A Stimuli Responsive Rotaxane-Au Catalyst: Regulation of Activity and Diastereoselectivity

M. Galli, J. E. M. Lewis, and S. M. Goldup*

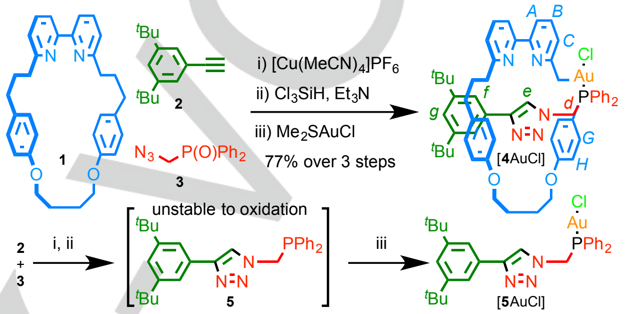
Abstract: We report a rotaxane-based Au catalyst and study the effect of the mechanical bond on its catalytic activity. Although the non-interlocked thread readily mediates the cyclopropanation of styrene, the rotaxane requires a catalytically innocent guest, the identity of which significantly influences both the yield and diastereoselectivity of the reaction. Under optimised conditions Au^{I} (the catalyst), Ag^{I} (to abstract the Cl^{-} ligand) and Cu^{I} (the cofactor) combine to produce a catalyst with excellent activity and selectivity.

Catalysts based on interlocked molecules have recently begun to receive increased attention.[1] The majority of systems reported take advantage of the well-studied ability of the mechanically bonded components to undergo large amplitude relative motion,[2] including examples in which motion alters reaction chemoselectivity,[3] machines inspired by DNA polymerase that employ an interlocked catalyst-substrate architecture to produce highly processive reactions,[4] and systems where the catalytic activity of the rotaxane is controlled by reversible shielding of organocatalytic moieties in the thread.[5,6,7]

In contrast to these applications of mechanical motion, comparatively little is known about the influence of the mechanical bond itself on the outcome of catalysed reactions.[8] In 2004, Takata and co-workers reported that an *achiral* imidazolium organocatalyst encircled by a chiral macrocycle mediates an enantioselective benzoin reaction, albeit in moderate *ee*.[9] Very recently, Leigh and co-workers reported a chiral [2]rotaxane ligand for Ni that exhibits higher enantioselectivity than a non-interlocked model complex, at the cost of reduced activity due to steric hindrance.[10] These results suggests that the sterically crowded environment provided by the mechanical bond could be used to engineer novel reaction fields to alter the stereoselectivity of catalysts that are hard to control using conventional scaffolds.

Although synthetically powerful, Au^{I}- mediated reactions are perhaps the quintessential example of an activation mode for which it is hard to engineer the ligand to sterically influence the reaction due to the linear coordination geometry of Au^{I}.[11] Here we report a rotaxane-Au catalyst[12,13] in which the mechanical bond influences both diastereoselectivity and catalytic activity, and demonstrate the stimuli responsive control of both of these important reaction parameters.

Rotaxane Au complex [**4**AuCl] was synthesised[14] in excellent yield over three steps from macrocycle **1**, alkyne **2** and azide **3** using our small macrocycle modification[15] of Leigh's active template Cu-mediated alkyne-azide cycloaddition[16] (AT-CuAAC) reaction,[17] followed by reduction of the phosphine oxide moiety and formation of the Au complex. Non-interlocked complex [**5**AuCl] was synthesised in an analogous manner.



Scheme 1. Synthesis of [**4**AuCl] and [**5**AuCl]. Reagents and Conditions: i) $[Cu(MeCN)_4]PF_6$, $^{i}Pr_2EtN$, EtOH, 80 °C, 18 h; ii) Cl_3SiH, Et_3N, PhMe-CH_2Cl_2 (6 : 1), 100 °C, 18 h; iii) Me_2SAuCl, CH_2Cl_2, rt, 1 h.

