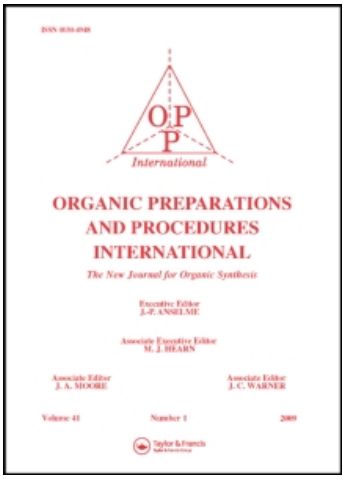

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AN IMPROVED SYNTHESIS OF (S)-3-METHYL-γ-BUTYROLACTONE

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(s, 1H), 7.30 (m, 6H); mass spectrum: 360, 358, 354 (M^+ for $^{35}Cl_3$), 319 (base peak, loss of Cl).

Anal. Calcd for $C_{17}H_{13}Cl_3O_2$: C, 57.41; H, 3.69; Cl, 29.91
Found: C, 57.34; H, 3.64; Cl, 29.89

2-Veratryl-3-chloro-5,6-dimethoxy-1H-inden-1-ol (3f).- The title compound was obtained in 3% purified yield by fractional recrystallization of the reaction product from a room temperature reaction of 1a with DMF-$POCl_3$ as colorless solid: mp. 189-190°. IR (mull): 3200-3400 cm^{-1}, ^{1}H-NMR ($CDCl_3$): δ 1.95 (d, J = 9 Hz, 1H), 3.88 (s, 12H), 5.40 (d, J = 9 Hz), 6.82-7.50 (m, 5H).

Anal. Calcd for $C_{19}H_{19}ClO_5$: C, 62.89; H, 5.28; Cl, 9.77
Found : C, 63.03; H, 5.24; Cl, 9.61

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AN IMPROVED SYNTHESIS OF (S)-3-METHYL-γ-BUTYROLACTONE

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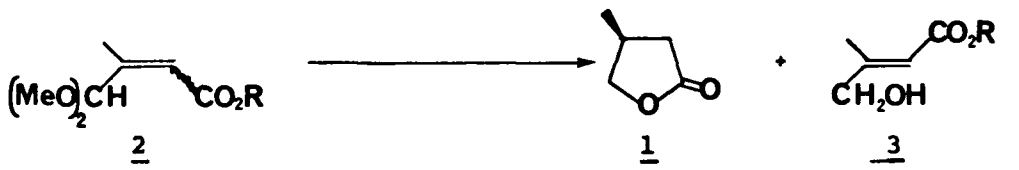
(S)-(-)-3-Methyl-γ-butyrolactone (1), a useful chiron for the synthesis of natural products[1] and of some intermediates for the construction of steroid side chains,[2] has been obtained by baker's yeast biohydrogenation of the unsaturated ethyl ester 2a.[3] Ethyl (S)-3-methyl 4-hydroxybutanoate and the (E)-unsaturated ester 3a are the initial products of the above biohydrogenation; the lactone 1 can be obtained by distillation from the cyclization reaction carried out subsequently on the crude fermentation products.

However, when the preparation of the lactone 1 was repeated by us on a gram scale, we were not able to obtain a quantitative cyclization, and the lactone 1 was always contaminated by



2 1 3

a) R = Et b) R = K

the corresponding saturated (S)-hydroxyester. The maximum recorded optical rotation of distilled lactone 1 was seldom superior to -19° (lit.[3]: $[\alpha]_D$ -24.7° for 97% ee). A few examples of the reduction of acids or salts (instead of the ester) by baker's yeast have been reported.[4,5] In the case of salts of 3-ketoacids, also a reverse enantioselectivity had been observed.[6] We therefore, prepared the potassium salt 2b from ethyl ester 2a with a 7:3 E/Z ratio[7] and incubated it with fermenting baker's yeast. After acidic work-up of the incubation mixture and distillation., the lactone was obtained in 60% yield with excellent optical purity ($[\alpha]_D$ -23°, 90% ee). It should be noted that the yields of lactone 1 obtained from the ethyl ester 2a strongly depended upon the E/Z ratio and was never superior to 40%; this suggests that the (Z)-isomer of 2a was indeed the substrate of the biohydrogenating system.[7] In the case of the potassium salt 2b, the initial ratio of the two isomeric salts did not influence the amount of saturated compound obtained by biohydrogenation. This fact makes it more advantageous to use of the potassium salt 2b for the preparation of lactone 1 in good yields and high optical purity.

EXPERIMENTAL SECTION

60-MHz ^{1}H-NMR spectra were recorded on a Varian EM 360 L spectrometer. Optical rotations were measured on a Perkin-Elmer Model 241 polarimeter. Gas chromatographic analyses were performed on a Carlo Erba Fractovap 2101. TLC analyses were carried out on silica gel Merck 60 F254 plates and column chromatographies were performed on silica gel Merck 60 (230-240 mesh). Distillations for analytical purposes were performed on a glass tube oven Buchi GKR-50.

Potassium Salt of 4,4-dimethoxy-3-methyl-2-butenoate (2b).- Ethyl 4,4-dimethoxy-3- methyl-2-butenoate (2a) (21 g, 0.11 mole) was added to a solution of potassium hydroxide (6.27 g) in ethanol (40 ml). The reaction mixture was refluxed for 4 hrs and when the hydrolysis was complete, evaporation of the solvent under reduced pressure afforded potassium salt 2b (21.7 g, 99%), which was directly used for the incubation. ^{1}H-NMR (D_2O): δ 1.7 and 1.8 (s, 3H, 0.9H Z and 2.1H E), 3.4 (s, 6H), 4.7 and 4.8 (s, 1H, 0.3H Z and 0.7H E), 5.9-6.1 (m, 1H).

(S)-(-)-3-Methyl-γ-butyrolactone (1).- To a solution of saccharose (85 g) in water (1.5 l), baker's yeast (170 g) was added. After 1 hr at 30°, the potassium salt 2b was added (21.7 g, 0.109 moles) and the reaction mixture was kept at 30° with stirring for 96 hrs. The progress of

the reaction was monitored by ^{1}H-NMR. The reaction mixture was filtered through a pad of Celite and the aqueous filtrate was treated with potassium hydroxide, concentrated to 200 ml under reduced pressure, acidified with conc. HCl and extracted with dichloromethane (5 x 400 ml). After drying on sodium sulfate, the solvent was evaporated and the crude oil distilled to yield the pure lactone 1 (6.54 g, 60%), bp. 140°/16 mmHg; ^{1}H-NMR ($CDCl_3$): δ 1.2 (d, 3H), 2.0-3.0 (m, 3H), 3.8-4.9 (m, 2H); $[\alpha]_D$-23° (c = 4, MeOH).

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A SIMPLE REDUCTION OF ARALKYL KETONES TO ALCOHOLS

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Catalytic transfer hydrogenation has been widely studied in the past three decades.[1] Palladium-catalysed ammonium formate reduction of aromatic halides,[2] nitriles,[3] nitro compounds[2,4] and α,β-unsaturated carbonyl compounds[5] has been reported. Aromatic ketones are reduced to the corresponding aromatic hydrocarbons using Pd/C-formic acid in refluxing ethanol;[6] aromatic aldehydes and ketones are also reduced to the hydrocarbons using palladium-carbon/cyclohexene or limonene.[7] The hitherto undescribed reduction of aralkyl