Effects of Cation Recognition on 1,3-Dipolar Cycloaddition of Crowned Diphenyldiazomethanes with Maleic Anhydride

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The rates of 1,3-dipolar cycloaddition of 12–21 membered ring crowned diphenyldiazomethanes with maleic anhydride were ion-selectively decelerated by addition of alkali metal perchlorates on account of the diminished FMO interaction associated with the cation recognition.

Crown ethers possessing multiple bonds or reactive functional groups are versatile building blocks for the construction of novel supramolecular architectures capable of binding cationic species with formation of well-defined host–guest compounds.[1] These designed compounds may also be very interesting from the viewpoint of cation-recognized control of reactions as well as the intriguing physicochemical properties.[2] Despite the great potentialities, relatively little attention is focused on reaction kinetics using these promising compounds as a substrate.[3] Our interest in the control of reactions by the non-covalent weak interaction led us to investigate the effects of cations on their intrinsic reactivities of functionalized crown compounds. We have therefore chosen a well-known 1,3-dipolar cycloaddition of crowned diazoalkanes 1 with maleic anhydride 3 as a model reaction in order to assess the effects of recognized cations on kinetic features as compared with a reference dimethoxy-substituted analogue 2.

1a n=0
1b n=1
1c n=2
1d n=3

2
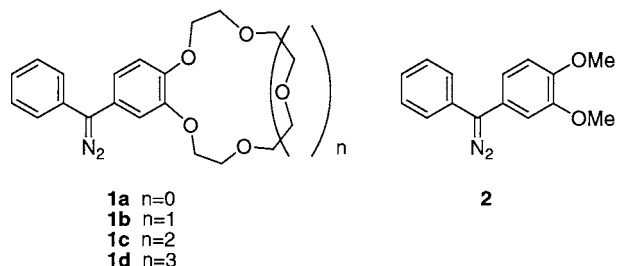
The reaction of 12–21 membered ring crowned diphenyldiazomethanes[4] **1a–d** with maleic anhydride 3 proceeded smoothly with decoloration of 1. In ^{1}H NMR measurement, it was found that a representative reaction of 18-membered **1c**
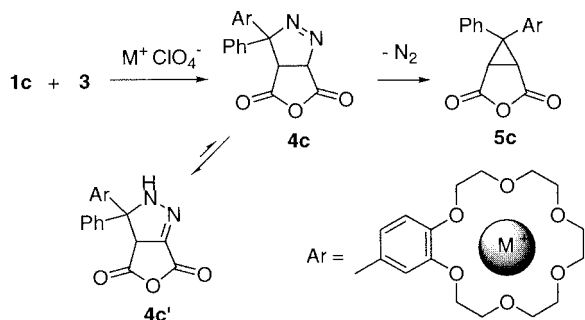
Scheme 1.

Table 1. Effects of metal perchlorates on the rates of 1,3-dipolar cycloaddition of **1a–d** and **2** with **3** at 30 °C[a,b]

Diazoalkane	$10k_2^0$ $(M^{-1} s^{-1})$	k_2^M / k_2^0				
		Li$^+$	Na$^+$	K$^+$	Rb$^+$	Cs$^+$
1a	1.47	0.81	0.80	0.93	0.98	0.97
1b	2.11	<u>0.55</u>	<u>0.48</u>	0.58	0.70	0.78
1c	2.12	0.90	<u>0.71</u>	<u>0.54</u>	<u>0.56</u>	0.61
1d	2.18	0.74	0.61	0.61	<u>0.60</u>	<u>0.61</u>
2	2.03	1.01	1.02	0.99	0.99	0.98

[a]Reactions were performed in acetonitrile using 20 equiv excess of **3** (20 mM) with respect to **1** and **2** (1 mM) in the presence and absence of alkali metal perchlorates (5 mM). The k_2^M and k_2^0 represent the rate constants for the presence and absence of added perchlorates, respectively. [b]Underscored values were obtained under the saturation kinetics.

with an equimolar amount of anhydride **3** in acetonitrile-d_3 almost quantitatively provides the corresponding cyclopropane **5c** and 2-pyrazoline **4c'** (ca. 1:1 mixture) via facile nitrogen extrusion and tautomerization of the primary dipolar adduct 1-pyrazoline **4c**, respectively (Scheme 1).[5]

