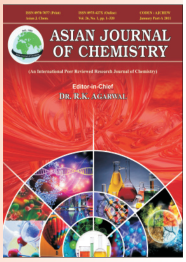
Asian Journal of Chemistry; Vol. 26, No. 24 (2014), 8463-8466

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2014.17949



Synthesis of Arylidene Propanedioic Acids by Knoevenagel Condensation for use in Ceramic Sols

Syed Salman Shafqat[1], Misbahul Ain Khan[2,3], Azham Zulkharnain[4],
Sinin Hamdan[1], Andrew Ragai Henry Rigit[1] and Amir Azam Khan[1,*]

[1]Department of Mechanical and Manufacturing Engineering, Faculty of Engineering, Universiti Malaysia Sarawak, 94300 Kota Samarahan, Sarawak, Malaysia
[2]Institute of Chemistry, University of the Punjab, Lahore, Pakistan
[3]Department of Chemistry, The Islamia University of Bahawalpur, Bahawalpur, Pakistan
[4]Department of Molecular Biology, Faculty of Resource Science & Technology, Universiti Malaysia Sarawak, 94300 Kota Samarahan, Sarawak, Malaysia

*Corresponding author: E-mail: akamir@feng.unimas.my

Received: 5 May 2014; *Accepted*: 26 August 2014; *Published online*: 1 December 2014; AJC-16382

This paper is primarily concerned with the synthesis of arylidene propanedioic acids by Knoevenagel condensation. Generally organic bases pyridine and piperidine are used as catalyst in Knoevenagel condensation which are costly and health hazard. In this research work, Knoevenagel condensation of various aromatic aldehydes (benzaldehyde, salicylaldehyde and *p*-chlorobenzaldehyde) and active methylenes (malonic acid and ethyl acetoacetate) was carried out in the presence of amino acids (glycine, lysine, hippuric acid, methionine and leucine) as catalyst. Using salicylaldehyde gave coumarin-3-carboxylic acid, a solvent free synthesis. These products were isolated and purified and were characterized through melting points, TLC, IR, mass and ^{1}H NMR. These acids are synthesized for eventual development of organically modified ceramic nano powders.

Keywords: Knoevenagel condensation, Amino acid catalysis, Ceramic sols.

INTRODUCTION

Knoevenagel condensation reaction is a versatile method for the formation of new carbon-carbon bonds by reaction between a carbonyl compound and an "active methylene" substrate. Among various classes of compounds produced through this reaction, acrylic acids are produced by the reaction of aldehydes and malonic acid. This reaction needs base catalysis and organic bases such as piperidine and pyridine are generally employed at a waterbath temperature. The reaction is accompanied by a decarboxylation. The intermediate dicarboxylic acid is seldom isolated[1]. During the course of our work on pyrazole carbaldehydes where we had utilized the reaction of 1-arylpyrazole-4-carbaldehydes, using ethanol as a solvent, we were surprised to find that the reaction with malonic acid as substrate did not undergo decarboxylation and a dioic acid product was obtained[2]. In our other area of research on the synthesis of triarylimidazoles[3] and Biginelli synthesis[4], we have found amino acids as efficient catalysts in these reactions. This led us to extend our work for efficacy of amino acids as catalysts in other organic reactions. Acrylic acid is an important molecule which has its main utility as the starting material in various polymer reactions and as such economically very important material[5]. Many aryl and hetaryl acrylic acids are reported in the literature, such as cinnamic acid, furylacrylic acid[6], pyrrole acrylic acid[7-10] and pyridine acrylic acid[11]. Some of these acids are being coupled as monomers which are later on used in polymer synthesis.

Knoevenagel condensation provides this material but utilizes pyridine or piperidine bases which are environmental hazards. As such there is a need to explore other catalysts which are environmentally benign. Amino acids thus seem to be of choice. Literature search shows that there are few references for the use of amino acids for catalyzing Knoevenagel condensation[12]. Amino acids and their derivatives have been investigated in the catalysis of reduction, oxidation, electrophilic α-fluorination and amination, carbon-carbon bond forming reactions[13-16], transamidation of carboxamide[17] as well as promoter of some of the reaction.

We are now extending our work of this eco-friendly catalyst in this condensation. Besides being non toxic these are well tolerated by physiological systems and are readily available. In this preliminary note we would like to report the findings of our work in the synthesis of organic-inorganic polymeric hybrid materials.

