g) was dissolved in dioxane (15 mL) and then diluted HCl (4.5%, 5 mL) was added. The solution was heated to reflux for 5 min. The solvent was evaporated and water added (25 mL). Filtration, after cooling in ice for 10 min, gave pure acid **7** with quantitative yields.

Registry No. **1a**, 17838-69-6; **1b**, 33691-09-7; **1c**, 91632-23-4; **1d**, 29969-62-8; **1e**, 62833-11-8; **1f**, 91632-24-5; **1g**, 91632-25-6; **1h**, 91632-26-7; **2a**, 17147-69-2; **2b**, 91632-27-8; **2c**, 91670-46-1; **2d**, 91632-28-9; **2e**, 91632-29-0; **2f**, 91632-30-3; **2g**, 91632-31-4; **2h**, 91632-32-5; **3a**, 91632-33-6; **3b**, 91632-34-7; **3c**, 91632-35-8; **3d**, 91632-36-9; **3e**, 91632-37-0; **3f**, 91632-38-1; **4a**, 91632-52-9; **4b**, 91632-53-0; **4c**, 91632-54-1; **4d**, 91669-97-5; **4e**, 91632-55-2; **4f**, 91632-56-3; **5a**, 91632-57-4; **5b**, 91632-58-5; **5c**, 91632-59-6; **5d**, 91632-60-9; **5e**, 91632-61-0; **5f**, 91632-62-1; **6a**, 91632-39-2; **6b**, 91632-40-5; **6c**, 91632-41-6; **6d**, 91632-42-7; **6e**, 91632-43-8; **6f**, 91632-44-9; **6g**, 91632-45-0; **7a**, 91632-46-1; **7b**, 91632-47-2; **7c**, 91632-48-3; **7d**, 91632-49-4; **7e**, 91632-50-7; **7f**, 91632-51-8; **7g**, 91670-47-2; $PhCH_2COOEt$, 101-97-3; ClC_6H_4-4-CH_2COOEt, 14062-24-9; BrC_6H_4-4-CH_2COOEt, 14062-25-0; $MeOC_6H_4$-4-CH_2COOEt, 14062-18-1; MeC_6H_4-4-CH_2COOEt, 14062-19-2; MeC_6H_4-3-CH_2COOEt, 40061-55-0; MeC_6H_4-2-CH_2COOEt, 40291-39-2; HCOOEt, 109-94-4; $HC(OEt)_3$, 122-51-0; NH_2OH, 7803-49-8; H_2O_2, 7722-84-1; MnO_2, 1313-13-9; ethyl 2-pyridylacetate, 2739-98-2.

Optically Active Nitrogen Ligands. 1. Synthesis of Two Optically Active Monoalkyl-Substituted 2-(2′-Pyridyl)pyridines

C. Botteghi,* G. Caccia, G. Chelucci, and F. Soccolini

Istituto di Chimica Applicata, Università di Sassari, 07100 Sassari, Italy

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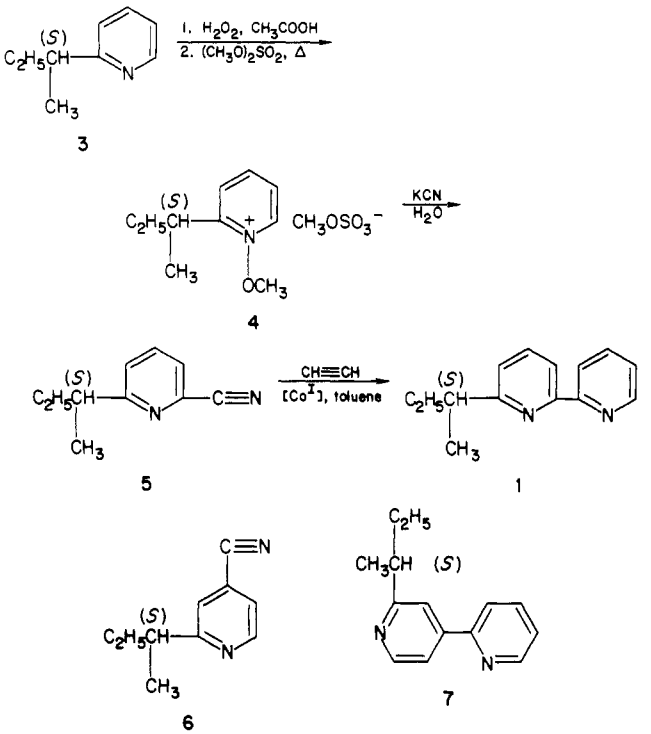
Rhodium(I) and iridium(I) complexes with 2,2′-bipyridines are reported to display a remarkable catalytic activity toward the reduction of olefins and ketones both by molecular hydrogen and by H-transfer at room temperature and atmospheric pressure.[1-3]

