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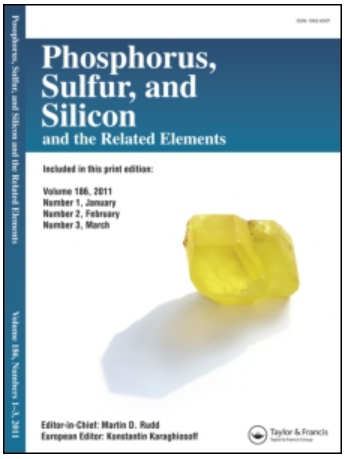

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SYNTHESIS AND BEHAVIOUR OF NADH MODELS BEARING A CHIRAL SULFOXIDE

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SYNTHESIS AND BEHAVIOUR OF NADH MODELS BEARING A CHIRAL SULFOXIDE

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Chiral 3-sulfinyl-1,4-dihydropyridine derivatives were synthesized by asymmetric oxidation of the parent 3-pyridine sulfides with Kagan's reagent ($Ti(OiPr)_4$/diethyl tartrate/H_2O/tBuOOH = 1/2/1/1). The chemoselective oxidation conditions of the sulfur atom were optimized. One chiral NADH mimic reagent so obtained was used in the reduction of prochiral α,α',α''-trifluoroacetophenone. During this reduction a side reaction occurred i.e. desulfenylation of the reagent. The by-product was identified after trapping with methyl propiolate. This side reaction did not occur in the quinoline series.

Key words: Chiral sulfoxides; NADH models; asymmetric reduction; desulfenylation

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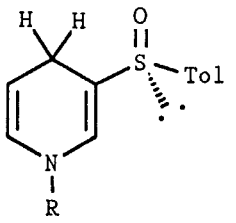
INTRODUCTION

NADH models bearing a chiral auxiliary have been widely studied.[1] Numerous asymmetric reductions have been performed with reagents consisting of 3-carbonylated (e.g., amide or ester) 1,4-dihydropyridines bearing a chiral group. Although this group is far from the active site (C_4 atom) of the molecule, some suitable substituents incorporated in this group have allowed the obtention of high e.e. For example, in our laboratory, chiral aminoalcohols were involved in asymmetric reductions performed with high optical yields.[2]

However, it must be stressed that very few NADH models containing at C-3 other groups than amides or esters have been synthesized. In this field, the first synthesis of the (S)-3-*p*-tolylsulfinyl-1,4-dihydropyridines **1a, b** was recently reported. They were efficient NADH model compounds in the asymmetric reduction of methyl benzoylformate (Figure 1).[3]

These derivatives were obtained after the reaction of 3-pyridylmagnesium bromide with (−)menthyl (S)-*p*-toluenesulfinate leading to 3-pyridyl *p*-tolylsulfoxide. This method is not easily expandable, so it appears that it would be of interest to find a totally different reaction scheme allowing variations about the structure of the chiral sulfinyl group. Moreover, with reagents **1a, b** the optical yields were



R = CH_3 : 1a
= CH_2Ph : 1b

FIGURE 1

high but the chemical yields were low or medium, especially when $Mg(ClO_4)_2$, $6H_2O$ was used instead of $Mg(ClO_4)_2$ as a catalyst. It could be assumed that water may have been involved in a secondary reaction which was responsible of this lowering of the yield. We will now describe a new method which will yield chiral sulfinyl NADH models, a study of the secondary reaction, which lowers the chemical yields and the design of new models allowing better chemical yields.

RESULTS AND DISCUSSION

1) Pyridine Series

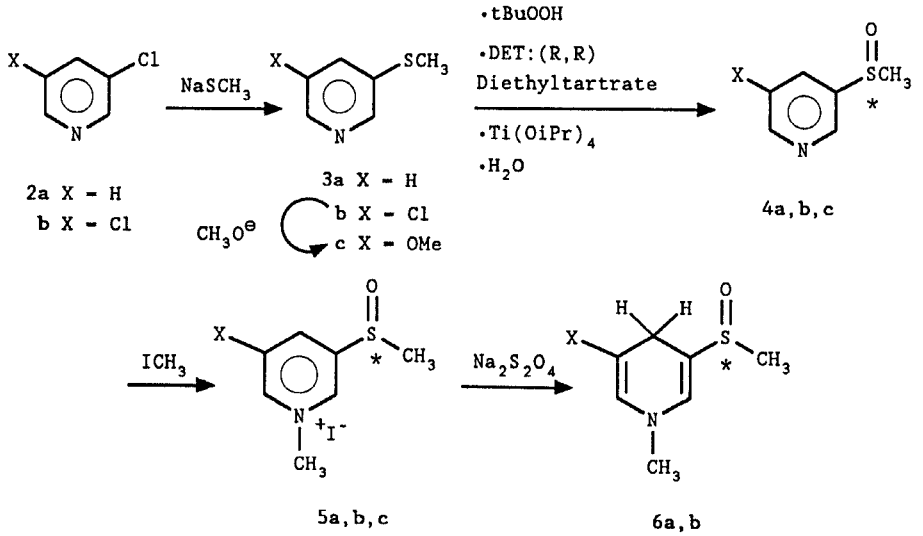
The general method is outlined in Scheme 1.

