

An efficient synthesis of Mikanecic acid using calcium chloride

S. Ravichandran

Assistant Professor in Chemistry , Saveetha School of Engineering, Saveetha University, Saveetha nagar, Thandalam, Chennai-602 105 (Tamilnadu).

Corres.author: ravichanduru@yahoo.com

Abstract: An efficient method for the synthesis of Mikanecic acid diesters from Baylis-Hillman adducts is reported using calcium chloride. The product is obtained in good yield.

Key Words: Mikanecic acid diesters, Baylis-Hillman adducts, Calcium chloride.

Introduction

Synthetic organic chemistry is one of the most developing, expanding and successful branches of science. During the last fifteen years, synthetic organic chemistry has seen enormous growth, not only in terms of development of new methodologies for construction of carbon-carbon and carbon-hetero atom bonds but also in terms of development of new reagents, catalysts, strategies, transformations and technologies often involving the concepts of atom economy.

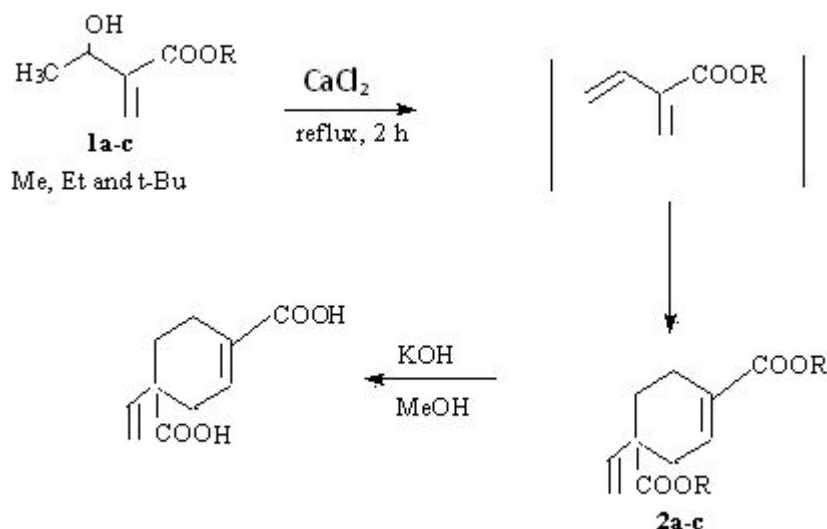
Recently use of inorganic solid supports¹⁻³ as catalysts has been developed resulting in milder conditions and easy experimental procedures. Calcium chloride catalyzed organic reactions⁴ are gaining importance owing to their inexpensive nature and special catalytic attributes in heterogeneous reactions.

Construction of quaternary carbon center has been one of the challenging and attractive areas in synthetic areas in synthetic organic chemistry, because

a number of biologically active natural products contain such structural sub-units⁵⁻⁸.

4-vinyl-1-cyclohexene-1,4-dicarboxylic acid (**Mikanecic acid**) is a terpenoid dicarboxylic acid, has attracted our attention owing to its special feature of having vinylic quaternary carbon center in a functionalized six membered cyclic system. Mikanecic acid was isolated in 1936 by Manske⁹ from the products of alkaline hydrolysis of the alkaloid Mikanoidine obtained from *Senecio mikakioides otto*. Many works have appeared regarding the history¹⁰, characterization and synthesis of racemic Mikanecic acid¹¹. The reaction of acetaldehyde with suitable acrylates in the presence of DABCO afforded Baylis-Hillman adducts¹²⁻¹⁷ (**1a-1c**) which on treatment with calcium chloride (0.168 g, 20 mol%) led directly to the formation of Mikanecic acid diesters (**2a-2c**), through Diels-Alder type self-dimerization of 1,3-butadiene-2-carboxylate (**Scheme 1, Table 1**).

Scheme 1 :

Table 1 . Synthesis of Mikanecic acid diesters^{a,b}

Substrate	Reaction time	product	Yield ^c (%)
1a	2	2a	42
1b	2	2b	48
1c	2	2c	49

^aAll reactions were carried out in 5 mm scale of Baylis-Hillman adduct in 5 ml Ethanol with CaCl_2 (0.168 g, 20 mol%) and the reaction mixture refluxed for 2 hr.

^bSatisfactory spectral data are obtained.

^cIsolated yield after column chromatography (2% ethylacetate in hexane).

Experimental

Melting points were determined in an open capillary tube with a Buchi melting point apparatus and are uncorrected. Elemental analyses were carried out using Perkin-Elmer 240C CHN-analyzer. IR spectra were recorded on a Perkin Elmer IR spectrophotometer. ¹H- NMR spectra was run in (CDCl_3) solvent at 200 MHz on a NMR spectrophotometer (chemical shifts in δ ppm).

General Procedure for the Synthesis of Mikanecic Acid:

All reactions were carried out in 0.01 mole scale of Baylis-Hillman adduct mixed with CaCl_2 (0.168 g, 20 mol%) in Ethanol (5ml) and the reaction mixture were refluxed for 2 hr. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature. Then the reaction mixture was acidified with 5 mL of concentrated HCl and the

lower layer was separated, washing the water layer with dichloromethane (DCM). The solid separated was filtered and recrystallized from methanol to give products, which were characterized by IR, NMR spectral data were obtained. The results obtained are very much consistent with literature report. The method reported here represents an indirect way of performing Diels-Alder reaction involving the same molecule as diene and dienophile generated *in situ* thus demonstrating the synthetic potentiality of the Baylis-Hillman reaction¹⁸⁻²⁴ leading to the synthesis of racemic Mikanecic acid.

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