water and concentrated sodium chloride solution, and dried ($MgSO_4$). Removal of the solvent and short-path distillation gave 5.50 g (97%) of methyl phenyldiazoacetate, boiling at a bath temperature of 62–64° (0.3 μ): $n^{25}D$ 1.5779; uv max (cyclohexane) 440 mμ (ε 65) 298 (sh, 5700), 280 (9300), 275 (sh, 9100), 253 (sh, 14,000), and 246 (15,000); ir (CCl_4) 2090 and 1715 cm^{-1}, among others; nmr ($CDCl_3$) τ 2.6–3.2 (m, 5, phenyl) and 6.3 (s, 3, COOMe).

Anal. Calcd for $C_9H_8N_2O_2$: C, 61.35; H, 4.58; N, 15.90. Found: C, 61.73; H, 4.94; N, 16.31.

Methyl *p*-Methoxyphenylglyoxylate Hydrazone.—Friedel–Crafts addition[11] of methyl chloroglyoxylate[12] to anisole gave, in 77% yield, a mixture of methyl *o*- and *p*-methoxyphenylglyoxylate (ratio *ca.* 20:80): bp 94–102° (1 μ), $n^{25}D$ 1.5486–1.5519, as a pale yellow oil which solidified on standing. Hydrazine hydrate (42 ml) was added slowly to a cooled mixture of 70 ml of glacial acetic acid and 70 ml of water, followed by 58.27 g of the above mixture of isomers and 200 ml of methanol. After the mixture had been stirred at room temperature for 64 hr, most of the methanol was removed under reduced pressure. Water and methylene chloride were added to the residue, the layers were separated, and the aqueous phase was extracted several times with methylene chloride. The combined extracts were washed with water, 5% hydrochloric acid, 5% sodium bicarbonate solution, and concentrated sodium chloride solution, and dried. Removal of the solvent gave 64.4 g of a semisolid, the nmr spectrum of which indicated that it was a mixture of methyl *o*- and *p*-methoxyphenylglyoxylate hydrazone (ratio 17:83). Crystallization from benzene (100 ml) gave 21.5 g (43%) of methyl *p*-methoxyphenylglyoxylate hydrazone, mp 140–142°. An analytical sample (ethyl acetate) had mp 142–143°; nmr ($CDCl_3$) 2.7–3.1 (m, 4, phenyl), 3.6 (broad singlet, 2, NH_2), and 6.2 (two singlets, separation 1.5 cps, three each, OMe and COOMe); uv max (dioxane) 270 mμ (ε 10,000) and 228 (13,100); ir (KBr) 3400, 3290, 3230, and 1715 cm^{-1}, among others; the N–H stretching region is insensitive to concentration changes (in CH_2Cl_2).

Anal. Calcd for $C_{10}H_{12}N_2O_3$: C, 57.68; H, 5.81; N, 13.46. Found: C, 57.69; H, 5.85; N, 13.54.

Methyl *p*-Methoxyphenyldiazoacetate.—To a solution of 61.1 g (weight after removal of the acetic acid) of lead tetraacetate in 400 ml of methylene chloride was added, with external cooling (ice bath), 19.17 g of methyl *p*-methoxyphenylglyoxylate hydrazone. The mixture was stirred at room temperature for 5 min, Celite and water (100 ml) were added, and the mixture was filtered after being stirred for 1 min. The layers of the filtrate were separated; the organic layer was washed with concentrated sodium chloride solution and dried. Removal of the solvent and crystallization of the residue from 30 ml of cyclohexane gave 15.06 g of methyl *p*-methoxyphenyldiazoacetate, mp 50.5–51.5°, in the form of orange crystals. An additional 0.82 g of this product was obtained by removal of the solvent from the mother liquor and crystallization of the residue from 6 ml of cyclohexane: combined yield 15.88 g (84%); nmr ($CDCl_3$) τ 2.6–3.1 (AB quartet, split further, 4, phenyl) and 6.2 (two singlets, three each, OMe and COOMe); uv max (cyclohexane) 450 mμ (ε 103), 283 (11,000), and 250 (18,000); ir (CCl_4) 2100, 1720 cm^{-1}; (KBr) 2095, 1705 cm^{-1}.

Anal. Calcd for $C_{10}H_{10}N_2O_3$: C, 58.24; H, 4.89; N, 13.59. Found: C, 58.01; H, 4.94; N, 13.25.

