

A NEW APPROACH TO THE SYNTHESIS OF CHIRAL TETRAAZACORONANDS DERIVED FROM L-ALANINE*

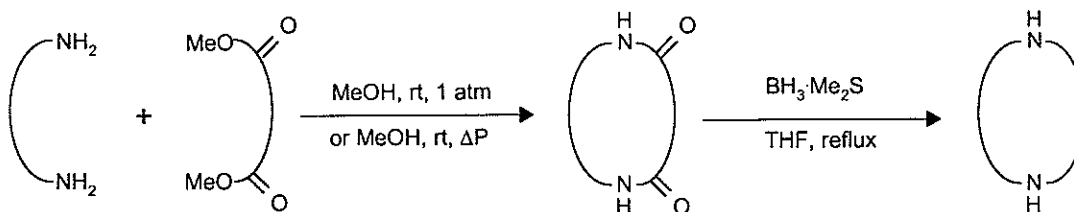
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Abstract - Dimethyl α,ω -dicarboxylates react under high pressure or ambient conditions with chiral primary diamino ethers derived from L-alanine to give the chiral cyclic diamides or tetramides in satisfactory yields. The effective preparation of chiral amino components starting from L-alanine is also described.

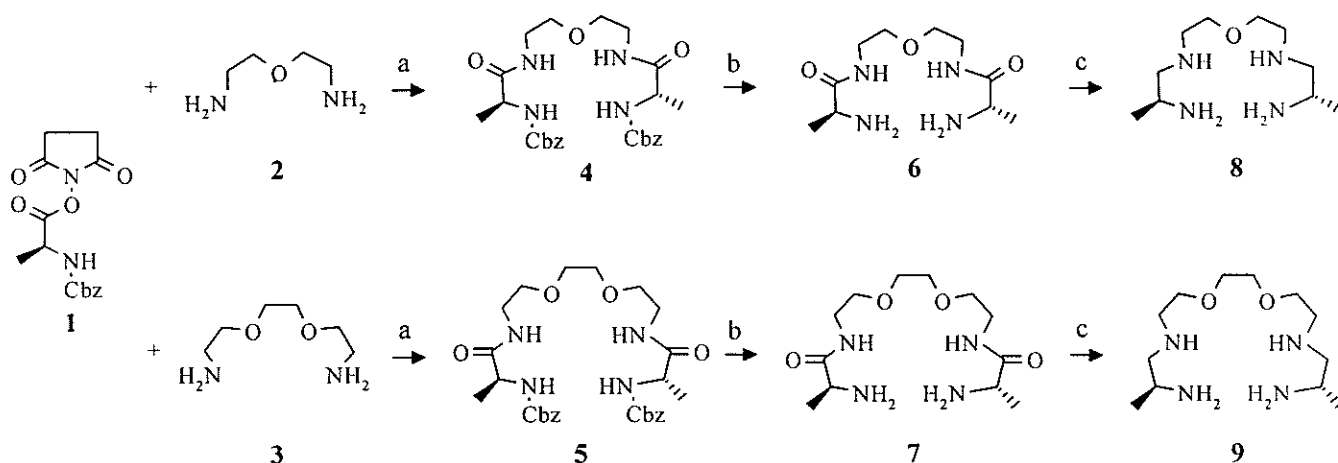
There are several papers describing the preparations of cyclic diamides as intermediates in the synthesis of diazacoronands.¹ An interesting approach to this problem has been reported by Tabushi *et al.*² as a condensation of primary α,ω -diamine with dimethyl ester of malonic or oligoglycolic acids in boiling ethanol. Recently, we have found³ that this method can be extended to other, more complex dicarboxylic esters. This finding constitutes a very efficient and versatile procedure for the synthesis of various macrocyclic diamides, as schematically shown in Scheme 1.



Scheme 1

*Dedicated to Professor Teruaki Mukaiyama on the occasion of his 73rd birthday.

