of some solvent (*ca.* 50 ml) by distillation caused precipitation of a solid. After cooling, there was obtained by filtration α-amyrenone (390 mg): mp 125–126°, $[\alpha]_D$ +124° (*c* 1.2, pyridine) [lit.[13] mp 125–126°, $[\alpha]_D$ +119° (pyridine)].

Action of Triphenylphosphine Dibromide on α-Amyrenone.—To a solution of triphenylphosphine dibromide (3.0 g) in dry dimethylformamide (25 ml) was added a solution of α-amyrenone (250 mg), and the mixture was stirred for 20 hr at 90° under a nitrogen atmosphere. The product was worked up in the usual way and chromatographed on Spence Type H alumina. Elution with petroleum ether–benzene (4:1, 100 ml) yielded an oil (positive Beilstein test) that crystallized from methanol to give **2α-bromours-12-en-3-one** as needles (90 mg): mp 184–187°, $[\alpha]_D$ +26° (*c* 1.0), λ^{CHCl_3} 5.80 μ.

Anal. Calcd for $C_{30}H_{47}BrO$: C, 71.53; H, 9.41. Found: C, 71.43; H, 9.32.

Further elution with petroleum ether–benzene (4:1, 75 ml) gave a product (negative Beilstein test) that crystallized from ether–methanol to give **ursa-1,12-dien-3-one** as small needles (110 mg): mp 177–178°, $[\alpha]_D$ +36° (*c* 1.4), λ^{EtOH} 232 mμ (ε 10,200), λ^{CHCl_3} 6.01 μ.

Anal. Calcd for $C_{30}H_{46}O$: C, 85.23; H, 10.98. Found: C, 85.35; H, 11.07.

Action of Bromine on α-Amyrenone.—A solution of bromine (18.9 mg) in acetic acid (5 ml) was added dropwise over 10 min to α-amyrenone (50 mg) in the same solvent (5 ml). The mixture was then stirred for a further 10 min, diluted with water, and extracted with ether. Evaporation of the washed and dried ether extract yielded the product which on crystallization from methanol gave 2α-bromours-12-en-3-one as needles: mp and mmp 184–187°, $[\alpha]_D$ +30° (*c* 1.3).

Dehydrobromination of 2α-Bromours-12-en-3-one.—The bromo ketone (25 mg) was added to collidine (5 ml), and the mixture was heated at 100° for 5 hr, cooled, diluted with water, and extracted with ether. The extract was washed successively with dilute hydrochloric acid, dilute sodium bicarbonate solution, and water. Evaporation of the dried extract gave a solid which crystallized from methanol to give ursa-1,12-dien-3-one as small needles (14 mg): mp and mmp 175–177°, $[\alpha]_D$ +32° (*c* 0.9), λ^{EtOH} 232 mμ (ε 10,100), λ^{CHCl_3} 6.00 μ.

Registry No.—I, 638-95-9; III, 2309-00-4; II, 2309-01-5; IV, 638-96-0; VI, 2308-99-8; V, 2672-44-8; triphenylphosphine dibromide, 1034-39-5.

(13) W. A. Jacobs and E. E. Fleck, *J. Biol. Chem.*, **88**, 137 (1930).

A Synthesis of 2-Deoxy-D-*erythro*-pentose[1]

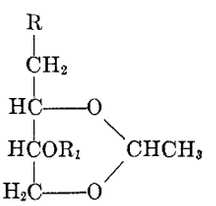
I. ZIDERMAN AND E. DIMANT

Laboratory of Organic and Biological Chemistry, The Hebrew University, Jerusalem, Israel

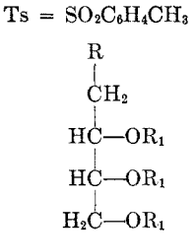
Received August 25, 1966

Nucleophilic displacement reactions of a 1-deoxy-1-halogeno-D-erythritol derivative or of a 1-*O*-(*p*-tolylsulfonyl)-D-erythritol derivative with a cyanide anion to form 2-deoxy-D-*erythro*-pentononitrile, followed by partial reduction of the nitrile, could offer a simple route to 2-deoxy-D-*erythro*-pentose. By this way no epimeric pair has to be separated, while it may also be used for labeling the anomeric carbon of the 2-deoxy sugar with radioactive carbon. Using 1-deoxy-2,4-*O*-ethylidene-1-iodo-D-erythritol (**5**), 2-deoxy-D-*erythro*-pentose was synthetized by the suggested procedure. When this work had been completed, a synthesis of 2-deoxy-D-*erythro*-pentose-(1-^{14}C), similar in its essential steps to the one described here, was reported by Bayly and Turner.[2]