Methyl *p*-nitrophenyldiazoacetate was prepared in 60% yield from methyl *p*-nitrophenylacetate by the method of Regitz.[4b] The product had mp 149–150° dec (crystallization from ethyl acetate); nmr ($CDCl_3$) 1.8–2.5 (AB quartet, split further, 4, phenyl) and 6.1 (s, 3, COOMe); uv max (cyclohexane) 440 (sh, ε 120), 330 (17,000), and 272 (11,000); ir (CCl_4) 2110, 1735 cm^{-1}; (KBr) 2100, 1715 cm^{-1}.

Anal. Calcd for $C_9H_7N_3O_4$: C, 48.87; H, 3.19; N, 19.00. Found: C, 48.66; H, 3.17; N, 18.74.

Methyl Cyanoglyoxylate Hydrazone.—To a stirred mixture of 11.0 g of methyl (*p*-dimethylaminophenylimino)cyanoacetate[10] and 250 ml of glacial acetic acid was added, dropwise, 12 g of anhydrous hydrazine. After the mixture had been stirred at 80° for 1 hr, most of the acetic acid was removed under vacuum. Methylene chloride and concentrated sodium chloride were added to the residue, the mixture was filtered, and the insoluble crystalline solid was washed with water and methylene chloride and dried, to give 0.51 g of methyl cyanoglyoxylate hydrazone. The layers of the filtrate were separated, and the aqueous phase was extracted repeatedly with methylene chloride (a total of 400 ml). The combined extracts were washed with concentrated sodium chloride solution and dried. Removal of the solvent gave another 1.05 g of methyl cyanoglyoxylate hydrazone, yield of crude product 1.56 g (25%). This material was used directly for the preparation of methyl cyanodiazoacetate. An analytical sample, mp 171–171.5°, was obtained by sublimation (1 μ; 100–110° bath temperature) followed by chromatography on Florisil (elution with tetrahydrofuran–methylene chloride 5:95) and crystallization from acetonitrile: nmr ($(CD_3)_2CO$) τ 0.7–1.8 (broad band, 2, NH_2) and 6.1 (s, 3, COOMe); uv max (MeCN) 280 mμ (14,100); ir (KBr) 3330, 3180, 2970, 2220, 1715, 1650, 1550 cm^{-1}, among others.

Anal. Calcd for $C_4H_5N_3O_2$: C, 37.80; H, 3.97; N, 33.06. Found: C, 37.53; H, 3.82; N, 33.06.

Methyl Cyanodiazoacetate.—A mixture of 244 mg of methyl cyanoglyoxylate hydrazone, 1.4 g of silver oxide, 2.4 g of magnesium sulfate, and 20 ml of methylene chloride was stirred at room temperature for 2 hr. Removal of the solvent from the filtered solution gave 241 mg of methyl cyanodiazoacetate as a yellow oil: ir (neat) 2225, 2140, and 1720 cm^{-1}, among others; nmr ($CDCl_3$) τ 6.1 (s, COOMe). To a solution of 230 mg of this material in 5 ml of ether was added 502 mg of triphenylphosphine. Methyl cyanodiazoacetate triphenylphosphazine (660 mg, 93% yield based on methyl cyanoglyoxylate hydrazone), mp 189–190° dec, precipitated immediately (the melting point remained unchanged on crystallization from benzene): nmr ($CDCl_3$) τ 2.1–2.7 (m, 15, phenyl) and 6.2 (s, 3, COOMe); uv max (MeCN) 325 mμ (ε 27,000), 275 (6500), 268 (6500) 262 (sh, 5600), and 225 (sh, 28,000); ir (KBr) 2200, 1735 cm^{-1}, among others.

Anal. Calcd for $C_{22}H_{18}N_3O_2P$: C, 68.21; H, 4.69; N, 10.85; P, 7.99. Found: C, 68.26; H, 4.61; N, 10.85; P, 7.90.

Registry No.—**1a** (*syn*), 22979-32-4; **1a** (*anti*), 22979-33-5; **1b** (*syn*), 22979-34-6; **2a**, 22979-35-7; **2b**, 22979-36-8; **2c**, 22812-58-4; **4** (*syn*), 22979-25-5; **5**, 22979-38-0; **6**, 23031-07-4.

