JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Communication

pubs.acs.org/JACS

Flexible, Linear Chains Act as Baffles To Inhibit the Intramolecular Rotation of Molecular Turnstiles

Chengyuan Yu,[†] Lishuang Ma,[†] Jiaojiao He,[†] Junfeng Xiang,[‡] Xuebin Deng,[†] Ying Wang,*[,†] Xuebo Chen,*[,†] and Hua Jiang*[,†]

[†]Key Laboratory of Theoretical and Computational Photochemistry and Key Laboratory of Radiopharmaceuticals, Ministry of Education; College of Chemistry, Beijing Normal University, Beijing 100875, China

[‡]Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China

Supporting Information

ABSTRACT: In artificial molecular devices, flexible, linear chains typically exhibit very weak capability in inhibiting molecular motion. Herein, we describe the dynamic properties of a series of molecular turnstiles consisting of a rigid frame and a phenyl rotator flanked with linear alkoxymethyl substituents. The long, flexible substituents act as elastic baffles to inhibit the rotations of the rotator at medium to fast speeds on the NMR time scale. When the rotator moves slowly, the substituents become more relaxed, thus obtaining an opportunity to completely thread through the cavity of the turnstiles. These findings reveal a basic but missing correlation between steric hindrance and speed of motion for flexible, linear chains in dynamic molecular devices, thus opening up a new direction toward molecular machines with more elaborate dynamic functions.

The development of new artificial molecular machines[1] is a field of ever-increasing interest and activities in the wake of their potential applications in sensing,[2] catalysis,[3] and nanotechnology.[4] Over the past decades, significant progress has been achieved in this field.[1] However, compared with the numerous efforts in exploring molecular features of frameworks and rigid moieties, the function of flexible, linear chains with respect to their application in molecular machines has not yet been extensively addressed,[5,6] leaving a knowledge void on their roles and applications in artificial molecular machines.

Motion inhibition is one of the basic tasks in the design of miscellaneous artificial molecular machines. To achieve this goal, rigid and bulky groups have been extensively utilized, as can be seen in a large number of ingenious dynamic systems, including molecular brakes,[7] molecular turnstiles,[8] shuttles,[9] rotaxanes,[10] and models of muscles.[11] By contrast, the use of flexible, linear chains for this purpose has seldom been considered. This is mainly due to their structural flexibility, which greatly decreases the steric hindrance of the chains and makes it difficult to evaluate kinetic factors. Consequently, flexible, linear chains are typically found to hardly affect the dynamics of the molecular machines, regardless of the actual chain length employed.[12,13] A possible strategy to overcome this obstacle is segregating the dynamics of molecular machines to a shorter time scale compared to the motion of the whole flexible chains themselves, as we previously applied in the construction of molecular shuttles with reversibly wrapped foldamers.[14]

Herein, we report that flexible, linear alkoxymethyl substituents on the rotator of molecular turnstiles clearly show the ability to act as elastic baffles to hinder the rotation of molecular turnstiles. The function depends on the motion speed of the rotator, being ineffective when the rotator moves slowly on the NMR time scale. Thus, the turnstiles move in two totally different modes, including oscillation and rotation, in a wide range of temperatures (Figure 1).

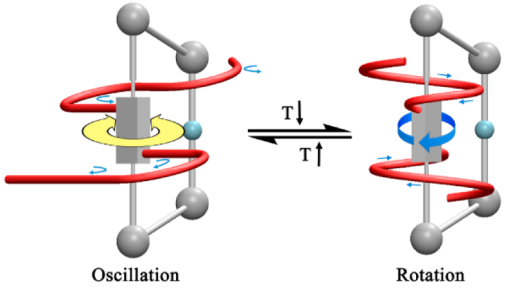

Figure 1. Cartoon illustration of two motion modes (oscillation and rotation) for the studied molecular turnstiles with flexible, linear substituents on the rotator.