1-Amino-1-deoxy-2,4-*O*-ethylidene-D-erythritol (**1**)[3] was hydrolyzed to 1-amino-1-deoxy-D-erythritol (**8**), and isolated as 1-[(benzyloxycarbonyl)amino]-1-deoxy-D-erythritol (**9**). Benzoylation of **9** formed 2,3,4-tri-*O*-benzoyl-1-[(benzyloxycarbonyl)amino]-1-deoxy-D-erythritol (**10**), which was converted by hydrogen bromide in acetic acid to 1-amino-2,3,4-tri-*O*-benzoyl-1-deoxy-D-erythritol hydrobromide (**11**). 2,3,4-Tri-*O*-benzoyl-1-chloro-1-deoxy-D-erythritol (**12**) was prepared from the amine (**11**), and 2,3,4-tri-*O*-benzoyl-1-bromo-1-deoxy-D-erythritol (**13**), was prepared from the mother compound (**10**) (without isolation of the amine) *via* the respective nitrosyl halides. 2,3,4-Tri-*O*-benzoyl-1-deoxy-1-iodo-D-erythritol (**14**) was prepared from the bromine analog (**13**) with sodium iodide.



1, R = NH_2; R_1 = H
2, R = OH; R_1 = H
3, R = Ts; R_1 = Ts
4, R = Ts; R_1 = H
5, R = I; R_1 = H
6, R = CN; R_1 = H
7, R = CHO; R_1 = H
Ts = $SO_2C_6H_4CH_3$ (*p*)



8, R = NH_2; R_1 = H
9, R = $NHCOOCH_2C_6H_5$; R_1 = H
10, R = $NHCOOCH_2C_6H_5$; R_1 = Bz
11, R = $NH_2 \cdot HBr$; R_1 = Bz
12, R = Cl; R_1 = Bz
13, R = Br; R_1 = Bz
14, R = I; R_1 = Bz
Bz = COC_6H_5

In attempted displacement reactions of **13** with sodium, silver, mercuric, or cuprous cyanide in refluxing *N*,*N*-dimethylformamide (DMF) no evidence for nitrile formation was found. On the other hand **13** reacted with sodium benzoate in DMF under reflux for 4 hr to form tetra-*O*-benzoylerythritol, as described by Kent, *et al.*,[4] for **12**. Nucleophilic displacements by cyanide anion of the *p*-toluenesulfonyloxy anion from a primary alcohol *p*-toluenesulfonate or of the iodide anion from 6-deoxy-6-iodo hexose and hexitol derivatives to form nitriles have recently been reported.[5]

In an alternative procedure, which is similar to that of Bayly and Turner,[2] 2,4-*O*-ethylidene-1-*O*-(*p*-totylsulfonyl)-D-erythritol (**4**)[6,7] was converted to 1-deoxy-

(1) (a) Taken from a thesis to be submitted by I. Z. to the Senate, The Hebrew University, Jerusalem, in partial fulfilment of the requirements for the degree of Ph.D. (b) A short communication of this paper has been presented at the 36th Meeting of the Israel Chemical Society, Oct 1966; *Israel J. Chem.*, **4**, 92p (1966).

(2) R. J. Bayly and J. C. Turner, *J. Chem. Soc., Org. Sect.*, 704 (1966).
(3) I. Ziderman and E. Dimant, *J. Org. Chem.*, **31**, 223 (1966).
(4) P. W. Kent, K. R. Wood, and V. A. Welch, *J. Chem. Soc.*, 2493 (1964).
(5) J. M. Sugihara, W. J. Teerlink, R. Macleod, S. M. Dorrence, and C. H. Springer, *J. Org. Chem.*, **28**, 2079 (1963).
(6) F. C. Hartman and R. Barker, *ibid.*, **28**, 1004 (1963).
(7) M. Ikehara and E. Ohtsuka, *Chem. Pharm. Bull.* (Tokyo), **11**, 1095 (1963).

