Facile and Rapid Synthesis of Some Optically Active Imide-Acid Derivatives Using Microwave Irradiation

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Abstract:

Imide acid derivatives are an important class of substrates for biological and chemical applications. In the chemical applications they are used for synthesis of new amino acid derivatives and peptides. In this paper rapid and highly efficient synthesis of six optically active imide-acid derivatives **4(a-f**) was achieved under microwave irradiation by using a domestic microwave oven from the reactions of six different chiral α-amino acid **2(a-f)** with phthalic anhydide **1** in the presence of small amount of N,N-dimethyl formamide (DMF) as a base. The reaction proceeded rapidly (100-150 sec), and as a result a series of chiral imide-acid derivatives **4(a-f**) were obtained in high yields (96-100 %). All of the synthesized compounds were fully characterized by their melting point, specific rotations, elemental analyses, ^{1}H-NMR and FT-IR spectroscopy.

KeyWords: Microwave-assisted reaction**,** Optically active imide-acids**,** α-Amino acids.

Introduction

In the recent years, the use of microwave technology in organic synthesis has received considerable attention [1-2], the reason is that this technology can increase the purity of the resulting products, enhance the chemical yield and shorten the reaction time [3]. It has been reported that a variety of reactions such as Diels-alder [4], Ene [5], Claisen reactions [6], Fischer cyclization [7], synthesis of heterocycles [8], hydrolysis of esters [9], hydrogenation [10], deprotection of benzyl ester [11], deacetylation of diacetates [12], oxazoline formation [13] and polymer synthesis [14-22] could be facilitated by microwave irradiation in a good energy transferring medium. In this article a facile and rapid method for the synthesis of some chiral imide-acid derivatives under microwave irradiation was reported (Scheme 1). By use of this method six chiral imide-acid derivatives **4(a-f)** have been synthesized in excellent yields (96-100%) in a short time. Comparing these results with recent published works by convention

thermal heating [23-29] and by microwave assisted reactions [30] shows that not only these imide-acid were obtained in high yield but also time of reactions dramatically is decreased.

Experimental

All chemicals were purchased from Aldrich Chemical Co. (Milwaukee, WI) and Merck Chemical Co. (Germany). Melting points were determined by using an electrothermal digital melting point apparatus. ^{1}H-NMR spectra were recorded on a Bruker 500 MHz instrument. Fourier transform infrared (FTIR) spectra were recorded on Galaxy series FTIR 5000 spectrophotometer (England). Spectra of solids were performed using KBr pellets. Vibrational transition frequencies are reported in wave number (cm^{-1}). Band intensities are assigned as weak (w), medium (m), shoulder (sh), strong (s) and broad (br). Specific Rotations were measured by an A-Kruss polarimeter. Elemental analyses were performed by the Research Institute of Petroleum Industry, Tehran, Iran. As the source of microwave irradiation, I used a Samsung domestic microwave oven (2450 MHz, 900 W) for carrying out reactions.

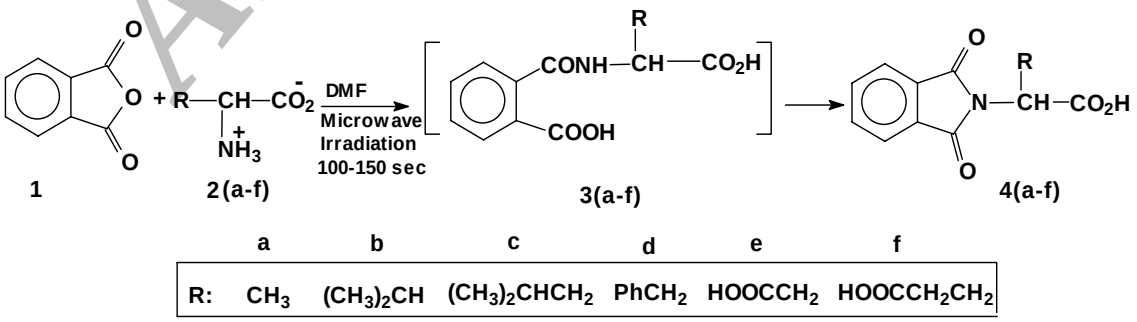
Synthesis of Chiral imide-acid derivatives 4(a-f)

These compounds were prepared according to a typical procedure that was shown in scheme 1.