The designed turnstiles, **1a–i**, consist of a trapezoidal framework and a phenyl rotator flanked with a pair of flexible, linear alkoxymethyl substituents (Figure 2), in which a self-assembly strategy based on strong coordinative binding of Pd^{2+} cation to bidentate pyridine-containing ligands was used to construct the macrocycle frame.[15] This type of turnstile was chosen as the platform in this proof-of-concept study because of the low rotation energy barrier (<1 kcal mol^{-1}) for diphenylacetylene,[16] allowing a fast rotation of the rotational component in the absence of intramolecular steric interactions. A series of alkoxymethyl substituents with different chain lengths were used in our design, aimed at gaining a correlation between the alkoxymethyl chain length (could be expressed in terms of the number of atoms other than hydrogens on the main chain, denoted N_{atom}) and the dynamics of the turnstiles. The incorporation of an oxygen atom was designed to simplify

Received: October 16, 2016
Published: November 29, 2016

DOI: 10.1021/jacs.6b10816
J. Am. Chem. Soc. 2016, 138, 15849–15852

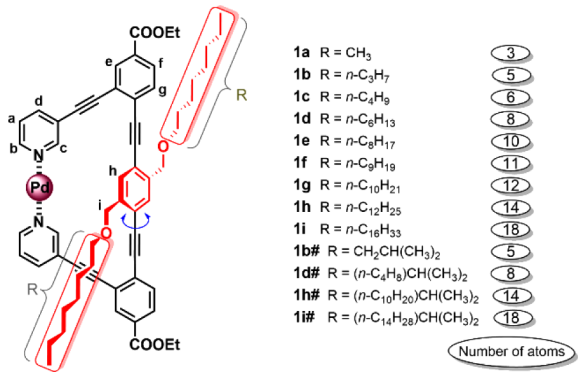

Figure 2. The studied molecular turnstiles. The number of atoms other than hydrogens on the main chain of the alkoxymethyl substituents (N_{atom}) is given on the right for each compound.

the ^{1}H NMR signal pattern of the two diastereotopic methylene protons (H_i) geminal to the phenyl rotator, providing a coupled AB spin system which could be utilized as a probe to detect the motion of the rotators.[8a]

The overall strategy for synthesizing the target precursors of the molecular turnstiles (ligands **9a**–**i**, Scheme S1 in the Supporting Information (SI)) is similar to that in our recent work on the triptycene-based coordination turnstiles,[15] except that a Williamson ether synthesis was employed to attach the flexible substituents to the rotator. Turnstiles **1a**–**i** were obtained quantitatively by mixing a solution of $Pd(MeCN)_2Cl_2$ in acetonitrile with the corresponding ligands in chloroform at room temperature, followed by concentration under a reduced pressure.

The formation of the Pd^{2+} complexes was first supported by ^{1}H NMR titration experiments (Figures S1–S13, SI), in which the signals of ligands gradually became weaker upon the addition of Pd^{2+} cations, along with the appearance of a new set of signals corresponding to the complexes. Evidence for the formation of a macrocycle was provided by the 2D NOESY spectrum of **1d**, in which the cross-peaks of H_c–H_i and H_c–H_h can be clearly observed (Figure S24, SI). The turnstile structure of the molecules was confirmed by single-crystal X-ray diffraction analysis on **1b** (Figure 3).

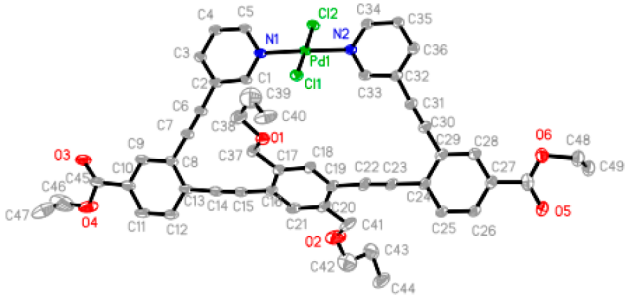

Figure 3. X-ray molecular structure of turnstile **1b**. Atoms are depicted with thermal ellipsoids set at the 50% probability level. Further details are reported in Tables S2 and S3, SI.