2,4-*O*-ethylidene-1-iodo-D-erythritol (**5**). The latter reacted with sodium cyanide to DMSO at 37° to form 2-deoxy-3,5-*O*-ethylidene-D-*erythro*-pentononitrile (**6**). Reduction of **6** with an excess of Raney nickel[8] in aqueous acetic acid (20%) at room temperature, yielded mainly the 2-deoxy pentose (**7**). The reduced reaction mixture was hydrolyzed and deionized, and the product was isolated in 23% yield (based on **6**) as its *N*-phenylglycosylamine.

Experimental Section[9]

1-[(Benzyloxycarbonyl)amino]-1-deoxy-D-erythritol (9).—1-Amino-1-deoxy-2,4-*O*-ethylidene-D-erythritol (**1**,[3] 14.7 g, 0.1 mole) dissolved in 1 *N* sulfuric acid (125 ml) was hydrolyzed for 48 hr at 60° in an open flask.[16] The solution was cooled to room temperature and sodium carbonate (anhydrous, 17.2 g, 0.162 mole) was added in small portions. Paper chromatography revealed in the solution only one new ninhydrin reactive compound [**8**, R_f (in c) 0.054, Whatman No. 1 paper]. Benzyloxycarbonyl chloride (21.3 ml, 0.15 mole) was added in five portions within 1 hr with effective magnetic stirring. Crystals started to appear and gas was evolved a short time after the start of the addition of the chloride. Stirring with ice-bath cooling was continued for 4 hr. The crystals were collected by suction and dried *in vacuo* over sodium hydroxide. The product (21.7 g, 85%) melted at 95–103°, and was crystallized from ethyl acetate: mp 109–110°, $[\alpha]^{28}D$ −10.5° (*c* 1.2, methanol).

Anal. Calcd for $C_{12}H_{17}NO_5$ (255.26): C, 56.46; H, 6.71; N, 5.49. Found: C, 56.59; H, 6.53; N, 5.72.

2,3,4-Tri-*O*-benzoyl-1-[(benzyloxycarbonyl)amino]-1-deoxy-D-erythritol (10).—Benzoyl chloride (53.0 ml, 0.45 mole) was added dropwise to an ice-cooled and stirred solution of 1-[(benzyloxycarbonyl)amino]-1-deoxy-D-erythritol (**9**, 25.5 g, 0.1 mole) in pyridine (250 ml). The reaction mixture was left overnight at room temperature, about 160 ml of pyridine was removed under vacuum at 45°, and the residue was poured with stirring into ice–water (2 l.). The benzoate was filtered by suction and taken up in benzene (300 ml), and the solution was washed with alkali, acid, and water and dried (calcium chloride). The benzene solution was concentrated to about 200 ml and petroleum ether (bp 60–80°) was added to turbidity. The crystalline benzoate, mp 95–98° (50.2 g, 89%), was collected by suction. Addition of petroleum ether to the filtrate yielded a second crop of mp 91–94° (1.6 g, 2.8%). Three crystallizations from the same solvents produced the analytically pure ester: mp 100°, $[\alpha]^{29}D$ −1.7° (*c* 8, chloroform).

Anal. Calcd for $C_{33}H_{29}NO_8$ (567.59): C, 69.83; H, 5.15; N, 2.46. Found: C, 70.09; H, 5.29; N, 2.39.

1-Amino-2,3,4-tri-*O*-benzoyl-1-deoxy-D-erythritol Hydrobromide (11).—2,3,4-Tri-*O*-benzoyl-1-[(benzyloxycarbonyl)amino)]-1-deoxy-D-erythritol (**10**, 5.7 g, 0.01 mole) was dissolved in hydrogen bromide–saturated glacial acetic acid (15 ml). The benzoate dissolved gradually with evolution of gas. The solution was left overnight at room temperature and poured with stirring into ether (250 ml). The oil that separated crystallized as fine needles which were dried under vacuum over sodium hydroxide. The salt (**11**) was crystallized from methanol and ether: mp 164–165° (4.1 g, 80%), $[\alpha]^{28}D$ +14.1° (*c* 1.1, methanol).