Starting from various 3-halogeno-5-substituted pyridines, the reaction of sodium methyl sulfide in dimethylformamide[4] yielded compounds **3a, b**. From **3b, 3c** was easily obtained after reaction with sodium methoxide.

The chemoselective oxidation of the sulfur atom under Kagan's conditions[5] leading to the sulfoxide **4b** was performed after a careful study of the influence of temperature. With compound **3b**, for example, large amounts of sulfone **4b'**, could be obtained, at room temperature. Large amounts of non oxidized product **3b** could be obtained at low temperature.

The optimum temperature for the obtention of **4b** was $-40°C$ as shown on Fig. 2. Compounds **4b** and **4b'** were identified in the ^1H NMR spectra of the crude product (see experimental part).

The optimum temperatures of the obtention of **4a** and **4c** were respectively $-50°C$ and $-40°C$ by following a similar method. After a simple purification by column chromatography, compounds **4a, b, c** were obtained chemically pure. The optical purity of these compounds is not known. It will be discussed later about compound



Scheme 1

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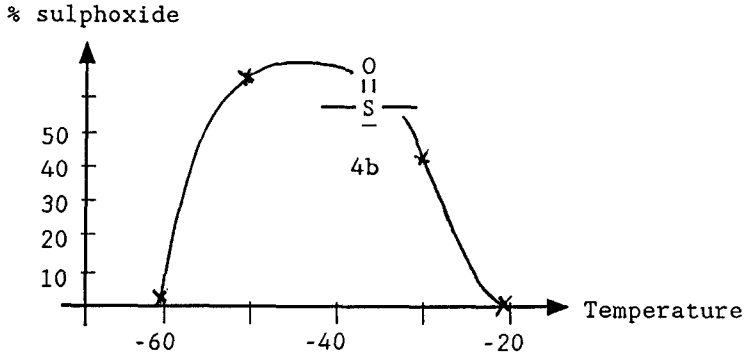


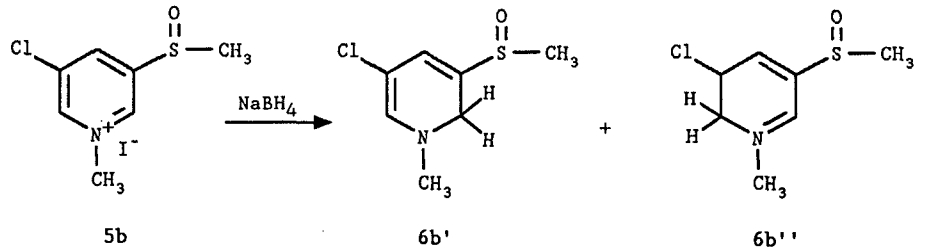
FIGURE 2

6b. However, it can be observed that the optical rotation of **4a, b, c** was positive. From the observations of Kagan[5] it can be assumed that these compounds possess the (R) configuration as they were obtained, by using (R) diethyl tartrate as chiral system during the oxidation.

Quaternization of **4** leading to **5** was quantitative and the regioselective reduction was performed with sodium dithionite as a reducing agent. The dihydropyridines **6a, b, c** showed different behaviour. The 5-methoxy compound **6c** was too unstable to be isolated. On the other hand, **6a** and **6b** could be identified; particularly, **6b** was used with a view to establishing if the reduction of **5b** with $Na_2S_2O_4$ was really regioselective in the 1,4-position. In a separate experiment **5b** was reduced with $NaBH_4$ leading to a possible mixture of **6b'** (and **6b''**) via a 1,2-reduction (Scheme 2).[6]

In the ^1H NMR spectra, a signal at 4 ppm can be related to the H_2 proton in **6b'** (or the H_6 proton in **6b''**), which are normally more deshielded than H_4 proton in **6b** (δ = 3.25 ppm). Moreover, in the UV spectra a strong absorption near 330 nm is also characteristic of a 1,4-dihydropyridine structure.[7]

Complexation of **6b** *with magnesium ions.* Most reductions performed with NADH models, occur with a divalent metal ion, generally magnesium perchlorate.[8] It is postulated that the hydrogen transfer is favoured by the occurrence of a ternary complex built with the reagent, the metal ion and the substrate. So, it was of interest to study the complexation of **6a** and **6b** in the presence of magnesium perchlorate. Unfortunately, **6a** was quickly destroyed by Mg^{2+} ions, so the study was limited to **6b**. The ^{13}C NMR spectra of **6b** in the presence of increasing amounts



5b 6b' 6b''

