Ultrasonics Sonochemistry 20 (2013) 1296–1301

Contents lists available at SciVerse ScienceDirect

Ultrasonics Sonochemistry

journal homepage: www.elsevier.com/locate/ultson

Amberlyst-15 and Amberlite-200C: Efficient catalysts for aldol and cross-aldol condensation under ultrasound irradiation

Achraf Lahyani, Manef Chtourou, Mohamed Hédi Frikha, Mahmoud Trabelsi *

Laboratory of Applied Chemistry: Heterocyclics, Fats and Polymers, Faculty of Sciences, University of Sfax, Route de Soukra Km 3,5, 3038- Sfax, Tunisia

ARTICLE INFO

Article history:
Received 11 May 2012
Received in revised form 28 January 2013
Accepted 31 January 2013
Available online 22 February 2013

Keywords:
Acid-resins
Solvent free
Ultrasound irradiation
trans-Chalcones
α,α′-Bis(arylmethylidene) cycloalkanones

ABSTRACT

This paper presents an improved synthesis of *trans*-chalcones and α,α′-bis(arylmethylidene) cycloalkanones under ultrasound irradiation in the presence of commercial acid-resins as catalysts in solvent free conditions. Several *trans*-chalcones and α,α′-bis(arylmethylidene) cycloalkanones were synthesized in good yields and excellent selectivity in a short reaction time.

1. Introduction

The 1,3-diaryl-2-propenones are generally synthesized by Claisen–Schmidt reaction between the aromatic aldehydes and aryl methyl ketones. These compounds are of high interest due to their use as intermediates in the synthesis of a series of heterocyclic compounds [1]. Some chalcones are used due to their antineoplastic, antispasmodic, antibiotic, bacteriostatic properties or because of their chemical flexibility as synthons for the synthesis of polycyclic compounds [2] or for the testing of their pharmacological activity [3]. Recent studies evaluating the biological activity of chalcones have showed that these compounds have several anticancer, anti-inflammatory, antimitotic, anti-tubercular, cardiovascular, anti-hyperglycemic [4], antimicrobial, anti-invasive [5], antileishmanial, anti-malarial activities and can be used in the inhibition of tyrosine [6].

trans-Chalcones are also key precursors in the synthesis of many biologically important heterocycles, such as benzothiazepines [7], the pyrazolines, and flavones [6]. Some chalcones are used as sweeteners, medications, sunscreen agents, varnishes, and sensitive photographic emulsions [8]; others have antifungal and anti-ulcer properties [9].

The cross-aldol condensation is an efficient synthesis of α,α′-bis(arylmethylidene) cycloalkanones. These compounds are the precursors for the synthesis of bioactive substances, such as pyrimidine derivatives [10].

The bis(arylmethylidene) cycloalkanones are compounds with multiple biological activities such as inhibition of HIV-1 integrase [11], cytotoxic properties [12], cancer chemo preventive [13] and antioxidant properties [14].

Due to their important biological and pharmacological properties, the bis(arylmethylidene) cycloalkanones have drawn attention in organic synthesis and in medical research [15].

Traditionally, chalcones can be obtained by Claisen–Schmidt condensation performed in acidic or basic medium under homogeneous conditions [16]. Some reagents such as sodium hydroxide, potassium hydroxide, the telluroxide (bis(*p*-methoxyphenyl)), $Ba(OH)_2$ and 2,2-bipyridine complex of $Co(OAc)_2$ were used as basic catalysts [9]. When KOH or NaOH are used as catalysts, the reaction time is sometimes very long (2–4 days), with a strong possibility of side reactions, such as Cannizzaro reaction and aldol condensation [4]. The acid-catalysed methodologies involve the use of $AlCl_3$, anhydrous HCl, $TiCl_4$, $RuCl_3$ [4], BF_3, B_2O_3, *p*-toluenesulfonic acid [1]. All these reactions are performed in the presence of organic solvents and required high temperatures, which were responsible for generating side products.

Under homogeneous conditions, several basic and acid catalysts have been used in the synthesis of α,α′-bis(arylmethylidene) cycloalkanones such as $(EtO)_4Si/CsF$ or KF, $Cp_2ZrH_2–NiCl_2$, Rh(III)-porphyrin, Cp_2TiPh_2, BMPTO under microwave irradiation, $RuCl_3$, $TiCl_3OTf$, $LiOH.H_2O$, $FeCl_3$-[bmim][BF_4], $KF–Al_2O_3$ under ultrasound irradiation, TMSCl–NaI, $H_2SO_4–SiO_2$, $Yb(OTf)_3$, Et_2NTMS–LPDE and $LiClO_4$–$TMSNEt_2$ [16–23].

