Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters
Tetrahedron Letters 46 (2005) 3369–3372

Stereoselective synthesis of tri- and tetrasubstituted oxepanes via *n*-Bu_3SnH mediated *7-endo-trig* vinyl radical cyclisation

Ponnusamy Shanmugam* and Paramasivan Rajasingh

Organic Chemistry Division, Regional Research Laboratory (CSIR), Thiruvananthapuram 695019, Kerala, India

Received 20 January 2005; revised 10 March 2005; accepted 15 March 2005
Available online 1 April 2005

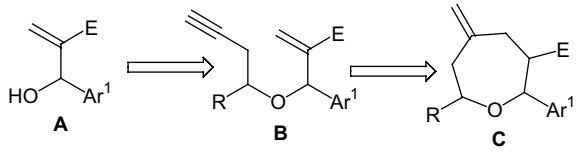
Abstract—A stereoselective *7-endo-trig* cyclisation of homopropargyl and phenyl homopropargyl derivatives of Baylis–Hillman adducts using *n*-Bu_3SnH/AIBN mediated vinyl radical cyclisation affords tri- and tetrasubstituted oxepanes, respectively, in good yields.
© 2005 Elsevier Ltd. All rights reserved.

1. Introduction

Amongst various carbon–carbon bond forming reactions, the Baylis–Hillman reaction is important, giving rise to densely functionalised molecules and is considered to be atom economic. Highly functionalised Baylis–Hillman adducts have been used as starting materials for various stereoselective preparations of functionalised intermediates and in natural product synthesis.[1] Seven-membered oxacycles are structural fragments of a variety of bioactive natural products,[2] besides their use in pharmacological applications.[3] Examples of their occurrence in Nature range from the monocyclic compounds zoapatanol, isolaurepinnacin and rogiolenyne to the highly complex ciguatoxin.[4] The presence of these units in complex molecules make them challenging synthetic targets, thus resulting in the development of a number of synthetic methods.[5] The number of methods for the construction of seven-membered oxacycles has steadily increased.[6] Tin radical mediated cyclisation has been developed as a potential method for preparing various types of cyclic compounds via intramolecular carbon–carbon bond-forming processes.[7] There are few examples in the literature for the construction of seven-membered ring systems by a tin hydride-mediated *7-endo-trig* cyclisation strategy.[8] Recently, we reported the vinyl radical cyclisation of isomerised Baylis–Hillman propargyl and homopropargyl derivatives for the synthesis of functionalised tetrahydrofuran and tetrahydropyran ring systems, respectively.[9c,d] In continuation of our research on the use of Baylis–Hillman adducts for the synthesis of functionalised oxacycles,[9] we envisaged that substituted oxepane rings could be synthesised stereoselectively from simple homopropargyl derivatives and phenyl homopropargyl derivatives of the Baylis–Hillman adducts. Radical addition reactions of Baylis–Hillman adducts have been carried out to investigate the 1,2-stereoinduction during the H-abstraction[10] step; thereby the stereochemistry of the products could be predicted and all such reactions were found to be intermolecular radical addition reactions. We intended to synthesise tri- and tetrasubstituted oxepanes from *O*-homopropargyl Baylis–Hillman derivatives and to study the 1,2-stereoinduction in the H-abstraction step[11] of the tin hydride-mediated vinyl radical cyclisation.

2. Results and discussion

The synthetic strategy is depicted in Scheme 1, thus, radical cyclisation of homopropargyl and aryl homopropargyl derivatives **B** would provide oxepanes **C**. The



Scheme 1. Synthetic strategy.

Keywords: *7-endo-trig*; Vinyl radical; Baylis–Hillman adduct; Oxepanes; *n*-Butyltin hydride.
* Corresponding author. Tel.: +91 471 2515275; fax: +91 471 2491712; e-mail: shanmu196@rediffmail.com

0040-4039/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2005.03.086

derivatives **B** could be synthesised from Baylis–Hillman adducts **A** by heating with the corresponding homopropargyl alcohol in the presence of eco-friendly Montmorillonite-K10 clay[9c] as catalyst, under neat conditions. They can also be prepared from bromide derivatives of Baylis–Hillman adducts with homopropargyl alcohol using bromide as the leaving group.[12]

The synthesis of trisubstituted oxepanes is outlined in Scheme 2. The Baylis–Hillman adducts were prepared according to the literature procedure.[13] The *O*-alkylation of Baylis–Hillman adducts **1a–f** with homopropargyl alcohol under clay-catalytic conditions[9c] afforded the key intermediates **2a–f** in moderate yields (Scheme 2, Table 1). Adducts bearing a nitrile group at the activated position, **2d–f**, were not isolated in pure form since they could not be separated from minor isomerised products. Hence, after passing through a silica gel column, the mixture was subjected to radical cyclisation and the pure compounds **3d–f** were isolated after column chromatography. Radical cyclisation of compound **2a** was carried out with 1.5 equiv of tri-*n*-butyltin hydride and a catalytic amount of AIBN in benzene at reflux for 12 h under an inert atmosphere to afford the crude stannylated compound, which was protiodestannylated in dichloromethane with pyridinium *p*-toluenesulfonate (PPTS) to give 2,3,5-trisubstituted oxepane **3a** in good yield (Scheme 2, Table 1). To show the generality of this reaction, we examined the cyclisations of homopropargyl derivatives **2b–f** all of which furnished the desired cyclised products **3b–f** in good yields. The results are summarised in Table 1. All new compounds were characterised by IR, ^{1}H and ^{13}C NMR, DEPT-135, 2D H–H COSY, X–H COSY and HRMS data.

