Table I. ^{13}C NMR Spectral Data of 2- and 4-Substituted Pyridines[a]

substituent	δ values C2 C6	C3 C5	C4	subst
2-SCH_3	159.0	118.1	134.8	12.2
	148.5	120.5		
4-SCH_3	148.6	119.3	149.6	13.1
	148.6	119.3		
2-I	117.7	134.3	137.0	
	150.0	122.4		
4-I	150.0	132.8	105.1	
	150.0	132.8		
2-$SiMe_3$	167.8	128.1	133.3	-2.3
	150.0	122.1		
4-$SiMe_3$	147.9	127.2	149.1	-2.6
	147.9	127.2		
4-$SeCH_3$	148.5	122.6	144.0	4.7
	148.5	122.6		

[a] Concentrations about 25% (v/v), solvent $CDCl_3$.

b. Metalation in Strongly Polar Medium. In the reaction flask (see a) was placed a solution of 0.11 mol of *t*-BuOK in 80 mL of THF, 0.20 mol of pyridine, and 40 mL of HMPT (dried by adding a sufficient quantity of a concentrated solution of lithium—3 g/100 mL—in liquid ammonia until the blue color persisted and subsequently distilling twice at 10–15 mmHg). The mixture was cooled to −105 to −110 °C and a solution of 0.10 mol of butyllithium in 70 mL of hexane was added in 10 min, with efficient stirring and cooling between −100 and −110 °C.

After the addition, the light-yellow solution was stirred for an additional 15 min at −100 °C; then Me_3SiCl (0.15 mol) or CH_3SSCH_3 (0.14 mol) was added in one portion. In the case of iodination and reaction with selenium first a solution of 0.12 mol of anhydrous lithium bromide was added at −100 °C and after 5 min a solution of 0.15 mol of iodine in 100 mL of THF was poured to the reaction mixture or 0.10 mol of powdered red selenium was introduced. After the addition of the reagents the temperature was allowed to rise to −10 °C. In the case of selenation 0.15 mol of methyl iodide was then added. The reaction mixtures were subsequently diluted with 200 mL of water or aqueous solution of 10 g of $Na_2S_2O_3$.

The aqueous layer was extracted 5–8 times with small portions of diethyl ether. The combined solutions were dried over K_2CO_3 and the concentrated in vacuo. In order to remove the HMPT present in the remaining liquid, water (100 mL) was added and ten extractions with 2:1 mixture of pentane and diethyl ether were carried out. Each extract was washed twice with 30-mL portions of water, the aqueous layers being added to the main aqueous layer. The combined extract were dried over K_2CO_3 and then concentrated in vacuo. Careful distillation of the remaining liquids afforded the reasonable pure 4-substituted pyridine in yields of 50–55% (the actual yields are about 20% higher, but the fractionated distillations gave rise to some losses).

4-Methylthiopyridine and 4-iodopyridine, were obtained in a pure state by crystallization at −20 °C from a 3:1 mixture of pentane and diethyl ether. Our 2-(methylseleno)pyridine has bp 100 °C/20 min, n_D^{20} min, n_D^{20} 1.6147. For physical constants of the pyridine derivatives, see ref 6–8; for ^{13}C NMR spectral data, see Table I.

c. Isolation of the Deuterated Pyridines. After the metalation (a) had been completed, the cold (−100 °C) reaction mixture was poured in 2–3 min into a vigorously stirred solution of 0.4 mol of deuteriomethanol in 100 mL of diethyl ether, with cooling below −20 °C (applying inverseorder addition gave appreciable amounts of dideuterated and nondeuterated pyridine).

After this quenching procedure a mixture of 40 mL of 36% hydrochloric acid and 60 mL of water was added. The layers were separated and the organic layer washed 1 time with 50 mL of water. The combined aqueous layers were freed from organic solvents by heating them in vacuo (rotary evaporator). Subsequently potassium hydroxide pellets (100 g) were added with shaking and cooling in ice–water. The deuterated pyridine liberated was isolated by extraction (5 times) with diethyl ether, drying the extracts over powdered KOH, and subsequently distilling at normal pressure. The yield of deuterated pyridine (~90% 2-isomer) was about 95%.