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Sodium Borohydride Reduction of Aza Lactones[1]

PRICE TRUITT AND J. CHAKRAVARTY

Department of Chemistry, North Texas State University, Denton, Texas 76203

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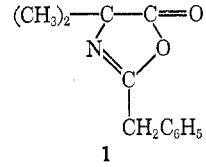
The recent report of Meyers and coworkers[2] concerning the sodium borohydride reduction of dihydrooxazines for the production of aldehydes prompted us to investigate the reduction of some 2-oxazoline-5-ones (aza lactones) with the view of producing aldehydes from these easily formed compounds.

2-Benzyl-4,4-dimethyl-2-oxazoline-5-one (**1**) and 2-phenyl-2-oxazoline-5-one (**2**) were selected as representative aza lactones for this study.



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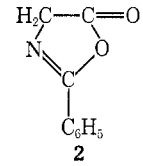

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(1) This investigation was supported by Research Grant No. CA-10530 from the National Cancer Institute.
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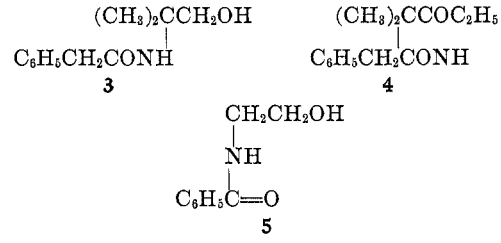
When **1** was treated with an excess of sodium borohydride, a compound **3** was obtained. Any doubt about the proposed structure for **3** was eliminated when acid hydrolysis of **3** afforded phenylacetic acid and the sulfate ester of 2-amino-2-methyl-1-propanol.[3] Compound **3** reacted with phenyl isocyanate to yield the corresponding carbamate. Spectral data also confirmed this structure.



3 **4**

5

The reduction of **1** with a stoichiometric quantity of reagent gave a mixture of starting material **1**, the alcohol **3**, and the ethyl ester **4**. This compound, **4**, was separated from **1** and **3** by chromatographing over acidic alumina. The same compound was obtained by esterification of α-methyl-N-phenylacetyl-α-alanine with ethanol and sulfuric acid.

The reduction of 2-phenyl-2-oxazoline-5-one (**2**), with an excess sodium borohydride resulted in a 90% yield of N-(2-hydroxyethyl)benzamide (**5**) as a thick liquid. This alcohol was identified by its reaction with phenyl isocyanate to form the known phenyl carbamate.[4]

Experimental Section

All melting points were taken with a Hoover–Johns melting point apparatus and are uncorrected; analyses were carried out by Mr. Ed Hoff. Nmr spectra were determined in $CDCl_3$ with TMS as an internal standard, using a Varian A-60 spectrometer. The infrared spectra wre obtained from potassium bromide disks on a Perkin–Elmer Model 237 spectrophotometer.

Sodium Borohydride Reduction of the Aza Lactone[5] 1.—The aza lactone **1** (500 mg) was dissolved in a mixture of tetrahydrofuran, ethanol, and water (15 ml, 1:1:1), sodium borohydride (50 mg) was added in small portions with stirring, and the reaction mixture was kept at room temperature for 20 hr. When the reaction mixture was worked up, a thick liquid (500 mg) was obtained. On chilling in a Dry Ice–acetone bath it solidified and was crystallized from ether in shining colorless cubes, mp 75–76° (470 mg, 91%); ν_{max} 3370 cm^{-1} (s), 3240 (s), 1645 (s), 1600 (m), 1580 (s), and 1080 (s). The nmr spectrum showed a sharp peak at δ 7.30 (5 H, phenyl), a broad peak between 5.65 and 5.90 (1 H, NH), a broad peak between 4.5 and 4.75, centered at 4.62 (1 H, OH), one sharp peak at 3.5 (4 H), and a sharp peak at 1.22 (6 H, methyls).

Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.62; H, 8.25; N, 6.77. Found: C, 69.66; H, 8.25; N, 6.55.

Reaction of **3** with phenyl isocyanate gave the expected phenyl carbamate as a white solid, which was crystallized from acetone in shining white needles, mp 157°.

Anal. Calcd for $C_{19}H_{22}N_2O_3$: C, 70.00; H, 6.80; N, 8.59. Found: C, 69.85; H, 6.67; N, 8.64.

