Alkali Metal Ion Mediated Cyclization of 4,4'-(3,6-dioxaocta-1,8-diyloxy)-bis(benzophenone)

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Abstract: The effect of alkali metal ions on the ratio of cyclization to polymer formation was investigated. The presence of potassium ions enhances the formation of macrocycles, while lithium ions suppress the reaction.

Aggregation and self-assembly are phenomena that have been used for synthetic purposes to a limited extent.¹ Recently, this concept has been taken to new heights by using base pair recognition to stimulate the synthesis of a self-replicating molecule.² A great deal remains to be learned from simpler, less constrained systems. In the present case, the templating effects of alkali metal ions are probed by comparing the relative yields of macrocycle and polymer being formed during photolysis of the title compound 1³ as shown in Scheme 1. Complexes between acyclic crown polyethers and alkali metal ions are known to exist and represent model compounds for the transport of cations across membranes.⁴ The work presented in this paper was predicated on the notion that the polyether segments of these diketones would coordinate to the metal ion (M⁺) in the ground-state and that radical intermediates formed during photolysis⁵ would couple under the influence of the complex and enhance the formation of macrocyclic rings at the expense of polymer.

Scheme 1



Diketone 1 was easily obtained by refluxing 4-hydroxybenzophenone (2.50 mmol), triethylene glycol di-p-tosylate (1.13 mmol), KOH (2.50 mmol) in 1-butanol for 3 days (Scheme 2). Filtration of the potassium tosylate salt and removal of the solvent yielded the crude products as an oil. The oil was taken up in methylene chloride and washed successively with 0.1 N NaOH and saturated brine, followed by drying over MgSO4. Removal of the solvent and crystallization from ethyl acetate / petroleum ether (8:1) yielded analytically pure 4,4'-(3,6-dioxaocta-1,8-diyloxy)-bis(benzophenone) 1 as a white crystalline solid in 64% yield.⁶

Scheme 2



The alkali metal chloride (MCl) solutions were prepared by dissolving the appropriate amount of MCl needed to make a 1.12 M solution in 2-propanol / water (20:1). Bis-benzophenone 1 was added as a solid to each of the metal chloride and to a control solutions to a final concentration of 1.96 mM. The samples were swirled with heating to solubilize the polyether. Each sample was purged with N₂ for 20 min and then photolyzed for 29 h using a medium pressure mercury (Hanovia) lamp. The solutions were concentrated and analyzed by size exclusion chromatography using a Zorbax[®] (DuPont) SPM-60 column and elution with 5% methanol in methylene chloride.

Scheme 3 shows the four products obtained in the photolysis.⁶ The degradation product 4 catalyzes the pinacol rearrangement of diol 2 to ketone 3. Table 1 lists the normalized percentages and the ratio of

Alkali metal salt	Polymer	Cyclized Product 3	4-HBP 4	Bis- benzo- phenone 1	Ratio of Cyclized / Polymer
control	29.2	28.7	36.9	5.3	0.98
LiCl	2.7	0.4	13.7	83.2	0.15
NaCl	6.7	38.6	39.2	15.4	5.76
KCl	4.9	32.1	57.7	5.3	6.55
RbCl	6.9	39.6	44.9	9.1	5.74
CsCl	13.2	33.1	48.6	5.1	2.51

Table 1Normalized percentages for the photolysis of 1.

Scheme 3



cyclized product 3 to polymer. The presence of the potassium ion leads to the highest ratio. In contrast to all of the other metal ions studied, Li⁺ completely suppresses both the photoreaction of 1 and its decomposition. This data clearly indicates that the photochemistry of this system is sensitive to the nature of the metal ion involved in the complex and that a more elaborate explanation of the process is necessary.

Normally, the lithium ion is not expected to quench the excited-state of a ketone, but that seems to be happening in this case. One explanation that is consistent with available data involves the complexation of Li⁺ to the carbonyls of the benzophenone moieties in the podand. This is a reasonable expectation, since Li⁺ is harder than the other alkali metal ions studied. Presumably, Li⁺ holds the podand in a conformation such that energy transfer between excited-state benzophenone and ground-state benzophenone quenchs the excited state.⁷ For large ions such as Na⁺, K⁺, and Rb⁺, the podand cavity relaxes to accommodate them. As a result, the benzophenone moieties would be separated in space to an extent that intramolecular quenching would be minimized. Under these conditions, excitation of a benzophenone moiety in 1 followed by hydrogen abstraction and coupling would increase the yield of the pinacol macrocycle 2. However, an unanticipated zwitterionic decomposition pathway leading to 4 competes successfully with macrocycle formation.⁸ In the presence of the

even larger Cs⁺ ion, the proportion of polymer increases due to the imperfect match between the podand cavity and the diameter of the ion. This observation is in line with previous experiments in this lab indicating that under certain conditions, the larger metal ions can actually promote polymer formation at the expense of macrocycle formation.³

This work demonstrates the template effect of the alkali metal ions to facilitate ring closure upon photolysis of a bis-benzophenone compound. The ratio of cyclized product to polymer is highly dependent on the diameter of the podand cavity. Coordination of the lithium ion led to enhanced intramolecular quenching of the ketones. Sodium, potassium, and rubidium ions led to more cyclized product over polymer. This result can be attributed to an optimum cation size. Cesium, a large cation, does not adopt a conformation favorable for macrocyclic ring formation and therefore a lower ratio of cyclized to polymer product distribution is observed.

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References and Notes

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