Mild esterification with diazomethane; Methyl-2E,4E-hexadienoate

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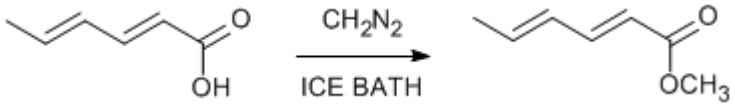
John MacMillan (john.macmillan@temple.edu)



Chemicals Used

Diazald 99% (Aldrich, D2,800-0)
trans,trans-2,4-Hexadienoic (Sorbic) acid (Aldrich, 24,019-9)
Potassium hydroxide, pellets, 85%, A.C.S reagent (Aldrich, 22147-3)
Glacial acetic acid, 99.7%, A.C.S. reagent (Aldrich, 24,285-3)
Ethyl Alcohol, 190 proof, 95+%, A.C.S. spectrophotometric grade (Aldrich, 49,351-1)
Sodium hydrogen carbonate, 99.7%, A.C.S. reagent, Aldrich, 43,144-3
Ether, anhydrous, 99.8%, A.C.S. reagent (Aldrich, 44,354-9)

Procedure

Diazomethane was generated "in situ" by the reaction of “Diazald” with base, described in the lead reference. The reaction was run in a totally rubber stopper fitted apparatus, consisting of a 100 ml 3 neck distilling flask fitted with dropping funnel ,water condenser, magnetic stirring bar, hot plate-magnetic stirrer and nitrogen inlet. The outlet of the condenser led with tygon tubing to a two holed rubber adapter fitting a 250 ml Erlenmeyer flask charged with 3.7 g (0.033 mole) sorbic acid in 100 ml anhydrous diethyl ether . The distilling flask was charged with 2.5 g of potassium hydroxide pellets, 4 ml deionized water and 13 ml 190 proof ethanol.. The addition funnel was charged with 12 g Diazald in 100 ml anhydrous diethyl ether. The distilling flask was warmed to ~ 65^0 C with a water bath and stirring was commenced. The Erlenmeyer flask containing the sorbic acid was cooled to ~ 0^0 C with an ice bath and equipped with a magnetic stirrer and hot plate-magnetic stirrer. Rubber Tygon tubing led from the Erlenmeyer flask to a second 100 ml rubber stoppered Erlenmeyer flask containing ~ 30 ml glacial acetic acid , in

order to trap any traces of unreacted diazomethane. Stirring was commenced in the cooled Erlenmeyer flask containing the sorbic acid, while the ether solution of Diazald was added dropwise over 3 hours to the warmed distilling flask containing the potassium hydroxide. Water bath temperatures were maintained at 65-70^0 C during the addition. A yellow solution of diazomethane in ether distilled into the cooled Erlenmeyer flask and reacted with the sorbic acid. After complete addition of the Diazald solution an additional 20 ml anhydrous ether was added through the dropping funnel into the distilling flask and distilled into the cooled 250 ml Erlenmeyer flask. The 250 ml Erlenmeyer flask was disassembled and the ether/methyl sorbate solution shaken 4 times with 20 ml portions of saturated sodium bicarbonate solution, then 6 times with 10 ml portions of deionized water. The extracts were then neutral to Litmus. The ether solution was dried over 5g anhydrous magnesium sulfate, decanted, and the ether removed on a rotary evaporator. Short path distillation of the residual oil at water aspirator pressure with an oil bath gave a center cut of 2.0 g (48%) of > 98% pure methyl sorbate isomers, determined by gas chromatography. The ester contained ~ 10% 2-E,4-Z isomer, which was also present in the commercial material. Other runs were typically ~50% yield of distilled ester. This procedure, while requiring a somewhat involved setup, is best for unsaturated carboxylic acids with a tendence to isomerize under the strongly acidic esterification methods commonly employed.

Author's Comments

Caution! Diazomethane should always be generated in situ. Do not store solutions of diazomethane, as explosions have been reported. Do not use fritted glassware with this reagent. Employ rubber holed fittings. As a precaution we ran these reactions behind a small lead based blast shield, although no incidents occurred.

Data

B.p 70^o (25mm), Ir (film) 3025(m), 3000(m), 2950(m), 2850(m), 1720 (vs),1645(s),1615(s),1430(s),1370(m).1315(s).1290(m),1260(s),1240(s).1210(m),1185(m),1135(s),1075(m),1025(m),990(s),930(m),915(w), 890(m),850(m),840(m),785(m) and 700(m) cm^{-1} Pmr (60Mhz), CCl_4 δ7.18(m, 1H, Hβ), 6.15(m, 2H, Hγ + Hβ), 5.71(d, 1H, J=16Hz, Hα), 3.66(s,3H, OCH_3), 1.83(d, J=6Hz, 3H, methyl).

The ester contained ~10%-2E,4Z-isomer. The spectrum becomes fully first order on addition of $Eu(fod)_3$ (fod= 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato).

The isomers are fully resolved with lanthanide chemical shift reagents. See other references. Coupling constants for the 2E,4E isomer are: Jαβ = 16 Hz, Jβγ = 10 Hz, Jγ∆ = 15 Hz, J∆-CH_3 = 6 Hz.

Lead Reference

Derivatization of Carboxylic Acids with Diazomethane and Trimethylsilyldiazomethane: Convenient Methods and Artifacts

http://userpage.chemie.fu-berlin.de/~tlehmann/krebs/files_diazoalkanes.pdf

Other References

John H. MacMillan and Stephen S. Washburne, "Lanthanide Chemical Shift Reagents as Tools for Determining Isomer Distributions in 2,4-Hexadieneoates and Related Compounds", Organic Magnetic Resonance, Vol. 6, p250, (1974) DOI: 10.1002/mrc.1270060414

http://jhm2.homestead.com/files/8.pdf

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