Scheme 2

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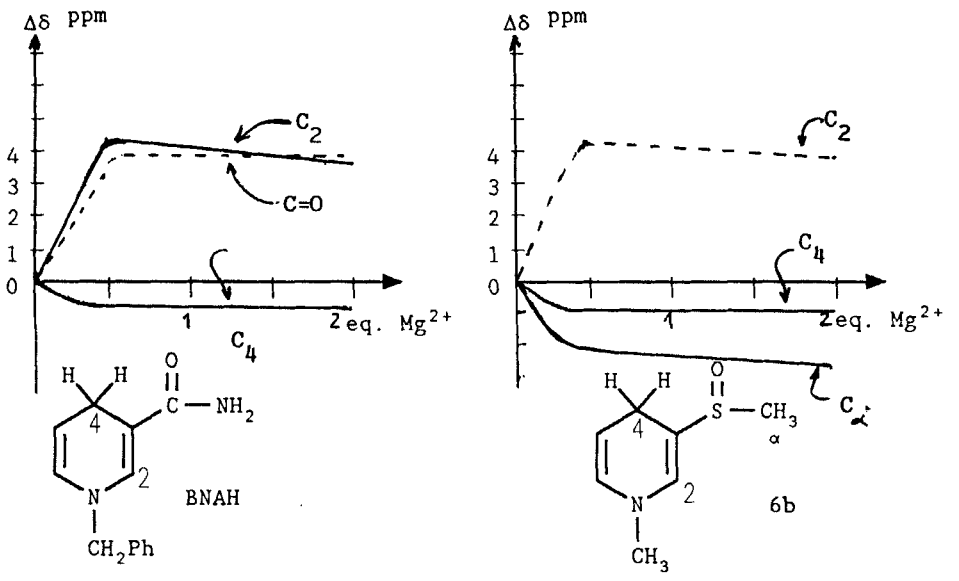

FIGURE 3

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of $Mg(ClO_4)_2$ were recorded in CD_3CN (Figure 3) and compared with the behaviour of BNAH, the most common NADH model compound, in the same conditions.[9]

The two compounds, as can be seen, show large similarities. That means that complexation of Mg^{2+} probably occurs through the sulfoxide group (compare with BNAH where complexation occurs through the carbonyl group). It is well known that this phenomenon is largely involved in the efficiency of the enantioselectivity of the hydrogen transfer with chiral NADH models in the BNAH series.

Reduction of a prochiral substrate with **6b**. The optical purity of **6b** was determined to be 60% by recording its ^1H NMR spectra in presence of (S)-N-(3,5-dinitrobenzoyl)-α-phenylethylamine.[10]

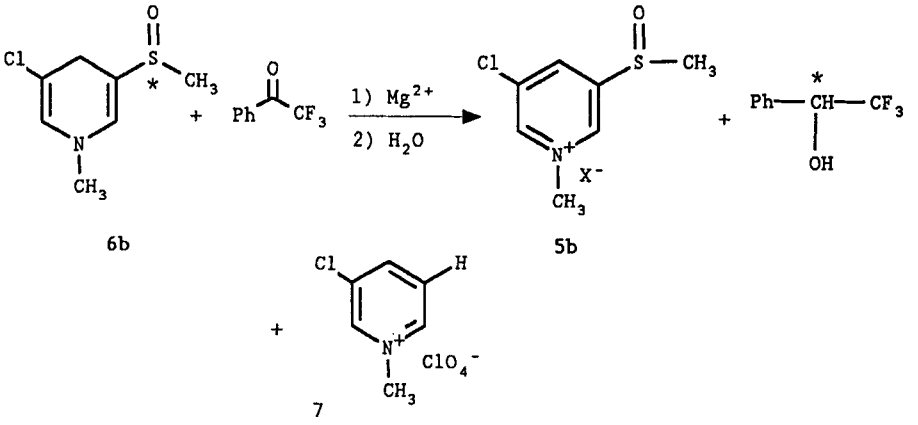
The reduction of α,α',α''-trifluoroacetophenone ($PhCOCF_3$) was performed under standard conditions.[2]

After work up of the reaction mixture, several products were isolated (Scheme 3).

Besides the normal products shown, i.e., the pyridinium salt **5b** and the chiral alcohol (70%) a secondary product **7** was isolated in about 25% yield.

a) Analysis of the chiral α,α',α''-trifluorophenyl-1 ethanol: The enantiomeric excess of the alcohol determined by optical rotation was 33%, and after correction of the optical purity of **6b** could be evaluated to 55%. The major enantiomer was the (R) and from previously reported work the structure of the ternary complex can be depicted in Figure 4.[2]

Magnesium ions are complexed with the sulfinyl group and the carbonyl group, with the two rings facing each other. By this mean steric hindrance caused by the methyl group favours the departure of the pro(R) hydrogen atom from C_4 leading preferentially to (R) (−) α,α',α''-trifluorophenyl ethanol.



Scheme 3

b) Analysis of **7**: The structure of this compound was established by ^1H NMR, IR and elemental analysis (see experimental part).