Anal. Calcd for $C_{25}H_{24}BrNO_6$ (514.38): C, 58.37; H, 4.70; N, 2.72. Found: C, 58.16; H, 4.70; N, 2.82.

2,3,4-Tri-*O*-benzoyl-1-chloro-1-deoxy-D-erythritol (12).—Nitrosyl chloride[17] (10 ml, 216 mmoles) was added to an ice-cooled solution of 1-amino-2,3,4-tri-*O*-benzoyl-1-deoxy-D-erythritol hydrobromide (**11**, 10 g, 195 mmoles) in chloroform (40 ml). The reaction mixture was left overnight at room temperature and concentrated (room temperature). The solid residue was dissolved in methanol and the solution was concentrated to dryness. Crystallizations from benzene–petroleum ether yielded needles, mp 152°.

Anal. Calcd for $C_{25}H_{21}ClO_6$ (452.90): C, 66.30; H, 4.67. Found: C, 66.02; H, 4.35.

Kent, *et al.*,[4] prepared **12** in a different way, mp 159–160°.

2,3,4-Tri-*O*-benzoyl-1-bromo-1-deoxy-D-erythritol (13).—2,3,4-Tri-*O*-benzoyl-1-[(benzyloxycarbonyl)amino]-1-deoxy-D-erythritol (**10**, 11.3 g, 20 mmoles) was added to a stirred solution of hydrogen bromide in glacial acetic acid (50% w/v, 25 ml), and complete solution was achieved at room temperature after 2 hr. The solution was stirred with ice-bath cooling, and sodium nitrite (5.5 g, 80 mmoles) was added during 3–4 hr. Crystals started to form and the solution became viscid. The reaction mixture was left overnight at room temperature, and the dark brown solid was suspended in iced water with stirring (hood, benzyl bromide fumes). The crystals were filtered by suction, washed with water, and dissolved in benzene. The benzene solution was washed with water until acid free, dried (calcium chloride), and concentrated to dryness. Crystallization from benzene yielded the product, mp 162° (5.9 g, 60%), raised by several recrystallizations from benzene to mp 167°, R_f [tlc, (b)] 0.67, $[\alpha]^{28}D$ +22° (*c* 2.0, chloroform).

Anal. Calcd for $C_{25}H_{21}BrO_6$ (497.35): C, 60.36; H, 4.25; Br, 16.06. Found: C, 60.65; H, 4.17; Br, 15.79.

2,3,4-Tri-*O*-benzoyl-1-deoxy-1-iodo-D-erythritol (14).—A solution of 2,3,4-tri-*O*-benzoyl-1-bromo-1-deoxy-D-erythritol (**13**, 4.0 g, 8 mmoles) and dried sodium iodide (2.4 g, 16 mmoles) in acetone (100 ml) in a sealed tube was maintained in a boiling water bath for 9 hr. The crystals formed were removed by suction. The filtrate was concentrated to dryness, and the residue was extracted with chloroform (four 35-ml portions). The combined extracts were washed with a dilute sodium thiosulfate solution and with water, and dried (sodium sulfate). The solution was concentrated to dryness and the residue was crystallized from benzene–petroleum ether (bp 60–80°): mp 167° (3.3 g, 75%). After treatment with Norit, the product was recrystallized twice from chloroform–methanol, once from ethanol, and finally from benzene–petroleum ether: mp 172°, $[\alpha]^{28}D$ +14.4° (*c* 1.0, chloroform).

Anal. Calcd for $C_{25}H_{21}IO_6$ (544.33): C, 55.16; H, 3.88. Found: C, 55.38; H, 4.07.

Displacement of the bromine atom of **13** with cyanide was attempted with sodium, potassium, silver, mercuric, or cuprous cyanide, in different solvents (ethanol, acetone, acetonitrile, benzene, DMF, DMSO), and different temperatures and time periods. The reaction mixtures were filtered, and the filtrate was distributed between benzene and water. No nitrogen-containing compound was found in the organic phase. Attempted displacements of **12** and of **14** with some of the mentioned cyanides were equally unsuccessful.