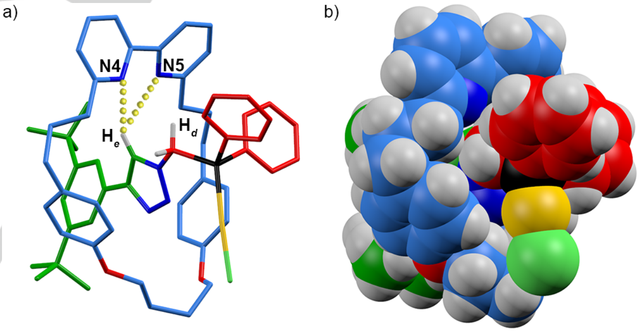


Figure 1. Single crystal X-ray structure of [**4**AuCl] in a) capped sticks with shorter of the N···H contacts indicated; b) space-filling representation. ^{1}H labelling as in Scheme 1. Selected interatomic distances: N4-H_d = 2.7 Å; N5-H_d = 3.1 Å; N4-H_e = 2.9 Å; N5-H_e = 2.7 Å; P-Au = 2.2 Å; Au-Cl = 2.3 Å; angle P-Au-Cl = 176°.

During the synthesis of **4** and **5** the first significant effect of the mechanical bond became apparent: although phosphine rotaxane **4** does not require special handling, non-interlocked **5** is extremely susceptible to oxidation and reverts to the corresponding phosphine oxide on standing in $CDCl_3$. Thus, the mechanical bond appears to stabilise the relatively electron rich alkyl phosphine moiety.[8] Single crystals of [**4**AuCl] suitable for X-ray analysis were grown by slow evaporation from $CDCl_3$.[18] The space filling representation of [**4**AuCl] (Fig 1b) clearly demonstrates the sterically hindered environment around the Au centre provided by the mechanical bond. In the solid-state, triazole proton H_e and one of methylene protons H_d participate in bifurcated C-H···N hydrogen bonds with the pyridine nitrogens.

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[a] Ms M. Galli, Dr J. E. M. Lewis, Dr S. M. Goldup
School of Chemistry
University of Southampton
Highfield, Southampton, SO17 1BJ.
E-mail: s.goldup@soton.ac.uk

Supporting information for this article, including full crystallographic data and characterisation of all novel compounds, is given via a link at the end of the document.

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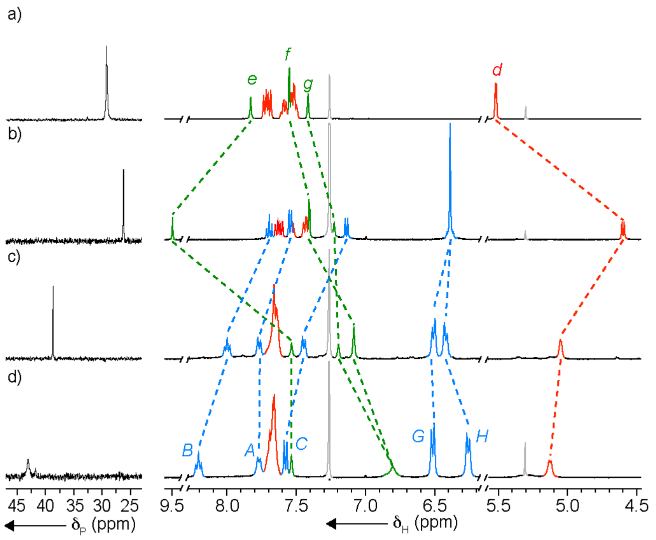


Figure 2. Partial ^{31}P (162 MHz) and ^{1}H (400 MHz) NMR (CDCl$_3$, 300 K) spectra for a) [**5**AuCl] b) [**4**AuCl], c) [**4**AuCl] + AgSbF$_6$; d) [**4**AuCl] + [Cu(MeCN)$_4$]PF$_6$ + AgSbF$_6$. Selected peaks are assigned with labelling as shown in Scheme 1. Solvent peaks are shown in dark grey.