Its formation is not very easy to explain: two alternatives may be proposed (Scheme 4):

i) The reagent **6b** attacks the sulfur atom of the sulfoxide leading, in the secondary pathway, to a sulfurane intermediate **6b'** which loses the unstable methyl sulfenic acid **8** easily, after action of water. The dihydropyridine so formed is very reactive since it does not contain a powerful electron withdrawing group. So, it allows the fast reduction of the remaining derivative **6b**. ii) The heterolysis of the C—S bond may occur directly at 60°C leading to a cationic species and then to the well stabilized pyridinium cation **7**. It must be mentioned that the proton could be furnished, in the two cases by the presence of water which could not be totally eliminated from the reaction mixture. The amount of **7** was enhanced with increasing amounts of water in the solvent (it must be remembered that the best chemical yields reported by Iwata et al.[3] were obtained by using anhydrous $Mg(ClO_4)_2$ instead of $Mg(ClO_4)_2$, $6H_2O$).

The validity of these propositions would be confirmed if the methylsulfenic acid **8** could be identified. However, compounds of this type are very unstable[11] and the formation of the sulfenic acid could be established by a trapping experiment[12]

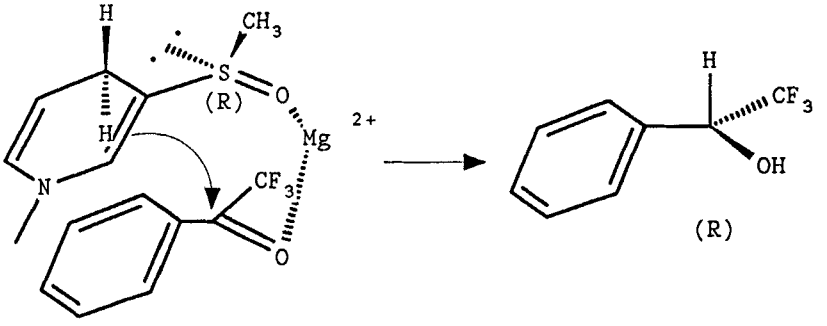


FIGURE 4

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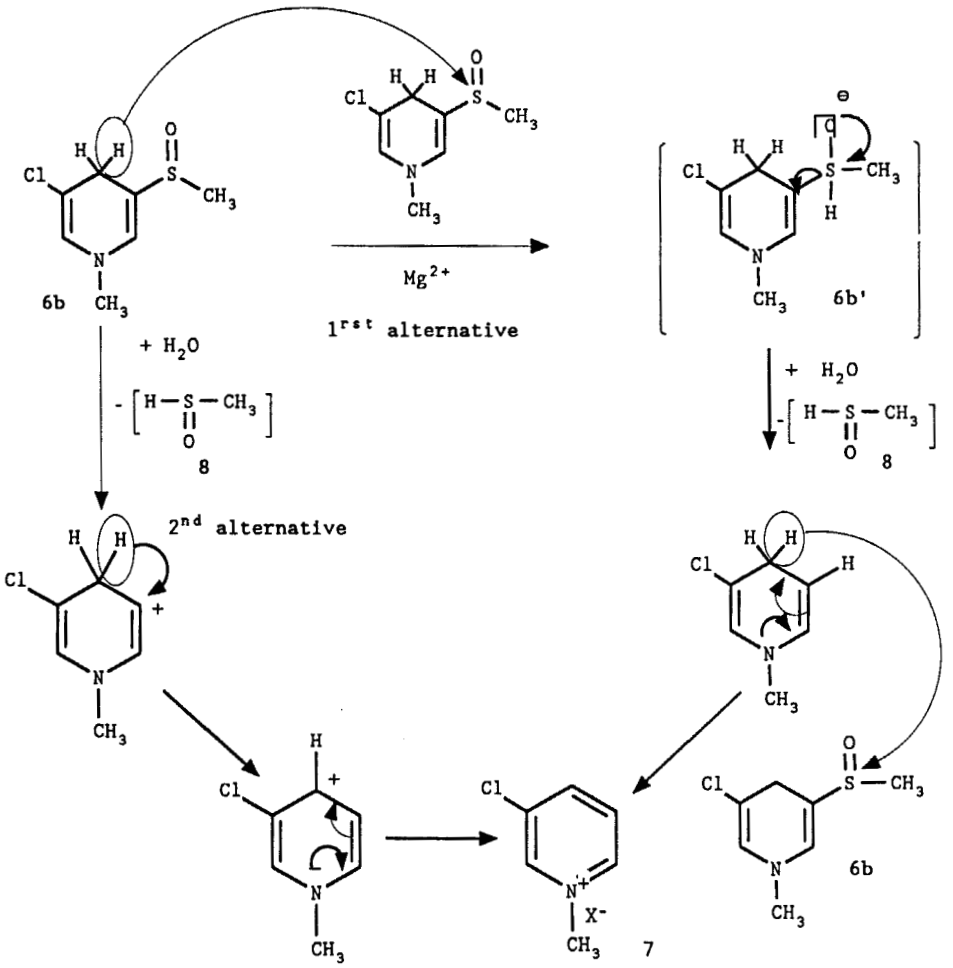

Scheme 4

where reagent **6** was used in the presence of methyl propiolate and magnesium ions (Scheme 5).

After purification, methyl (E)-methylsulfinyl acrylate **9** was isolated and identified.

