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Tetrahedron Letters 46 (2005) 3151–3155
Tetrahedron Letters

Microwave assisted cyclocondensation of dialdehydes with chiral diamines forming calixsalen type macrocycles

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Received 29 December 2004; revised 5 March 2005; accepted 15 March 2005

Abstract—Microwave irradiation of various dialdehydes and chiral diamines afforded chiral macrocyclic imines in moderate to good yields. Linked dialdehydes predominantly form [2+2] macrocycles whereas dialdehydes without linkers yield [3+3] macrocycles. This is the first report of template-free synthesis of calixsalen-type macrocycles formed in shorter reaction times under microwave conditions. In all the reactions, the salts of chiral diamines were used in contrast to the free diamines normally employed.

Over the past few decades, macrocyclic compounds have been extensively studied for their molecular recognition and supramolecular structures. Macrocycles containing a Schiff base and hydroxyl moieties[1] are particularly attractive as they form multi-metal complexes which exhibit catalytic and fluorescent properties.[2] Gawronski et al.[3] introduced a synthetic strategy for the synthesis of chiral macrocyclic hexaimines via a [3+3] cyclocondensation of 1,4- and 1,3-dialdehydes and enantiopure diamines under dilute reaction conditions. Kuhnert et al.[4] have synthesized similar chiral macrocycles containing up to 42-membered rings using a variety of dialdehydes. Indeed, many examples of macrocyclic polyimines formed by [2+2] and [3+3] cyclocondensation reactions are known.[5] Jablonski and co-workers[6] synthesized hydroxyl-containing [2+2] chiral macrocyclic calixsalens using a metal ion template. Apart from applications in supramolecular chemistry, these macrocyclic salen compounds are also used as fluorescent sensors[2] and as chiral ligands for a variety of asymmetric catalytic reactions like epoxidation,[6a] alkyne addition[7] and epoxide ring-opening reactions.[8] Jacobsen et al.[8] employed a chiral cyclic oligosalen ligand, which is an oligomeric mixture, for asymmetric epoxide ring-opening reactions. Although many examples of chiral macrocyclic Schiff bases have been reported, a short and efficient synthesis of this type of macromolecule remains a challenge for synthetic chemists since the existing methods involve the need for a template, dilute reaction conditions, long reaction times and enantiomerically pure diamines.

Herein, we report the first synthesis of calixsalen type chiral macrocyclic polyimines using salts of cyclic as well as acyclic diamines under microwave irradiations. The reaction is very rapid and does not require harsh conditions.

Scheme 1 represents the general procedure for the formation of calixsalen type macrocycles from linked dialdehydes and chiral diamines. The process involves microwave irradiation (unmodified domestic microwave oven) of a mixture containing the dialdehyde and the salt of a chiral diamine with an excess of potassium carbonate in 1:1 water–ethanol for 5 min (the corresponding thermal reaction takes 2–3 h which predominantly forms linear polymers with lower yield of macrocycles).

Condensation of 5,5′-methylene-bis-salicylaldehyde[6a] **1** with (1*R*,2*R*)-diammoniumcyclohexane mono-(+)-tartrate[9a] **2** gave a mixture of [1+1], [2+2] and [3+3] cyclocondensation products in 55% yield (Table 1, entry 1). The MALDI-TOF spectra of this mixture clearly showed predominant peaks due to [1+1], [2+2] and [3+3] macrocycles (*m*/*z* 334, 668, and 1002). These macrocycles were analyzed as a mixture and the individual components were not isolated. With a cyclic diamine

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Keywords: Macrocycles; Schiff bases; Microwave.

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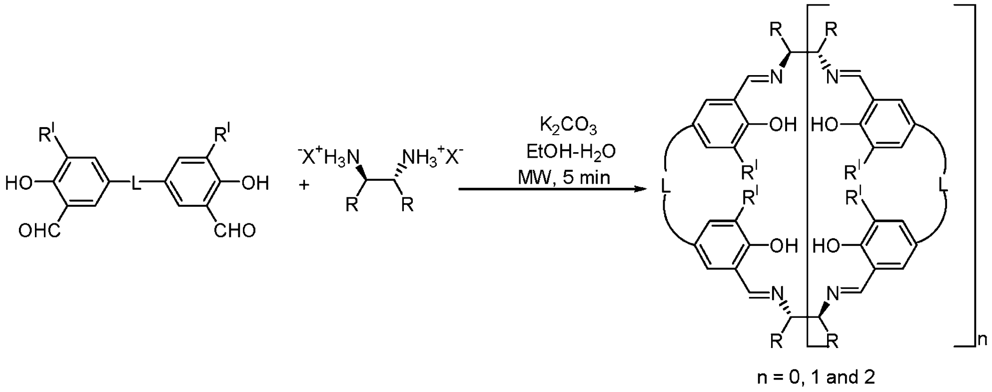
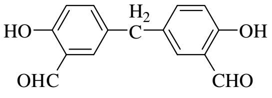
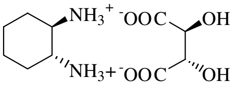
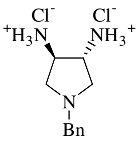
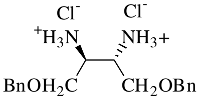
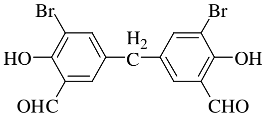
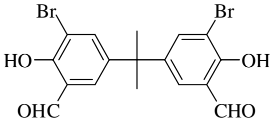
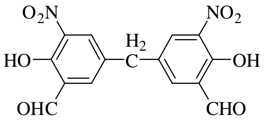
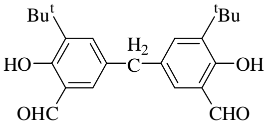
doi:10.1016/j.tetlet.2005.03.089



Scheme 1. Cyclocondensation of linked dialdehydes with chiral diamines under microwave irradiation.

Table 1. [2+2] Cyclocondensation of linked dialdehydes with chiral diamines

Entry	Dialdehyde	Chiral diamine	Yield (%)
1	 **1**	 **2**	55[a]
2		 **3**	31[b]
3		 **4**	26[b]
4	 **5**	**2**	45[b]
5		**3**	52[b]
6	 **6**	**2**	41[b]
7		**3**	47[b]
8	 **7**	**2**	ND
9	 **8**	**4**	25[b]