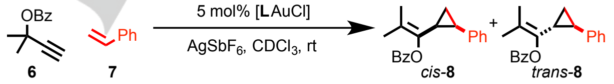
Despite the unusual nature of the Au coordination environment in [**4**AuCl], the ^{31}P NMR spectra of the thread (Fig 2a) and rotaxane (Fig 2b) AuCl complexes are similar, exhibiting single resonances at 26.2 and 29.2 ppm respectively. In contrast, their ^{1}H NMR spectra are very different; as well as the expected shielding of thread resonances (e.g. H_d, H_f and H_g), triazole proton H_e resonates at 9.5 ppm in the rotaxane-Au complex, 1.7 ppm higher than in [**5**AuCl], suggesting that the C-H···N hydrogen bond between H_e and the bipyridine N atom observed in the solid state is at least partially maintained in solution.

To investigate the effect of the mechanical bond on the catalytic behaviour of [**4**AuCl] we selected Toste's Au^{I}-mediated modification of the Ohe-Uemura cyclopropanation reaction as a simple, well-understood model system.[19,20] As in many Au^{I}-mediated reactions, the active catalyst is proposed to be an LAu^{+} π-acid, typically generated by abstraction of the Cl ligand from LAuCl by Ag^{I} salts.[11] ^{31}P NMR analysis of the product of treating [**4**AuCl] with AgSbF$_6$ (Fig 1c) revealed a new resonance at higher chemical shift (38.7 ppm) consistent with Cl abstraction and formation of a solvated PAu^{+} complex. [21] However, in the presence of AgSbF$_6$, [**4**AuCl] failed to mediate the reaction between propargylic ester **6** and styrene (**7**) to produce cyclopropanes **8** (entry 1). Despite the lack of activity of [**4**AuCl], *in situ* NMR analysis of reactions containing [**4**AuCl] confirmed the presence of [**4**Au]$^{+}$ under the reaction conditions. In contrast, non-interlocked complex [**5**AuCl] (entry 2) successfully produced **8** with moderate selectivity in good yield.[20a]

Comparison of the ^{1}H NMR of [**4**AuCl] and [**4**Au]$^{+}$ provided a clue as to the origin of the rotaxane catalyst's lack of activity: on abstraction of the Cl anion, the resonance corresponding to triazole proton H_e shifts from 9.5 to 7.5 ppm, suggesting that the C-H···N interaction present in [**4**AuCl] is at least partially interrupted in [**4**Au]$^{+}$. This observation is consistent with the Au^{+} centre interacting with the N donor atoms of the macrocycle, interrupting the weaker hydrogen bonding interaction. The proposed N-Au interaction would be expected to temper the catalytic activity of [**4**Au]$^{+}$ by reducing the π-acidity of the metal centre and preventing coordination of the substrate.[22] Based on this hypothesis, a solution suggested itself: addition of a guest that coordinates in the macrocyclic cavity and is able to effectively compete with the N-Au interaction should remove the inhibition and switch the catalyst "on".[23]

Addition of TsOH, [Cu(MeCN)$_4$]PF$_6$, Zn(OTf)$_2$ or Cd(OTf)$_2$ to a solution of [**4**AuCl] in CDCl$_3$ led to dramatic changes in the ^{1}H NMR, but minimal change in the ^{31}P resonance (∂_P = 24.5, 23.9, 27.7 and 24.4 ppm respectively; see supporting information for full details), suggesting the P-Au bond is unaffected by guest binding. Addition of AgSbF$_6$ to [**4**AuCl] and [Cu(MeCN)$_4$]PF$_6$ in CDCl$_3$ resulted in formation of a complex with a broad ^{31}P resonance consistent with the desired PAu^{+} species (Fig 2d). Furthermore, in the presence of 1 equiv. of TsOH (table 1, entry 3) [**4**AuCl] produced cyclopropanes **8** in reasonable yield in just 1 h. More effective still, both Cu^{I} and Zn^{II} (entries 4 and 5 respectively) resulted in rapid reactions and excellent yields of **8**. Replacing Zn(OTf)$_2$ with Cd(OTf)$_2$ (entry 6) led to a diminished yield. In contrast, to the behaviour of the rotaxane, reactions mediated by [**5**AuCl] were unaffected by the presence of Zn^{II} (entry 7), while addition of Cu^{I} (entry 8) led to partial decomposition of the catalyst and a diminished yield of **8**.[24] In the absence of Au^{I} the additives have no intrinsic catalytic behaviour (entry 9).