When the same reaction was carried out with a stoichiometric quantity of sodium borohydride under the same experimental conditions a mobile liquid was obtained. The crude liquid in the infrared showed the presence of some unreacted aza lactone (ν_{max} 1805 cm^{-1}), hydroxy (ν_{max} 3400 cm^{-1}), and ester (ν_{max} 1725 and 1180 cm^{-1}). On chromatography over acidic alumina with petroleum ether–ether as the eluting agent (4:1), a white solid was obtained in 31% yield, mp 101°, which was crystallized from a petroleum ether–ether mixture in fine silky needles: mp 101°, ν_{max} 3230 (s) 1725 (s), 1640 (s), 1602 (w), 1565 (s), and 1180 cm^{-1} (s). The nmr spectrum showed a sharp peak at δ 7.31 (5 H, phenyl), a broad peak between 6.25 and 6.10 (1 H, NH), a quartet between 4.30 and 3.95 (J = 7 cps, 2 H, OCH_2CH_3), one sharp peak at 3.5 (2 H, $CH_2C_6H_5$), one sharp peak at 1.5 (6 H, methyls), and a triplet between 1.34 and 1.11 (J = 7 cps, 3 H, CH_2CH_3).

Anal. Calcd for $C_{14}H_{19}NO_3$: C, 67.53; H, 7.69; N, 5.63. Found: C, 67.56; H, 7.68; N, 5.48.

The same compound was obtained by esterification of α-methyl-N-phenylacetyl-α-alanine with ethanol and sulfuric acid, mp 101°, alone or mixed with the above compound.

The ether eluent afforded colorless solid alcohol **3** in 60% yield, mp 75–76°, alone or mixed with the known sample of the alcohol.

Hydrolysis of 3 with Sulfuric Acid.—The compound **3**, mp 75–76° (400 mg), was hydrolyzed with sulfuric acid (15 ml, 30%) for 4 hr. A white solid (270 mg) was obtained, which was crystallized from petroleum ether in shining white flakes, and was confirmed to be phenylacetic acid (yield 100%), mp 78–79°, alone or mixed with the authentic sample of phenylacetic acid.

The aqueous sulfuric acid solution was then neutralized with barium hydroxide solution, and the precipitated barium sulfate was filtered off. The filtrate was evaporated to dryness on a steam bath. A brown gummy material was left. On trituration with a few drops of methanol, a white amorphous solid (about 50 mg) was separated, which on crystallization from methanol melted at 260–262° (with vigorous evolution of gas). Buckles and Mock[3] reported the melting point of the sulfate ester of 2-amino-2-methyl-propanol as 253–255° dec.

Sodium Borohydride Reduction of the Aza Lactone[6] 2.—The azalactone **2** (1.6 g) was reduced with sodium borohydride (190 mg) in a solution of tetrahydrofuran, ethanol, and water (30 ml, 1:1:1). The thick liquid (1.4 g; 88%) had ν_{max} 3380 (s), 3220 (hump), 1645 (s), 1600 (m), 1565 (s), and 1090 cm^{-1} (s). Reaction of this compound with phenyl isocyanate gave the known phenyl carbamate which was crystallized from acetone in white flakes, mp 197°.[4]

Registry No.—Sodium borohydride, 1303-74-8; **1**, 22929-09-5; **2**, 1199-01-5; **3**, 1569-06-8; **3** phenyl isocyanate, 22929-14-2; **4**, 29292-12-0; **5**, 18838-10-3.

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Total Synthesis of (±)-Karahana Ether

ROBERT M. COATES AND LAWRENCE S. MELVIN, JR.[1]

Department of Chemistry and Chemical Engineering, University of Illinois, Urbana, Illinois 61801

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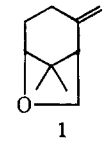
Three new monoterpenes have recently been isolated from Japanese hop, "Shinshu-wase."[2] One of the two ether components is karahana ether, to which structure **1** was assigned on the basis of chemical and spectroscopic evidence. We report here a brief total synthesis of (±)-karahana ether from geraniol (**2a**) which confirms this structural assignment.[3]



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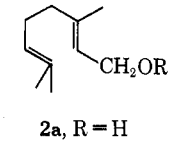

2a, R = H
b, R = Ac

(1) National Science Foundation Undergraduate Research Participant, Summer 1968.

(2) Y. Naya and M. Kotake, *Tetrahedron Lett.*, 1645 (1968).

(3) Another component, karahanaenone, has recently been synthesized: E. Demole and P. Enggist, *Chem. Commun.*, 264 (1969).