In general, organic synthesis catalyzed with homogeneous basic or acid medium has various disadvantages, such as catalyst

---

* Corresponding author. Fax: +216 74 676 606.
E-mail address: Mah.Trabelsi@fss.rnu.tn (M. Trabelsi).

1350-4177/$ - see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.ultsonch.2013.01.017

recovery and generation of secondary products [24]. In addition, most organic syntheses catalyzed under homogeneous conditions involve the use of hazardous solvents, expensive and toxic reagents, and special efforts needed to prepare catalysts and starting materials [25].

Recently, the solvent-free condition and the use of heterogeneous catalysts has emerged as an eco-friendly alternative of great importance within organic synthesis, as it reduces environmental pollution and brings down handling costs due to simplification of work up technique [6].

Different heterogeneous acid or basic catalysts have been investigated in the synthesis of *trans*-chalcones, such as commercial acid-clays [3], potassium hydroxide impregnated silica gel [3], Bamboo char sulfonic acid [5], amino grafted zeolites [24], and Amberlyst-15 under solvent-free condition, but severe, conditions (at 120 °C for 24 h) [5] and in the synthesis of α,α'-bis(arylmethylidene) cycloalkanones such as carbon-based solid acid [26], silica sulfuric acid [20] and SiO_2-OK [27]. The development of ion exchange resins with strong acid sites and large specific area made this kind of catalyst even more attractive. These acid-resins have been used in many organic syntheses such as etherification [28], acylation [29], aza-michael addition [30], isomerisation [31] and aldol condensation [5].

We purpose in this work the synthesis of *trans*-chalcones and α,α'-bis(arylmethylidene) cycloalkanones catalyzed with acid-resins under ultrasound irradiation and solvent-free conditions. This method allows for high yield in a short time and at moderate temperatures reaction. Herein we report a reusable, easily separable, eco-friendly and highly effective resin-catalyst.

2. Experimental

2.1. Materials

Two acid-resins (Amberlyst-15 and Amberlite-200C) were used as catalysts for the preliminary reactions between benzaldehyde and acetophenone. Amberlyst-15, Amberlite-200C, arylbenzaldehydes (98–99%) and aryl-acetophenones (98–99%) were purchased from Fluka and used as received. The cationic resin (Na^+) A-200C was activated by hydrochloric acid. All other reagents (cyclohexanone, cyclopentanone) were also pure products ($\geqslant$97%).

2.2. General procedure for the synthesis of trans-chalcones

For a typical synthesis, 0.4 g of resin, 0.02 mol of aryl-benzaldehyde and 0.02 mol of methyl aryl-ketone were charged in a 10 mL glass reactor. The reaction mixture was heated in an oil bath at 60 ± 2 °C. The ultrasound probe was immersed directly in the reactor. An ultrasonic generator (Bioblock Scientific 750 W) emits the sound vibration into the reaction mixture. Sonification was achieved at low frequencies of 20 kHz (amplitude of 30%). The reaction time was fixed at 1 h. After cooling to room temperature, dichloromethane (50 mL) was added, the reaction mixture was filtered, and the catalyst washed with hot ethanol (50 mL). Solvent was then evaporated and the dried crude products were crystallized from 95% ethanol, except for nitro-chalcones, which were crystallized from acetone, filtrated and finally dried under vacuum for 48 h. The melting points of the isolated products were measured on a Reichert–Heizbank apparatus. The yields of the reactions were determined by gas chromatography on a Shimadzu 2014-GC apparatus using chloroform as solvent. The capillary column was DB-5 and the carrier gas was nitrogen.

2.3. General procedure for the synthesis of α,α'-bis(arylmethylidene) cycloalkanones

For a typical synthesis, 0.5 g of resin, 0.02 mol of aryl-benzaldehyde and 0.01 mol of cycloalkanone were charged in a 10 mL glass reactor. The reactor was placed in a water bath and the reactions were performed with water cooling at 20–30 °C. The ultrasound probe was immersed directly in the reactor. The ultrasonic generator (Bioblock Scientific 750 W) emits the sound vibration into the reaction mixture. Sonification was achieved at low frequencies of 20 kHz (amplitude of 30%). The reaction time was fixed at 90 min. After this time, dichloromethane (50 mL) was added, the reaction mixture was filtered, and the catalyst washed with hot ethanol (50 mL). Solvent was then evaporated and the dried crude products were crystallized from a mixture of 95% ethanol and ethyl acetate (50/50), filtrated and finally dried under vacuum for 48 h. The melting points of the isolated products were measured on a Reichert–Heizbank apparatus. The yields of the reactions were calculated from the mass of the isolated pure product.