With the aim of making a new class of chiral complexes available and of investigating their effectiveness in asymmetric homogeneous catalysis, we undertook a study on a generalizable procedure to obtain optically active 2-(2′-pyridyl)pyridines (2,2′-bipyridines) with high optical purity. To our knowledge, no optically active title compounds have been reported in the literature so far; even monoalkyl-substituted 2,2′-bipyridines are very seldom described.[4-6]

In this paper the results obtained in the synthesis of (+)-(*S*)-2-(2′-pyridyl)-6- (**1**) and (+)-(*S*)-2-(2′-pyridyl)-4-*sec*-butylpyridine (**2**) are presented.

The reaction sequence leading to **1** is shown in Scheme I. Starting with the readily accessible (+)-(*S*)-2-*sec*-butylpyridine[7] (**3**) we obtained the key intermediate nitrile **5** by treatment of the *N*-oxide with dimethyl sulfate followed by reaction of the pyridinium compound **4** with potassium cyanide[8] (Scheme I). The overall yield was 60%; as expected,[8] the isomeric 2-*sec*-butyl-4-cyanopyridine (**6**) (Scheme I) was formed too: the ratio of the two isomers **5** and **6** was 70/30 (determined by GLC). Isomerically pure **5** was easily obtained by column chromatography on silica gel using benzene as the eluant.[9] The yield of pure **5** was about 30% based on starting **3** (Scheme I).

Scheme I[a]



[a] [Co^I] = (π-Cyclopentadienyl)cobalt 1,5-cyclooctadiene.

The cyclization reaction with acetylene was carried out by using (π-cyclopentadienyl)cobalt 1,5-cyclooctadiene as the catalytic precursor and toluene as the solvent following the procedure described by Bönneman and Brinkmann[10] and produced the expected bipyridine **1** in about 80% yield free from other heterocyclic byproducts.

(+)-(*S*)-2-(2′-Pyridyl)-6-*sec*-butylpyridine (**1**) was isolated in about 25% overall yield based on starting **3** as a 99% pure oil, and its identity was confirmed by NMR and MS analysis (see Experimental Section).

For the preparation of the 2,2′-bipyridine **2**, the crucial intermediate 1,5-dialdehyde (**9**) was easily provided by rhodium-catalyzed hydroformylation of (+)-(*S*)-1,1-diethoxy-3-*sec*-butyl-3-butene (**8**), prepared in turn with about 95% optical purity from (+)-(*S*)-*sec*-butylallylmagnesium chloride.[11] Compound **9** was converted into compound **10** by reaction with 2-lithiopyridine at −70 °C,[12,13] followed by oxidation of the resulting pyridinecarbinol with activated MnO_2 at room temperature[14] (Scheme II).