Kinetic reactions were carried out at 30 °C in acetonitrile under pseudo-first-order conditions using 20-equiv excess of **3** (20 mM) relative to **1** and **2** (1 mM) with or without added metal perchlorates (5 mM). The progress of reactions was monitored with a UV spectrometer at λ_{max} = 530 nm (ε = ca. 100) by following the disappearance of diazo-color of **1** and **2**. The second-order rate constants k_2^0 for the absence of added salts were collected along with the rate ratios, k_2^M/k_2^0, where k_2^M represent the observed rate constants for the presence of salts (Table 1). In the absence of metal salts, all diphenyldiazomethanes used provided the comparable rate constants ranging from 2.1–2.2×10^{-1} M^{-1} s^{-1} except **1a** (1.5×10^{-1} M^{-1} s^{-1}) irrespective of bearing cyclic or non-cyclic substituents. However,
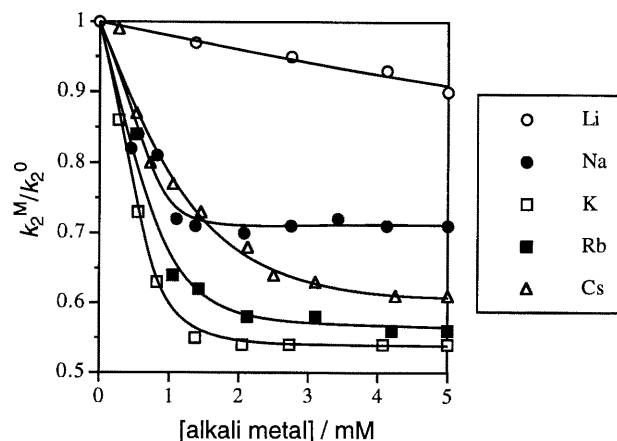

Figure 1. Plots of k_2^M/k_2^0 for the reaction of 18-membered **1c** (1 mM) with 20 equiv excess of **3** on various concentrations of added alkali metal perchlorates in acetonitrile.
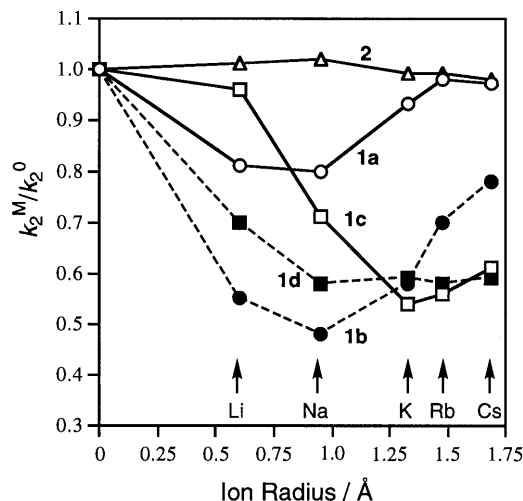
Figure 2. Plots of k_2^M/k_2^0 vs ion radius (Å) for 1,3-dipolar cycloaddition of **1a–d** and **2** with **3**. [**1** or **2**] = 1 mM, [**3**] = 20 mM and [$M^+ClO_4^-$] = 5 mM in acetonitrile.

a survey of table shows that the added metal salts brought about an appreciable rate-retardation depending on the combination of crowned **1** and the metal ions, although the reference **2** essentially remained unaffected. A preliminary experiment on the dependence of the k_2^M on metal concentration revealed that the saturation kinetics was satisfactorily performed even on 5 mM salt for the significant complexation of **1b** with Li$^+$ and Na$^+$, **1c** with Na$^+$–Rb$^+$, and **1d** with Rb$^+$ and Cs$^+$ as represented for **1c** (Figure 1 and Table 1). The leveling-off values of k_2^M/k_2^0 refer to the complexation of almost all of the crowned diphenyldiazomethanes. The negligible salt effects for **2** obviously rule out the possible acceleration or deceleration by way of a sort of metal coordination on the components **2** and/or **3**. Therefore, the rate-decelerating salt effects for crowned **1** can be explained by the cation recognition in light of the host–guest complexation of crown compounds.

