Enantioselective Synthesis of Mechanically Axially Chiral Rotaxanes

Peter Gallagher,[1,†] Andrea Savoini,[1,†] Patrick W. V. Butler,[1] Graham J. Tizzard,[1] and Stephen M. Goldup*[,1,2]

[1]Chemistry, University of Southampton, University Road, Southampton, SO17 1BJ.

[2]School of chemistry, University of Birmingham, Edgbaston, Birmingham B15 2TT, U.K.

[†]These authors contributed equally

Supporting Information Placeholder

ABSTRACT: The chiral mechanical axial stereogenic unit of rotaxanes was only recently recognized, despite equivalent mechanically axially chiral catenanes being discussed in the early 1960s. Here we demonstrate that a single H-bond between the groups that differentiate the faces of the macrocycle and axle appears sufficient to deliver high diastereocontrol (80% *de*) in the mechanical bond forming step and extend this observation to the first direct enantioselective approach in up to 70% *ee*.

The synthesis of rotaxanes and catenanes whose covalent subcomponents are achiral, but which nevertheless exist as non-superimposable mirror images due to the presence of a mechanical stereogenic unit, has progressed significantly in the last decade.[1] Historically, enantioenriched samples of such mechanically chiral molecules[2] were only made available by chiral stationary phase HPLC (CSP-HPLC) separation of a racemic sample of their enantiomers. In 2014,[3] we introduced a chiral derivatization strategy that allowed access to mechanically planar chiral (MPC) rotaxanes without CSP-HPLC, which was subsequently extended to a chiral auxiliary approach for to MPC rotaxanes[4] and catenanes.[4b,5] In addition to auxiliary approaches, Kawabata and co-workers,[6] and Zhu and Tian and co-workers,[7] have demonstrated the stereoselective synthesis of MPC rotaxanes by post-synthetic modification using kinetic resolution and desymmetrization strategies respectively, and Leigh and co-workers demonstrated a chiral leaving group approach that gave rise to an MPC rotaxane with 50% *ee* in the mechanical bond forming step.[8]

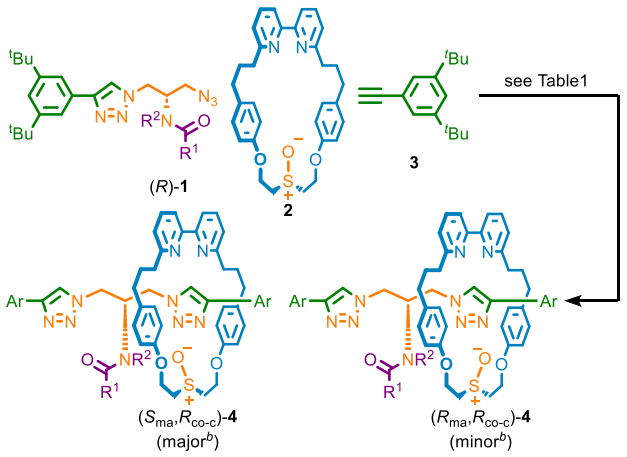
The MPC stereogenic unit arises when two oriented (C_{nh}) rings are interlocked (catenanes) or an oriented ring encircles an axle whose ends are distinguishable (C_{nv}, principle axis parallel to the axle) and thus does not depend on the relative positions of the interlocked subcomponents. However, co-conformational motion can also give rise to stereochemistry. In 2008, Leigh and co-workers demonstrated that a covalent prochiral center could be desymmetrized by an encircling macrocycle.[9] Similarly, Saito and co-workers, [10] and Credi, Baroncini and co-workers[11] reported co-conformationally mechanically planar chiral rotaxanes whose stereochemistry arises due to displacement of an oriented ring from the internal mirror plane of an otherwise centrosymmetric axle and we have highlighted the equivalent phenomenon in the context of catenanes.[5b]

Recently, we took advantage of co-conformational covalent stereochemistry to demonstrate the first stereoselective synthesis of mechanically axially chiral (MAC) catenanes,[12] structures that are composed of two facially dissymmetric macrocycles. The simplest way to achieve such facial dissymmetry is through the presence of one or more covalent prochiral units in each ring. Recognizing this allowed us to develop a synthetic approach by which covalent stereochemistry was first converted to mechanical and co-conformational stereochemistry, the latter of which could be removed after separation of the diastereomers produced to generate the enantiopure mechanically axially chiral target. The same analysis also revealed a hitherto unrecognized rotaxane mechanical stereogenic unit in which a prochiral ring encircles a prochiral axle. We termed such structures "mechanically axially chiral rotaxanes" by analogy with their catenane cousins. This stereogenic unit also yielded to our chiral co-conformational auxiliary approach.

