

*Dedicated to the memory of  
Professor Cristofor I. Simionescu (1920–2007)*

## A NEW ALTERNATIVE METHOD FOR THE SYNTHESIS OF CINNAMIC ACIDS FROM AROMATIC ALDEHYDES AND ZINC ACETATE

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Cinnamic acids have been prepared in 58-85% yields by a new synthetic route from aromatic aldehydes and zinc acetate in acetic acid and *N*-methyl-2-pyrrolidinone (NMP) as solvents, at reflux (185-195°C), for 8-12 hours.

### INTRODUCTION

Condensation reaction, one of the most popular methods for the formation of new C-C bonds, is still an active research field allowing the development of new approaches and synthetic strategies, comprising the identification of novel reagents able to react readily and selectively, according to a specific purpose.

In this context, zinc mediated condensation reactions<sup>1</sup> are useful tools in exploring new alternatives for C–C and C-hetero bond formation.<sup>2</sup> Zinc salts (zinc acetate, zinc acetylacetonate, zinc arsenide, zinc bromide, zinc carbonate, zinc chloride, zinc fluoride, zinc iodide, zinc nitrate, zinc stearate) are widely used in organic and macromolecular chemistry due to their specific properties induced by zinc atom.

Zinc acetate is commonly known as a Lewis acid. According to the frontier molecular orbital (FMO) theory, a Lewis acid is a species which reacts *via* its lowest unoccupied molecular orbital (LUMO), being often said to have a vacant orbital. Due to its character of transition metal, zinc atom determines a special behaviour of zinc acetate which makes it a borderline Lewis acid among heavy metal Lewis acids (according to Pearson's HSAB classification).<sup>3</sup> Zinc acetate is often used for its special characteristics as catalyst<sup>4</sup> and complex<sup>5</sup> and, seldom, as condensing agent.<sup>6</sup>

Cinnamic acids compose a relatively large family of organic acids which appear to have antibacterial, antifungal and antiparasitical activities. They are also used in macromolecular synthesis as very important building blocks for various classes of polymers, having attractive properties, especially a high photoreactivity due to the presence, in the main or side chains, of the cinnamoyl group, well known as photoresponsive unit. For their use in perfume production, the food industry, pharmaceuticals, medicine and technical applications, cinnamic acids are synthesized on a commercial scale.

In the field of direct synthesis of cinnamic acids we do have some recent contributions<sup>7</sup> and our constant preoccupation yielded in a new synthetic approach which we are introducing herein.

In this paper, we are exploring the ability of zinc acetate to generate methylene active group as driving force in its condensation reaction with aromatic aldehydes. We also present the reaction mechanism in order to explain the particular function of zinc acetate as reagent in this synthesis.

### RESULTS AND DISCUSSION

Cinnamic acids have been prepared from aromatic aldehydes and aliphatic carboxylic anhydrides in the presence of bases, particularly

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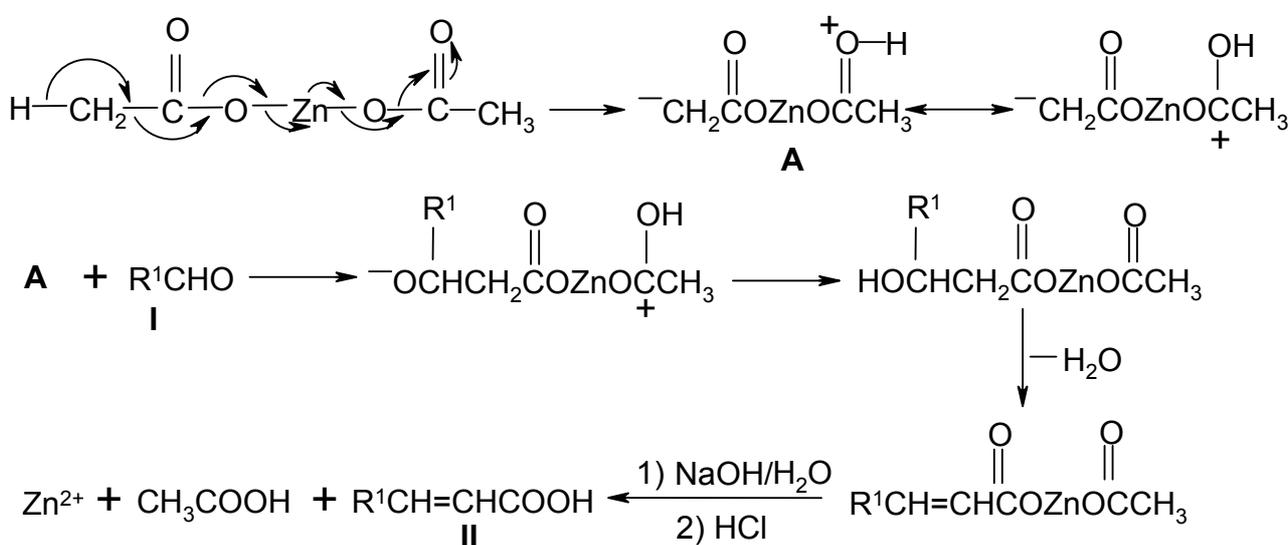
electron withdrawing groups were obtained in good yields, following the general procedure (see "Experimental" section).