The complexation caused considerable changes of absorption bands of the ligands. The best fit to the UV–vis titration curves in a 1:1 binding model yielded the association constants of **1a**, **1b**, **1d**, **1f**, and **1h** to be in the range of $(1.8–2.8) \times 10^5$ M^{-1} (Table S1, SI) in 3:1 (v/v) $CHCl_3$/MeCN. The narrow range here indicates that the length of the chains has no significant impact on the coordination process as well as the stability of the complexes.

By comparing the ^{1}H NMR spectra of turnstiles **1a**–**i** in 96:4 (v/v) $CDCl_3$/acetonitrile-d_3 at 298 K (Figure S14, SI), we deduced that the internal rotation of the turnstiles hinges on the chain length of the alkoxymethyl substituents. For instance, the turnstile with shorter alkoxymethyl substituents, **1a**, was found to rotate faster on the NMR time scale at room temperature, as evidenced by the well-resolved singlets of protons H_i in its ^{1}H NMR spectrum. However, for the other molecules with longer substituents, the pair of protons H_i became diastereotopic (appearing as an AB quartet), indicating that the longer substituents are capable of, at least, slowing down the rotation of the rotators.

To further explore the relationship between N_{atom} and the motion of the turnstiles, variable-temperature (VT) ^{1}H NMR experiments were carried out on **1a**–**i**. The range of temperatures investigated was chosen to be near the coalescence temperature for each compound, at which the intramolecular exchange is medium on the NMR time scale. For **1a** in $CDCl_3$, decreasing the temperature slowed down the rotation of the rotators, giving rise to broadening followed by splitting of the resonance of H_i (Figure 4a). A decoalescence of

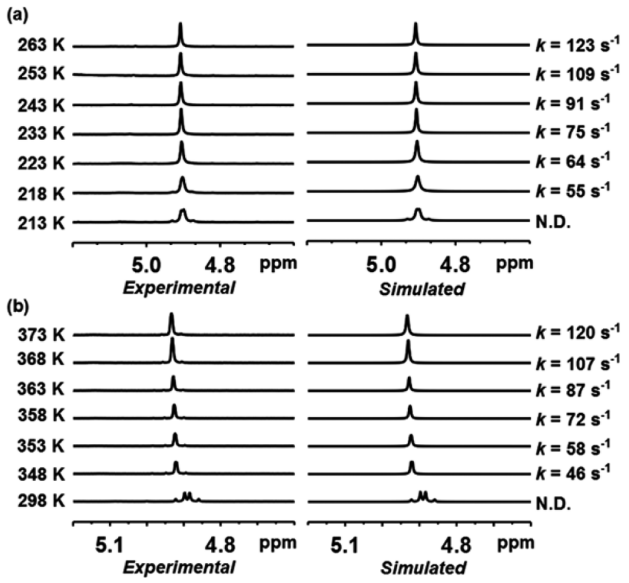

Figure 4. Experimental and simulated VT ^{1}H NMR spectra (500 MHz) of (a) **1a** (2 mM) and (b) **1e** (2 mM) at the region of H_i in $CDCl_3$ and $CDCl_2CDCl_2$, respectively. The temperature (T, K) and calculated rate constants (k, s^{-1}) are given for each trace.

the protons was observed at 218 K. VT ^{1}H NMR experiments on **1b**–**i** were performed on the solutions of the compounds in 1,1,2,2-tetrachloroethane-d_2, a solvent that has polarity similar to that of $CDCl_3$ but a higher boiling point. In these cases, coalescence was observed at ca. 322 K for **1b** and in a temperature range of 340–360 K for **1c**–**i** (Figure 4b and Table S5 and Figures S35–S42, SI). These coalescences suggest that the methylene groups adjacent to the rotators are capable of passing through the cavities of the turnstiles.