We investigated the usefulness of this method for the preparation of chiral polyazacoronands derived from L-alanine. After protecting the amino group, we synthesized the active *N*-hydroxysuccinimide ester (**1**), which was subjected to reactions with amines (**2**) and (**3**), respectively (Scheme 2). The resulting products (**4**) and (**5**) were treated with hydrogen in the presence of the 5% Pd/C catalyst to afford the amines (**6**) and (**7**), respectively, which were then reduced using $\text{BH}_3 \cdot \text{Me}_2\text{S}$ (BMS) to form amines (**8**) and (**9**), respectively.



Scheme 2. Reagents and conditions: (a) THF, rt; (b) H_2 , 5% Pd/C, MeOH, rt; (c) $\text{BH}_3 \cdot \text{Me}_2\text{S}$, THF, reflux.

Table 1. Double-amidation reactions leading to chiral tetraazacoronands^{a,b}

Entry	Diamine	Diester	Tetraaza-coronand	Pressure	Time	Yield [%]	$[\alpha]_D^{20}$
1	6	10	13	10 kbar	24 h	9	-5.0
2	6	11	14	10 kbar	24 h	10	-21.1
3	6	12	15	10 kbar	24 h	11	-19.8
4	7	10	16	10 kbar	24 h	10	-12.8
5	7	11	17	10 kbar	24 h	10	-2.0
6	7	12	18	10 kbar	24 h	8	-7.9
7	8	10	19	10 kbar	24 h	37	-15.8
8	8	10	19	1 atm	7 days	66	
9	8	11	20	10 kbar	24 h	23	-7.6
10	8	11	20	1 atm	7 days	18	
11	8	12	21	10 kbar	24 h	43	-5.8
12	8	12	21	1 atm	7 days	55	
13	9	10	22	10 kbar	24 h	37	-3.3
14	9	10	22	1 atm	7 days	54	
15	9	11	23	10 kbar	24 h	29	-5.2
16	9	11	23	1 atm	7 days	30	
17	9	12	24	10 kbar	24 h	34	-2.6
18	9	12	24	1 atm	7 days	41	

^a All reactions were carried out at room temperature and in methanol as a solvent.

^b Optical rotations were measured for 1% solutions in ethanol.

The resulting amines (8) and (9), as well as starting amines (6) and (7), were subjected to cyclisation reactions with the methyl esters of carboxylic acids derived from di-, tri-, and tetraethylene glycols (10, 11, and 12, respectively) as shown in Table 2.^{4,5} The reaction yields are shown in Table 1. The yields are generally good and they are higher for amines (8) and (9) than for (6) and (7).

