Journal of Inclusion Phenomena and Molecular Recognition in Chemistry 7: 309–311, 1989.

One-step Alkali Metal Ion Promoted Macrobicyclization. Synthesis of (*m*-xylyl 2.2)-Cryptand

MAREK PIETRASZKIEWICZ,* RAFAŁ GASIOROWSKI, and
MAŁGORZATA KOŹBIAŁ
Institute of Physical Chemistry, Polish Academy of Sciences, 01224 Warszawa, Kasprzaka 44/52, Poland

(Received: 16 February 1988; in final form: 1 September 1988)

Abstract. A single step, alkali metal ion-assisted macrobicyclization reaction between α,α′-diamino-*m*-xylene and either *bis*(2-iodoethoxy)ethane or *bis*(2-*p*-toluenesulphonyloxyethoxy)ethane affords (*m*-xylyl 2.2)-cryptand in good yield. Clear evidence for a template effect is found with the sodium cation. This method offers an alternative route to 4,13-diaza-18-crown-6.

Key words. Cryptand, macrobicyclization, template synthesis.

1. Introduction

Although the high dilution technique has enjoyed considerable popularity in the formation of macropolycyclic molecular receptors, there has been remarkable interest in the metal ion-assisted syntheses of macrocyclic polyazamacrocycles [1–5] and cryptates [6–8].

Template synthesis may be considered as a complementary method to a high dilution procedure. On the other hand, the removal of the template ion from the macrocyclic complex may be problematic in particular cases.

Successful syntheses of lariat crown ethers involving metal ions as templates encouraged us to use this strategy in macrobicyclizations leading to cryptand structures. The title compound has previously been obtained using the high dilution method [9].

We now report on the template synthesis of 4,13-diaza-18-crown-6 bridged with a *m*-xylylene unit.

2. Experimental

All reagents were of analytical grade and used without further purification, except acetonitrile which was distilled over CaH_2.

2.1. SYNTHESIS OF (*m*-XYLYL 2.2)-CRYPTAND 3

To the suspension of sodium carbonate (250 g, 2.35 mol) in acetonitrile (500 mL) two solutions containing diamino-*m*-xylene **1** (27.2 g, 0.2 mol) and triethylene

---

* Author for correspondence.

Presented at the International Symposium on Inclusion Compounds, Jaszowiec, Poland, 24–26 September 1987.

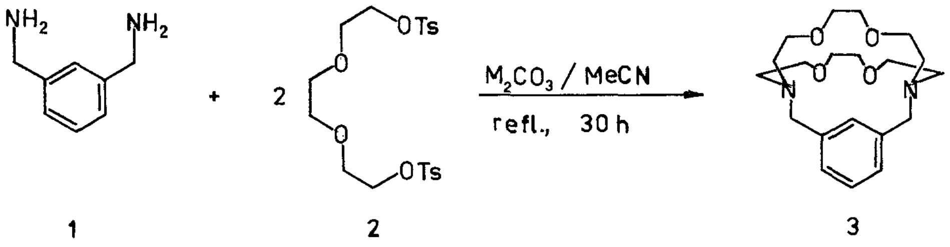
glycol bistosylate **2** (183.2 g, 0.4 mol) in MeCN (1000 mL) each were added simultaneously with efficient stirring and reflux over a 3 h period. Stirring and refluxing was maintained for 30 h. The solution was filtered while warm, washed with MeCN and evaporated. The residue was treated with water (150 mL) and extracted with $CHCl_3$ (2 x 250 mL), saturated with CO_2 and filtered. Evaporation yielded an orange residue which was extracted with boiling heptane. The product **3** was crystallized from ethyl acetate. Yield 18.2 g (25%).

Hydrogenation of **3** was achieved on Pd/C-10% in ethanol solution and H_2 at atmospheric pressure to form 4,13-diaza-18-crown-6 quantitatively.

Six additional condensations were performed with diamino-*m*-xylene **1** (1 mmol) and *bis*(2-iodoethoxy)ethane (2 mmol) in MeCN (30 mL) for 30 h at 80°C. Samples of the resulting solutions were taken for yield determination by an HPLC method: column RP–18 5 μm, length 100 mm, diameter 4.6 mm, flow rate 0.6 ml/min, UV 254 nm detection; eluent: H_2O 90%, EtOH 10%, H_3PO_4; 6×10^{-2} M, KH_2PO_4; 3×10^{-2} M, Et_2NH; 3×10^{-2} M.

3. Results and Discussion

We found that the macrobicyclization can be achieved in one step in 25% yield according to the scheme shown.



The α,α'-diamino-*m*-xylene **1** reacted in boiling acetonitrile with two molecules of triethylene glycol *bis*-*p*-toluenesulphonate **2** to form the macrobicyclic compound **3** (mp: 103°C) whose analytical data were in agreement with those reported previously [9] (MS: 364, M^+).

Table I. Relative yields[a] of macrobicyclization

Carbonate	Yield
Li_2CO_3	0.66
Na_2CO_3	1
K_2CO_3	0.9
$CaCO_3$	0.47
$BaCO_3$	0.45
$PbCO_3$	0.18

[a] Relative to that obtained with Na_2CO_3.

In order to optimize the yield, we performed several macrobicyclizations involving *bis*(2-iodoethoxy)ethane [7] and diamine **1**, using different salts as templates and bases. The final yields were estimated by an HPLC method. The results are collected in Table I.

The best yield was achieved with sodium carbonate, indicating the most efficient template effect.

This approach offers an alternative route to macrobicyclic structures and, in this case, the facile synthesis of 4,13-diaza-18-crown-6.

Acknowledgement

This work was supported by grant CPBR-3.20 from the Polish Academy of Sciences.

References

1. S. Kulstad and L. A. Malmsten, *Acta Chem. Scand.*, **B33,** 469 (1979).
2. V. J. Gatto and G. W. Gokel, *J. Am. Chem. Soc.*, **106**, 8240 (1984).
3. V. J. Gatto, K. A. Arnold, A. M. Viscariello, S. R. Miller and G. W. Gokel. *Tetrahedron Lett.*, **327**, 1986.
4. V. J. Gatto, K. A. Arnold, A. M. Viscariello, S. R. Miller and G. W. Gokel, *J. Org. Chem.*, **51**, 5373 (1986).
5. K. A. Arnold, L. Echegoyen, F. R. Fronczek, R. D. Gandour, V. J. Gatto, B. D. White and G. W. Gokel, *J. Am. Chem. Soc.*, **109**, 3716 (1987).
6. S. Kulstad and L. A. Malmsten, *Tetrahedron Lett.*, **643**, 1980.
7. J. M. Lehn, B. Alpha, R. Deschenaux, E. Anklam and M. Pietraszkiewicz, unpublished results.
8. B. Alpha, Doctoral Dissertation: 'Cryptates Photoactifs de Lanthanides – de Nouveaux Marqueurs Luminescents', Université Louis Pasteur de Strasbourg, 21 December 1987.
9. W. Wehner and F. Vögtle, *Tetrahedron Lett.*, **2603**, 1976.