A series of free energy of activation values ($\Delta G^{\ddagger}$) for the movements of the studied molecules were calculated using the Eyring equation.[17] Since the VT ^{1}H NMR measurements were carried out at temperatures in different ranges for different turnstiles, for comparison, the kinetic data at 353 K were

DOI: 10.1021/jacs.6b10816
J. Am. Chem. Soc. 2016, 138, 15849–15852

obtained, in which the data for **1a** were calculated by the linear extrapolation method.[18,19] The results (Figure 5 and Table S5, SI) show that the $\Delta G^{\ddagger}$ value increases considerably with the increase of N_{atom} up to 10 (from 16.7 kcal mol^{-1} for **1a** to 18.0 kcal mol^{-1} in the case of **1e**), then slightly decreases and finally stabilizes at a level around 17.5 kcal mol^{-1} when $N_{atom} \geq 12$. This is different from what we hypothesized, as we had expected that progressively increasing the chain length of the flexible substituents would produce a steady increase in their steric hindrance, thus hindering the rotation of the turnstile more effectively. A possible explanation for this inconsistency is that the turnstiles containing long, flexible substituents on the rotator may move differently from those incorporating short ones.

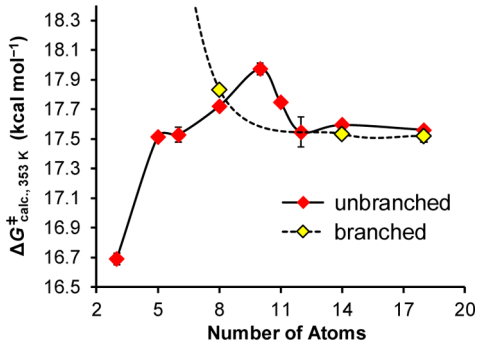

Figure 5. Plots of the calculated free energy of activation ($\Delta G^{\ddagger}$) at 353 K for the turnstiles' motion versus the length of the main chain of the unbranched and the branched alkoxymethyl substituents on the rotator.

To obtain detailed dynamic features of the turnstiles, we prepared another four molecules, **1b#**, **1d#**, **1h#**, and **1i#**, incorporating a pair of alkoxymethyl substituents with a branched end on the rotator (Figure 2), as controls for **1b**, **1d**, **1h**, and **1i**, respectively. The branched substituent, which could be regarded as a methyl derivative of the linear one, was designed to possess a bulky subunit at the end of the chain, serving as a stopper to prevent a complete threading of the flexible strand through the turnstile cavity but, at the same time, provide the whole substituent a steric hindrance approximately equal to that of its unbranched counterpart.

VT ^{1}H NMR investigation on **1b#** in 1,1,2,2-tetrachloroethane-d_2 showed that protons H_i appeared as an AB quartet at all temperatures studied, even at the high-temperature limit of 383 K (Figure S43, SI). This indicates that, much different from **1b**, the turnstile **1b#** is conformationally locked and cannot undergo rotation in the whole range of temperatures examined. Given that the structural difference between **1b#** and **1b** lies only on the termini of the substituents, the big difference in turn demonstrates that the rotator of **1b** indeed undergoes rotation. This agrees with the results of density functional theory (DFT) computations (Figure S49, SI), which predicted the propoxymethyl substituent is small enough to pass through the cavity. By contrast, the H_i signals of **1d#**, **1h#**, and **1i#**, turnstiles with N_{atom} = 8, 14, and 18, respectively, showed patterns very similar to those of their linear counterparts at room temperature, and coalesced at almost the same temperature as well. Furthermore, the measured rotational barriers for **1d#**, **1h#**, and **1i#** were found to be almost identical to those of **1d**, **1h**, and **1i**, respectively (Figure 5 and Table S5, SI). These observations indicated that, during the movement of turnstiles with long, flexible substituents, there were in fact no steric interactions at all between the termini of the substituents and the macrocycle frameworks. Consequently, the terminal segments of the flexible substituents never passed through the cavities in the motion of the molecules, providing an explanation for why the chain length of the rotor substituents has no significant impact on the motion barrier when $N_{atom} \geq 8$ (Figure 5). Considering that the methylene groups adjacent to the rotators are capable of passing through the cavities in all cases except that of **1b#**, one can conclude that, in the process of motion for such molecules, the flexible substituents partially pass through the cavity (to give a chemical exchange between two probe diastereotopic methylene protons) by a head-in rather than an end-in threading mechanism, and then undergo unthreading (rotating back), presumably driven by the chain tension presenting in the transition state of the molecules as well as Brownian motion, thus giving rise to an overall motion in the mode of oscillation (Figure 1). In this process, the chain segments are governed partially by Brownian motion and partially by collective motions imposed by the rest of the rotator component.[20] The indirect interaction between the terminal segment and the phenyl rotator depends on the chain length, becoming weaker in the systems incorporating a longer chain. When $N_{atom} \geq 12$, this interaction might tend to be negligible.