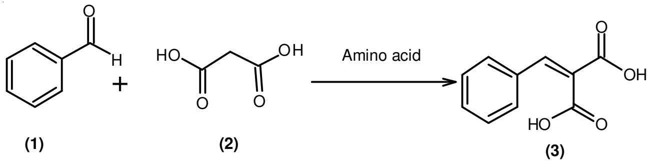
Organic-inorganic polymeric hybrid materials are synthesized by sol-gel processing of organofunctional metal alkoxides. These hybrid materials were initially termed as "ormosil" (organically modified silane) and latter "oromocers" (organically modified ceramis). Ormocers based on acrylic acids will be synthesized to explore their utility as multipurpose coatings. Acrylic co-polymers and acrylic acids modified terpolymer-silica hybrinano composite[18] as well as poly-(oxyethylenemethacrylate) (POEM) modified silica nanoparticles[19] with improved properties have been synthesized and characterized. Acrylics were first made commercially available in the 1950. The worldwide production of acrylic acid in 1994 was estimated to be approximately 2 million tonnes[5].

EXPERIMENTAL

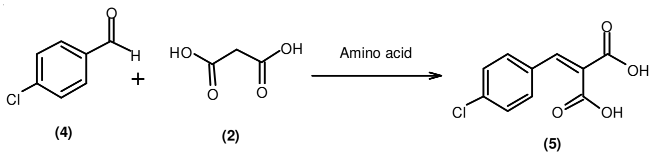
Most of the chemicals used during this research work were of commercial quality and were purified through normal techniques. Commercial TLC plates were used and UV light was used as a spot locating agent. Infrared spectra (IR) were recorded on Perkins Elmer FTIR (spectrum RXI) spectrometer. Mass spectra were recorded on mass spectrometer (MAT 312 Model). ^{1}H NMR spectra were recorded on Bruker NMR AM-400 MHz and 300 MHz.

Preparation of arylidene propanedioic acids: A mixture consisting of 0.2 mol of benzaldehyde (**1**), 0.2 mol of malonic acid (**2**) and 0.01 g of an amino acid in a 50 mL round bottomed flask was heated on a water bath for 2 h. The reaction mixture was cooled to room temperature and poured into 20 mL cold water. After 15 min standing it was filtered, washed with water, dried and recrystallized from ethanol to give benzylidene propanedioic acid (**3**) (**Scheme-I**).

***p*-Chlorobenzylidene propanedioic acid (5):** From *p*-chlorobenzaldehyde (**4**) and malonic acid (**2**) in 5 mL ethanol, *p*-chlorobenzylidene propanedioic (**5**) was isolated which was recrystallized from hot water. The results are presented in the Table-2 (**Scheme-II**).

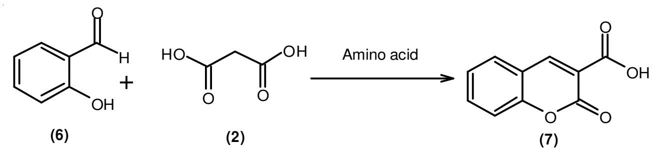


Scheme-I



Scheme-II

Coumarin-3-carboxylic acid (7): Following the general procedure, from salicylaldehyde (**6**) malonic acid (**2**) and an amino acid gave coumarin-3-carboxylic acid (**7**) which was recrystallized from hot water. The results are given in the Table-3 (**Scheme-III**).



Scheme-III

Ethyl-2-(4-chlorobenzylidene)-3-oxobutanoate (9): A reaction of *p*-chlorobenzaldehyde (**4**) ethyl acetoacetate (**8**) and an amino acid gave ethyl-2-(4-chlorobenzylidene)-3-oxobutanoate (**9**). It was recrystallized thrice from hot water. The results are presented in Table-4 (**Scheme-IV**).