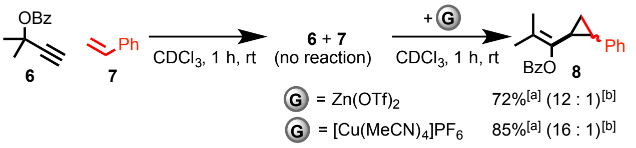
Table 1. Effect of additives on the catalytic activity of [**4**AuCl] and [**5**AuCl].



Entry	[LAuCl]	Additive	Yield[a] (*cis-trans*[b])
1	[**4**AuCl]	-	n.r.
2	[**5**AuCl]	-	85% (10 : 1)
3	[**4**AuCl]	TsOH	62% (15 : 1)
4	[**4**AuCl]	[Cu(MeCN)$_4$]PF$_6$	93% (16 : 1)
5	[**4**AuCl]	Zn(OTf)$_2$	76% (13 : 1)
6	[**4**AuCl]	Cd(OTf)$_2$	58% (11 : 1)
7	[**5**AuCl]	Zn(OTf)$_2$	86% (10 : 1)
8	[**5**AuCl]	[Cu(MeCN)$_4$]PF$_6$	68% (9 : 1)
9	-	H^{+}, Cu^{I}, Zn^{II} or Cd^{II}	n.r.

[a] Determined by ^{1}H NMR with Cl$_2$CHCHCl$_2$ as internal standard. [b] Determined by HPLC analysis.

The effect of guest binding on the catalytic behaviour of [**4**AuCl] is noteworthy on a number of counts. Firstly, and most obviously, the activity of the catalyst is strongly dependent on the presence of the guest. Building on these results we performed *in situ* switching experiments with [**4**AuCl] and the best performing guests, Cu^{I} and Zn^{II} (Scheme 2). After 1 h no reaction was observed in the absence of additives. Addition of Zn(OTf)$_2$ or [Cu(MeCN)$_4$]PF$_6$ led to rapid production of cyclopropanes **8** in comparable yield and diastereoselectivity to the reaction in which the guest was introduced prior to the substrate. Thus, [**4**AuCl] behaves as a switchable catalyst, with an extremely large difference in activity between the “off” and “on” states.



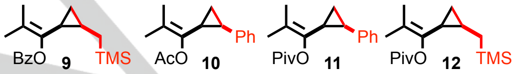
Scheme 2. Switching Experiment. Reagents and Conditions: [**4**AuCl] (5 mol%), $AgSbF_6$ (5 mol%), $CDCl_3$, rt, 1 h then addition of guest (5 mol%) and a further 1 h at rt. [a] Determined by ^1H NMR with $Cl_2CHCHCl_2$ as internal standard. [b] Determined by HPLC analysis.

Secondly, the selectivity observed in the presence of Cu^I or TsOH are among the highest values achieved by monodentate phosphines for these substrates.[25] As diastereoselectivity in Toste’s cyclopropanation reaction is correlated with ligand steric hindrance[20] we examined the steric demand of the rotaxane ligand using Nolan’s % buried volume ($\%V_{bur}$) parameter, a gross measure of the volume around the metal centre occupied by the ligand atoms.[26] Applying the calculation[27] to the solid-state structure of [**4**AuCl] (Fig 1) revealed a value of $\%V_{bur}$ of 44%, significantly higher than that of PPh_3 (30%) and even sterically hindered ligand P^tBu_3 (38%).[26]

Finally, and perhaps most strikingly, each guest examined gives rise to a *different degree of diastereoselectivity.* This variation is tentatively attributed to the modulation of the reaction field provided by the mechanical bond upon guest binding; as well as disrupting the N-Au coordination, the binding of guests into the macrocycle cavity will alter the co-conformation between the macrocycle and thread, rigidifying the catalyst framework and modifying the space around the reaction site in a manner akin to allosteric modulation of enzymatic catalysts.