1-Deoxy-2,4-*O*-ethylidene-1-iodo-D-erythritol (5).—A solution of 2,4-*O*-ethylidene-1-*O*-(*p*-tolylsulfonyl)-D-erythritol (**4**,[18] 37.4 g, 0.124 mole) and dried sodium iodide (37.4 g, 0.248 mole) in dry acetone (260 ml) was maintained in a closed vessel in a boiling water bath for 5 hr. The calculated amount of sodium *p*-toluene-

(8) B. Staskun and O. G. Backeberg, *J. Chem. Soc.*, 5880 (1964).

(9) Cyanide salts were dried under vacuum over phosphorus pentoxide. DMSO was dried with alumina followed by vacuum distillation. Reaction mixtures were stirred magnetically. Evaporations were carried out under vacuum. Melting points were determined in a Buchi melting point apparatus (Tottali) and were not corrected. Unless otherwise stated, chromatography was carried out on thin layers of silica gel[10] using the solvents (a) ethyl acetate–cyclohexane, 4:1; (b) ethyl acetate–cyclohexane, 1:1; (c)[11] 1-butanol–ethanol–water, 45:5:50. Compounds were detected with naphthoresorcinol–phosphoric acid[12] or with iodine vapor. Amines were identified with ninhydrin,[13] reducing sugars were identified with alkaline silver nitrate,[14] and 2-deoxy pentoses were identified with diphenylamine reagent.[15] Silicic acid used for column chromatography was an analytical reagent, 100 mesh (Mallinckrodt). Infrared spectra were obtained with a Perkin-Elmer grating spectrophotometer, Model 337. Microanalyses were carried out by the Microanalysis Laboratory of the Weizmann Institute of Science, Rehovoth, Israel.

(10) Kieselgel D-5, silica gel for tlc was produced by Camag, Muttenz, Switzerland.

(11) S. M. Partridge, *Biochem. J.*, **42**, 238 (1948).

(12) K. Randerath, "Thin-Layer Chromatography," D. D. Libman, Translator, Verlag Chemie, Weinheim, 1963, p 200.

(13) R. J. Block, E. L. Durrum, and G. Zweig. "Paper Chromatography and Paper Electrophoresis," 2nd ed, Academic Press Inc., New York, N. Y., 1958, p 124.

(14) Reference 13, p 178.

(15) Z. Dische, *Mikrochemie*, **2**, 4 (1930), cited in Z. Dische, *Methods Carbohydrate Chem.*, **1**, 505 (1962).

(16) C. E. Ballou, *J. Am. Chem. Soc.*, **82**, 2585 (1960).

(17) J. R. Morton and H. W. Wilcox, *Inorg. Syn.*, **4**, 48 (1953).

(18) Compound **4** was prepared according to Ikehara and Ohtsuka.[7] The concomitantly formed 2,4-*O*-ethylidene-1,3-di-*O*-(*p*-tolylsulfonyl)-D-erythritol (**3**), mp 65–67° (lit.[19] mp 65–67°), was removed from crude **4** by crystallization from dilute methanol. Pure **4** was obtained from the filtrate, mp 63–64°, $[\alpha]^{30}D$ −42.8° (*c* 0.95, methanol) (lit.[2] mp 64.5–65° $[\alpha]D$ −41.5°).

(19) S. A. Barker, A. B. Foster, A. H. Haines, J. Lehmann, J. M. Webber, and G. Zweifel, *J. Chem. Soc.*, 4161 (1963).

sulfonate was collected by filtration of the cooled reaction mixture. The filtrate was concentrated to dryness and the residue was thoroughly extracted with cold benzene. The combined extracts were concentrated to a small volume and petroleum ether was added to turbidity. The crystalline product (mp 53–54°, 19.3 g, 60%) and an additional crop obtained from the mother liquor (mp 53°, 10.1 g, total yield 91.5%) were recrystallized from the same solvents: mp 54°; R_f (a) 0.58, (b) 0.36; $[\alpha]^{28}D$ −48.2° (*c* 1.0, chloroform) (lit.[2] mp 47–55°, $[\alpha]D$ −43.4°).