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(9) An alternative experimental procedure can be followed for getting isomerically pure **1**. Cyclization of the 70/30 mixture of cyanopyridines **5** and **6** under the usual conditions gives a mixture of bipyridines **1** and **7** (Scheme I) in 82% yield with practically identical composition. Column chromatography under the same conditions on the bipyridine mixture affords quite pure **1** in 22% yield based on starting **3**.
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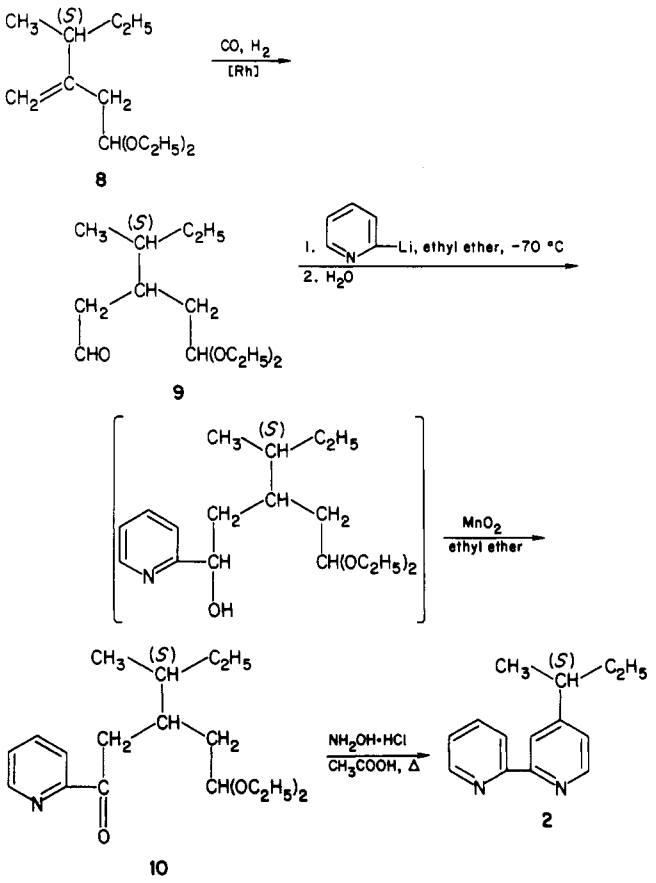
0022-3263/84/1949-4290$01.50/0

Scheme II



For the conversion of **10** into **2**, hydroxylamine hydrochloride in dry acetic acid was found to be the best reagent[15]: up to 40% yield of **2** was reached by heating **10** under these conditions for 6 h (Scheme II). The main byproduct (23%) of this reaction was unsubstituted 2-(2′-pyridyl)pyridine, which was isolated and identified by comparison of its MS and NMR spectra with those of an authentic sample. This compound is formed presumably by dealkylation during the cyclization of **10**.

The enantiomeric purity of **1** was determined by using the lanthanide shift reagents (LSR) method.[16] The ^1H NMR spectrum of the europium complexes of **1**, $[\alpha]^{25}_D$ +21.4° (*c* 2.03, cyclohexane), with tris[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]europium(III)[17] showed distinctly resolved signals for the pyridine H-3 protons in a ratio of 4.4:1. At a molar ratio of LSR to **1** of about 1:1, the chemical shift of H-3 protons was 11.70 ppm for the *S* and 11.95 ppm for the *R* enantiomer.

From these data, an enantiomeric purity of about 63% can be calculated for **1**, which is very close with that of pyridine **3**, $[\alpha]^{25}_D$ +25.5° (neat), used as the starting material (Scheme I).[7]

We were not able to establish the enantiomeric purity of **2** by the chiral LSR method. However, we believe that no racemization occurs during the preparation of **2** from **8** (Scheme II): in fact, starting with **8** having 95% minimum optical purity, we obtained two samples of **2** through two distinct preparations (Scheme II) with very similar optical rotations, $[\alpha]^{25}_D$ +17.96° (cyclohexane) and $[\alpha]^{25}_D$ +17.82° (cyclohexane), respectively.

Table I. UV and CD Bands of Alkylbipyridines 1 and 2 in *n*-Heptane

compound	UV λ_{max}	UV $\epsilon_{max} \times 10^{-3}$	CD λ_{max}	CD $\Delta\epsilon_{max}$
(+)-(*S*)-2-(2′-pyridyl)-6-*sec*-butylpyridine	286	17.35	274	+0.51[a]
	238	12.35		
	194	46.80		
(+)-(*S*)-2-(2′-pyridyl)-4-*sec*-butylpyridine	282	15.10	265	+0.27[a]
	238	11.73		
	193	37.40		

[a] Extrapolated to 100% optical purity.

