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Zinc/Glacial Acetic Acid Assisted Novel Reduction of Cross-conjugated a, a´-(E,E)-Bis(Benzylidene) Cyclopentanones to Benzylidene Cyclopentanols

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Abstract

α,α´-*(E,E)*-bis(benzylidene)cyclopentanone on treatment with zinc dust and glacial acetic acid in dry CH2Cl2 undergoes reduction of one enone unit to the corresponding alcohol leaving the other double bond intact. The reaction procedure is simple, effective and produce valuable benzylidene cyclopentanols with a high yield.

Key words : Reduction, zinc dust, glacial acetic acid

Introduction

Though most of the well known organic reactions are recognized to proceed by two-electron transfer process, radical chemistry as well as many biological transformations generally stands on single-electron transfer (SET) mechanism. Radicals can be generated by the homolytic cleavage at elevated temperatures are highly reactive species and form valuable products. SET reactions dominate many interesting research fields that include electrochemistry, electron transfer catalysis promoted by various metals or organometallic chemistry.[1]

In case of reduction of α,β-unsaturated ketones, employing SET reaction protocols, a wide array of products, ranging from corresponding saturated ketones, hydrocarbons and pinacols, were generally obtained.[2] Reductive dimers were also isolated due to β,β-coupling between the radicals formed.[3] For this type of reduction, reducing metals such as Mg[4] or Al[5] or Zn[6] were generally involved.

In this connection we have used zinc dust as reducing agent to reduce cross-conjugated α,α´-*(E,E)*-bis (benzylidene) cyclopentanone in glacial acetic acid medium. Zinc is an essential trace element for humans,[7] animals,[8] plants[9] and plays "ubiquitous biological roles".[10] It

being cheap and easily available alternative to the precious metal complexes of palladium, ruthenium and iridium has found many applications as catalyst in organic synthesis.[11] Thus it becomes metal of choice for this purpose.

In our previous study on the reduction of substituted cross-conjugated α,α´-*(E,E)*-bis (benzylidene) cycloalkanones bearing five- and six-membered rings respectively using zinc-amalgam/ glacial acetic acid reaction medium and refluxing in dry toluene, yielded corresponding C=C bond reduced products and reductive C-C coupled dimers with the carbonyl functions remaining unaffected.[12] Moreover, we have also observed that the ring conformations influenced the extent of reduction of the monomers and C-C coupled dimers. In the present study, we have employed zinc dust to reduce cross-conjugated α,α´-*(E,E)*-bis (benzylidene) cyclopentanone in glacial acetic acid medium and found that one enone system was reduced to alcohols keeping the other double bond unaffected. As a result benzylidene cyclopentanols were isolated with a very good yield as a sole product.

Materials and Methods

General Methods

All chemicals and solvents were purchased from Merck (Germany) and Sigma-Aldrich. Zn was purchased from s-d. fine Chem. and used without further activation. Glacial acetic acid were obtained as AR grade and distilled prior to use. Dichloromethane were purchased as AR grade, distilled and dried over moleculer sieves (4A) before use. Melting points were determined in open capillary tubes on Kofler block apparatus and are uncorrected. IR spectra were recorded in KBr discs with a Perkin- Elmer RXI FT-IR spectrophotometer. NMR spectra (^{1}H, ^{13}C) were recorded in $CDCl_3$ solution in 5 mm BBO probe fitted with a pulse field gradient and working with Topsin 1.3 programme in a Bruker AV-300 Supercon NMR spectrometer (chemical shifts in d ppm and J in Hz). Mass spectrometry was performed on a Q-Tof Micromass Waters Limited mass spectrometer. Chromatography columns were prepared from silica gel (100-200 mesh; Spectrochem Pvt. Ltd., India) and petroleum ether *(b.p. 60-80˚C)*-ethyl acetate mixture were used as eluant.