2) *Quinoline Series*

From the above results it can be seen that 3-methylsulfinyl 1,4-dihydropyridine derivatives are a little unstable since some of them could not be isolated or some others can be involved in secondary reactions which affect their efficiency during the reduction of a substrate. With a view to enhancing the overall stability and also the optical purity of this type of NADH models, it was decided to prepare an isoster in the quinoline series (Scheme 6).

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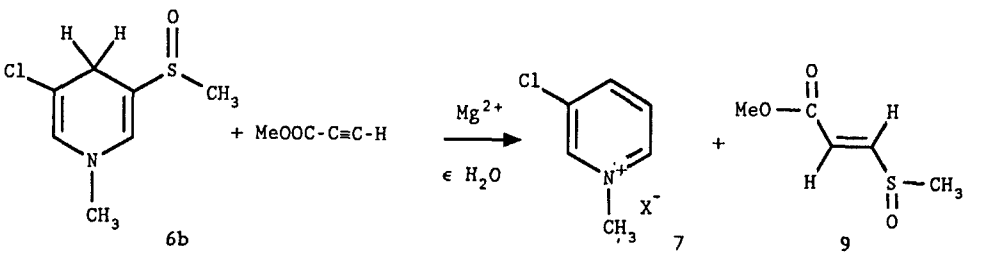
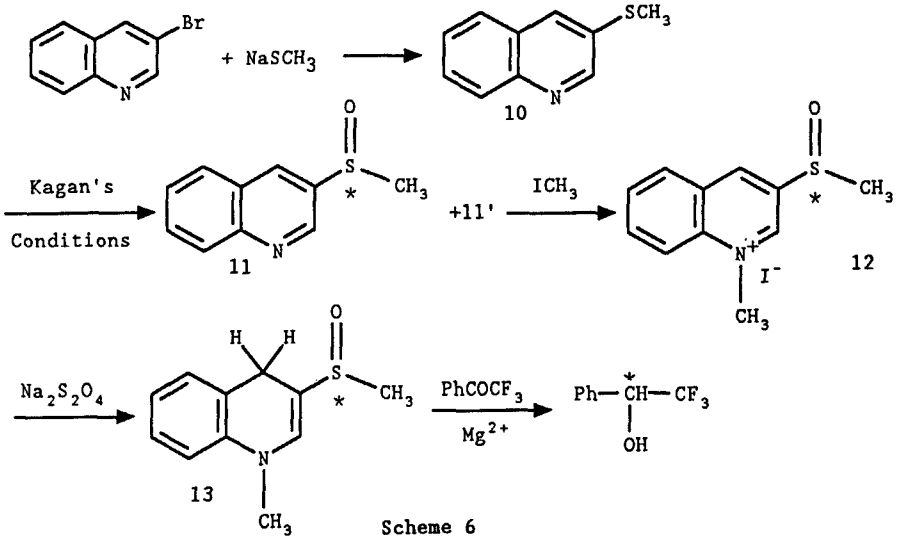


Scheme 5



Scheme 6

The optimum temperature for the oxidation of the sulfide **10** was found to be −40°C. The sulfoxide **11** so obtained, was 66% optically pure. The resolution of the enantiomers was tried by using chiral 2,2′-dihydroxy-1,1′-binaphthyl.[13] After three treatments the optical purity of **11** reached 78% and the further obtained reagent **13** was used in the reduction of α,α',α''-trifluoroacetophenone. The results were the following: i) chemical yield: 100%; ii) e.e.: 50% (after correction of optical purity); iii) no occurrence of the secondary reaction leading to desulfenylation of the reagent **13**.

CONCLUSION

The behaviour of chiral 3-methylsulfinyl-1,4-dihydropyridines was investigated in the reduction of α,α',α''-trifluoroacetophenone. Besides the normal reaction leading to the alcohol with a good e.e. a side reaction occurs. The by products formed

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during this reaction were identified. Moreover, in the quinoline series, a chiral 3-methylsulfinyl-1,4-dihydroquinoline was also synthesized which was very much more stable and allows the reduction of the substrate in quantitative chemical yields, without the intervention of the side reaction. The method leading to the chiral sulfoxides can be expanded to substituents other than methyl group. Thus, it can be hoped that larger substituents could enhance the stereoselectivity of the hydrogen transfer.

EXPERIMENTAL

IR spectra were recorded with a Beckman 4250 spectrophotometer. ^{1}H NMR spectra were determined on a 60 MHz VARIAN EM 360L spectrometer or on a 400 MHz BRUCKER AM 400 spectrometer. Microanalyses were obtained from a Carlo Erba 1106 apparatus. Optical rotations were determined on a Perkin Elmer 241 micropolarimeter.

Reaction of Halogeno Pyridines or Quinoline with Sodium methane thiolate. Obtention of **3a, b, c** *and* **10**. Compound **3b** was obtained by following the method described in the literature,[4] i.e., reaction of 3,5-dichloropyridine with 1.1 equivalent of sodium methane thiolate in DMF at 20°C for 1 hour. Compound **3c** was obtained by substitution of the chlorine atom of **3b** with 4 equivalents of sodium methoxide in DMF at 80°C for 2 hours. Compound **3a** could be obtained only by using harder conditions: 10 equivalents of sodium methane thiolate in DMF at 80°C for 24 hours. Compound **10** was obtained under the same conditions as compound **3a** (reaction time 48 hours).