The findings presented above demonstrated that long, flexible, linear substituents could act as elastic baffles to inhibit rotation when the rotator moves at a medium or fast speed on the NMR time scale. We then anticipated that slowing down the intramolecular oscillation of the studied molecules, to a time scale comparable to or even longer than that of the local dynamics of the whole flexible chains, would allow the chain segments to relax more, thus providing the chain an opportunity to completely thread through the turnstile cavity. To test our hypothesis, VT ^{1}H NMR investigations on **1h** and **1h#** in 1,1,2,2-tetrachloroethane-d_2 at temperatures in a wider range (363−313 K, compared 367−342 K for **1h#** in previous investigations) were carried out, and the results are shown in Figure 6. For **1h**, a linear Eyring plot can be observed, indicating that the activation enthalpy and the entropy indeed remain constant in the whole range of temperatures examined. In contrast, the data points of **1h#** do not fit linearly in the investigated temperature range. While the plotted points in the range of 363−335 K almost overlap with those of **1h**, the ones at relatively low temperatures (335−313 K), at which the rotator moves slowly on the NMR time scale (as evidenced by the obvious AB quartet ^{1}H NMR signal of H_i), gradually

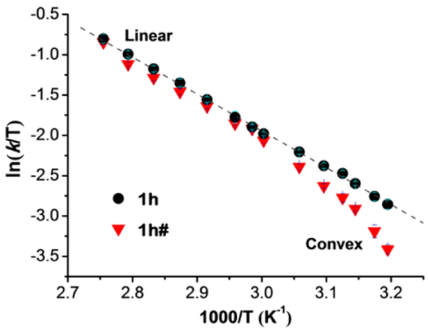

Figure 6. Eyring plots of the rates of exchange obtained from line width analysis of protons H_i on **1h** and **1h#**.

DOI: 10.1021/jacs.6b10816
J. Am. Chem. Soc. 2016, 138, 15849−15852

deviated downward from the previous trend line upon decreasing the temperature, thus giving a convex Eyring plot. Again, this deviation could only be attributed to the steric interaction between the terminal stopper and the framework, which further suggests that the termini of the unbranched substituents of **1h** could access to the turnstile cavity at relatively low temperatures. In view of the small steric hindrance of the termini of the unbranched chains, it is reasonable to conclude that a complete threading of these flexible chains may occur under such conditions, thus giving rise to a rotation of **1h**. Clearly, the occurrence of rotation depends on the temperature, becoming more frequent as the temperature decreases in the studied cases.

For **1h**, the linear Eyring plot suggests that switching the mode of motion between oscillation and rotation gives no obvious changes in the motion barriers. Consequently, when the turnstile oscillates, the collision between the flexible baffle and the framework might be an elastic one (giving negligible changes in the overall energy of the molecule). This is supported by our DFT calculations, which predict that the terminal segments of long, flexible substituents, in fact, hardly affect the energy of the molecules in motion (Figure S50, SI). Notably, this prediction also agrees well with the observation shown in Figure 5 and some other dynamic systems.[12,19]

In conclusion, we have shown that long, flexible, unbranched alkoxymethyl chains could be used as a baffle to hinder the rotation of the rotator of molecular turnstiles. The function depends on the speed at which the overall chain moves. At relatively low temperature, the whole chain moves slowly, so that the chains become much more flexible and thus can no longer serve as a baffle. We expect that these thermodynamic and kinetic features can be utilized advantageously in the future development of new ultraminiaturized devices, in which the mode of motion or any other functions could be precisely modulated.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b10816.