The serendipitous isolation of [**4**(H)(AuCl)]$AuCl_2$ as a minor by-product during the synthesis of [**4**AuCl] provides insight into the effect of guest binding on the steric environment around the gold. In the solid-state structure of $[\mathbf{4}(H)(AuCl)]^+$ (see supporting information) the proton guest is located between a triazole nitrogen and one of the bipyridine nitrogens. This binding event causes a co-conformational rearrangement compared with [**4**AuCl]; the Au-Cl bond of [**4**(H)(AuCl)]$AuCl_2$ is projected towards rather than away from the bipyridine unit (*cf* Fig 1), clearly altering the three dimensional environment around the Au centre. The calculated $\%V_{bur}$ of 42% for [**4**(H)(AuCl)]$AuCl_2$ also differs from that of [**4**AuCl], albeit by only 2%. Although neither [**4**AuCl] or [**4**(H)(AuCl)]$AuCl_2$ is of direct catalytic relevance, the large co-conformational change observed on protonation provides evidence for the proposed allosteric role of the guest.

To investigate the generality of these observations we compared the reactions of substrates with different steric properties mediated by $^tBu_3PAuCl$, [**5**AuCl] or [**4**AuCl] (Fig 3). In keeping with previous reports, alkyl substituted cyclopropanes **9** and **12** were formed in low selectivity in the presence of $^tBu_3PAuCl$, whereas variation of the ester moiety between OAc (**10**) and pivolate (OPiv; **11**) led to no significant change in selectivity.[20a] This trend was repeated in the case of [**5**AuCl], although in all cases the selectivity was inferior to that of the bulkier $^tBu_3P$ ligand. Reactions mediated by [**4**AuCl] gave the target cyclopropane in significantly higher selectivity than produced with either non-interlocked catalyst further demonstrating the sterically hindered environment provided by the mechanical bond. Once again, the diastereoselectivity of reactions mediated by [**4**AuCl] varied in a guest dependent manner. However, whereas [**4**AuCl] produced benzoate esters **8** and **9** in higher *dr* in the presence of Cu^I than Zn^{II}, this trend was reversed in the case of alkyl ester derived products **10**-**12** Thus, although the guest-dependent behaviour of [**4**AuCl] is reproducible across the substrates investigated, the optimal guest appears to depend on the detailed structure of the reagents. This suggests that, in addition to a simple steric component, specific interactions between substrate and catalyst that vary with the identity of the guest may play a significant role.



	9	10	11	12
$^tBu_3PAuCl$	1.4 : 1	14 : 1	15 : 1	1.4 : 1
[**5**AuCl]	1.3 : 1	13 : 1	13 : 1	1.3 : 1
[**4**AuCl] + Zn^{II}	2.1 : 1	19 : 1	20 : 1	1.8 : 1
[**4**AuCl] + Cu^I	2.4 : 1	15 : 1	15 : 1	1.6 : 1

Figure 3. Comparison of $^tBu_3PAuCl$, [**5**AuCl] and [**4**AuCl] with representative substrates. Selectivity determined by ^1H NMR. Conditions as in table 1.

In conclusion, we have demonstrated a rotaxane-based Au catalyst and identified a new approach to the development of stimuli responsive interlocked catalysts more generally. Although such behaviour has previously been demonstrated in organocatalytic rotaxanes,[5] this is the first example of a rotaxane-based metal complex with stimuli responsive catalytic activity. Once switched on by guest binding, the flexible but sterically crowded[28] environment of the mechanical bond has been shown to influence strongly the diastereoselectivity of an Au-mediated reaction, demonstrating the potential of interlocked molecules for the design of new reaction fields for hard to influence transformations. The influence of the mechanical bond is also responsive to external stimuli, depending as it does on the nature of the guest, the first time that such stimuli responsive stereoselectivity has been observed in a rotaxane catalyst. The origin of this effect is tentatively proposed to be similar to allosteric modulation in enzymes in which cofactor binding subtly influences the environment of the active site. Modification of the reaction field by guest binding in such rotaxane architectures offers a supramolecular approach to the optimisation of catalyst activity and selectivity, the potential for catalytic signal application for the development of sensors,[29] and the possibility of controlling not just the stereoselectivity but also the chemoselectivity of metal catalysed reactions in a stimuli responsive manner.