TABLE-1
YIELD OF COMPOUND **3** EMPLOYING VARIOUS AMINO ACID CATALYSTS TOGETHER WITH THE ^{1}H NMR, FTIR AND MASS SPECTRA

Catalyst	Colour	Yield (%)	m.p. (°C)	Lit. m.p.[20]	IR (cm^{-1})	Mass (*m/z*)	^{1}H NMR
Glycine	Pale yellow	65	185	191°C	1677cm^{-1} (C=O); 1628cm^{-1}(C=C)	192(25 %)M$^+$; 174(100 %); 146(52 %); 129(26 %); 118(50 %); 102(51 %); 77(98 %).	(CDCl$_3$, 300 MHz) δ: 7.24–.11(5H, m, Ar-H, H-2-H-6)
Lysine	Yellow	56	188				
Methionine	White	68	186				
Hippuric acid	White	65	190				
Leucine	Pale yellow	64	182				

TABLE-2
SUMMARY OF CONDENSATION OF *p*-CHLOROBENZALDEHYDE WITH MALONIC ACID

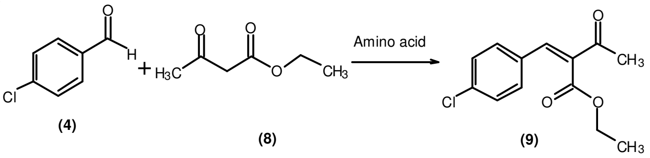
Catalyst	Colour	Yield (%)	m.p. (°C)	Lit. m.p.[21]	IR (cm^{-1})	Mass (*m/z*)
Glycine	White	58	210	215 °C	1677 cm^{-1} (C=O); 1623 cm^{-1} (C=C)	226 (45 %) M$^+$; 228 (16 %) M$^+$; 180 (100 %); 173 (72 %); 165 (24 %); 152 (19 %); 136 (27 %); 101 (39 %); 75 (28 %).
Lysine	White	76	205			
Methionine	Yellow	55	198			
Hippuric acid	White	65	207			
Leucine	Light yellow	70	202			

TABLE-3
COMPOUND (**7**) FROM THE CONDENSATION OF SALICYLDEHYDE WITH MALONIC ACID

Catalyst	Colour	Yield (%)	m.p. (°C)	Lit. m.p.[22]	IR	Mass (*m/z*)	^{1}H NMR
Glycine	White	66	181	189-192 °C	1704 cm^{-1} (C=O)	190 (31 %) M$^+$; 146 (100 %); 118 (67 %); 89 (60 %); 63 (64 %).	CDCl$_3$, 300 MHz 9.97 (1H, 5, H-4), 8.03 (1H, dd, *J* = 8.5, 2.0 H$_2$, H-5). 7.24 (1H, ddd, *J* = 8.5, 2.0, 2.0 H$_2$, H-6), 7.80 (1H, ddd, *J* = 8.0, 7.5 2.0 Hz, H-7) 7.44 (1H, dd, *J* = 8.0, 2.5 H$_2$, H-8)
Lysine	White	75	182				
Methionine	White	68	180				
Hippuric acid	White	73	184				
Leucine	White	76	189				

TABLE-4
COMPOUND (**9**) FROM THE CONDENSATION OF *p*-CHLOROBENZALDEHYE WITH ETHYL ACETOACETATE

Catalyst	Physical appearance	Yield (%)	m.p. (°C)	IR (cm^{-1})	Mass (*m/z*)
Glycine	Pale yellow	63	154	1739 cm^{-1} (C=O); 1623 cm^{-1} (C=C)	252 (100 %) M$^+$; (254 (30 %) M$^+$; 237 (66 %); 217 (%); 207 (46 %); 178 (27 %); 165 (77 %); 141 (29 %); 101 (28 %); 83 (58 %);
Lysine	White	65	155		
Methionine	Yellow	55	158		
Hippuric acid	White	50	155		
Leucine	White	68	156		



Scheme-IV

RESULTS AND DISCUSSION

Benzylidene propanedioic acid: Condensation of benzaldehyde (**1**) with malonic acid (**2**) was carried out in the presence of glycine as catalyst. This reaction gave good yield of benzylidene propanedioic acid (**3**). With a successful reaction it was then carried out in the presence of some other amino acids (Table-1). The product in each case was characterized through its TLC, m.p., IR, mass spectrum and ^{1}H NMR and were found to be identical with the product obtained with glycine (m.p., mixed m.p., TLC, IR 1677 cm^{-1} (C=O); mass (*m/z* 192 (25 %) M$^+$) and ^{1}H NMR: δ 7.24-8.11 (5H, m, Ar-H, H-2-H-6).