The plots of k_2^M/k_2^0 vs alkali metal ion radius more explicitly showed the cation recognized rate-retarding features for **1** as compared with the reference **2** (Figure 2). The numerical value of 1 for metal-free reactions was plotted on the ion radius zero as abscissa. Although 12-membered **1a** underwent almost a similar poor rate retardation at smaller sized Li$^+$ (ion radius 0.60 Å) and Na$^+$ (0.95 Å), 15-membered **1b** notably dropped to a distinct bottom at size-fitted Na$^+$ and rose again in going to Cs$^+$. The next larger 18-membered **1c** exhibited the bottom at the favorite K$^+$ (1.33 Å) in conformity with the ion-in-the-hole concepts.[6] The largest 21-membered **1d** provided the monotonous horizontal line for the Na$^+$ to Cs$^+$ (1.40 Å). This may be due to the high flexibility of the macrocyclic ring, which would enable **1d** to wrap even the smaller Na$^+$–Rb$^+$ (1.69 Å).

Considering that diazoalkanes are classified as one of the typical HOMO controlled dipoles,[7] the reactivity of **1** and **2** with electron deficient maleic anhydride **3** is controlled by the dominant HOMO (diazoalkanes)–LUMO (anhydride) interaction as well as their orbital coefficients.[8] The reaction would be accelerated or decelerated by the substitution of electron-releasing or -withdrawing group on the 1,3-dipole, respectively.[9] In fact, substituted diphenyldiazomethanes are known to provide

fairly negative Hammett ρ values in the 1,3-dipolar reactions with tetracyanoethylene (ρ = –2.67)[10a] and chloranil (–1.67).[10b] In line with this, the rate-retarding effects of alkali metal cations on 1,3-dipolar cycloaddition of **1** can be explained by the electron-withdrawing electrostatic influence of the bound metal ions, which tends to withdraw electron density from the aromatic ring and lowers the energy of the HOMO of 1,3-dipole **1**.

Such a reduction of HOMO level was confirmed by a cyclic voltammetry. The oxidation potential E_p^{ox} of 18-membered **1c** (1 mM) in acetonitrile was shifted by addition of metal ions (5 mM) and the potential plot was quite similar to the k_2^M/k_2^0 rate profile (Figure 2) as indicated by the excellent regression equation;[11]

$$E_p^{ox} = -0.110\, k_2^M/k_2^0 + 0.825 \qquad (r = 0.96).$$

In conclusion, the 1,3-dipolar cycloaddition of 12–21 membered ring crowned diphenyldiazomethanes **1a–d** with maleic anhydride **3** was decelerated by selective cation binding of the crown rings. These kinetic features were interpreted in terms of the reduced FMO interaction owing to the lowered HOMO of **1** by cation recognition.

References and Notes
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4   Oily diazomethanes were stably isolated by literature method without any purification; J. Osterodt, M. Nieger, P.-M. Windscheif, and F. Vögtle, *Chem. Ber.*, **126**, 2331 (1993). New compounds **1a** and **1d** were characterized by ^{1}H NMR (CDCl$_3$). **1a:** δ 3.81 (s, 4H), 3.85–3.87 (m, 4H), 4.15–4.21 (m, 4H), 6.89–6.93 (m, 2H), 7.02 (d, 1H, J = 8.6 Hz), 7.15 (t, 1H, J = 7.6 Hz), 7.23 (d, 2H, J = 7.6 Hz), 7.37 (t, 2H, J = 7.6 Hz). **1d:** δ 3.68 (s, 8H), 3.73–3.83 (m, 8H), 3.89–3.95 (m, 4H), 4.11–4.21 (m, 4H), 6.85 (s, 1H), 6.87 (d, 1H, J = 8.2 Hz), 6.93 (d, 1H, J = 8.2 Hz), 7.14 (t, 1H, J = 7.6 Hz), 7.22 (d, 2H, J = 7.6 Hz), 7.36 (t, 2H, J = 7.6 Hz).
5   The **4c'** was quantitatively converted into **5c** by heating at 80 °C in benzene. Both the compounds **4c'** and **5c** consist of ca. 1:1 ratio of *endo-* and *exo-*isomers (by NMR).
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11 E_p^{ox} of **1c** (0.723 V vs SCE) was shifted to 0.718 V (Li), 0.751 (Na), 0.772 (K), 0.758 (Rb) and 0.751 (Cs).