Here we investigate and optimize the stereoselective synthesis of these newly identified MAC rotaxanes and show that, surprisingly, a single intercomponent hydrogen bond appears sufficient to control the reaction outcome.[13] Using this information, we demonstrate a one pot synthesis of a MAC rotaxane in 78% *ee* and the first direct enantioselective synthesis of a MAC rotaxane in 67% *ee*.

Previously we reported[12] that the active-template[14] Cu-mediated alkyne-azide cycloaddition (AT-CuAAC[15,16]) reaction of azide (*R*)-**1a**, macrocycle **2**, and alkyne **3** gave rotaxanes (S_{ma},$R_{co\text{-}c}$)[17]-**4a** (major) and [R_{ma},$R_{co\text{-}c}$]-**4a** (minor), which have the same co-conformational configuration and opposite mechanical axial configuration, in 50% *de* (Table 1, entry 1). The solid state structure obtained by single crystal x-ray diffraction (SCXRD) of an analogous catenane[12] suggests a close contact between the N-H of the carbamate unit and the S-O of the sulfoxide unit. Thus, we proposed that an H-bond between these groups may play a role in the observed stereoselectivity.[18] To test this proposal, here we performed the same reaction in EtOH, a more competitive solvent, and found that the *de* was reduced (14%, entry 2). Furthermore, the reactions of acetamide azides **1b**-**d** to give rotaxanes **4b**-**d** (entries 3-5 respectively) proceeded with diastereoselectivities that paralleled the polarization of the N-H unit; trifluoro acetamide **1d** produced rotaxane **4d** in the highest selectivity (70% *de*), followed by trichloroacetamide **4c** (48% *de*) then acetamide **4b** (36% *de*). The solid state structure of the major isomer of **4d** obtained by SCXRD (Figure 1) revealed the same [S_{ma},$R_{co\text{-}c}$] configuration as observed for **4a** with the proposed NH•••O H-bond observed between the acetamide and sulfoxide units. As expected, methylated derivative **4e** reacted in poor stereoselectivity (10% de, entry 6), consistent with the NH•••O H-bond contributing to the observed stereoselectivity.

Scheme 1. Synthesis of rotaxanes **4**[a]



[a]Reagents and conditions: (*R*)-**1** (1.1 equiv.), **2** (1 equiv.), **3** (1.1 equiv.), $[Cu(CH_3CN)_4]PF_6$ (0.96 equiv.), $^iPr_2NEt$ (2 equiv.). For conditions see Table 1. [b]The absolute stereochemistry of the major isomers of **1a** and **1d** were determined crystallographically (ref. 12 and Figure 1 respectively). That of **1b**, **c** and **e** is presumed by analogy. Ar = 3,5-di-^{t}Bu-C_6H_3.

Table 1. Effect of reaction conditions and substrate on the AT-CuAAC diastereoselective synthesis of rotaxanes **4**

entry	Substrate	Conditions	Selectivity[a]
1	**1a** (R^1 = OtBu, R^2 = H)	CH_2Cl_2, rt	50% *de*
2	**1a** (R^1 = OtBu, R^2 = H)	EtOH, rt	14% *de*
3	**1b** (R^1 = Me, R^2 = H)	CH_2Cl_2, rt	36% *de*
4	**1c** (R^1 = CCl_3, R^2 = H)	CH_2Cl_2, rt	48% *de*
5	**1d** (R^1 = CF_3, R^2 = H)	CH_2Cl_2, rt	70% *de*
6	**1d** (R^1 = CF_3, R^2 = H)	EtOH, rt	16% *de*
7	**1e** (R^1 = CF_3, R^2 = Me)	CH_2Cl_2, rt	10% *de*
8	**1a** (R^1 = OtBu, R^2 = H)	CH_2Cl_2, –40 °C	72% *de*
9	**1a** (R^1 = OtBu, R^2 = H)	CH_2Cl_2, –78 °C	80% *de*
10	**1d** (R^1 = CF_3, R^2 = H)	CH_2Cl_2, –40 °C	82% *de*
11	**1d** (R^1 = CF_3, R^2 = H)	CH_2Cl_2, –78 °C	70% *de*

[a]Determined by ^1H NMR analysis of the crude reaction product.