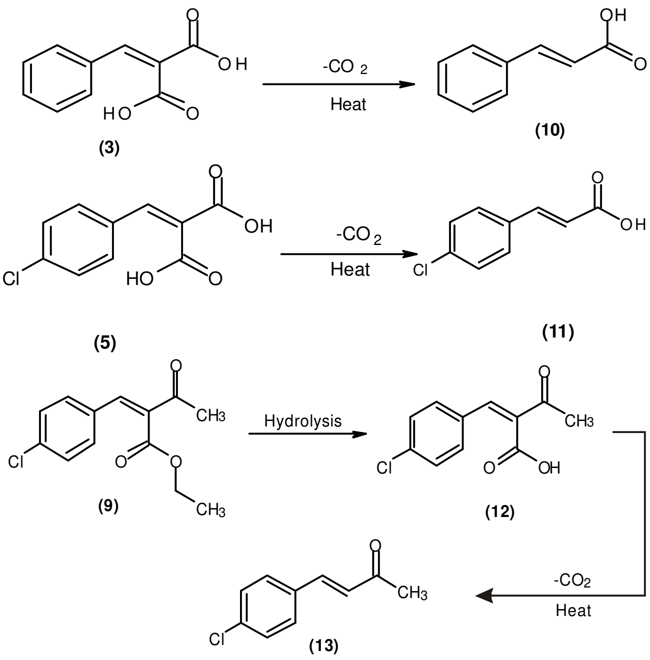
***p*-Chlorobenzylidene propanedioic acid:** A similar condensation of *p*-chlorobenzaldehyde (**4**) with malonic acid (**2**) with different amino acids as catalyst gave 4-chloro-benzylidene propanedioic acid (**5**) characterized through its TLC, m.p., IR and mass spectra (Table-2). All the products were similar as characterized through IR and mass.

Coumarin-3-carboxylic acid: Condensation of salicylaldehyde (**6**) with malonic acid (**2**) was carried out in the presence of amino acids as catalyst (Table-3). The most important characteristic of this reaction is that it is a solvent free synthesis of coumarin derivatives. The product, coumarin-3-caboxylic acid (**7**) was fully characterized through its TLC, m.p., IR, mass and ^{1}H NMR. The characteristic features of the spectra are as follows; IR (KBr, ν_{max}, cm^{-1}): 1704 (C=O); mass (*m/z*): 190 (31 %) M$^+$; 146 (100 %); 118 (67 %); 89 (60 %); 63 (64 %). ^{1}H NMR: (CDCl$_3$, 300 MHz): 9.97 (1H, 5, H-4), 8.03 (1H, dd, J = 8.5, 2.0, H2, H- 5). 7.24 (1H, ddd, J = 8.5, 2.0, 2.0 H$_2$, H-6), 7.80 (1H, ddd, J = 8, 7.5 2.0 Hz, H-7) 7.44 (1H, dd, J = 8.0, 2.5 H$_2$, H-8).

Ethyl-2-(4-chlorobenzylidene)-3-oxobutanoate: Condensation of *p*-chlrobenzyldehyde (**4**) with ethyl acetoacetate (**8**) was carried out in the presence of amino acids as catalyst. The product, ethyl-2-(4-chlorobenzylidene)-3-oxobutanoate (**9**) in each case was characterized through its TLC, m.p., IR and mass. All the products were similar as characterized through IR, mass and ^{1}H-NMR (Table-4). The salient features of these spectra are as follows; IR (KBr, ν_{max}, cm^{-1}): 1739 (C=O); 1623 (C=C). Mass (*m/z*): 252 (100 %) M$^+$; (254 (30 %) M$^+$; 237 (66 %); 217 (45 %); 207 (46 %); 178 (27%); 165 (77 %); 141 (29 %); 101 (28 %); 83 (58 %).

It was expected that the use of amino acids will not only catalyze the condensation but also help decarboxylation during the course of the reaction since it was conducted at the water bath (100 °C). But to our surprise in all the three reactions and with all the amino acid catalysts (Tables 1-3) dioic acids (**3** and **5**) and coumarin-3-carboxylic acid (**7**) were isolated. There was no indication of corresponding decarboxylated product.

These dioic acids[3,5] could easily be decarboxylated to yield the corresponding acrylic acids[10,11] and the product also could easily be selectively converted to compounds **10, 11** and **13** (**Scheme-V**).



Scheme-V

In this preliminary note amino acids are shown to be efficient catalysts in the Knoevenagel condensation. Further work is in progress in our laboratories.