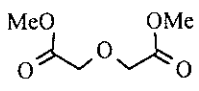
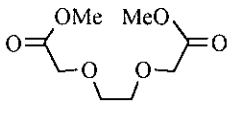
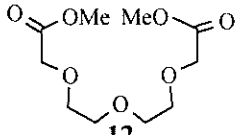
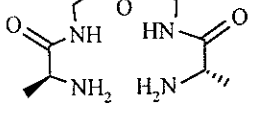
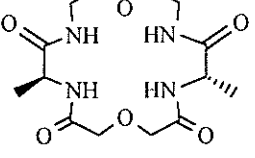
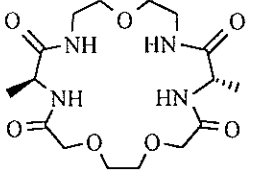
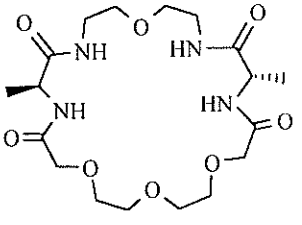
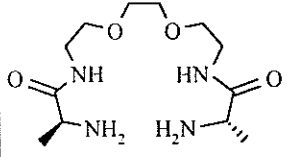
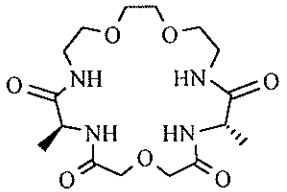
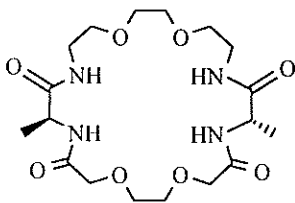
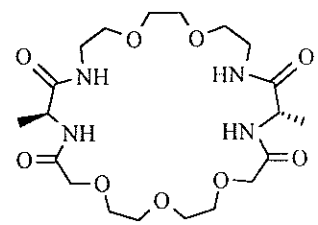
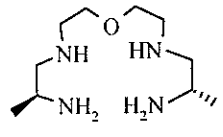
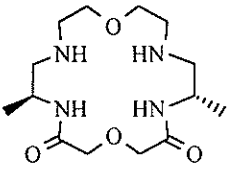
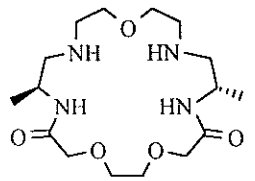
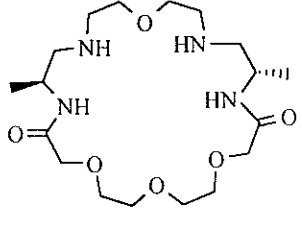
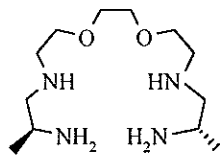
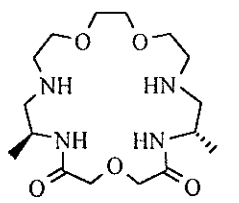
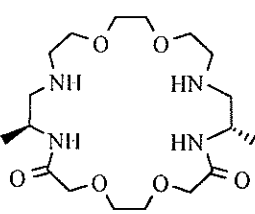
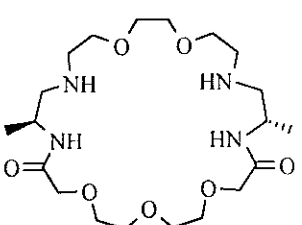
	 10	 11	 12
 6	 13	 14	 15
 7	 16	 17	 18
 8	 19	 20	 21
 9	 22	 23	 24

Table 2

The results presented here demonstrate that chiral α,ω -diamines obtained from L-alanine can be efficiently transformed into various macrocyclic diamides and tetraamides with satisfactory yields. Investigations on the application of other α -amino acids to this problem are in progress.

ACKNOWLEDGEMENTS

Financial support from the National Committee for Scientific Research (KBN grant 3 T09A 127 15) is gratefully acknowledged.

REFERENCES AND NOTES

1. For recent comprehensive reviews see:
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 - b) T. Stankiewicz and J. Jurczak, *Polish J. Chem.*, 1992, **66**, 1743.
 - c) J. Jurczak, P. Lipkowski, T. Stankiewicz, and Z. Urbańczyk-Lipkowska, *Supramol. Chem.*, 1995, **6**, 87.
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 - d) P. Lipkowski, D. T. Gryko, J. Jurczak, and J. Lipkowski, *Tetrahedron Lett.*, 1998, **39**, 3833.
4. All macrocyclic compounds obtained (**13-24**) have correct high-resolution MS, and ^1H and ^{13}C NMR spectra.
5. Typical procedure: An equimolar 0.1 M methanolic solution of α,ω -diamine and dimethyl α,ω -dicarboxylate was left at ambient temperature over a period of 7 days. Then the solvent was evaporated and the residue was chromatographed on the silica gel column using 0.5-3% mixtures of MeOH in CHCl_3 . The high-pressure procedure was identical to that reported earlier: D. T. Gryko, P. Piatek, and J. Jurczak, *Synthesis*, 1999, 336.

Received, 28th April, 1999