Anal. Calcd for $C_6H_{11}IO_3$ (258.95): C, 27.92; H, 4.29; I, 49.18. Found: C, 28.16; H, 4.30; I, 49.27.

2-Deoxy-3,5-*O*-ethylidene-D-*erythro*-pentononitrile (6).—1-Deoxy-2,4-*O*-ethylidene-1-iodo-D-erythritol (**5**, 5.16 g, 0.02 mole), sodium cyanide (1.078 g, 0.022 mole), and DMSO (20 ml) were stirred at 36° for 17.5 hr. The reaction mixture was passed through a silicic acid column (100 g) and eluted with a mixture of ethyl acetate–cyclohexane, 4:1. The eluate was collected in 5-ml fractions, which were analyzed by tlc. Fractions containing the product were pooled and concentrated. The residue was crystallized from ethyl acetate–petroleum ether (bp 40–60°) yielding the nitrile **6**, mp 102° (1.5 g, 48%). Two further crops from the mother liquor raised the total yield to 78%. Recrystallization of the first crop from the same solvents formed the pure nitrile: mp 102–103°; R_f (a) 0.39, (b) 0.13; $[\alpha]^{28}D$ −44° (*c* 0.9, chloroform); infrared 2245 cm^{-1} (C≡N) (lit.[2] mp 105–105.5°, $[\alpha]D$ −38°).

Anal. Calcd for $C_7H_{11}NO_3$ (157.17): C, 53.50; H, 7.05; N, 8.90. Found: C, 53.73; H, 7.16; N, 8.66.

2-Deoxy-*N*-phenyl-*erythro*-pentosylamine.—Raney nickel was prepared[8] from Raney's alloy (1.25 g), added in portions to 2 *N* sodium hydroxide (24 ml) with stirring. The suspension was stirred for 30 min and the catalyst was washed free of alkali with several changes of water (litmus). The catalyst was suspended in aqueous acetic acid (20%, 7.5 ml) and 2-deoxy-3,5-*O*-ethylidene-D-*erythro*-pentononitrile (**6**, 314 mg, 2 mmoles) was added. The mixture was stirred for 10 min. The catalyst was removed by gravity filtration and was washed with water until free of reducing material (Fehling). The combined filtrates and Amberlite IR-120(H) (4–5 g) were stirred for 2–3 hr in an oil bath (90°) while nitrogen was bubbled through the mixture. The original green solution turned colorless and tlc revealed a 2-deoxypentose, which could not be separated from 2-deoxy-D-*erythro*-pentose, R_f (c) 0.43 (Pfanstiehl). The resin was washed with water until free of reducing material. The filtrates were passed through a Duolite A-4 column (26 ml, 13 × 175 mm), and the column was washed with water until freed of reducing material. The eluate was concentrated under vacuum to a syrup, to which aniline (0.28 ml, 3 mmoles) was added, and the deoxy sugar derivative was crystallized from water and methanol, mp 164° (96 mg, 23%). Recrystallization from ethanol raised the melting point to 167–168°, $[\alpha]^{28}D$ +169° (*c* 0.58, pyridine, 10 min) [lit.[20] mp 171–172°, $[\alpha]^{17}D$ +164° (pyridine after 10 min)]. The product showed no change in melting point when mixed with a sample prepared from authentic 2-deoxy sugar.

Registry No.—2-Deoxy-D-*erythro*-pentose, 7640-21-3; **9**, 7718-67-4; **10**, 7721-91-7; **11**, 7705-70-6; **12**, 7705-71-7; **13**, 7718-68-5; **14**, 7705-72-8; **5**, 7284-12-0; **6**, 7705-74-0.

(20) L. Hough, *J. Chem. Soc.*, 3066 (1953).