Registry No. CH_3SSCH_3, 624-92-0; Me_3SiCl, 75-77-4; pyridine, 110-86-1; 2-potassiopyridine, 91238-49-2; 3-potassiopyridine, 91238-50-5; 4-potassiopyridine, 91238-51-6; iodine, 7553-56-2; selenium, 7782-49-2; deuteriomethanol, 1455-13-6; 2-(methylseleno)pyridine, 88871-79-8; 2-(methylthio)pyridine, 18438-38-5; 4-(methylthio)pyridine, 22581-72-2; 2-iodopyridine, 5029-67-4; 4-iodopyridine, 15854-87-2; 2-(trimethylsilyl)pyridine, 13737-04-7; 4-(trimethylsilyl)pyridine, 18301-46-7; 4-(methylseleno)pyridine, 91238-52-7; pyridine-2-d_1, 1807-97-2.

(10) When this work was finished a paper of Martin et al. (*J. Org. Chem.* **1983**, *48*, 4158) dealing with the ortho-metalation of pyridines with lithium tetramethylpiperidide came to our attention.

A Convenient Synthetic Route to (*E*)-2-Penten-1-ol

Alicia E. Gastaminza,* Nilda N. Ferracutti, and Nora M. Rodriguez

Laboratorio de Química Orgánica, Departamento de Ciencias Exactas, Universidad Nacional del Sur, 8000 Bahía Blanca, Argentina

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(*E*)-2-Penten-1-ol (**1**) is of interest as a common precursor for the synthesis of the achiral aliphatic components of some insect sex pheromones which have a terminal unsaturated five-C atom unit of *E* configuration.[1] In connection with our work on this synthetic area, we required comparatively large amounts of **1**.

The few procedures reported in the literature for its preparation involve allylic rearrangements[2] or stereospecific hydrogenation of 2-pentyn-1-ol.[3] The former procedures give a mixture of geometrical isomers, while the latter is not suitable for large-scale preparations. Consequently, efforts were focused on the development of a convenient and economically feasible route for preparing **1**.

Our approach was based upon the selective reduction of (*E*)-2-pentenoic acid(**2**) and/or its derivatives which, to the best of our knowledge, has not been reported. **2** was obtained in good yield by Knoevenagel–Doebner condensation between propionaldehyde and malonic acid. Stereocontrol of the reaction was achieved at 20 °C in absence of light, and the thermodynamically more stable *E* isomer was formed almost quantitatively. It should be noted that in the case of α,β-unsaturated acids and esters the β-carboxylic or β-carbalkoxy group, respectively, has a deshielding effect on the *cis*-vinylic proton. The differential shielding of the *cis*- and *trans*-vinylic protons allows calculation of the cis/trans isomer distribution.[4]

Initial attempts at reducing **2**, (*E*)-2-pentenoic acid chloride (**2a**), and methyl (*E*)-2-pentenoate (**2b**) by pro-

(1) For a comprehensive review, see: Rossi, R. *Synthesis* **1977**, 817.
(2) (a) Delaby, R. C.R. Hebd. *Seances Akad. Sci.* **1923**, *176*, 1898; **1925**, *181*, 722. (b) Bouis, M. *Liebigs Ann. Chem.* **1928**, *9*, 402. (c) Meisenheimer, J.; Link, J. *Liebigs Ann. Chem.* **1930**, *479*, 211.
(3) Smith, L. M.; Smith, R. G.; Loehr, T. M.; Daves, G. D.; Daterman, G. E.; Wohleb, R. H. *J. Org. Chem.* **1978**, *43*, 2361.
(4) Jackman, L. M. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry"; Pergamon Press: Oxford, 1962; pp 119–120.

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cedures described in the literature for other closely related α,β-unsaturated compounds[5] gave either disappointingly low reduction yields or poor chemoselectivity. Furthermore, we found that **1** can be isolated from any of the unchanged substrates by fractional distillation, but it is virtually impossible to obtain pure **1** not contaminated with pentan-1-ol when the saturated alcohol is also formed during reduction.