3-methylsulfenylpyridine (**3a**). Calc. for C_6H_7NS: C, 57.60; H, 5.60; N, 11.20. Found: C, 57.2; H, 5.9; N, 11.1. ^{1}H NMR ($CDCl_3$): 2.45 (s, 3H); 7.05–7.30 (m, 1H); 7.40–7.70 (m, 1H); 8.30–8.40 (m, 1H); 8.55 (d, 1H).

5-chloro 3-methylsulfenylpyridine (**3b**). Calc. for C_6H_6ClNS: C, 45.14; H, 3.79; N, 8.77. Found: C, 44.6; H, 3.6; N, 8.8. ^{1}H NMR ($CDCl_3$) 2.5 (s, 3H); 7.5 (t, 1H); 8.4 (t, 2H).

5-methoxy 3-methylsulfenylpyridine (**3c**). Calc. for C_7H_9NOS: C, 54.19; H, 5.81; N, 9.03. Found: C, 53.9; H, 5.8; N, 8.9. ^{1}H NMR ($CDCl_3$): 2.5 (s, 3H); 3.8 (s, 3H); 7.1 (t, 1H); 8.1 (m, 2H).

3-methylsulfenylquinoline (**10**). Calc. for $C_{10}H_9NS$: C, 68.53; H, 5.18; N, 7.99. Found: C, 68.1; H, 5.1; N, 7.7. ^{1}H NMR ($CDCl_3$): 2.6 (s, 3H); 7.4–8.2 (m, 5H); 7.83 (d, 1H).

Oxidation of Sulfides. In a flask, flushed with argon, were introduced 1.49 ml (0.005 mol) of titanium isopropoxide, 1.71 ml (0.01 mol) of (R,R) diethyl tartrate, 50 ml of dry dichloromethane (distilled on H_2Ca, filtered on basic alumina and stored over molecular sieves 3 A) and 0.09 ml (0.005 mol) of water. After stirring for 20 minutes, 0.005 mol of sulfide **3a, b, c** or **10** was added, the mixture was cooled (for precise temperature see table 1), then 1.67 ml (0.0055 mol) of 3.3 M *tert*-butyl hydroperoxide in toluene[14] was added. The reaction mixture was maintained at the desired temperature (for time see table 1) then 0.90 g of water was added and the cooling bath was removed. After 1 hour at room

TABLE 1

Optimum conditions for oxidation of sulfides

Starting sulphide	Temperature	Time	% Starting material	% sulfoxide	% sulfone
3a	-50°C	72 h	42	55	3
3b	-40°C	20 h	25	75	-
3c	-40°C	20 h	30	70	-
10	-45°C	48 h	20	80	-

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temperature, the white precipitate was filtered (a small amount of alumina was added to the solution to help the filtration) and thoroughly washed with dichloromethane. The filtrate was kept in the presence of 5% NaOH and brine for 1 hour and then separated. The organic phase was dried and concentrated to give the crude product. Analysis of this one shows the presence of sulfoxide sulfide and sulfone (see table 1).

The mixture was chromatographed (silica Kieselgel 60, elution with ether/AcOEt: 50/50). A mixture of sulfone and sulfide is first eluted, then the sulfoxide is obtained in a pure form.

When sulfone was formed, the mixture with sulfide was washed with ether. The sulfone is not soluble and was then obtained pure.

3-methylsulfinylpyridine (**4a**). Oil. Calc for C_6H_7NOS: C, 51.06; H, 4.96; N, 9.93. Found: C, 49.6; H, 4.8; N, 9.5. IR (ν S=O) 1145 cm^{-1}. ^1H NMR ($CDCl_3$) 2.80 (s, 3H); 7.35–7.70 (m, 1H); 8.0–8.3 (m, 1H); 8.70–8.90 (m, 2H).

5-chloro-3-methylsulfinylpyridine (**4b**). m.p. 59°C Calc. for C_6H_6ClNOS: C, 41.02; H, 3.42; N, 7.98. Found: C, 41.1; H, 3.4; N, 8.0. IR (ν S=O) 1145 cm^{-1}. ^1H NMR ($CDCl_3$) 2.90 (s, 3H); 8.15 (t, 1H); 8.75 (m, 2H).

5-methoxy-3-methylsulfinylpyridine (**4c**). m.p. 85°C Calc. for $C_7H_9NO_2S$: C, 49.12; H, 5.26; N, 8.19. Found: C, 48.9; H, 5.1; N, 7.7. IR (ν S=O) 1060 cm^{-1}. ^1H NMR ($CDCl_3$): 2.85 (s, 3H); 3.95 (s, 3H); 7.65 (m, 1H); 8.30–8.50 (m, 2H).

