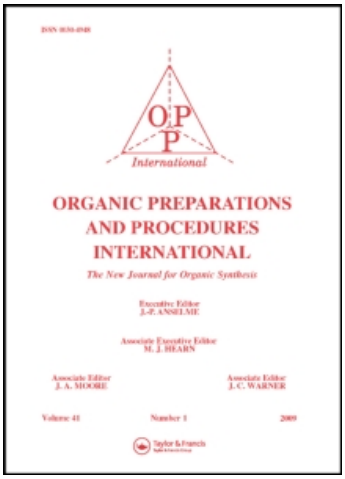

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SYNTHESIS OF EVERNIPENTANONE BY ADDITION OF *n*-BUTYLLITHIUM ON ETHYL EVERNINATE

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SYNTHESIS OF EVERNIPENTANONE BY ADDITION OF *n*-BUTYLLITHIUM ON ETHYL EVERNINATE

Submitted by (03/30/92)

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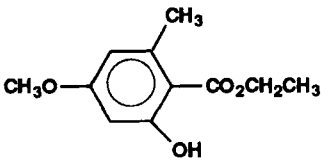
The preparation of tertiary alcohols by addition of organolithiums to esters has been suggested to proceed *via* the intermediate ketones from theoretical deductions and demonstrated by infrared spectroscopy of the Li-complexes in solution.[1] The present work describes the synthesis of 2-hydroxy-4-methoxy-6-methylvalerophenone (evernipentanone, **2**) by addition of *n*-butyllithium to ethyl everninate (**1**), thus adding a major argument to the theory.

When *n*-butyllithium was added to methyl 2,4,6-trimethylbenzoate, the starting material was



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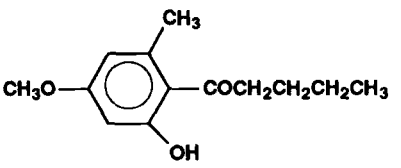

2

recovered quantitatively because of steric hindrance, whereas methyl 2-hydroxy-4-methoxybenzoate gave the expected tertiary alcohol. It therefore appeared that the formation of evernipentanone (**2**) is

the result of two effects, namely steric hindrance and the stabilization of the ketone through chelation of the carbonyl group with the hydroxy group at the *o*-position. Evernipentanone (**2**), obtained in 80% yield, does not appear to have been reported so far; evernipentanone (**2**) is obtained in only 60% yield with *n*-BuLi and tetraethylenediamine (TMED).[2]

EXPERIMENTAL SECTION

Melting points were determined on a Kofler apparatus using a microscope and are corrected. The MS (electron impact) were determined on an AEI MS 50 spectrometer and the ^{1}H NMR spectra on a Bruker 200 MHz apparatus, ppm from zero TMS. Thin layer chromatography was carried out on Schleicher-Schull SiO_2 fluorescent films for analytical purposes, and on 1 mm thickness plates for preparative isolation, UV observation at 254 nm with a Desaga lamp and extraction from the scraped layer with ethyl acetate. The reagents were all purchased from Aldrich-Europe Chemie.

Evernipentanone (2).- Ethyl everninate (**1**) was prepared from the commercially available ethyl orsellinate by methylation with methyl iodide at reflux in anhydrous acetone in presence of freshly ignited K_2CO_3, according to a reported method.[3] Diazomethane also methylates the *para* OH group of ethyl orsellinate selectively, albeit in poorer yield .

To a solution of ethyl everninate (**1**) (1 mM) in anhydrous THF (8 ml) at -78° (dry N_2), was added a cold *n*-BuLi (7 mM; from a 15% solution in hexane) with a syringe through a rubber septum with stirring. The reaction mixture was kept for 1 hr at -78° and then for 18 hrs at room temperature. Hydrolysis was carried out at 0° by adding cold 2N HCl with stirring, until pH 1. The organic products were extracted by ethyl acetate (50 ml x 2) after addition of water (50 ml), further washing the organic phase with H_2O (20 ml), prior to drying over Na_2SO_4 and evaporation. The reaction products were isolated from the concentrates by preparative SiO_2 TLC (pentane-ethyl acetate 95:5). The product **2** was purified further on TLC films for analytical purposes (Rf 0.55) and spontaneously crystallized as colorless prisms (135 mg, 80% yield), mp. 59-63°. MS m/z (%): 222 M^+ (95), 180 M-42$^+$ (20) McLafferty rearrangement, 166 M-56$^+$ (92), 165 M-57$^+$ (100) oxonium ion; UV (MeOH) λ_{max} [nm,(ε)] 218 (7.7 x 10^3), 270 (4.6 x 10^3). ^{1}H NMR ($CDCl_3$): δ 13.55 (s, 1H, phenolic chelated OH), 6.30 and 6.32, (s, 1H each, aromatic protons, J = 2 Hz), 3.85 (s, 3H, OCH_3), 2.90 (t, 2H, CH_2CO, J = 7.5 Hz), 2.58 (s, 3H, CH_3 at C-6), 1.70 (q, 2H, C-3, J = 7.5 Hz), 1.38 (sext., 2H, CH_2, C-4, J = 7.5 Hz), 0.96 (t, 3H, CH_3 aliphatic, J = 7.5 Hz).

Anal. Calcd. for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C 70 42; H, 8.28

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SYNTHESIS OF β- AND γ-ALKOXY AND β-DIMETHYLAMINO 1- AND 2-SUBSTITUTED-1,3-CYCLOPENTADIENES

Submitted by: (02/03/92) William S. Rees, Jr.* and Kerstin A. Dippel

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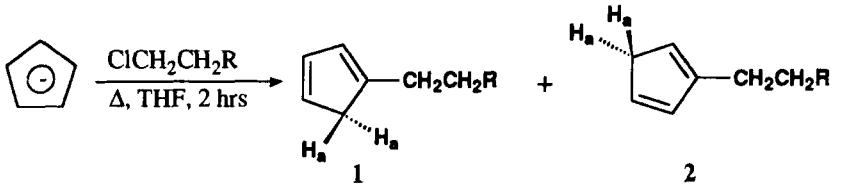
As part of our research effort directed at the preparation of volatile organometallic compounds of the group 2 elements Ca, Sr, and Ba,[1] we needed cyclopentadienide anions exocyclically β- or γ-substituted with ether or amine functionality capable of intramolecular coordination to the central metal atom. Although many ring-, and a few α-exocyclic heteroatom-substituted cyclopentadienes are known,[2] they were not useful to our need which required the presence of an alkylene chain linker between the cyclopentadiene and the heteroatom of appropriate length and flexibility to coordinate with the metal center.[3]

Compounds **1** and **2** were prepared as regioisomeric mixtures[4] by reaction of the appropriate primary alkyl chlorides with cyclopentadiene anion. Although reduced pressure distillation may be employed for all these purifications, it was necessary only for the complete purification of **1c, 2c**. All new regioisomeric mixtures of compounds were characterized by ^1H and ^{13}C NMR, low and high resolution MS, and combustion analyses. They have been utilized in the preparation of elementocene compounds of main group and transition elements.[5] Although not necessary in this instance, presumably, the regioisomers could be separated if desired.



1 **2**

a) R = OMe b) R = OEt c) R = CH_2OEt d) R = NMe_2

EXPERIMENTAL SECTION

All reactions were carried out following standard techniques for the manipulation of air-sensitive compounds[6] in oven dried glassware (130°) under an atmosphere of oxygen- and moisture-free nitrogen. Nitrogen was dried by sequential passage through 50 mm x 1 m columns of Ridox[7] and Sicapent.[8]