The strategy for defining the best preparative method was to explore each substrate/reducing agent/solvent system by factorial experiments.[6] Selective reduction[7] of **2** and **2b** by LAH/ether, LAH/benzene, LAH–$AlCl_3$/ether, of **2a** by $NaBH_4$–Al_2O_3/ether, and of **2b** by LAH–EtOH/ether was studied by systematic variation of a single factor at a time (substrate/reducing agent concentration ratio, temperature, time, and addition order) while holding all remaining factors constant.[8] Application of this methodology showed that the highest selective reduction yields were obtained for substrate **2b**. A remarkable solvent effect was observed in reductions by LAH.[9] When ether was used, functional group selectivity no better than 60% could be achieved; by changing the solvent to benzene, the chemoselectivity was dramatically enhanced to 88%. However, long times of reaction are needed (14.5 h, 50 °C), and the yield of isolated **1** diminishes due to emulsion formation during the workup of the reaction mixture.

From the preparative point of view, reduction of **2b** by LAH–$AlCl_3$ in ether gave the best results; experimental conditions are described in which reduction yield is the highest for the regiospecific reaction. It should be emphasized that these conditions are critical to the success of the procedure; as already mentioned, minor deviations lead to lower reduction yields or loss of the regiospecificity with concomitant formation of the undesirable saturated alcohol.

In conclusion, we believe that this route to **1** has some distinct advantages in comparison with previously reported methods. Preparation of **1** is achieved in a three-step sequence from ready available and relatively inexpensive reagents. Operationally simple procedures are involved, and it is suitable for large-scale preparation.

Experimental Section

All compounds are known and were identified by their physical and spectroscopic properties. IR spectra were recorded in liquid films on a Perkin-Elmer Model 137 spectrometer. ^1H NMR spectra were obtained for solutions in CCl_4 with Me_4Si as internal standard on a Varian A60 spectrometer.

(*E*)-2-Pentenoic Acid (2). This compound was obtained by a modification of the known general procedure for preparing β-alkyl-substituted acrylic acids.[10] To 1.3 mol of dry pyridine, placed in an ice–water-cooled flask provided with two consecutive reflux condensers fitted with a drying calcium chloride tube were added 1 mol of malonic acid and 1.25 mol of propionaldehyde. The ice–water bath was removed; the whole apparatus was protected from light; and the reaction mixture was kept for 2 days at 20 °C with occasional shaking. Two 0.25-mol portions of malonic acid were added, one on each of two consecutive days. After a total of 6 days, the reaction mixture was poured into an excess of 50% sulfuric acid and the resulting solution was kept in a refrigerator until most of **2** could be separated as a clear oil. The remaining aqueous layer was extracted several times with ether; the combined organic extracts were dried over anhydrous $MgSO_4$ and the solvent was removed. The crude product was twice fractionally distilled under diminished pressure through a Vigreux column to give pure **2** (>99% by ^1H NMR, 88% yield): bp 92 °C (8 mm) (lit.[11] bp 99 °C, 10 mm); IR 3400–2960 (COOH), 1710 (C=O), 1675 (C=C), 985 (*trans*-HC=CH) cm^{-1}; ^1H NMR δ 7.12 (dt, 1, J = 16 Hz, J' = 6 Hz, HC_3=C), 5.75 (dt, 1, J = 16 Hz, J' = 2 Hz, HC_2CO), 2.25 (m, 2, CH_2), 1.08 (t, 3, J = 7 Hz, H_3C).

Methyl (*E*)-2-Pentenoate (2b). Fischer esterification of **2** gave **2b** (85% yield): bp 50–52 °C (25 mm) (lit.[12] bp 50.5–51 °C, 26 mm); IR 2980 (CH_2), 1730 (C=O), 1660 (C=C), 1164 (COC), 985 (*trans*-HC=CH) cm^{-1}; ^1H NMR δ 6.90 (dt, 1, HC_3=C), 5.60 (dt, 1, HC_2CO), 3.50 (s, 3, OCH_3), 2.14 (m, 2, CH_2), 1.02 (t, 3, H_3C).