Experimental Section

Switching experiment: $CDCl_3$ (0.5 mL) was added to a sealed vial containing rotaxane [**4**AuCl] (7.1 mg, 0.0062 mmol) and $AgSbF_6$ (2.2 mg, 0.0062 mmol). After 5 min **6** (23.0 mg, 0.122

mmol) and **7** (50.9 mg, 0.489 mmol,) were added as solutions in $CDCl_3$ (2.5 mL). A solution of 1,1,2,2-tetrachloroethane in $CDCl_3$ (1.22 M, 0.1 mL) was added and the resulting mixture was stirred for 1 h and analysed by ^{1}H NMR. The mixture was transferred into a vial containing the guest (0.0062 mmol). After 1 h the reaction was analysed by ^{1}H NMR and HPLC.

Keywords: rotaxane • supramolecular • catalyst • molecular machine • gold

[1] For recent reviews: a) S. F. M. van Dongen, S. Cantekin, J. A. A. W. Elemans, A. E. Rowan, R. J. M. Nolte, *Chem. Soc. Rev.* 2014, *43*, 99–122; b) E. A. Neal, S. M. Goldup, *Chem. Commun.* **2014**, *50*, 5128–5142; c) D. A. Leigh, V. Marcos, M. R. Wilson, *ACS Catal.* **2014**, *4*, 4490–4497.

[2] For recent reviews on interlocked molecules see: a) S. J. Loeb, *Chem. Soc. Rev.* **2007**, *36*, 226–235; b) E. R. Kay, D. A. Leigh, F. Zerbetto, *Angew. Chem. Int Ed.* **2007**, *46*, 72–191; c) J. F. Stoddart, *Angew. Chem. Int. Ed.* **2014**, 11102–11104; d) N. H. Evans, P. D. Beer, *Chem. Soc. Rev.* **2014**, *43*, 4658-4683.

[3] Y. Suzaki, K. Shimada, E. Chihara, T. Saito, Y. Tsuchido, K. Osakada, *Org. Lett.* **2011**, *13*, 3774–3777.

[4] a) P. Thordarson, E. J. A. Bijsterveld, A. E. Rowan, R. J. M. Nolte, *Nature* 2003, *424*, 915–918; b) B. Lewandowski, G. De Bo, J. W. Ward, M. Papmeyer, S. Kuschel, M. J. Aldegunde, P. M. E. Gramlich, D. Heckmann, S. M. Goldup, D. M. D'Souza, A. E. Fernandes, D. A. Leigh, *Science.* **2013**, *339*, 189–193; c) S. F. M. van Dongen, J. Clerx, K. Nørgaard, T. G. Bloemberg, J. J. L. M. Cornelissen, M. A. Trakselis, S. W. Nelson, S. J. Benkovic, A. E. Rowan, R. J. M. Nolte, *Nat. Chem.* **2013**, 1–8; d) G. De Bo, S. Kuschel, D. A. Leigh, B. Lewandowski, M. Papmeyer, J. W. Ward, *J. Am. Chem. Soc.* 2014, *136*, 5811–5814.

[5] a) V. Blanco, A. Carlone, K. D. Hänni, D. A. Leigh, B. Lewandowski, *Angew. Chem. Int. Ed.* **2012**, *51*, 5166–5169; b) V. Blanco, D. A. Leigh, U. Lewandowska, B. Lewandowski, V. Marcos, *J. Am. Chem. Soc.* **2014**, *136*, 15775–15780; c) V. Blanco, D. A. Leigh, V. Marcos, J. A. Morales-Serna, A. L. Nussbaumer, *J. Am. Chem. Soc.* **2014**, *136*, 4905–4908; d) J. Beswick, V. Blanco, G. De Bo, D. A. Leigh, U. Lewandowska, B. Lewandowski, K. Mishiro, *Chem. Sci.* **2015**, *6*, 140.