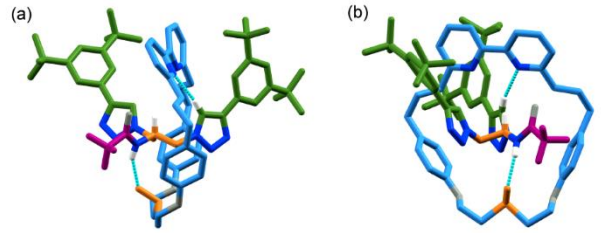
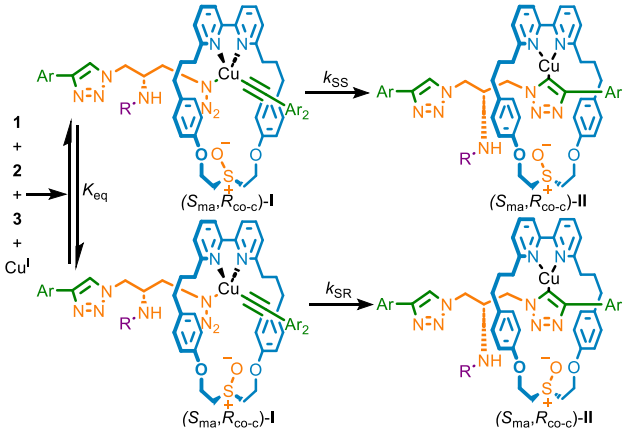


Figure 1. Solid state structure of major stereoisomer [S_{ma},$R_{co\text{-}c}$]-**4d** showing the proposed key intercomponent H-bond (colors as in Scheme 1, including the sulfoxide (SO) moiety to highlight the differentiation of the macrocycle faces, except N [dark blue], O [grey], H [white]). Majority of H omitted. (a) side-view. (b) front-view.

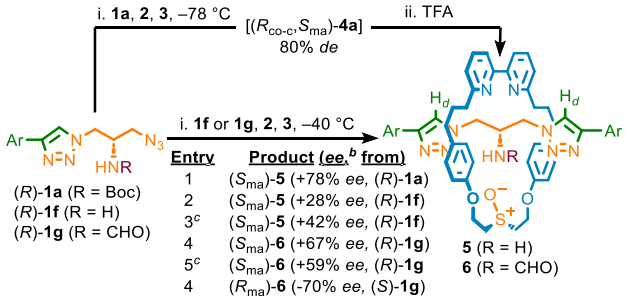
The effect of temperature on the stereoselectivity of the reactions of **1a** and **1d** was more complicated. Whereas reducing the reaction temperature in the synthesis of **4a** from rt (entry 1), to –40 °C (entry 8), to –78 °C (entry 9) increased the observed selectivity, that for **4d** was higher at –40 °C (entry 10) and then reduced at –78 °C (entry 11). This counterintuitive observation can be rationalized in broad terms by considering that the AT-CuAAC reaction takes place over several steps[19] that include a pre-equilibrium between diastereomeric azide/acetylide complexes **I** followed by irreversible formation of the corresponding triazolides **II** (Scheme 2).[20] The observed stereoselectivity is thus a composite function of the pre-equilibrium step (K_{eq}) and the relative rates (k_{SS}, k_{SR}) at which intermediates **I** progress to triazolides **II**. The effect of temperature on the reaction to produce **4d** suggests the pre-equilibrium and kinetic resolution steps respond to differently to changes in temperature, resulting in the observed behavior.[21]

Scheme 2. Proposed AT-CuAAC mechanism highlighting pre-equilibrium and kinetic resolution steps[a]



Trivially, the optimized conditions for the diastereoselective formation of **4a** (entry 9) allows the synthesis of highly enantioenriched rotaxane **5** in one-pot (Scheme 3, entry 1); AT-CuAAC coupling of (*R*)-**1a** followed by TFA-mediated removal of the Boc group gave rotaxane (S_{ma})-**5** in good stereoselectivity (+80% *ee*) in agreement with that observed for **4a** (80% *de*). The same reaction with (*S*)-**1a** gave (R_{ma})-**5** (77% *ee*).