The 1,2-stereoinduction during H-abstraction leads to the aryl and ester groups being in a *cis* orientation in order to reduce steric interactions. The relative stereochemistry of the oxepane **3a** was established by NOE irradiation studies. Irradiation of H_a at δ 4.6 enhanced the resonance corresponding to H_b at δ 2.85 by 1.6%. Similarly, for compound **3f**, irradiation of H_a enhanced the signal corresponding to H_b by 3.2%. This indicated that they were *cis* to one another. Hence, the relative stereochemistry of the substituents is assigned as shown in Figure 1.

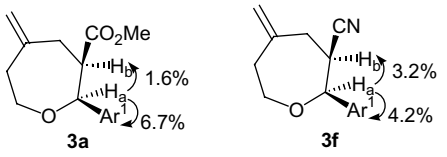
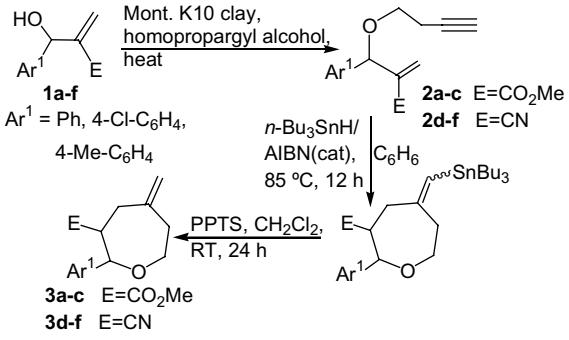
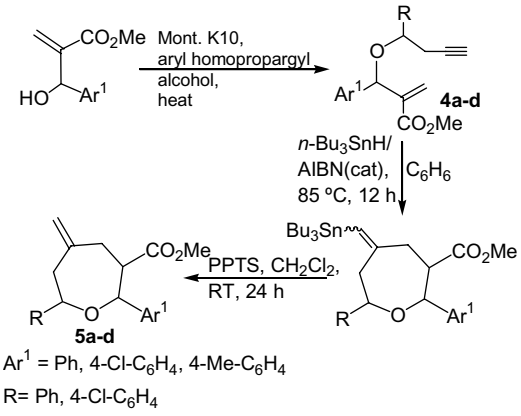


Figure 1. NOE correlations in trisubstituted oxepanes **3a** and **3f**.

In order to synthesise tetrasubstituted oxepanes, we prepared phenyl substituted homopropargyl alcohols from their corresponding aldehydes.[14] The phenyl substituted *O*-homopropargyl derivatives **4a–d** were synthesised following the procedure reported for compounds **2a–f**. Radical cyclisation of **4a** with 1.5 equiv of tri-*n*-butyltin hydride and a catalytic amount of AIBN in benzene at reflux for 12 h afforded a crude stannylated compound which was protiodestannylated, without purification, with PPTS to give 2,3,5,6-tetrasubstituted oxepane **5a** in good yield (Scheme 3, Table 2). The cyclisations of **4b–d** all furnished the desired cyclised products **5b–d** in good yields. The results are summarised in Table 2. All new compounds were characterised by IR, ^{1}H and ^{13}C NMR, DEPT-135, 2D H–H COSY, X–H COSY and HRMS data.



Scheme 2. Synthesis of trisubstituted oxepanes.



Scheme 3. Synthesis of tetrasubstituted oxepanes.

Table 1. Synthesis of trisubstituted oxepanes **3a–f**

Entry	Ar^1	E	Enyne ether	Yield (%)	Oxepane	Yield (%)
1	Ph	CO_2Me	**2a**	34	**3a**	58
2	4-Cl-C_6H_4	CO_2Me	**2b**	37	**3b**	61
3	4-Me-C_6H_4	CO_2Me	**2c**	36	**3c**	63
4	Ph	CN	**2d**	45[a]	**3d**	57
5	4-Cl-C_6H_4	CN	**2e**	48[a]	**3e**	48
6	4-Me-C_6H_4	CN	**2f**	44[a]	**3f**	58

[a] Combined yield with isomerised compounds.

Download English Version:

https://daneshyari.com/en/article/5279852

Download Persian Version:

https://daneshyari.com/article/5279852

Daneshyari.com