UV and CD spectra of **1** and **2** were carried out in the 330–180-nm spectral region in *n*-heptane. The UV spectra of both compounds show three main groups of absorption bands at about 280, 240, and 190 nm (Table I) associated with the electronic $\pi \rightarrow \pi^*$ transitions of the aromatic system of the bipyridine chromophore. The spectral data obtained are in agreement with those reported in the literature for 2-(2′-pyridyl)pyridine in cyclohexane.[18]

As for the CD measurements, we were able to detect only one band connected with the low-energy electronic transition: this is located at about 270 nm and is finely structured and positive for both **1** and **2** (Table I). As expected, the observed dissymmetry factor ($g = \Delta\epsilon/\epsilon$) is very low ($2–3 \times 10^{-5}$): this CD band is related to an electrically allowed transition[18] which acquires optical activity only by means of the weak chiral perturbation due to the small difference between the methyl and methyl groups of the *sec*-butyl substituent.

Experimental Section

Boiling points are uncorrected. GLC analyses were performed on Perkin-Elmer 900 and 3920 B gas chromatographs, using the columns and the temperature specified. NMR spectra at 80 MHz were obtained with a Varian CFT-20 spectrometer, and at 90 MHz with a Bruker WH 90 spectrometer in $CDCl_3$ and CCl_4 solutions using tetramethylsilane as an internal standard ($\delta = 0$). Optical rotations were taken on a Perkin-Elmer 241 polarimeter in 1-dm tubes. Mass spectra were obtained with a Hitachi-Perkin-Elmer RMU-6L mass spectrometer. IR spectra were recorded with a Beckmann 4250 spectrometer. Microanalyses were performed by a CHN 240 B Perkin-Elmer analyzer.

Materials. Two samples of (+)-(*S*)-2-*sec*-butylpyridine with 78% and 64% minimum optical purities, respectively, were prepared through reaction of samples of the corresponding optically pure (+)-(*S*)-2-methylbutanenitrile[19] with acetylene in the presence of (π-cyclopentadienyl)cobalt 1,5-cyclooctadiene[7,20] in about 80% yield. (+)-(*S*)-1,1-Diethoxy-3-*sec*-butyl-3-butene (**8**), $[\alpha]^{25}_D$ +14.75° (*c* 1.972, cyclohexane), was obtained by reaction of (+)-(*S*)-*sec*-butylallylmagnesium chloride and phenyl diethyl orthoformate in THF in 80% yield.[11]

(+)-(*S*)-2-Cyano-6-*sec*-butylpyridine (5). Compound **3** (7.8 g, 0.058 mol), $[\alpha]^{25}_D$ +31.28° (78% minimum optical purity), was converted into the *N*-oxide by oxidation with 30% hydrogen peroxide in glacial acetic acid at 75–80 °C for 100 h according to Ochiai.[20] The solvent was removed in vacuo (10 mm) and the formed *N*-oxide used as such in the following step. To the crude *N*-oxide was added 7.6 g (0.06 mol) of dimethyl sulfate slowly such a rate that the temperature of the reaction mixture was kept at 65 °C throughout the addition.[8] When the addition was complete (about 8 min), the solution was heated at 100 °C for an additional

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3 h. Upon cooling the crystallization salt was filtered, washed with anhydrous acetone, and used for the following step without any further purification.

A solution of 1-methoxypyridinium methyl sulfate salt dissolved in 20 mL of water was added slowly (10 min) under stirring to a solution of 8.6 g (0.17 mol) of potassium cyanide dissolved in 30 mL of water and cooled at 0 °C. After the addition the reaction mixture was allowed to rise to room temperature and stirred at 25 °C overnight. After extraction with ethyl ether (150 mL), drying over Na_2SO_4, and removal of the solvent, 5.2 g (0.033 mol; 57% yield) of reaction product were obtained: bp 65 °C (0.4 mm). A GLC analysis (2 m × 2.5 mm column packed with OV 17 2% on Chromosorb G at 200 °C) showed that this product contained about 35% of (+)-(*S*)-4-cyano-4-*sec*-butylpyridine (**6**). Pure compound **5** was obtained by column chromatography using silica gel as packing material (100 g/1 g of product) and benzene as the eluant: 2.09 g (23% yield); bp 60 °C (0.1 mm); $[\alpha]^{20}_D$ +29.51° (*c* 2.057, cyclohexane); IR (neat) $\nu_{C\equiv N}$ 2238 cm^{-1}; ^1H NMR (CCl_4) δ 7.81–7.36 (m, 3 H), 2.87 (m, 1 H), 1.71 (m, 2 H), 1.28 (d, 3 H), 0.83 (t, 3 H); mass spectrum, *m/e* (relative intensity) 132 (100), 145 (75), 131 (61.8), 105 (19.5), 78 (17.6), 104 (14.7), 119 (13.3), 77 (13), 27 (13), 40 (11.8), 160 (M^+, 7.8).