Scheme 3. Synthesis of enantioenriched mechanically axially chiral rotaxanes **5** and **6**[a]



[a]Reagents and conditions: i. **1** (1.1 equiv.), **2** (1 equiv.), **3** (1.1 equiv.), $[Cu(CH_3CN)]PF_6$ (0.96 equiv.), $^iPr_2NEt$ (2 equiv.), CH_2Cl_2, 16 h; ii. TFA, CH_2Cl_2, –78 °C to rt, 6 h. [b]Determined by analytical CSP-HPLC (e.g., Figure 2a). [c]Reaction was conducted at –78 °C. Ar = 3,5-di-^{t}Bu-C_6H_3.

More excitingly, the high stereoselectivity observed in the AT-CuAAC reaction of azides **1** bearing a polarized NH presents the opportunity for the direct synthesis of MAC rotaxanes without the need for first forming separable co-conformational diastereomers; if the N substituent is too small to trap the macrocycle in one triazole-containing compartment, the only fixed stereochemistry in the product is provided by the mechanical axially stereogenic unit. Accordingly, reaction of primary amine-containing azide (*R*)-**1e** with macrocycle **2** and alkyne **3** at rt gave rotaxane **5** directly but in low stereoselectivity (16% *ee*), which increased when the reaction was performed at –40 °C (28% *ee*, entry 2) and improved further still at –78 °C (42% *ee*, entry 3). CSP-HPLC analysis of a sample of rotaxane (S_{ma})-**5** produced from (*R*)-**1a** and comparison with the same product from (*R*)-**1f** confirmed that the latter also produces (S_{ma})-**5** as the major stereoisomer (Figure 2a).

When instead formamide-containing azide (*R*)-**1g** was reacted with **2** and **3**, even at rt rotaxane **6** was obtained in reasonable stereopurity (58% *ee*), which was improved further at –40 °C (68% *ee*, entry 4). Conducting this reaction at –78 °C reduced the observed stereoselectivity (59% *ee*, entry 5), suggesting that, as with azide **1d**, the pre-equilibrium and kinetic resolution steps result in an unusual temperature dependence. CSP-HPLC analysis of a sample of rotaxane (S_{ma})-**6** produced by formylation of a sample of rotaxane (S_{ma})-**5** of known stereopurity and comparison with the same compound produced from (*R*)-**1g** confirmed that the latter produces (S_{ma})-**6** as the major stereoisomer. When (*S*)-**1g** was reacted instead (R_{ma})-**6** was produced (70% *ee*, entry 6). The solid-state structure of **6** obtained by SCXRD (Figure 2b) did not display the expected intermolecular NH•••O H-bond; instead, the same interaction was found to occur in an intermolecular fashion within the unit cell.

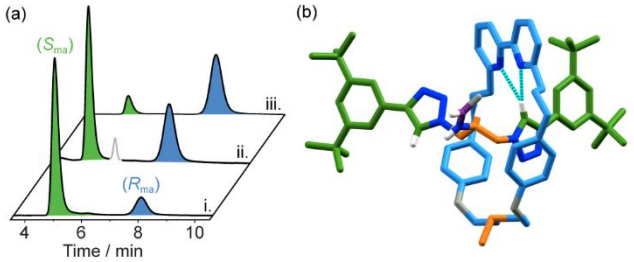


Figure 2. (a) CSP-HPLC analysis of: i. (S_{ma})-**6** (67% *ee*) produced from (*R*)-**1g**; ii. (S_{ma})-**6** (21% *ee*) produced from (S_{ma})-**5** (21% ee; minor impurity highlighted in grey), and iii. (S_{ma})-**6** (70% *ee*) produced from (*R*)-**1g**. (b) Solid state structure of *rac*-**6**, in which the N-H•••O bond between the SO unit and the amide is intermolecular (colors as in Scheme 1, including the sulfoxide (SO) moiety to highlight the differentiation of the macrocycle faces, except N [dark blue], O [grey], H [white]).