Experimental and computational details and characterization data, including X-ray analysis of **1a**, NMR spectra, and Eyring plot analyses (PDF)

X-ray crystallographic data for **1a** (CIF)

■ AUTHOR INFORMATION

Corresponding Authors

*ywang1@bnu.edu.cn

*xuebochen@bnu.edu.cn

*jiangh@bnu.edu.cn

ORCID

Hua Jiang: 0000-0002-9917-2683

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the National Natural Science Foundation of China (21332008 and 21572023), the Youth Scholars Program of Beijing Normal University (2014NT08) and the Fundamental Research Funds for the Central Universities for financial support.

■ REFERENCES

(1) (a) Balzani, V.; Credi, A.; Raymo, F. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2000**, *39*, 3348−3391. (b) Kay, E. R.; Leigh, D. A.; Zerbetto, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 72−191. (c) Michl, J.; Sykes, E. C. H. *ACS Nano* **2009**, *3*, 1042−1048. (d) Erbas-Cakmak, S.; Leigh, D. A.; McTernan, C. T.; Nussbaumer, A. L. *Chem. Rev.* **2015**, *115*, 10081−10206.

(2) Shi, K.; Dou, B.; Yang, C.; Chai, Y.; Yuan, R.; Xiang, Y. *Anal. Chem.* **2015**, *87*, 8578−8583.

(3) (a) Neal, E. A.; Goldup, S. M. *Chem. Commun.* **2014**, *50*, 5128−5142. (b) Galli, M.; Lewis, J. E. M.; Goldup, S. M. *Angew. Chem., Int. Ed.* **2015**, *54*, 13545−13549. (c) Pan, T.; Liu, J. *ChemPhysChem* **2016**, *17*, 1752−1758.

(4) Peplow, M. *Nature* **2015**, *525*, 18−21.

(5) Xue, Z.; Mayer, M. F. *J. Am. Chem. Soc.* **2010**, *132*, 3274−3276.

(6) (a) Monnereau, C.; Ramos, P. H.; Deutman, A. B. C.; Elemans, J. A. A. W.; Nolte, R. J. M.; Rowan, A. E. *J. Am. Chem. Soc.* **2010**, *132*, 1529−1531. (b) van Dongen, S. F. M.; Elemans, J. A. A. W.; Rowan, A. E.; Nolte, R. J. M. *Angew. Chem., Int. Ed.* **2014**, *53*, 11420−11428. (c) Andersen, S. S.; Share, A. I.; Poulsen, B. L. C.; Kørner, M.; Duedal, T.; Benson, C. R.; Hansen, S. W.; Jeppesen, J. O.; Flood, A. H. *J. Am. Chem. Soc.* **2014**, *136*, 6373−6384.

(7) (a) Nikitin, K.; Bothe, C.; Müller-Bunz, H.; Ortin, Y.; McGlinchey, M. J. *Organometallics* **2012**, *31*, 6183−6198. (b) Tan, W. S.; Chuang, P.-Y.; Chen, C.-H.; Prabhakar, C.; Huang, S.-J.; Huang, S.-L.; Liu, Y.-H.; Lin, Y.-C.; Peng, S.-M.; Yang, J. S. *Chem. - Asian J.* **2015**, *10*, 989−997.

(8) (a) Bedard, T. C.; Moore, J. S. *J. Am. Chem. Soc.* **1995**, *117*, 10662−10671. (b) Zhou, Z.; Zhang, X.; Liu, Q.; Yan, Z.; Lv, C.; Long, G. *Inorg. Chem.* **2013**, *52*, 10258−10263. (c) Wang, G.; Xiao, H.; He, J.; Xiang, J.; Wang, Y.; Chen, X.; Che, Y.; Jiang, H. *J. Org. Chem.* **2016**, *81*, 3364−3371.