(0.025 mole) of freshly powdered phthalic anhydide **1** and (0.025 mole) of chiral amino acid **2(a-f)** were placed in a reaction vessel and the mixture was ground until fine powder formed, then proper amount of N,N-dimethyl formamide (DMF) (almost between 0.3-0.5 ml) added to reaction mixture as a base. Then the reaction mixture was irradiated in microwave oven at full power for 100-150 sec. Progress of the reaction was monitored by Thin Layer Chromatography. Then the reaction mixture was poured into 50 mL of water. After the usual workup, the chiral imide-acide derivatives **4(a-f)** were recrystallized with proper solvent (Table 1).

Results and discussion

Thus several chiral amino acid 2(a-f) undergo condensation with phthalic anhydrid when subjected to microwave irradiation in the presence of small amount of N,N-dimethyl formamide as a base (Scheme 1). From the results summarized in Table 1 the generality of the reaction is evident, as a variety of chiral amino acid 2(a-f) reacts to form chiral imide-acid derivatives 4(a-f) in good yields (96-100 %) within a very short time of irradiation (100-150 sec). The conversions were fairly clean and were free from common byproducts.



Scheme 1

Table 1 Microwave assisted synthesis of chiral imide acid derivatives 4(a-f**)**

Entry	Amino acid compound	R	mp (^{O}C)	Irradiation time (sec)	Yield of **4** (%)	[a] $[\alpha]_D^{25}$
4a	L-Alanine	CH_3	145-146	100	100	-23.5
4b	L-Valine	$(CH_3)_2CH$	114-115	100	98	-68.5
4c	L-Lucine	$(CH_3)_2CHCH_2$	120-122	120	98	-25.0
4d	L-Phenyl alanine	$PhCH_2$	181-183	120	96	-210.0
4e	L-Aspartic acid	$HOOCCH_2$	223-225	150	99	-57.0
4f	L-Glutamic acid	$HOOCCH_2CH_2$	158-160	150	96	-45.0

[a] Measured at a concentration of 0.5g/dL in EtOH at 25^{o}C.

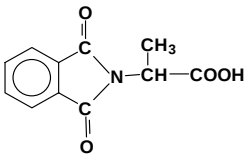
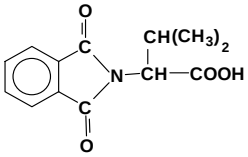
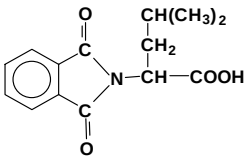
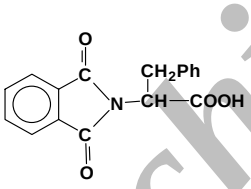
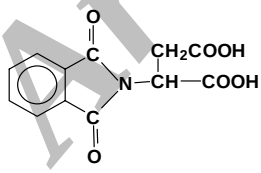
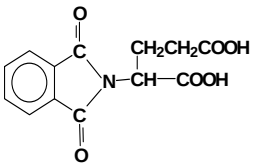
The yields of the resulting imide-acid derivatives 4(a-f) obtained by microwave assisted reaction were compared with those obtained with conventional thermal reactions and results show the internal heat generation of reaction mixture under the microwave irradiation is much more effective for the progress of reaction in a shorter reaction time.

The FT-IR spectra of imide-acid derivatives 4(a-f) showed strong peak between 2500-3500 cm^{-1} which was assigned to the O-H of acid group in these compounds. Absorption bands between 1780-1700 cm^{-1} which were characteristic peaks for two asymmetric and symmetric stretching of carbonyl groups in imid ring and carbonyl groups in acid groups. Absorption bands around 1390-1360 cm^{-1} and 740-710 showed the presence of the imide heterocyle in these compounds. The elemental analysis values of the resulting polymers are in good agreement with the calculated values for the proposed structures (Table 2).

Conclusion

Imide acid derivatives are an important class of substrate for biological and chemical applications. In the chemical synthesis imide acid derivatives are used for protecting amino acids. The above results demonstrate that microwave heating is an efficient method (shorter reaction time and high efficiency of energy) for synthesis of imide acid derivatives in compare to solution reaction. We are currently using this method for the synthesis of novel monomer, polymer and modification of polymer.