The reaction that we are introducing in this paper is a different one because, usually, the reaction between aromatic aldehydes and aliphatic carboxylic acids and their salts, *i.e.* acetic acid and its salts such as NaOAc, Ca(OAc)<sub>2</sub>, Ba(OAc)<sub>2</sub>, Hg(OAc)<sub>2</sub> etc, is not possible.

Zinc acetate is a Lewis soft acid, a borderline acid between strong and soft acids, with an electron-withdrawing effect.<sup>18</sup> The acetate group is capable of binding to metal ions in a variety of ways through its two oxygen atoms and several

connectivities are observed for the various hydrates of zinc acetate. Anhydrous zinc acetate adopts a polymeric structure consisting of zinc coordinated to four oxygen atoms in a tetrahedral environment, each tetrahedron being connected to neighbors by the acetate groups.

Due to its particular nature, zinc acetate is able to undergo an activation process, under certain conditions, which makes it suitable for the subsequent condensation reaction. Based on our experimental results and taking into account theoretic considerations,<sup>11,19-21</sup> we can state that the following mechanism can occur (Scheme 2):



Scheme 2 – Mechanism of the synthesis of cinnamic acids from aromatic aldehydes and zinc acetate.

Given the experimental conditions, one methylene group from zinc acetate is activated by the other acetate group and by Zn atom, as presented in Scheme 2 (structure A). If the bond O-Zn-O wouldn't be partially covalent, the activation couldn't take place. The activated methylene group is then able to undergo a condensation reaction with aromatic aldehydes I, resulting in cinnamic acids II and acetic acid and Zn(OH)<sub>2</sub> as by-products.

This new synthetic pathway substantiates that the bond O-Zn-O is partially covalent, especially at high temperatures (150-200°C). Even more, the same partially covalent linkage O-Zn is responsible of the lower fusion points of (CH<sub>3</sub>COO)<sub>2</sub>Zn·2H<sub>2</sub>O (100°C) and (CH<sub>3</sub>COO)<sub>2</sub>Zn (240°C), compared to other metal acetates. In terms of an entirely ionic O-Zn-O bond, the activation couldn't take place and, consequently, in the absence of the active methylene group the reaction is not possible.

In conclusion, we have found a new synthetic approach for the preparation of cinnamic acids from aromatic aldehydes, using a novel active methylene group reagent, namely zinc acetate. Its capability to undergo an activation process makes it appropriate for this type of condensation, offering an effective alternative to the conventional Perkin synthesis. The reaction and its mechanism we propose are reasonable proofs to confirm the theoretic premise of our approach.

## EXPERIMENTAL

General procedure for the synthesis of cinnamic acids: In a 100 mL three-necked Claisen flask fitted with a thermometer, 4.4 g (0.024 mole) anhydrous zinc acetate, 2.8 g (0.02 mole) aromatic aldehyde I, 2 mL NMP and 3.5 mL acetic acid were added. Then, an air cooled reflux condenser was fitted and the acetic acid was removed by distillation, until the temperature in the flask increased up to 185-187°. The obtained solution

was heated under reflux at 185-195°C for 8-12 h (see Table 1). At the end of the reaction, the final solution was treated with 70-80 mL water and with NaOH solution 20% to pH=9-10, at room temperature, and then filtered. The filtrate was treated with HCl solution 15-20% until pH=1-2, when cinnamic acid **II** precipitated. After stirring for 2-3 h and cooling with ice, the final product **II** obtained is filtered, washed with 15-20 mL cold water and dried. Yields ranged from 58 to 85% (Table 1).

IR spectra were recorded on a Bruker Vertex 79 FTIR spectrophotometer, using the KBr pellet technique. Melting points were determined with a Gallenkamp hot-block point apparatus. <sup>13</sup>C-NMR spectra were recorded on a Bruker Avance DRX 400 device. All solvents and reagents were purchased from Fluka and were used, when necessary, after purification.