3-methylsulfinylquinoline (**11**). m.p. 96°C Calc. for $C_{10}H_9NOS$: C, 62.80; H, 4.74; N, 7.32. Found: C, 62.7; H, 4.8; N, 7.4. IR (ν S=O) 1050 cm^{-1}. ^1H NMR ($CDCl_3$): 2.90 (s, 3H); 7.65 (t, 1H); 7.85 (t, 1H); 7.95 (d, 1H); 8.20 (d, 1H); 8.60 (d, 1H); 9.00 (d, 1H).

3-methylsulfonylpyridine (**4a'**). m.p. 50°C (dec) Calc. for $C_6H_7NO_2S$: C, 45.86; H, 4.46; N, 8.92. Found: C, 46.2; H, 4.5; N, 8.9. IR (ν SO_2: 1310–1160 cm^{-1}). ^1H NMR ($CDCl_3$): 3.15 (s, 3H); 7.40–7.70 (m, 1H); 8.15–8.45 (m, 1H); 8.95 (m, 1H); 9.25 (m, 1H).

5-chloro-3-methylsulfonylpyridine (**4b'**). m.p. 124°C Calc. for $C_6H_6NO_2SCl$: C, 37.60; H, 3.13; N, 7.31. Found: C, 37.8; H, 3.0; N, 7.2. IR (ν SO_2, 1300–1140 cm^{-1}). ^1H NMR ($CDCl_3$): 3.20 (s, 3H); 8.25 (m, 1H); 8.85 (d, 1H); 9.05 (d, 1H).

5-methyloxy-3-methylsulfonylpyridine (**4c'**). m.p. 129°C Calc. for $C_7H_9NO_3S$: C, 44.92; H, 4.81; N, 7.48. Found: C, 45.0; H, 4.9; N, 7.3; IR (ν SO_2 1300–1135 cm^{-1}). ^1H NMR ($CDCl_3$): 3.15 (s, 3H); 3.95 (s, 3H); 7.75 (m, 1H); 8.6 (d, 1H); 8.75 (d, 1H).

3-methylsulfonylquinoline (**11'**). m.p. 139°C Calc. for $C_{10}H_9NO_2S$: C, 57.95; H, 4.38; N, 6.76. Found: C, 57.9; H, 4.3; N, 6.6. IR (ν SO_2 1310–1180 cm^{-1}). ^1H NMR ($CDCl_3$): 3.2 (s, 3H); 7.6–8.2 (m, 4H); 8.75 (d, 1H); 9.3 (d, 1H).

Quaternization of Sulfoxides: Obtention of Pyridinium Salts (**5a, b, c**) *and Quinolinium Salt* (**12**). In a flask were dissolved the above sulfoxides (0.005 mol) in 20 ml of acetonitrile and 1 ml (large excess) of methyl iodide. The mixture was refluxed for 12 hours (**4a, b, c**) or for 24 hours (**11**). After concentration, ether was added and the precipitated salt was filtered and dried.

1-methyl-3-methylsulfinylpyridinium iodide (**5a**). m.p. 148°C Calc. for $C_7H_{10}INOS$: C, 29.68; H, 3.53; N, 4.95. Found: C, 29.7; H, 3.5; N, 4.9. IR (ν S=O 1060 cm^{-1}). ^1H NMR (DMSO/d_6) 2.95 (s, 3H); 4.40 (s, 3H); 8.10–8.40 (m, 1H); 8.70–8.95 (m, 1H); 9.0–9.15 (m, 1H); 9.25 (m, 1H).

1-methyl-5-chloro-3-methylsulfinylpyridinium iodide (**5b**). m.p. 158°C Calc. for $C_7H_9ClINOS$: C, 26.46; H, 2.83; N, 4.41. Found: C, 26.5, H, 2.7; N, 4.4. IR (ν S=O 1070 cm^{-1}). ^1H NMR (DMSO/d_6) 3.10 (s, 3H); 4.50 (s, 3H); 9.05 (s, 1H); 9.35 (s, 1H); 9.60 (s, 1H).

1-methyl-5-methoxy-3-methylsulfinylpyridinium iodide (**5c**). m.p. 146°C. Calc. for $C_8H_{12}INOS$: C, 30.67; H, 3.83; N, 4.47. Found: C, 30.4; H, 3.9; N, 4.3. IR (ν S=O 1050 cm^{-1}). ^1H NMR (DMSO/d_6): 2.95 (s, 3H); 4.00 (s, 3H); 4.35 (s, 3H); 8.40 (m, 1H); 8.80–9.00 (m, 2H).

1-methyl-3-methylsulfinylquinolinium iodide (**12**). m.p. 208°C. Calc. for $C_{11}H_{12}INOS$: C, 39.65; H, 3.63; N, 4.10. Found: C, 39.6; H, 3.4; N, 4.1. IR (ν S=O 1070 cm^{-1}). ^1H NMR (DMSO/d_6): 3.00 (s, 3H); 4.65 (s, 3H); 8.10 (t, 1H); 8.35 (t, 1H); 8.45 (m, 2H); 9.35 (s, 1H); 9.50 (s, 1H).