Table 2. [1]H-NMR and FTIR Spectral and Elemental Analyses Data of Imide-acid derivatives **4 (a-f)**

Compd. (Formula)	Structure	Spectral Deta
4a ($C_{11}H_9NO_4$)		**[1]H-NMR (90MHz, DMSO-d_6): 1.5-1.7 (d, 3H, 6Hz), 4.2-4.5 (q, 1H, 5 Hz), 8.0-8.5 (m, 4H), 6.9-7.0 (br, 1H) ppm.** **FTIR (KBr):** 2900-3500 (s, br), 1764 (s), 1703 (s), 1485 (m), 1402 (s, br), 1197 (m), 1074 (m), 847 (m), 750 (m), 725 (m) cm^{-1}. Analysis: Calculated for $C_{11}H_9NO_4$: C, 60.27; H, 4.13; N, 6.39; found: C, 60.0, H, 4.3, N, 6.1.
4b ($C_{13}H_{13}NO_4$)		**[1]H-NMR (500MHz, DMSO-d_6): 1.20-1.25 (d, 6H, 6Hz), 2.60-2.80 (m, 1H), 4.90-4.97 (m, 1H), 6.40-6.45 (s, br, 1H), 8.00-8.20 (m, 4H) ppm.** **FTIR (KBr):** 2900-3500 (s, br), 2966 (m), 1770 (s), 1693 (s), 1467 (m), 1398 (s, br), 1197 (m), 1097 (m), 904 (m), 750 (m), 729 (m) cm^{-1}. Analysis: Calculated for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.29; N, 5.66; found: C, 63.2, H, 5.2, N, 5.4.
4c ($C_{14}H_{15}NO_4$)		**[1]H-NMR (500MHz, DMSO-d_6): 0.90-95 (d, 6H, 7Hz), 1.70-1.90 (m, 1H), 2.40-2.60 (m, 2H), 4.20-4.30 (t, 1H, 7Hz), 6.50-6.60 (s, br, 1H), 8.10-8.20 (m, 4H) ppm.** **FTIR (KBr):** 2800-3500 (s, br), 2964 (m), 2878 (m), 1770 (m), 1722 (s), 1465 (m), 1386 (s, br), 1290 (m), 869 (m), 750 (m), 722 (m) cm^{-1}. Analysis: Calculated for $C_{14}H_{15}NO_4$: C, 64.35; H, 5.78; N, 5.36; found: C, 64.3, H, 5.9, N, 5.2.
4d ($C_{17}H_{13}NO_4$)		**[1]H-NMR (500MHz, DMSO-d_6): 2.80-3.00 (dd, 2H, 6Hz), 4.40-4.70 (t, 1H, 7Hz), 6.70-6.90 (s, br, 1H), 7.00-7.20 (m, 5H), 8.00-8.20 (m, 4H) ppm.** **FTIR (KBr):** 2800-3500 (s, br), 2989 (m), 2870 (m), 1772 (s), 1714 (s), 1604 (w), 1500 (m), 1383 (s, br), 1282 (s), 1105 (m), 847 (m), 750 (m), 720 (m) cm^{-1}. Analysis: Calculated for $C_{17}H_{13}NO_4$: C, 69.14; H, 4.43; N, 4.74; found: C, 69.3, H, 4.3, N, 4.5.
4e ($C_{12}H_9NO_6$)		[1]H-NMR (500MHz, DMSO-d_6): **2.90-3.20 (m, 2H), 4.70-4.80 (t, 1H, 8Hz), 8.00-8.20 (m, 4H), 8.30-8.50 (s, br, 2H) ppm.** **FTIR (KBr):** 2600-3500 (s, br), 1795 (m), 1710 (s), 1605 (w), 1400 (m), 1382 (s, br), 1271 (s), 1170 (m), 902 (m), 750 (m), 725 (m) cm^{-1}. Analysis: Calculated for $C_{12}H_9NO_6$: C, 54.76; H, 3.44; N, 5.32; found: C, 54.9, H, 3.6, N, 5.2.
4f ($C_{13}H_{11}NO_6$)		[1]H-NMR (500MHz, DMSO-d_6): **2.10-2.40 (m, 2H), 3.20-3.40 (t, 2H, 7Hz), 5.10-5.30 (t, 1H, 8Hz), 8.00-8.20 (m, 4H), 8.30-8.50 (m, br, 2H) ppm.** **FTIR (KBr):** 2700-3500 (s, br), 1790 (m), 1710 (s), 1605 (w), 1400 (m), 1380 (s, br), 1270 (s), 1170 (m), 750 (m), 720 (m) cm^{-1}. Analysis: Calculated for $C_{13}H_{11}NO_6$: C, 56.32; H, 3.99; N, 5.05; found: C, 56.5, H, 4.1, N, 5.0.

