)sulfinyl]oxy]methyl-substituted derivative (Scheme II). This behavior argues in favor of a concerted reaction[10] for formation of compound **1** from the intermediate **4** (and **7** and **9**). Also, if the reactions of 2,6-lutidine and *s*-collidine to produce 2,2,2-trifluoroethyl-substituted pyridines are mechanistically similar, the conversion of **4** into **2** should be a nonconcerted process since the comparable transformation (**10** → **8**) for *s*-collidine cannot be concerted. From among the simplest intermediates for this reaction (**4** → **2**), only **6a** can be excluded rigorously because $CF_3SO_2^-$ is stable under the reaction conditions and, thus, cannot be a source of the CF_3 group.

The reaction between *s*-collidine and triflic anhydride also was conducted with diphenylmethane as the solvent. It was anticipated that if the trifluoromethyl radical were involved in this reaction, 1,1,2,2-tetraphenylethane (**11**) would be formed; however, no **11** was produced. Although the negative CIDNP (repeated with *s*-collidine with the same result as described above for 2,6-lutidine) and diphenylmethane experiments are not conclusive, they argue against the intermediacy of a radical pair such as **5** in the formation of **2** (Scheme I). The combined effect of this information is to favor the intermediate **6b**.

Finally, the case for using a highly hindered base such as 2,6-di-*tert*-butyl-4-methylpyridine[11] (**12**) when preparing reactive triflates is strengthened by the present study. Compound **12** does not react with triflic anhydride. When salts such as **3** cannot be formed, reactions such as those described here do not take place.

Acknowledgment. We appreciate the helpful suggestions of Professor A. H. Andrist and the financial support of The Standard Oil Company of Ohio.

Registry No. **1**, 85371-04-6; **2**, 85371-05-7; **7**, 85371-06-8; **8**, 85371-07-9; 2,6-lutidine, 108-48-5; triflic anhydride, 358-23-6; *s*-collidine, 108-75-8.

(9) Characterizing data for compound **7**: ^1H NMR ($CDCl_3$) δ 6.92 (s, H-3, H-5), 5.26, 5.05 (CH_2, J = 12.7 Hz), 2.42 (s, CH_3), 2.22 (s, CH_3); ^{13}C NMR ($CDCl_3$) δ 158.46 (C_6), 152.98 (C_2), 148.69 (C_4), 124.32 (C_5), 123.14 (q, CF_3, $^1J_{CF}$ = 338.32 Hz), 120.32 (C_3), 70.42 (CH_2), 24.09 (CH_3), 20.92 (CH_3) (off-resonance decoupling produced the expected multiplicity for each signal); mass spectrum (CI, methane), m/z (rel intensity) 254 (31), 136 (11), 121 (46), 120 (100). Compound **7** was homogeneous by TLC and VPC but, like compound **1**, decomposed upon standing. Characterizing data for compound **8**: bp 173-175 °C; ^1H NMR ($CDCl_3$) δ 6.81 (s, H-3, H-5), 3.21 (q, CH_2, $^3J_{HF}$ = 10.6 Hz), 2.46 (s, CH_3(2)); ^{13}C NMR ($CDCl_3$) δ 158.35 (C_2, C_6), 139.25 (C_4), 125.33 (q, CF_3, $^1J_{CF}$ = 276.81 Hz), 121.65 (C_3, C_5), 39.60 (q, CH_2, $^2J_{CF}$ = 30.11 Hz), 24.40 (CH_3(2)) (off-resonance decoupling produced the expected multiplicity for each signal); mass spectrum (CI, methane), m/z (rel intensity) 230 (3), 218 (15), 190 (100), 170 (42). Compound **8** was homogeneous by TLC and VPC. Anal. Calcd for $C_9H_{10}F_3N$: C, 57.14; H, 5.34; N, 7.40. Found: C, 56.99; H, 5.30; N, 7.49.

(10) This reaction appears to be an example of a [2,3] sigmatropic rearrangement: Woodward, R. B.; Hoffman, R. "The Conservation of Orbital Symmetry"; Verlag Chemie: Weinheim, West Germany, 1971; p 130.

(11) Anderson, A. G.; Stang, P. J. *J. Org. Chem.* **1976**, *41*, 3034; *Org. Synth.* **1981**, *60*, 34.

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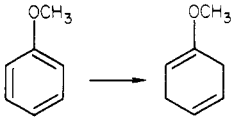
Birch Reductions of Methoxyaromatics in Aqueous Solution

Summary: A Birch-like electroreduction of methoxyaromatics in aqueous solutions was achieved, probably through the intermediacy of a tetrabutylammonium amalgam.

Sir: The Birch reduction[1] using an alkali metal in ammonia has often been applied to methoxyaromatics. As shown for anisole, the dihydroaromatic products are



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formed regioselectively and many of these products have been found to be useful in the synthesis of complex molecules.[2] Reduction of simple aromatics has also been achieved by electrochemically generating lithium metal in an amine solvent[3] or in HMPA.[4] Benzene and toluene have also been cathodically reduced in diglyme.[5] In the present study we set out to develop an electrochemical alternative to the tedious, somewhat dangerous alkali metal, ammonia procedure. Ultimately, it should be possible to develop a procedure that is as effective and less expensive by using electricity in place of the alkali metal and an aqueous electrolyte in place of ammonia. In this communication we report that cathodic reduction using

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(3) Benkeser, R. A.; Kaiser, E. M.; Lambert, R. F. *J. Am. Chem. Soc.* **1964**, *86*, 5272. Benkeser, R. A.; Kaiser, E. M. *Ibid.* **1963**, *85*, 2858.
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