Reduction of Quaternized Derivatives with Sodium Dithionite: Obtention of Dihydro Compounds **6a, b** *and* **13**. In a flask flushed with argon were introduced 0.002 mol of the above pyridinium or quinolinium salts in 10 ml of deoxygenated water. A solution of 1 g or $Na_2S_2O_4$ and 1 g of Na_2CO_3, 10 H_2O in 10 ml of water was added. After stirring for 10 minutes, the reaction mixture was extracted with 5 × 20 ml $CHCl_3$ and after drying and evaporation the crude dihydro derivatives were obtained and used as soon as possible.

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1-methyl-3-methylsulfinyl-1,4-dihydropyridine (**6a**). Yield 40%. IR (ν S=O 1020 cm^{-1}). ^1H NMR ($CDCl_3$): 2.55 (s, 3H); 2.90 (s, 3H); 3.25 (m, 2H); 4.55–4.85 (m, 1H); 5.55–5.8 (m, 1H); 6.45 (m, 1H).

1-methyl-5-chloro-3-methylsulfinyl-1,4-dihydropyridine (**6b**). Yield 40%. IR (ν S=O 1025 cm^{-1}). ^1H NMR ($CDCl_3$): 2.60 (s, 3H); 3.00 (s, 3H); 3.45 (d, 2H); 6.00 (s, 1H); 6.50 (s, 1H).

1-methyl-3-methylsulfinyl-1,4-dihydroquinoline (**13**). Yield 62%. IR (ν S=O 1070 cm^{-1}). ^1H NMR ($CDCl_3$): 2.70 (s, 3H); 3.20 (s, 3H); 3.90 (m, 2H); 6.6–7.4 (m, 5H).

Optical Purity of **6b**. The spectra of an equimolar mixture of **6b** and the chiral amide[10] in $CDCl_3$ were recorded on a Brucker 400 MHz apparatus. The signals attributed to the methyl protons of the two enantiomers appear at 2.531 and 2.546 ppm. From the integration curve the optical purity of **6b** was established as 60% and from the assumption of the literature the major enantiomer was assumed to have (R) configuration.[5]

The optical purity of **10** was determined by the same method.

Attempt to obtain optically pure **10**. In a flask 0.5 g (0.0017 mol) of (S)-2,2'-dihydroxy-1,1'-binaphthyl and 1.75 g of 3-methylsulfinyl quinoline **10** were dissolved in 20 ml of benzene and 20 ml of hexane. The solution was stirred at room temperature for 2 days. A yellow gum was formed. The above solution was separated, concentrated and the residue was chromatographed (silica, eluent: ether/hexane: 50/50). It was recovered 1.3 g of 3-methylsulfinylquinoline. The optical purity determined by the above method was 71%. The same treatment was repeated, leading to an optical purity of 78%.

Reduction of α,α',α''-trifluoroacetophenone.

a) With **6b** *or* **13**. In a flask stoppered with a septum and flushed with argon, were introduced 0.174 g (0.001 mol) of α,α',α''-trifluoroacetophenone, (0.0011 mol) of crude **6b** or **13**, 0.245 g (0.0011 mol) of anhydrous magnesium perchlorate of 5 ml of anhydrous acetonitrile. The mixture was warmed at 60°C for 24 hours. After cooling, 5 ml of water were added and the mixture was extracted with 5 × 10 ml of CH_2Cl_2. After drying and evaporation R(−) α,α',α''-trifluoroethanol was obtained. Yield 70% $[\alpha]_D^{20} = -4.1°$ (C = 1.00/benzene). The enantiomeric excess was 34%.[10] After correction of the optical purity the e.e. could be estimated as 55%.

In the same conditions the results with **13** were: Chemical yield: 100%; e.e. (after correction): 50%.

In another experiment, with **6b**, the reaction mixture was treated with 2 drops of water, carefully concentrated and the residue purified by t.l.c. (acetonitrile as eluent). By this mean 1-methyl-3-chloropyridinium perchlorate **7** was isolated. Yield 25%. m.p. 85°C. Calc. for $C_8H_7NO_4Cl_2$: C, 31.58; H, 3.07; N, 6.14. Found: C, 30.9; H, 2.8; N, 5.7. ^1H NMR (CD_3CN): 4.30 (s, 3H); 7.8–8.2 (m, 1H); 8.3 (m, 1H); 8.5 (m, 1H); 8.8 (m, 1H).

b) Trapping of methylsulfenic acid **8**. In a flask flushed with argon were introduced the same components as described in the above experiment except α,α',α''-trifluoroacetophenone. Methyl propiolate (0.84 g, 0.01 mol) was introduced and the mixture warmed at 60°C for 2 days. After evaporation of the solvent, the residue was purified by t.l.c. (eluent: ethylacetate/diethylether 1/1). Methyl (E), methylsulfinyl acrylate **9** was isolated in 15% yield. Calc. for C_5H_8OS: C, 40.52; H, 5.45. Found: C, 41.0; H, 5.1. IR (ν S=O 1070 cm^{-1}). ^1H NMR ($CDCl_3$): 2.73 (s, 3H); 3.83 (s, 3H); 6.6 (d, 1H, J = 15 Hz); 7.6 (d, 1H, J = 15 Hz).

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