The different co-conformational behaviors of **4a**, **5** and **6** are clear from analysis of their respective ^{1}H NMR spectra. Diastereomers (S_{ma},$R_{co\text{-}c}$)-**4a** and (R_{ma},$R_{co\text{-}c}$)-**4a** are separable species; heating a mixture diastereomers **4a** resulted in no change in their ratio (Figure S50), confirming that the macrocycle cannot shuttle between the two compartments due to the large NHBoc unit. In contrast, the diastereotopic triazole resonances H$_d$ of amine rotaxane **5** appear as two sharp singlets at 298 K, indicating that (S_{ma},$R_{co\text{-}c}$)-**5** and (R_{ma},$R_{co\text{-}c}$)-**5** are in fast exchange on the ^{1}H NMR timescale through rapid shuttling of the macrocycle between the two triazole-containing compartments (Figure S89). The same resonances for formylated rotaxane **6** are broad at 298 K, although once again only two signals are observed (Figure S99). This observation is consistent with (S_{ma},$R_{co\text{-}c}$)-**6** and (R_{ma},$R_{co\text{-}c}$)-**6** exchanging on the ^{1}H NMR timescale, albeit more slowly than (S_{ma},$R_{co\text{-}c}$)-**5** and (R_{ma},$R_{co\text{-}c}$)-**5**, in keeping with the larger steric bulk of the formamide group of **6**. Accordingly, increasing the temperature resulted in sharpening of the two resonances corresponding to H$_d$ (Figure S110).

In conclusion, we have investigated the factors leading to stereoselectivity in the synthesis of rotaxanes containing a mechanical axial stereogenic unit based on a facially dissymmetric sulfoxide macrocycle. Our results suggest that a single H-bond between the substituents that define the two prochiral centers is sufficient to direct the relative orientation of macrocycle and axle in the AT-CuAAC reaction and thus give rise to the MAC stereogenic unit in reasonable stereoselectivity, particularly at lower temperatures and in non-competitive solvents. Our optimized conditions led to a synthesis of a highly enantioenriched MAC rotaxane (80% *ee*) using a two-step, one-pot procedure without separation of diastereomers. These insights ultimately led us to a direct enantioselective approach to MAC rotaxanes in which the prochiral unit of the axle is small enough to allow the macrocycle to escape the compartment it initially encircles, directly giving rise to a product in which the only fixed stereogenic unit arises from the mechanical bond in up to 67% *ee*. With a better understanding of the factors that control the formation of the MAC stereogenic unit, this newly identified form of mechanical stereochemistry is ripe for investigation in chiral molecular switches,[11a,22] catalysis[23] and sensing.[24]

ASSOCIATED CONTENT

Supporting Information

Procedures and full characterization data (NMR, MS, CD, SCXRD, HPLC as appropriate) for all novel compounds and supplementary discussions.

AUTHOR INFORMATION

Corresponding Author

s.goldup@bham.ac.uk

ACKNOWLEDGMENT

S.M.G. thanks the ERC (Agreement No. 724987) for funding and the Royal Society for a Wolfson Research Fellowship (RSWF\FT\180010). P.B. thanks the University of Southampton for a Presidential Scholarship. A.S. thanks the Royal Society and University of Birmingham for funding. P.G. thanks the University of Southampton and the University of Birmingham for funding.

(1) Maynard, J. R. J.; Goldup, S. M., Strategies for the Synthesis of Enantiopure Mechanically Chiral Molecules. *Chem* **2020,** *6* (8), 1914.

(2) (a) Jamieson, E. M. G.; Modicom, F.; Goldup, S. M., Chirality in rotaxanes and catenanes. *Chem. Soc. Rev.* **2018,** *47* (14), 5266. (b) Evans, N. H., Chiral Catenanes and Rotaxanes: Fundamentals and Emerging Applications. *Chem. Eur. J.* **2018,** *24* (13), 3101. (c) Pairault, N.; Niemeyer, J., Chiral Mechanically Interlocked Molecules - Applications of Rotaxanes, Catenanes and Molecular Knots in Stereoselective Chemosensing and Catalysis. *Synlett* **2018,** *29* (6), 689. (d) Nakazono, K.; Takata, T., Mechanical Chirality of Rotaxanes: Synthesis and Function. *Symmetry* **2020,** *12* (1), 144.

(3) Bordoli, R. J.; Goldup, S. M., An efficient approach to mechanically planar chiral rotaxanes. *J Am Chem Soc* **2014,** *136* (13), 4817.

(4) (a) Jinks, M. A.; de Juan, A.; Denis, M.; Fletcher, C. J.; Galli, M.; Jamieson, E. M. G.; Modicom, F.; Zhang, Z.; Goldup, S. M., Stereoselective Synthesis of Mechanically Planar Chiral Rotaxanes. *Angew. Chem. Int. Ed.* **2018,** *57* (45), 14806. (b) Zhang, S.; Rodríguez-Rubio, A.; Saady, A.; Tizzard, G. J.; Goldup, S. M., A chiral macrocycle for the stereoselective synthesis of mechanically planar chiral rotaxanes and catenanes. *Chem* **2023,** *9* (5), 1195. (c) de Juan, A.; Lozano, D.; Heard, A. W.; Jinks, M. A.; Suarez, J. M.; Tizzard, G. J.; Goldup, S. M., A chiral interlocking auxiliary strategy for the synthesis of mechanically planar chiral rotaxanes. *Nat Chem* **2022,** *14* (2), 179.