Conclusion

In conclusion, we have described a general and highly efficient procedure for the preparation of some arylidene propanedioic acids. It is concluded from this work that amino acids in addition to be used in the synthesis employed as catalyst in other Knoevenagel condensations as well as other C-C bond forming reactions. In the present work the procedure for the synthesis of coumarin involved a solvent less system which is also environmentally benign. These acids have a potential use for applications in synthesis of organometallic sols for ceramic nano powders.

Future prospects

In our future work, organically modified ceramics will be synthesized by sol-gel method and their dioic acids will be grafted on organically modified ceramics to produce composite materials. The applications of these composite materials can further be explored as protective, decorative and/or as optical brightener coatings.

ACKNOWLEDGEMENTS

The authors are grateful to the Department of Mechanical and Manufacturing Engineering, Faculty of Engineering, Universiti Malaysia Sarawak (UNIMAS), 94300 Kota Samarahan, Sarawak, Malaysia for supporting this work under the DPI grant No 02(DPI08)/824/2011(08). The authors would also like to thank the Institute of Chemistry, University of the Punjab, Lahore, Pakistan, for their valuable help in conducting experiments.

REFERENCES

1. G. Jones, Organic Reactions Wiley, New York (1967).
2. F. Chaudhry, N. Asif, M.N. Khan, J. Ribeiro, A.Q. Ather, S. Hina, M.A. Munawar, M. Nasrullah, Q.T. Ain, F. Suhail and M.A. Khan, *Asian J. Chem.*, **25**, 7879 (2013).
3. F. Ijaz, M.N. Khan, S. Naureen, M.A. Khan, M.A. Munawar and A.M.R. Bernardino, *Asian J. Chem.*, **24**, 5114 (2012).
4. A.M. Zafar, M.N. Khan, M. Azad, M.A. Munawar and M.A. Khan, *Asian J. Chem.*, **25**, 3244 (2013).
5. T. Ohara, T. Sato, N. Shimizu, G. Prescher, H. Schwind, O. Weiberg, K. Marten and H. Greim, Ullmann's Encyclopedia of Industrial Chemistry (2003).
6. K. Budde, F. Quella, A. Mathes, W. Melchior, H. Müller, O. Nuyken and S. Spiegel, *Die Angew. Makromol. Chem.*, **194**, 103 (1992).
7. C.-L. Lin and W.-Y. Chiu, *J. Polym. Sci. A Polym. Chem.*, **44**, 1648 (2006).
8. A. Bhattacharya, A. De and S.N. Bhattacharyya, *Synth. Met.*, **65**, 35 (1994).
9. W. Wang, L. Lu, T. Chen and M. Rao, *J. Appl. Polym. Sci.*, **126**, 974 (2012).
10. Q. Li, J. Wu, Z. Tang, Y. Xiao, M. Huang and J. Lin, *Electrochim. Acta*, **55**, 2777 (2010).
11. C.S. Marvel, L.E. Coleman and G.P. Scott, *J. Org. Chem.*, **20**, 1785 (1955).
12. F.S. Prout, *J. Org. Chem.*, **18**, 928 (1953).
13. K. Sakthivel, W. Notz, T. Bui and C.F. Barbas, *J. Am. Chem. Soc.*, **123**, 5260 (2001).
14. L.A. Al-Momani, *ARKIVOC*, 101 (2012).
15. B. List, *Tetrahedron*, **58**, 5573 (2002).
16. A.J. Cobb, D.M. Shaw, D.A. Longbottom, J.B. Gold and S.V. Ley, *Org. Biomol. Chem.*, **3**, 84 (2005).
17. N.V. Shitole, K.F. Shelke, S.S. Sonar, S.A. Sadaphal, B.B. Shingate and M.S. Shingare, *Chem. Inform.*, **41**, i (2010).
18. S. Patel, A. Bandyopadhyay, V. Vijayabaskar and A.K. Bhowmick, *J. Mater. Sci.*, **41**, 927 (2006).
19. J.T. Park, J.A. Seo, S.H. Ahn, J.H. Kim and S.W. Kang, *J. Ind. Eng. Chem.*, **16**, 517 (2010).
20. C.A. Kingsbury, D. Draney, A. Sopchik, W. Rissler and D. Durham, *J. Org. Chem.*, **41**, 3863 (1976).
21. J.S. Bindra, Enkephalinase Enzyme Inhibiting Compounds, US Patent 4,329,495 (1982).
22. L.L. Woods and J. Sapp, *J. Org. Chem.*, **30**, 312 (1965).