Pure cyanopyridine **6** was obtained too (1.1 g, 12% yield): bp 45 °C (0.1 mm); $[\alpha]^{20}_D$ +26.2° (*c* 2.357, cyclohexane); IR (neat) $\nu_{C\equiv N}$ 2240 cm^{-1}; ^1H NMR (CCl_4) δ 8.74 (d, 1 H), 7.39 (m, 2 H), 2.89 (m, 1 H), 1.70 (m, 2 H), 1.30 (d, 3 H), 0.84 (t, 3 H); mass spectrum, *m/e* (relative intensity) 132 (100), 145 (92), 131 (64.9), 104 (17.5), 119 (15.8), 78 (15.8), 27 (15.8), 77 (14.9), 105 (14), 52 (12), 160 (M^+, 6.1).

In a second preparation a 67/33 mixture of **5** and **6** was obtained in 65% yield from **3** ($[\alpha]^{25}_D$ +25.51°, 64% minimum optical purity) according to the above experimental procedure. The mixture was not separated into its components and was used as such in the following cyclization with acetylene (see later).

(+)-(*S*)-2-(2′-Pyridyl)-6-*sec*-butylpyridine (1). A solution of **5** (2.09 g, 13.0 mmol) and (π-cyclopentadienyl)cobalt 1,5-cyclooctadiene (0.18 g) in degassed toluene (18 mL) (freshly distilled under nitrogen) was introduced by suction into a 0.2-L autoclave, evacuated from the air (0.1 mm). The reaction vessel was pressurized to 13 atm with acetylene and then rocked and heated to 120 °C. During 20 h the theoretical amount of gas required was adsorbed. After cooling and releasing of the residual gas, the solvent was evaporated and the brown residue distilled under reduced pressure to give **1** as a slightly reddish oil. Column chromatography of this product on silica gel (65 g/1 g of product) using benzene–ethyl ether (10:1) as the eluant gave 2.3 g (10.8 mmol, 83% yield) of colorless and gas chromatographically (2 m × 2.5 mm column, SE-30 5% on Chromosorb W at 160 °C) pure **1**: bp 100 °C (0.1 mm); $[\alpha]^{25}_D$ +25.87° (*c* 2.076, cyclohexane); ^1H NMR ($CDCl_3$) δ 8.65 (m, 1 H, 6′-H), 8.60–8.15 (m, 2 H, 4- and 4′-H), 7.92–7.60 (m, 2 H), 7.15–7.06 (m, 2 H), 2.86 (q, 1 H), 1.72 (m, 2 H), 1.33 (d, 3 H), 0.87 (t, 3 H); mass spectrum, *m/e* (relative intensity) 184 (100), 197 (60), 183 (52.8), 78 (21.3), 155 (14.6), 185 (13.5), 156 (11.2), 52 (10.1), 212 (M^+, 7.8).

Anal. Calcd for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60; N, 13.19. Found: C, 79.14; H, 7.84; N, 12.91.

In a second preparation a mixture of **5** and **6** (67/33, 19 mmol) in the presence of the above cobalt catalyst (0.15 g) was reacted with acetylene under the same reaction conditions to give a mixture of **1** and **7** with practically identical composition in 80% yield. Column chromatography on silica gel (50 g/1 g of product) using benzene as the eluant gave pure **1** (1.7 g), $[\alpha]^{25}_D$ +21.40° (*c* 2.03, cyclohexane), and **7** (0.72 g): bp 110 °C (0.05 mm); $[\alpha]^{25}_D$ +14.64° (*c* 2.25, cyclohexane); ^1H NMR ($CDCl_3$) δ 8.80-8.60 (m, 2 H), 7.85–7.60 (m, 4 H), 7.45–7.23 (m, 1 H), 2.88 (m, 1 H), 1.74 (m, 2 H), 1.35 (d, 3H), 0.86 (t, 3 H); mass spectrum, *m/e* (relative intensity) 184 (100), 197 (68.9), 183 (58.6), 78 (20.5), 212 (M^+, 19.5), 155 (16.0), 185 (15.5), 42 (12.6), 156 (12.5), 170 (11.5).