(5) (a) Denis, M.; Lewis, J. E. M.; Modicom, F.; Goldup, S. M., An Auxiliary Approach for the Stereoselective Synthesis of Topologically Chiral Catenanes. *Chem* **2019,** *5* (6), 1512. (b) Rodriguez-Rubio, A.; Savoini, A.; Modicom, F.; Butler, P.; Goldup, S. M., A Co-conformationally "Topologically" Chiral Catenane. *J. Am. Chem. Soc.* **2022,** *144* (27), 11927. (c) Noel Pairault, F. R., David Lozano, Ellen M. G. Jamieson, Graham J. Tizzard & Stephen M. Goldup, A catenane that is topologically achiral despite being composed of oriented rings. *Nat. Chem.* **2023**.

(6) Imayoshi, A.; Lakshmi, B. V.; Ueda, Y.; Yoshimura, T.; Matayoshi, A.; Furuta, T.; Kawabata, T., Enantioselective preparation of mechanically planar chiral rotaxanes by kinetic resolution strategy. *Nat. Commun.* **2021,** *12* (1), 404.

(7) Li, M.; Chia, X. L.; Tian, C.; Zhu, Y., Mechanically planar chiral rotaxanes through catalytic desymmetrization. *Chem* **2022**.

(8) Tian, C.; Fielden, S. D. P.; Perez-Saavedra, B.; Vitorica-Yrezabal, I. J.; Leigh, D. A., Single-Step Enantioselective Synthesis of Mechanically Planar Chiral [2]Rotaxanes Using a Chiral Leaving Group Strategy. *J. Am. Chem. Soc.* **2020,** *142* (21), 9803.

(9) Alvarez-Perez, M.; Goldup, S. M.; Leigh, D. A.; Slawin, A. M., A chemically-driven molecular information ratchet. Ibid.**2008,** *130* (6), 1836.

(10) Mochizuki, Y.; Ikeyatsu, K.; Mutoh, Y.; Hosoya, S.; Saito, S., Synthesis of Mechanically Planar Chiral rac-[2]Rotaxanes by Partitioning of an Achiral [2]Rotaxane: Stereoinversion Induced by Shuttling. *Org. Lett.* **2017,** *19* (16), 4347.

(11) Corra, S.; de Vet, C.; Groppi, J.; La Rosa, M.; Silvi, S.; Baroncini, M.; Credi, A., Chemical On/Off Switching of Mechanically Planar Chirality and Chiral Anion Recognition in a [2]Rotaxane Molecular Shuttle. *J. Am. Chem. Soc.* **2019,** *141* (23), 9129.

(12) Maynard, J. R. J.; Gallagher, P.; Lozano, D.; Butler, P.; Goldup, S. M., Mechanically axially chiral catenanes and noncanonical mechanically axially chiral rotaxanes. *Nat. Chem.* **2022,** *14* (9), 1038.

(13) For a related system in which a single H-bond is used to control the formation of rotaxane geometric isomers see: *chemrxiv*.

(14) Denis, M.; Goldup, S. M., The active template approach to interlocked molecules. *Nat Rev Chem* **2017,** *1* (8), 0061.

(15) Aucagne, V.; Hanni, K. D.; Leigh, D. A.; Lusby, P. J.; Walker, D. B., Catalytic "click" rotaxanes: a substoichiometric metal-template pathway to mechanically interlocked architectures. *J. Am. Chem. Soc.* **2006,** *128* (7), 2186.

(16) Saady, A.; Goldup, S. M., Triazole formation and the click concept in the synthesis of interlocked molecules. *Chem* **2023,** *9* (8), 2110.

(17) The suffix "ma" indicates that the label refers to the mechanical axial stereogenic unit. The suffix "co-c" indicates that the stereochemical label refers to the co-conformational covalent stereogenic unit.[12]

(18) We note that the previously reported SCXRD structure of minor diastereomer (R_{ma},$R_{co\text{-}c}$)-**4a**[12] contains the same interaction but in this case it occurs intermolecularly between neighboring molecules in the unit cell, as observed for **4d** (Figure 2).