## REFERENCES

1. a) S. Pinet, S. U. Pandya, P. Y. Chavant, A. Ayling and Y. Vallee, *Org. Lett.*, **2002**, *4*, 1463; b) L. Zani, S. Alesi, P. G. Cozzi and C. Bolm, *J. Org. Chem.* **2006**, *71*, 1558; c) K.-Y. Lee, C.-G. Lee, J.-E. Na and J.-N. Kim, *Tetrahedron Lett.*, **2005**, *46*, 69; d) B. Jiang and Y.-G. Si, *Tetrahedron Lett.*, **2003**, *44*, 6767; e) C. Fischer and E. M. Carreira, *Org. Lett.*, **2004**, *6*, 1497; f) B. Jiang and Y.-G. Si, *Angew. Chem., Int. Ed.*, **2004**, *43*, 216.
2. a) R. Varala, N. Sreelatha and S. R. Adapa, *J. Org. Chem.*, **2006**, *71*, 8283; b) R. Varala, A. Nasreen, E. Ramu and S. R. Adapa, *Tetrahedron Lett.*, **2007**, *48*, 69; c) R. Varala, N. Sreelatha and S. R. Adapa, *Synlett*, **2006**, 1549; d) R. Varala, E. Ramu and S. R. Adapa, *Synthesis*, **2006**, *22*, 3825; e) S. V. Ryabukhin, A. S. Plaskon, D. M. Volochnyuk, S. E. Pipko, A. N. Shivanyuk and A. A. Tolmachev, *J. Comb. Chem.*, **2007**, *9*, 1073.
3. R. Pearson, "Chemical Hardness", Wiley-VCH, Weinheim, Germany, 1997, p. 3-4.
4. Y. Motoyama and H. Nishiyama, "Mg(II) and Zn(II) Lewis Acids" in H. Yamamoto (ed.) "Lewis Acids in Organic Synthesis", vol.1, Edition-Sept. 2000, Wiley-VCH, Weinheim, Germany.
5. H. Ozeki and Yoshiaki Kobuke, *Tetrahedron Letters*, **2003**, *44*, 2287.
6. a) W. Siegel and I. Troetsch-Schaller, US Patent 5347047, Sept 13, 1994; b) S. Greenberg, A. B. P. Lever and C. C. Leznoff, *Can. J. Chem.*, **1988**, *66*, 1064.
7. a) C. I. Chiriac, F. Tanasa and M. Onciu, *Tetrahedron Lett.*, **2003**, *44*, 3579; b) C. I. Chiriac, F. Tanasa and M. Onciu, *Molecules*, **2005**, *10*, 481; c) C. I. Chiriac, F. Tanasa and M. Onciu, *Rev. Roum. Chim.*, **2005**, *50*, 627.
8. J. R. Johnson, *Org. React.*, **1942**, *1*, 210.
9. P. Kalnin, *Helv. Chim. Acta*, **1928**, *11*, 977.
10. T. Reetz, *J. Am. Chem. Soc.*, **1960**, *82*, 5039.
11. G. P. Miklukhin, *Doklady Akad. Nauk SSSR*, **1950**, *73*, 117, (*Chem. Abstr.* **1951**, 545e).
12. G. H. Cleland, *J. Org. Chem.* **1961**, *26*, 3362.
13. H. Zimmerman, *J. Am. Chem. Soc.*, **1959**, *81*, 2091.
14. B. S. Fedorov, *Prom. Org. Sin. Akad. Nauk SSSR*, **1967**, 173 (*Chem. Abstr.* **1962**, **1968**, 68, 77903h)
15. Y. Urushibara and M. Hirota, *Nippon Kagaku Zasshi*, **1961**, *82*, 351 (*Chem. Abstr.* **1962**, *56*, 10025g).
16. C. J. Pouchert, "The Aldrich Library of FT-IR spectra" vol. 2, ed II., Wiley&Sons, Milwaukee, 1997.
17. C. J. Pouchert and J. Behnke, "The Aldrich Library of <sup>13</sup>C and <sup>1</sup>H NMR spectra" vol. 2, ed. I, Wiley&Sons, Milwaukee, 1993.
18. R. G. Pearson and J. Songstad, *J. Am. Chem. Soc.*, **1963**, *85*, 3533; **1967**, *89*, 1827.
19. A. V. Capilla and R. A. Aranda, *Cryst. Struct. Commun.*, **1979**, *8*, 795.
20. G. Givaja, A.J. Blake, C. Wilson, M. Schröder and J. B. Love, *Chem. Commun. (Camb)*, **2005**, *21*, 4423.
21. K. Sakai, J. Nakajima, M. Niimura, R. Uchida and Y. Yamane, *Bull. Environ. Contam. Tox.*, **1995**, *54*, 142.