References

1- Michael, D., Mingos, P. and Baghurst, R., *Chem. Soc. Rev*, **20**, 1 (1991).
2- Galema, S. A., *Chem. Soc. Rev*., **26**, 233 (1997).
3- Caddick, S., *Tetrahedron*, **51**, 10403 (1995).
4- . Giguere, R. J. and et al, *Tetrahedron Lett*, **28**, 6553 (1987).
5- Giguere, R. J., Bary, T. L. and Duncan,S. M., *Tetrahedron Lett***., 27**, 4945 (1986).
6- Srikrishna, S. and Nagaraju, J., *Chem. Soc. Perkin. Trans*, 311 (1992).
7- Abramovitch, R. A. and Bulman, A.*, Synlett*, 795 (1992).
8- Alaharin, R. and Baguero, J. J., *J. L. Garcia Navio and J. Alvarez-Builla, Synlett*., 297 (1992).
9- Ley, S. V. and Mynett, D. M., *Synlett*, 793 (1993).
10- Bose, K., Banik, B. K., Barakat, K. J. and Manhas, M. S., *Synlett*, 575 (1993).
11- Varma, R. S., Chatterjee, A. K. and Varma, M., *Tetrahedron Lett*, **34**, 4608 (1993).
12- Varma, R. S., Chatterjee, A. K. and Varma, M., *Tetrahedron Lett*, **34**, 3207 (1993).
13- Qussaid, J., Berlan, M. and Soufiaoui, B., *Synth. Commun*, **25**, 659 (1995).
14- Imai, Y., Nemoto, H., Watanabe, S.and Kakimoto, M. A., *Polym. J.,* **28**, 256 (1996).
15- Wei, J., Hawley, M. C. and Delong, J. D., *Polym Engineering and Sci*., **33**, 1132 (1993).
16- Faghihi, Kh., Zamani, Kh., Mirsamie, A. and Sangi, R., *Europ. Polym. J*., **39**, 247 (2003).
17- Faghihi, Kh. and Hajibeygi, M., *Europ. Polym*. J., **39**, 2307 (2003).
18- Faghihi, Kh., Zamani, Kh., Mirsamie, A. and Mallakpour, S., *J. of Appl. Polym. Sci*., **91,** 516 (2004).
19- Faghihi, Kh., Zamani, Kh. and Mallakpour, S., *Polym. Inter*., **53**, 1226 (2004).
20- Faghihi, Kh. and Hajibeygi, M., *J. of Appl. Polym. Sci*., **92**, 3447 (2004).
21- Faghihi, Kh., *Macromol Research*, **12,** 258 (2004).
22- Faghihi**,** Kh., *Polym. J*., **37**, 449 (2005).
23- Fling, M. and Minard, F. N., S. W. Fox, *J. of Am. Chem. Soc*., **69**, 2466 (1947).
24- Billman, J. H. and Harting, W. F., *J. of Am. Chem. Soc*., **70**, 2466 (1948).
25- Tipson, R. S., *J. of Org. Chem*., **21**, 1353 (1956).
26- Bose, K., Greer, F. and Price,C. C., *J. of Org. Chem*., **23**, 1353 (1958).
27- Hoffmann, E. and Shernhav,H. S., *J. of Org. Chem*., **27**, 1353 (1962).
28- Bose, K. and Strube, R. E., *J. of Pharmaceutical Sci*., **52**, 847 (1963).
29- Khadilkar, M. and Madyar, V. R., *Indain J. of Chem*., **41B,** 1083 (2002).
30- Hajipour, A. R., Mallakpour, S. E. and Imanzadeh, G. H., *Indain J. of Chem*., **40B,** 250 (2001).