(19) (a) Neal, E. A.; Goldup, S. M., Competitive formation of homocircuit [3]rotaxanes in synthetically useful yields in the bipyridine-mediated active template CuAAC reaction. *Chem Sci* **2015,** *6* (4), 2398. (b) Neal, E. A.; Goldup, S. M., A Kinetic Self-Sorting Approach to Heterocircuit [3]Rotaxanes. *Angew. Chem. Int. Ed.* **2016,** *55* (40), 12488. (b) Modicom, F.; Jamieson, E. M. G.; Rochette, E.; Goldup, S. M., Chemical Consequences of the Mechanical Bond: A Tandem Active Template-Rearrangement Reaction. *Angew Chem Int Ed Engl* **2019,** *58* (12), 3875.

(20) Winn, J.; Pinczewska, A.; Goldup, S. M., Synthesis of a rotaxane Cu(I) triazolide under aqueous conditions. *J Am Chem Soc* **2013,** *135* (36), 13318.

(21) We note that our results cannot rule out that either K_{eq} or $k_{SS/SR}$ depends on a large negative entropy of reaction or activation respectively, which may also account for the unexpected temperature dependence of the AT-CuAAC reaction.

(22) (a) Gaedke, M.; Witte, F.; Anhauser, J.; Hupatz, H.; Schroder, H. V.; Valkonen, A.; Rissanen, K.; Lutzen, A.; Paulus, B.; Schalley, C. A., Chiroptical inversion of a planar chiral redox-switchable rotaxane. *Chem. Sci.* **2019,** *10* (43), 10003. (b) Corra, S.; de Vet, C.; Baroncini, M.; Credi, A.; Silvi, S., Stereodynamics of E/Z isomerization in rotaxanes through mechanical shuttling and covalent bond rotation. *Chem* **2021,** *7* (8), 2137. (c) Wang, Y.; Gong, J.; Wang, X.; Li, W. J.; Wang, X. Q.; He, X.; Wang, W.; Yang, H. B., Multistate Circularly Polarized Luminescence Switching through Stimuli-Induced Co-Conformation Regulations of Pyrene-Functionalized Topologically Chiral [2]Catenane. *Angew. Chem. Int. Ed.* **2022**, e202210542.

(23) (a) Cakmak, Y.; Erbas-Cakmak, S.; Leigh, D. A., Asymmetric Catalysis with a Mechanically Point-Chiral Rotaxane. *J. Am. Chem. Soc.* **2016,** *138* (6), 1749. (b) Heard, A. W.; Goldup, S. M., Synthesis of a Mechanically Planar Chiral Rotaxane Ligand for Enantioselective Catalysis. *Chem* **2020,** *6* (4), 994. (c) Pairault, N.; Zhu, H.; Jansen, D.; Huber, A.; Daniliuc, C. G.; Grimme, S.; Niemeyer, J., Heterobifunctional Rotaxanes for Asymmetric Catalysis. *Angew. Chem. Int. Ed.* **2020,** *59* (13), 5102. (d) Heard, R. W.; Suarez, J. M.; Goldup, S. M., Controlling catalyst activity, chemoselectivity and stereoselectivity with the mechanical bond. *Nat. Rev. Chem.* **2022,** *6* (3), 182.

(24) (a) Hirose, K.; Ukimi, M.; Ueda, S.; Onoda, C.; Kano, R.; Tsuda, K.; Hinohara, Y.; Tobe, Y., The Asymmetry is Derived from Mechanical Interlocking of Achiral Axle and Achiral Ring Components -Syntheses and Properties of Optically Pure [2]Rotaxanes. *Symmetry* **2018,** *10* (1), 20. (b) Lim, J. Y. C.; Marques, I.; Felix, V.; Beer, P. D., A Chiral Halogen-Bonding [3]Rotaxane for the Recognition and Sensing of Biologically Relevant Dicarboxylate Anions. *Angew. Chem. Int. Ed.* **2018,** *57* (2), 584. (c) Mitra, R.; Thiele, M.; Octa-Smolin, F.; Letzel, M. C.; Niemeyer, J., A bifunctional chiral [2]catenane based on 1,1'-binaphthyl-phosphates. *Chem. Commun.* **2016,** *52* (35), 5977.