Anal. Calcd for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60; N, 13.19. Found: C, 78.88; H, 7.93; N, 13.02.

Determination of Enantiomeric Purity of 1. The ^1H NMR spectra of **1** were run on a Varian-XL 100 spectrometer using deuteriochloroform as the solvent and tetramethylsilane as an internal standard. The chiral shift reagent employed was tris-[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]europium(III)[17] supplied by Sigma Chemical Corp.

The most satisfactory spectrum for enantiomeric excess determination was obtained by using a sample containing 5 mg of **1**, $[\alpha]^{25}_D$ +21.40° (*c* 2.03, cyclohexane), and 25 mg of the chiral shift reagent in 0.5 mL of the solvent.

(*S*)-3-*sec*-Butyl-5,5-diethoxypentanal (9). Compound **8** (20 g, 0.1 mol) in 40 mL of dry benzene and 11.5 mL of triethylamine was hydroformylated with a mixture of CO and H_2 (1:1) at 90 atm and 105 °C in the presence of 0.3 g of $RhCl(CO)(PPh_3)_2$ according to the procedure described elsewhere.[11] After 40 h ~70% of the substrate had reacted (GLC). After cooling and releasing, the reaction mixture was evaporated under reduced pressure (30 mm) and the residual aldehyde was purified by distillation through a short-path column. The product **9** was obtained in ~98% pure (14 g, 60% yield), bp 71 °C (0.04 mm).[11]

(*S*)-2-(3-*sec*-Butyl-5,5-diethoxypentanoyl)pyridine (10). 2-Bromopyridine (7.9 g, 0.05 mol) in ethyl ether (20 mL) was slowly added to 2 M solution of butyllithium (27.5 mL, 0.055 mol) in *n*-hexane cooled at −60 °C.[12] After the addition, the reaction mixture was allowed to rise to −45 to −35 °C and held at this temperature for 30 min. Compound **9** (11.5 g, 0.05 mol) in ethyl ether (10 mL) was dropwise added (30 min) at −70 °C under stirring to the solution of 2-lithiopyridine thus obtained. The mixture was allowed to rise slowly to room temperature, and the stirring was maintained for an additional 24 h. After hydrolysis with cold water (50 mL) and extraction with ether, the ethereal phase (150 mL) was separated and dried over Na_2SO_4.

The ethereal solution containing the crude (*S*)-1-(2′-pyridyl)-3-*sec*-butyl-5,5-diethoxypentanol was treated with activated MnO_2 (40 g, 0.46 mol), and the reaction mixture was stirred at room temperature for 5 days.[14] Then the solid products were filtered under reduced pressure and washed with CH_2Cl_2 (200 mL). Evaporation of the solvent and fractional distillation in vacuo of the residual oil gave compound **10** (7.6 g, 49.5% yield), bp 125 °C (0.3 mm), which was ~90% pure on GLC analysis (2 m × 2.5 mm column packed with SE-30 5% on Chromosorb W at 240 °C): $[\alpha]^{25}_D$ +6.08° (*c* 2.04, cyclohexane); IR (neat) $\nu_{C=O}$ 1704 cm^{-1}; ^1H NMR (CCl_4) δ 8.60–8.33 (m, 1 H, 6-H), 8.00–7.10 (m, 3 H, pyridine ring protons), 4.38 (t, 1 H, $CH(OR)_2$), 3.72–2.95 (m, 6 H), 2.56–2.02 (m, 1 H), 1.70–0.67 (m, 17 H).