2.4. Spectroscopic analysis

The IR analysis was performed using a spectrometer type Perkin Elmer Spectrum version 10.

The NMR spectra of the isolated products were recorded in solution in $CDCl_3$ on a spectrometer type AC Bruker (^1H at 400 MHz and ^{13}C at 75 MHz). The internal reference was $CDCl_3$.

The spectral data of some isolated compounds, taken as representative examples, are summarized below.

2.4.1. 1,3-Diphenyl-propenone (3ab)

IR [ν, cm^{-1}] 3052 (C=C–H, Ar–H), 1662.3 (C=O), 1604.3 (C=C, Ar), 1575.2; ^1H NMR [δ, ppm] 8.03 (2H, d, J = 6.9 Hz) , 7.82 (1H, d, $J_{H\alpha-H\beta}$ = 15.9 Hz), 7.54 (1H, d, $J_{H\alpha-H\beta}$ = 15.9 Hz), 7.52 (2H, t, J = 6.9 Hz et J = 7.5 Hz), and 6H between 7.42 and 7.66 ppm; ^{13}C NMR [δ, ppm] 190.6, 144.9, 138.3, 134.9, 133.1, 132.8, 130.6, 129.0, 128.7 (2C), 128.5, 128.5, 128.2, 127.5, 122.2.

2.4.2. 3-(2-Chlorophenyl)-1-(4-nitrophenyl)-propenone (3ec)

IR[ν, cm^{-1}] 3083.29 (C=C–H, Ar–H), 1660.54 (C=O), 1588.81 (C=C, Ar), 1344.12 (NO_2); ^1H NMR [δ, ppm] 8.36 (d, 2H, J_{H-H} = 8.2 Hz), 8.14 (d, 2H, J_{H-H} = 8.2 Hz), 8.21 (d, 1H, $J_{H\alpha-H\beta}$ = 15.9 Hz), 7.76 (dd, 1H, J_{H-H} = 7.2 Hz), 7.43 (d, 1H, $J_{H\alpha-H\beta}$ = 15.9 Hz), 7.47 (dd, 1H, J_{H-H} = 9.3 Hz), 7.37 (m, 1H, J_{H-H} = 9.3 Hz), 7.36 (m, 2H, J_{H-H} = 7.2 Hz); ^{13}C NMR [δ, ppm] 189.2, 150.3, 143.1, 142.8, 135.9, 132.9, 132.0, 130.7, 129.9 (2C), 128.1, 127.6, 124.3, 124.0 (2C).

2.4.3. 3-(2-Methoxyphenyl)-1-(4-nitrophenyl)-propenone (3fc)

IR [ν, cm^{-1}] 3076.67 (C=C–H, Ar–H), 2968.9, 2839.96, 1655.18 (C=O), 1592.55 (C=C, Ar), 1337.86 (NO_2); ^1H NMR [δ, ppm] 3.93 (3H, s), 8.34 (2H, d, J_{H-H} = 8,7 Hz), 8.12(1H, d, $J_{H\alpha-H\beta}$ = 15.6 Hz), 8.02 (2H, d, J_{H-H} = 9 Hz), 7.57(d, 1H, $J_{H\alpha-H\beta}$ = 15.6 Hz), and 4H between 6.95 and 7.63 ppm; ^{13}C NMR [δ, ppm] 189.1, 162.4, 150.0, 146.8, 143.5, 131.0, 130.7, 129.4 (2C), 127.1, 123.9, 123.9, 114.7, 114.4, 119.0, 55.6.

2.4.4. 2,5-Bis(4-methoxybenzylidene) cyclopentanone (5cf)

IR [ν, cm^{-1}] 2940.35, 2842.95, 1695.89 (C=O), 1594.16 (C=C, Ar); ^1H NMR [δ, ppm] 7.58 (2H, s), 7.56 (4H, d, J_{H-H} = 8.7 Hz), 6.96 (4H, d, J_{H-H} = 8.7 Hz), 3.85 (6H, s), 3.07 (4H, s); ^{13}C NMR [δ, ppm] 196.4, 160.5 (2C), 135.2 (2C), 133.3 (2C), 132.5 (2C), 128.7 (4C), 114.3 (4C), 55.4 (2C), 26.5 (2C).

2.4.5. 2,6-Bis(benzylidene) cyclohexanone (5ag)

IR [ν, cm^{-1}] 2933.21, 2863.15, 2845.62, 1661.00 (C=O), 1572.04 (C=C, Ar); ^1H NMR [δ, ppm] 7.75 (2H, s), 10H between 7.25 and