(*E*)-2-Penten-1-ol (1). A solution of LAH (5.70 g, 0.15 mol) in 150 mL of Na-dried ether was prepared in a well-dried round-bottom flask equipped with an equalizing dropping funnel and a condenser to whose top was attached a calcium chloride tube. As soon as possible, the ice–water bath was removed and the suspension was magnetically stirred at room temperature for 30 min. A solution of anhydrous $AlCl_3$ powder (6.67 g, 0.05 mol) in 250 mL of dry ether was added to the ice–water-cooled ethereal LAH suspension. After the addition was complete, the stirring was continued at room temperature for at least 30 min. **2b** (9.12 g, 0.08 mol) in 50 mL of dry ether was added at 5–10 °C with vigorous stirring and at such a rate as to avoid refluxing. Immediately after addition was complete, the temperature of the water bath was raised to 20 °C and the reaction mixture was left for exactly 50 min. Then 25 mL of 20% sulfuric acid were carefully added to destroy excess AlH_3, and the stirring was continued for another 45 min. The crude product (98.8% reduction by ^1H NMR) was fractionally distilled under diminished pressure to give **1** (6.33 g, 92% yield, >99% pure by ^1H NMR). At this scale, no significant yield difference was observed when the reaction was carried out under a nitrogen atmosphere. The product gave bp 72–73 °C (46 mm) (lit.[2c] bp 50–51 °C, 17 mm): IR 3300 (OH), 2850 (CH_2), 1665 (C=C); 1020 (C=CCH_2OH), 965 (*trans*-HC=CH) cm^{-1}; ^1H NMR δ 5.55 (m, 2 H, J = 16 Hz, *trans*-HC=CH), 3.98 (m, 2, H_2CO), 2.07 (m, 2, CH_2), 1.02 (m, 3, H_3C).

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Registry No. 1, 1576-96-1; **2**, 13991-37-2; **2b**, 15790-88-2; malonic acid, 141-82-2; propionaldehyde, 123-38-6.

(5) (a) Marfat A.; McGuirk, P. R.; Helquist, P. *J. Org. Chem.* **1979**, *44*, 1345. (b) Riley, R. G.; Silverstein, R. M. *J. Org. Chem.* **1974**, *39*, 1957. (c) Santaniello, E.; Farachi, C.; Manzocchi, A. *Synthesis* **1979**, 912. (d) Martin, C. J.; Schepartz, A. I.; Daubert, B. F. *J. Am. Chem. Soc.* **1948**, *70*, 2601. (e) Davidson, R. S.; Günther, W. H. H.; Waddington-Feather, S. M.; Lythgoe, B. J. *J. Chem. Soc.* **1964**, 4907. (f) Sum, F. W.; Weiler, L. *Tetrahedron* **1981**, *37*, 303. (g) Tsuboi, S.; Masuda, T.; Takeda, A. *J. Org. Chem.* **1982**, *47*, 4478.

(6) Brownlee, K. A. "Industrial Experimentation", 4th ed.; Chemical Publ.: New York, 1953.

(7) For a detailed review and discussion on this subject, see: (a) Brown, H. C.; Krishnamurthy, S. *Tetrahedron* **1979**, *35*, 567. (b) Brown, H. C.; Krishnamurthy, S. *Aldrichimica Acta* **1979**, *12*, 3.

(8) Those studies will be separately published.

(9) (a) Snyder, E. I. *J. Org. Chem.* **1967**, *32*, 3531. (b) Brown, H. C.; Ichikawa, K. *J. Am. Chem. Soc.* **1961**, *83*, 4372. (c) Jorgensen, M. J.; Thacker, A. F. *J. Chem. Soc. D* **1968**, 973.

(10) Shabtai, J.; Ney-Igner, E.; Pines, H. *J. Org. Chem.* **1981**, *46*, 3795.

(11) Auwers, K. V. *Liebigs Ann. Chem.* **1923**, *432*, 63.

(12) Hine, J.; Kanagasabapathy, V. M.; Ng, P. *J. Org. Chem.* **1982**, *47*, 2745.