(+)-(*S*)-2-(2′-Pyridyl)-4-*sec*-butylpyridine (2). A solution of **10** (3.93 g, 0.013 mol) in dry acetic acid (25 mL) was refluxed for 2 h and then, after cooling, hydroxylamine hydrochloride (2.7 g) in the same solvent (12 mL) was added. This mixture was refluxed for 6 h and then alkalized with 10% sodium hydroxide, and the organic products were extracted with ethyl ether. Drying over Na_2SO_4 and distillation yielded compound **2** (2.1 g) containing 30% of 2-(2′-pyridyl)pyridine (GLC). Column chromatography separation on silica gel (50 g/1 g of product) using benzene as the eluant gave 1.1 g (40% yield) of 99% pure **2**: bp 110 °C (0.05 mm); $[\alpha]^{25}_D$ +17.96° (*c* 2.16, cyclohexane); ^1H NMR ($CDCl_3$) δ 8.82 (m, 1 H, 6′-H), 8.57 (m, 1 H, 6-H), 8.50–8.35 (m, 1 H), 8.27 (m, 1 H), 7.93–7.70 (m, 1 H), 7.40–7.09 (m, 2 H), 2.71 (q, 1 H), 1.63 (m, 2 H), 1.29 (d, 3 H), 0.85 (t, 3 H); mass spectrum, *m/e* (relative intensity) 184 (100), 183 (67.4), 197 (52.6), 212 (M^+, 35.8), 78 (22.0), 156 (18.9), 185 (14.7), 51 (14.6), 170 (12.6), 168 (8.8).

Anal. Calcd for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60; N, 13.19. Found: C, 79.05; H, 8.00; N, 12.89.

Duplicated Preparation of 2. Following the above procedure, compound **8** (8.8 g, 0.044 mol), $[\alpha]^{25}_D$ +14.75° (*c* 1.972, cyclohexane), was converted into **2** (1.2 g, 13% overall yield) showing $[\alpha]^{25}_D$ +17.82° (*c* 2.013, cyclohexane).

UV and CD Measurements. UV and CD spectra were carried out with a JASCO UVIDEC 710 and a JASCO J 500-C spectrometer, respectively, using 0.5–0.01-cm cells and concentrations ranging between 1×10^{-3} and 2×10^{-3} mol/L in *n*-heptane. The particularly unfavorable dissymmetry factor ($g = 2–3 \times 10^{-5}$), which made the CD measurements difficult, was partially overcome by a DP 500-N data processor on line with the JASCO 500-C spectrometer: each CD spectrum represents the average of 16 scans. The signal/noise ratio was then improved by a factor of 4.

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Registry No. (*S*)-**1**, 91759-87-4; (*S*)-**2**, 91759-88-5; (*S*)-**3**, 55740-78-8; (*S*)-**3** *N*-oxide, 91759-95-4; (*S*)-**4**, 91759-90-9; (*S*)-**5**,

91759-91-0; (S)-6, 91759-92-1; (S)-7, 91759-93-2; (S)-8, 78156-22-6; 9, 78156-24-8; 10, 91759-94-3; $(PhO)(EtO)_2CH$, 14444-77-0; HC≡CH, 74-86-2; $NH_2OH·HCl$, 5470-11-1; (+)-(S)-2-methylbutanenitrile, 25570-03-0; (+)-(S)-2-*sec*-butylallylmagnesium chloride, 91759-96-5; (π-cyclopentadienyl)(1,5-cyclooctadiene)-(+)-(S)-2-*sec*-butylallylmagnesium chloride, 12184-35-9; 2-bromopyridine, 109-04-6; 2-lithiopyridine, 17624-36-1; 2-[1-hydroxy-3-(2,2-diethoxyethyl)-4-methylhexyl]pyridine, 91759-97-6.