Reaction Procedure

Formation of Product 2

Distilled glacial acetic acid (10 mL) and zinc dust (20 mmol) were added to α,α´-*(E,E)*-bis (benzylidene) cyclopentanone 1 (5 mmol) dissolved in dry dichloromethane (60 mL) and stirred at room temperature for 4 hours. The reaction mixture was filtered and solvent was removed under reduced pressure. To the residue a large volume of water was added and extracted with $CHCl_3$ three times. Chloroform layer was washed with water several times till

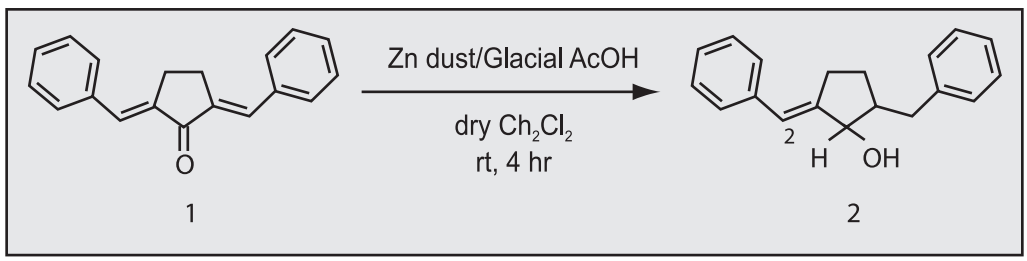
neutral to pH paper. Then it was dried over Na_2SO_4, concentrated and then resolved by chromatography over a column of silica gel by eluting with ethyl acetate-petroleum ether mixtures of increasing polarities.

(E)-2-benzyl-5-benzylidenecyclopentanol (2) :

White crystal, Yield 1.01 gm (80%), Mp 116-118 ˚C, IR υ_{max} (KBr) 3395, 3022, 2917, 1330, 1104, 692 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ_H 1.29-1.35 (1H, m), 1.84-1.95 (2H, m), 2.45-2.86 (4H, m), 2.86-2.93 (1H, dd, J_1 = 5.1 Hz, J_2 = 8.1 Hz), 4.13 (1H, d, J = 7.2 Hz), 6.43-6.46 (1H, m), 7.08-7.28 (10H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 27.6, 27.9, 38.8, 48.9, 81.0, 123.1, 126.0, 126.5, 128.3, 128.4, 128.5, 128.9, 137.7, 140.6, 146.6. Anal. calcd for (264.15): C 86.32, H 7.63%. Found: C 86.30, H 7.61%.

Results and Discussion

In search for optimum reaction condition, reduction of α,α´-*(E,E)*-bis (benzylidene) cyclopentanone, 1 (5 mmol) with varied amounts zinc dust and glacial acetic acid at room temperature using dry dichloromethane as solvent (Scheme 1), were studied and the results have been summarized in **Table 1.**



Scheme 1. Zinc/glacial AcOH mediated reduction of α,α´-*(E,E)*-bis(benzylidene) cyclopentanone, **1**

It is evident from Table 1 that the activation of zinc dust by standard procedure [13] had negligible efficacy in this specific reduction in excess glacial acetic acid as only 8% of the product was isolated even after 48 hours of stirring (entry 1, Table 1). Employing non-activated zinc dust, in same solvent reduced the time (8 hr) with increased yield of the product alcohol, 2 (entry 2, Table 1). As the starting material was not soluble in glacial acetic acid, we dissolved it in dry CH_2Cl_2 and diminished the acetic acid amount. We have observed that in presence of 20 mmol zinc dust with less volume of acetic acid the yield of the product was considerably increased to 40% within 6 hours (entry 3, Table 1). However, further increasing the quantity of zinc dust (25 mmol) the yield of the product was reduced to 20% (entry 4, Table 1). Reducing

the volume of glacial acetic acid more the yield of the product was increased dramatically (entries 5 and 6, Table 1). Finally, the optimum condition was achieved with the reaction being carried out at room temperature for 4 hours by using zinc dust (20 mmol)/10 mL glacial acetic acid in 60 mL dry CH_2Cl_2 when 80% of the desired product was obtained (entry 6, Table 1).

