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Facile synthesis of Mikanecic acid using calcium sulphate

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Abstract: In view of the emerging importance of the green chemistry principles in chemical and pharmaceutical industries, an efficient method for the synthesis of Mikanecic acid diesters from Baylis-Hillman adducts is reported using calcium sulphate ($CaSO_4.2H_2O$) as an environmental friendly and recycled catalyst. The product is obtained in good yield.

Key Words: Mikanecic acid diesters, Baylis-Hillman adducts, Solvent-free reactions, calcium sulphate.

INTRODUCTION

Due to environmental awareness, the development of simple, efficient and environmentally benign chemical processes or methodologies for the synthesis of complex structures are the major challenges for chemists. 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.

Due to the ever mounting environmental concern in the field of chemistry, it is advisable to easily recover and recycle catalysts, especially toxic metallic ones. Additionally, the challenge for a sustainable environment calls for clean procedures to avoid harmful organic solvents. 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-1cyclohexene-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 sulphate (15 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).

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 (CDCl₃) 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 CaSO₄.2H₂O (15

mol%) and the reaction mixture were refluxed for 1 hr in a water bath. The reaction was monitored by TLC using ethyl acetate/hexane (4/6). After completion of the reaction, the reaction mixture was cooled to room temperature and diluted with EtOH (20 mL). The resulting suspension was filtered through a Büchner funnel to recover the catalyst and the filtrate was poured into ice cold water (30 mL). The resulting precipitate was collected and recrystallized in EtOH to give the pure products, which were characterized by IR, NMR spectral data. The results obtained are very much consistent with literature report.

Scheme 1 :



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

Substrate	Product	Yield ^c (%)
1a	2a	52
1b	2b	60
1c	2c	54

^aAll reactions were carried out in 10 mm scale of Baylis-Hillman adduct with CaSO₄(15 mol%) and the reaction mixture refluxed for 1 hr.

^bSatisfactory spectral data are obtained.

^cIsolated yield after column chromatography.

The spectral and analytical data of the compounds (2a-2c) are given below.

224 (M·) ; *Anal.* Calcd for $C_{12}H_{16}O_4$: C, 64.28; H, 7.14 %. Found: C, 62.36; H, 6.82%.

2b: IR (neat): 1720, 1733, 1775 cm⁻¹; ¹H-NMR (200 MHz, CDCl3): δ 1.23 (3H, t), 1.27 (3H, t), 3.10-3.60 (6H, m), 4.13 (2H, 2q, J= 7 Hz), 5.85-6.21 (3H, m), 6.84 (1H, m) ; EI-MS: *m/z* 252 (M·) ; *Anal.* Calcd for C₁₄H₂₀O₄: C, 66.66; H, 7.93%. Found: C, 65.36; H, 7.76%.

2c: IR (neat): 1700, 1650 cm⁻¹; ¹H-NMR (200 MHz, CDCl3): δ 1.48 (9H, s), 1.49 (9H, s), 1.60-2.41 (6H, m), 5.08 (1H, dd), 5.88 (1H, dd), 6.84 (1H, m) ; EI-MS: *m*/*z* 308 (M·) ; *Anal.* Calcd for C₁₈H₂₈O₄: C, 70.12; H, 9.09 %. Found: C, 69.38; H, 8.47%.

Spectral data for Mikanecic acid

IR (KBr): 1690, 1640 cm⁻¹; ¹H-NMR (200 MHz, CDCl3): δ 1.67-2.82 (6H, m), 5.02-5.29 (1H, m), 5.75-6.04 (1H, m), 6.85 (1H, m), 12.42 (2H, s, br); ¹³C-NMR (50 MHz, CDCl3): δ 21.58, 29.09, 31.70, 46.53, 114.55, 129.31, 136.78, 140.29, 167.66, 175.21; EI-

REFERENCES

- K. Reshetova and Y. A. Ustynyuk, Russ. Chem. Bull., 53,335 (2004)
- G. Zhao, T. Jiang, H. Gao, B. Han, J. Huang and D. Sun, Green Chem., 6, 75 (2004).
- 3. A. Zoupy, A. Petit, F. Hamelin and D. Mathe, Synthesis, 1213 (1998)
- 4. B.Gangadasu, P.Narender, B.Chinna Raju and V.Jeyathirtha Rao, Indian J. Chem., 45B, 1259(2006).
- 5. S.F.Martin, Tetrahedron, 36, 419 (1980).
- 6. D.Romo, A.I.Mayer, Tetrahedron, 47, 9503 (1991).
- 7. J.Angelo, F.Dumas, A.Guingant, Tetrahedron Asymmetry, 3, 459 (1992).
- 8. K.Fuji, Chem. Rev., 93, 2037 (1993).
- 9. R.H.F.Manske, Canad. J. Res, 14B, 6 (1936).

MS: m/z 196 (M·); *Anal.* Calcd for C₁₀H₁₂O₄: C, 61.22; H, 6.12 %. Found: C, 57.48; H, 6.50 %.

CONCLUSION

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. The easy handling and workup combined with the easy available, non expensive, non toxic and recycled catalyst; good yields, **s**hort reaction periods and the needless reaction solvents are salient features of the catalyst that render the presented procedure relatively environmentally acceptable.

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- L.K.Sydnes, L.Skattbol, C.Chapleo, D.G. Lappord, Helv. Chim. Acta, 58, 2061(1975).
- 11. D.Basavaiah, S.Pandiaraju, P.K.S.Sharma, Tetrahedron Lett., 35, 4227 (1994).
- 12. V.V.L.Gowriswari, Ph.D. Thesis, University of Hyderabad, India (1989).
- 13. S.Ravichandran, Synth.Commun., 31,2059 (2001).
- S. Rafel, J.W. Leahy, J. Org. Chem., 62, 1521 (1997).
- D Basavaiah, A. J. Rao, T.Satyanarayana, Chem. Rev., 103, 811(2003).
- 16. P. Radha Krishna, E.Raja Sekhar, V. Kannan, Synthesis, 857 (2004).
- 17. P.Krishna, M. Narsingam, V.Kannan, Tetra hedron Lett., 45, 4773 (2004).
- 18. S.Ravichandran, Synth.Commun., 31, 2055 (2001).

- 19. V.V. Karpyak, M. D. Obushak, M. I. Ganushchak, Molecules, 8, 263 (2003).
- 20. C. Yu, B. Liu, L.Hu, J. Org. Chem., 67, 219 (2002).
- M. K. Kundu, S. B. Mukherjee, R.Padmakumar, S. V. Bhat, Synlett, 444 (1994).
- 22. V.Aggarwal, I.Emme, S. H. Fulford, J. Org. Chem., 68, 692 (2003).
- 23. V.K. Aggarwal, A.Meeru, Chem. Commun., 2311(1999).
- 24. J.Cai, Z.Zhou, G. Zhao, C.Tang, Org. Lett., 4, 4723 (2002).