Organic Reactions at High Pressure. Preparation of Wittig Phosphonium Salts at Ambient Temperature[1]

William G. Dauben,* John M. Gerdes, and Richard A. Bunce[2]

Department of Chemistry, University of California, Berkeley, California 94720

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As applications of the versatile Wittig reaction[3,4] are directed toward the synthesis of more complex olefins, the requisite phosphonium salts must frequently incorporate labile functional groups and stereochemically sensitive centers.[3a,d] The presence of sensitive functionality may limit the use of standard elevated temperature conditions (80–140 °C) for salt formation[3,4] and, therefore, provide impetus for developing a new mild method for quaternization of triphenylphosphine. In an S_N2 type of displacement reaction which results in ionization, the reaction possesses a negative volume of activation, $\Delta V^{\ddagger}$, and such a reaction should be accelerated under very high pressure (15 kbar, 1.5 GPa). The most typical process of this type is the Menshutkin reaction which involves an amine and an alkyl halide, tne $\Delta V^{\ddagger}$ having been reported to lie between −20 and −50 $cm^3\ mol^{-1}$.[5]

$$R_3N + R'X \rightarrow R_3N^+R'\ X^-$$

The accelerated rates observed for this type of charge developing reaction at high pressure are understood by considering the components of the $\Delta V^{\ddagger}$ parameter,[6] which include the intrinsic term or van der Waals volumes and the solvation term related to changes in the volume of the solvating medium brought about by the solute. Reduction of the intrinsic and solvation volumes, resulting from the new bond formation between two molecules and electrostriction of the dipolar medium,[7] respectively, also occurs during the reaction of a trialkyl phosphite with an alkyl iodide, the initial process of the Arbuzov reaction. The observed rate enhancement at elevated pressure, a factor of ten-fold at 2.5 kbar pressure[8] due in part to a charge development along the reaction course, should also be found in the reaction of triphenylphosphine with primary and secondary halides. The present work shows the great utility of high pressure rate enhancement in the formation of phosphonium salts, permitting reaction to occur between 20 and 40 °C.

$$Ph_3P + RX \rightarrow PH_3P^+R\ X^-$$

A variety of alkyl bromides and chlorides have been evaluated in their reaction with triphenylphosphine in different solvents, at different temperatures, and at high (15 kbar, 1.5 GPa) and low (1 bar) pressure, and the results are summarized in Table I. All reactions at elevated pressure were carried out at either 20 °C or 40 °C for 24 or 36 h. The melting points of the resultant, analytically pure salts were compared with those previously reported. Ambient (1 bar) pressure control experiments were performed using identical ratios of reagents and solvent and were allowed to react at 20 °C and 80 °C for the indicated times.

The advantages in using high pressure are very apparent in the preparation of phosphonium salts from alkyl bromides. As shown in entry 1, *n*-butyl bromide in acetonitrile under high pressure at 20 °C for 24 h was converted to the phosphonium salt in 72% yield. At 1 atm pressure at the same temperature in the same solvent but for 36 h reaction time, no reaction occurred; at 80 °C, however, a 55% yield of salt was obtained. Of special interest are the increased 15 kbar salt formation yields of 89% and 82% which result from using the more effective 7:3 mole ratio of benzene: toluene solvent system (low dielectric constant)[7] and the mole to mole ratio of reactants, respectively. The other primary bromides (entries 2 and 3) also quaternized triphenylphosphine best at elevated pressure. The required heating for the ambient pressure reaction of the bromo ketal (entry 3), brought about deketalization, thus making the carbonyl protected salt only preparable by use of the high pressure procedure. The same is true for the primary chloride (entry 4) which at 80 °C and atmospheric pressure gave only a 13% yield of salt, whereas with high pressure at 40 °C the yield was raised to 33% (not optimized).

Turning attention to secondary bromides, which are known to react sluggishly in the S_N2 displacement reaction, the few known examples of phosphonium salt preparations[10,11] (entries 5 and 6) all required extreme heating (120–140 °C). These substrates were ideally suited for this high pressure procedure. The atmospheric pressure control experiment of *sec*-butyl bromide (entry 5) showed no reaaction at 20 °C but when heated neat at 120 °C (sealed tube) yielded the salt in 95% yield. Under the standard high pressure conditions at 40 °C using either a 2:1 or 1:1 molar ratio of reactants, yields of 58% and 55% were obtained. With cyclopentyl bromide (entry 6), a temperature of 200 °C was needed for the 1 atm pressure control and the yield was only 43%. Under high pressure at 20 °C, a 52% yield was obtained and this could be raised to 79% by using a large excess of the bromide.[14] An

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(2) National Institutes of Health Postdoctoral Fellow, 1981–1983. Present address: Department of Chemistry, Oklahoma State University, Stillwater, OK 74078.

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