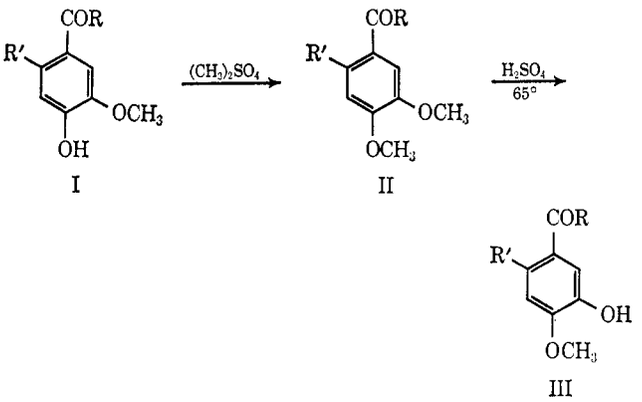
Selective Demethylation of 3,4-Dimethoxy-Substituted Aromatic Aldehydes and Ketones

A. BROSSI, H. GURIEN, A. I. RACHLIN, AND S. TEITEL

Chemical Research Department, Hoffmann-La Roche Inc., Nutley, New Jersey 07110

Received December 5, 1966

It has been shown that acid hydrolysis of 6,7-dimethoxy-3,4-dihydroisoquinolines causes preferential cleavage of the 7-methoxyl group.[1] These compounds may be visualized as aminocarbonyl derivatives in which ether cleavage occurs at the methoxyl group *meta* to the potential carbonyl function. The two 3,4-dimethoxy-substituted aromatic aldehydes, veratraldehyde (IIa) and 6-methylveratraldehyde (IIb), and the ketone, 3,4-dimethoxyacetophenone (IIc), which can be prepared easily from the readily available monomethyl ethers, vanillin (Ia), 6-methylvanillin (Ib), and 4-hydroxy-3-methoxyacetophenone (Ic), respectively, could be expected to react in an analogous fashion and were therefore chosen for model experiments. Our assumption proved to be correct[2] and we now wish to report a facile conversion of the two 4-hydroxy-3-methoxy-substituted aromatic aldehydes (Ia and Ib) and the ketone (Ic) into the corresponding 3-hydroxy-4-methoxy isomers (IIIa, IIIb, and IIIc, respectively) by acid hydrolysis of the intermediate O-dimethyl ether derivatives.



a, R = R′ = H
b, R = H; R′ = CH_3
c, R = CH_3; R′ = H

Thus veratraldehyde (IIa) and 6-methylveratraldehyde (IIb) on treatment with concentrated sulfuric acid at 65°, are converted to isovanillin (IIIa) and 6-methylisovanillin (IIIb) in yields of 61 and 64%, respectively. 6-Methylisovanillin (IIIb), a new compound, was different from the known isomeric 6-methylvanillin (Ib)[3] and both compounds on methylation gave the same known product (IIb).[4] Under the same conditions 3,4-dimethoxyacetophenone (IIc) is converted to acetoisovanillone (IIIc) in 58% yield.

Experimental Section[5]

6-Methylisovanillin (IIIb).—6-Methylveratraldehyde (IIb,[4] 225 g, 1.25 moles) was dissolved in 1125 ml of stirred, concentrated sulfuric acid at room temperature under nitrogen. The solution was heated to and stirred at 65° for 20 hr under nitrogen and then it was cooled and poured onto 7.5 kg of ice. After stirring for 15 min the mixture was filtered and the filter cake was washed with 500 ml of water. The filtrate, including the washes, was extracted with six 250-ml portions of methylene chloride. The combined methylene chloride extracts, the filter

(1) H. Bruderer and A. Brossi, *Helv. Chim. Acta.*, **48**, 1945 (1965).

(2) This is in marked contrast to the behavior of 3,4,5-trimethoxybenzaldehyde which, under acidic conditions, is preferentially cleaved at the *para* position to give syringaldehyde: I. A. Pearl and D. L. Beyer, *J. Am. Chem. Soc.*, **74**, 4262 (1952).

(3) J. P. Koetschet, *Helv. Chim. Acta.*, **13**, 479 (1930). This compound was kindly prepared by Dr. A. Focella and had mp 175–176°.

(4) A. St. Pfau, *ibid.*, **22**, 550 (1939).

(5) All melting points (corrected) were taken in open capillary tubes with a Thomas–Hoover melting point apparatus. Thin layer chromatography employed silica gel G plates and the infrared spectra were taken in chloroform.