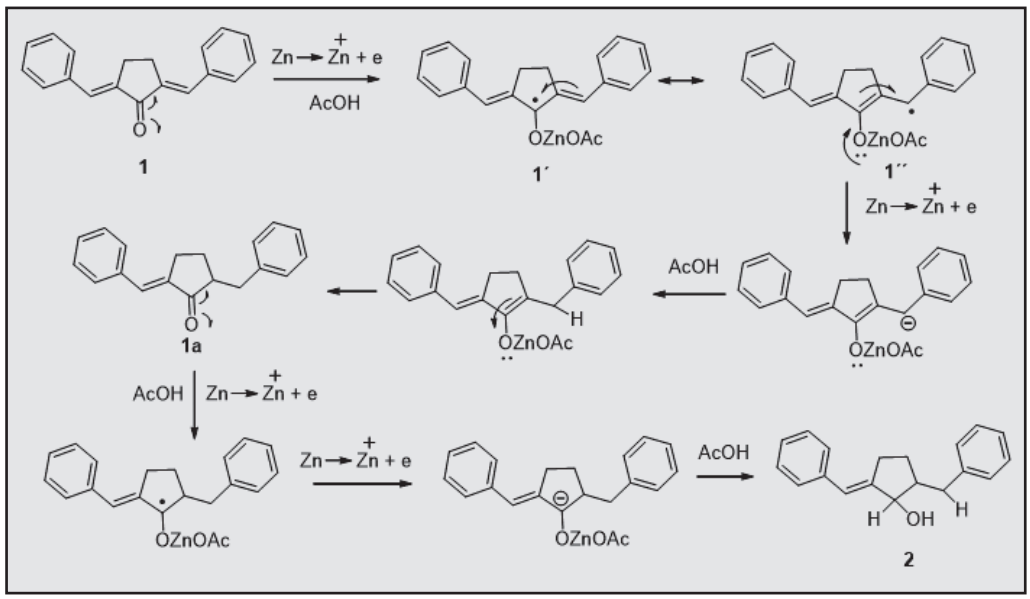
Table 1. Optimization of the reaction condition for the formation of product, **2**[a]

Entry	Zinc (in mmol)	Conditions	Time (hr)	Yield[b] (%)
1	15 (activated)	Excess AcOH (100 mL)	48	8
2	15	Excess AcOH (130 mL)	8	22
3	20	AcOH (70 mL) in CH_2Cl_2 (50 mL)	6	40
4	25	AcOH (70 mL) in CH_2Cl_2 (50 mL)	6	20
5	20	AcOH (15 mL) in CH_2Cl_2 (50 mL)	6	70
6	20	AcOH (10 mL) in CH_2Cl_2 (60 mL)	4	80

[a] **Reaction :** α,α´-*(E,E)*-bis(benzylidene) cyclopentanone, 1 (5 mmol), Zn-dust, glacial AcOH, CH_2Cl_2, rt = room temperature. [b] Isolated and optimized yield.

A plausible mechanistic pathway was presented (Scheme 2) for the reduction of planar α,α´-*(E,E)*-bis (benzylidene) cyclopentanone, **1** to explain the formation of **2** in presence of zinc dust in glacial acetic acid medium. Reduction of one enone function to alcohol could be suggested to occur in a stepwise manner. Initially an electron was transferred from zinc surface to the carbonyl function forming stable allylic radical, 1´ which undergo delocalization to benzyl radical, 1´´. Now this stable radical would accept an additional electron from metal to form the benzyl anion. This anion in acidic medium quenched with proton to form the reduced product, **1a** where one exocyclic double bond was reduced leaving behind other enone unit intact at the other end of the molecule. Further reduction of the second olefinic bond could not be achieved as already observed in our previous work. [13]This could be attributed to the possible steric hindrance towards proper orientation and interaction of **1a** with the zinc surface.

Instead the carbonyl function was reduced to alcoholic group via electron transfer from zinc metal to keto group and ultimately quenched by acid as depicted in **Scheme 2**.



Scheme 2. A plausible mechanistic pathway to the formation of 2 by zinc/AcOH assisted SET reaction

Conclusion

In conclusion, we have developed a simple zinc/glacial acetic acid mediated reduction procedure of cross-conjugated α,α´-*(E,E)*-bis (benzylidene) cyclopentanone producing one exocyclic double bond reduced product, benzylidene cyclopentanol in high yield.

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