(9) (a) Barrell, M. J.; Leigh, D. A.; Lusby, P. J.; Slawin, A. M. Z. *Angew. Chem., Int. Ed.* **2008**, *47*, 8036−8039. (b) Berná, J.; Alajarín, M.; Orenes, R. *J. Am. Chem. Soc.* **2010**, *132*, 10741−10747.

(10) (a) Wenz, G.; Han, B.-H.; Müller, A. *Chem. Rev.* **2006**, *106*, 782−817. (b) Harada, A.; Hashidzume, A.; Yamaguchi, H.; Takashima, Y. *Chem. Rev.* **2009**, *109*, 5974−6023. (c) Ma, X.; Tian, H. *Chem. Soc. Rev.* **2010**, *39*, 70−80.

(11) Bruns, C. J.; Stoddart, J. F. *Acc. Chem. Res.* **2014**, *47*, 2186−2199.

(12) (a) Deutman, A. B. C.; Monnereau, C.; Elemans, J. A. A. W.; Ercolani, G.; Nolte, R. J. M.; Rowan, A. E. *Science* **2008**, *322*, 1668−1671. (b) Deutman, A. B. C.; Cantekin, S.; Elemans, J. A. A. W.; Rowan, A. E.; Nolte, R. J. M. *J. Am. Chem. Soc.* **2014**, *136*, 9165−9172. (c) Cantekin, S.; Markvoort, A. J.; Elemans, J. A. A. W.; Rowan, A. E.; Nolte, R. J. M. *J. Am. Chem. Soc.* **2015**, *137*, 3915−3923.

(13) Peck, E. M.; Liu, W.; Spence, G. T.; Shaw, S. K.; Davis, A. P.; Destecroix, H.; Smith, B. D. *J. Am. Chem. Soc.* **2015**, *137*, 8668−8671.

(14) Gan, Q.; Ferrand, Y.; Bao, C.; Kauffmann, B.; Grélard, A.; Jiang, H.; Huc, I. *Science* **2011**, *331*, 1172−1175.

(15) Wang, G.; Xiao, H.; He, J.; Xiang, J.; Wang, Y.; Chen, X.; Che, Y.; Jiang, H. *J. Org. Chem.* **2016**, *81*, 3364−3371.

(16) Okuyama, K.; Hasegawa, T.; Ito, M.; Mikami, N. *J. Phys. Chem.* **1984**, *88*, 1711−1716.

(17) Sandstrom, J. *Dynamic NMR Spectroscopy*; Academic Press: London, 1982.

(18) Such strategy has been widely used in other molecular kinetic studies. For examples, see: (a) Dial, B. E.; Pellechia, P. J.; Smith, M. D.; Shimizu, K. D. *J. Am. Chem. Soc.* **2012**, *134*, 3675−3678. (b) Sun, W.-T.; Huang, S.-L.; Yao, H.-H.; Chen, I.-C.; Lin, Y.-C.; Yang, J.-S. *Org. Lett.* **2012**, *14*, 4154−4157. (c) Chen, Y.-C.; Sun, W.-T.; Lu, H.-F.; Chao, I.; Huang, G.-J.; Lin, Y.-C.; Huang, S.-L.; Huang, H.-H.; Lin, Y.-D.; Yang, J.-S. *Chem. - Eur. J.* **2011**, *17*, 1193−1200.

(19) Young, P. G.; Hirose, K.; Tobe, Y. *J. Am. Chem. Soc.* **2014**, *136*, 7899−7906.

(20) Baumgärtner, A. *Annu. Rev. Phys. Chem.* **1984**, *35*, 419−435.

DOI: 10.1021/jacs.6b10816
J. Am. Chem. Soc. 2016, 138, 15849−15852