[6] Selected recent reviews on stimuli responsive catalysis: a) S. Monsaert, A. Lozano Vila, R. Drozdzak, P. Van Der Voort, F. Verpoort, *Chem. Soc. Rev.* **2009**, *38*, 3360–3372; b) R. S. Stoll, S. Hecht, *Angew. Chem. Int. Ed.* **2010**, *49*, 5054–5075; c) M. J. Wiester, P. A. Ulmann, C. A. Mirkin, *Angew. Chem. Int. Ed.* **2011**, *50*, 114–137; d) B. M. Neilson, C. W. Bielawski, *ACS Catal.* **2013**, *3*, 1874–1885; e) J. Escorihuela, M. I. Burguete, S. V Luis, *Chem. Soc. Rev.* **2013**, 5595–5617; f) V. Blanco, D. A. Leigh, V. Marcos, *Chem. Soc. Rev.* **2015**, *44*, 5341–5370.

[7] Other examples of rotaxanes that influence chemical reactions include: a) C. B. Caputo, K. Zhu, V. N. Vukotic, S. J. Loeb, D. W. Stephan, *Angew. Chem. Int. Ed.* **2013**, *52*, 960–963; b) J. Berná, M. Alajarín, R.-A. Orenes, *J. Am. Chem. Soc.* **2010**, *132*, 10741–10747.

[8] For representative examples where mechanical bonding alters the reactivity of functional groups see: a) A. H. Parham, B. Windisch, F. Vögtle, *Eur. J. Org. Chem.* **1999**, 1233–1238; b) T. Oku, Y. Furusho, T. Takata, *Org. Lett.* **2003**, *5*, 12384–12385; c) E. Arunkumar, C. C. Forbes, B. C. Noll, B. D. Smith, *J. Am. Chem. Soc.* **2005**, *127*, 3288–3289; d) C. M. S. Yau, S. I. Pascu, S. A. Odom, J. E. Warren, E. J. F. Klotz, M. J. Frampton, C. C. Williams, V. Coropceanu, M. K. Kuimova, D. Phillips, S. Barlow, J.-L. Brédas, S. R. Marder, V. Millar, H. L. Anderson, *Chem. Commun.* **2008**, 2897–2899; e) D. M. D'Souza, D. A. Leigh, L. Mottier, K. M. Mullen, F. Paolucci, S. J. Teat, S. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 9465–9470; f) J. Winn, A. Pinczewska, S. M. Goldup, *J. Am. Chem. Soc.* **2013**, *135*, 13318-13321.

[9] *Y.* Tachibana, N. Kihara, T. Takata *J. Am. Chem. Soc.* **2004**, *126*, 3438-3439

[10] S. Hoekman, M. O. Kitching, D. A. Leigh, M. Papmeyer, D. Roke, *J. Am. Chem. Soc.* **2015**, *37*, 7656–7659.

[11] For recent reviews on ligand effects in Au catalysis see: a) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev.* **2008**, *108*, 3351–3378; b) Y. M. Wang, A. D. Lackner, F. D. Toste, *Acc. Chem. Res.* **2014**, *47*, 889–901.

[12] Selected examples of supramolecular approaches to Au catalysts: a) Z. J. Wang, C. J. Brown, R. G. Bergman, K. N. Raymond, F. D. Toste, *J. Am. Chem. Soc.* **2011**, *133*, 7358–7360; b) A. Cavarzan, A. Scarso, P. Sgarbossa, G. Strukul, J. N. H. Reek, *J. Am. Chem. Soc.* **2011**, *133*, 2848–2851; c) L. Adriaenssens, A. Escribano-Cuesta, A. Homs, A. M. Echavarren, P. Ballester, *Eur. J. Org. Chem.* **2013**, 1494–1500.

[13] Although Au^I-templated synthesis of catenanes has been reported, the catalytic behaviour of the products was not assessed: a) C. P. McArdle, S. Van, M. C. Jennings, R. J. Puddephatt, *J. Am. Chem. Soc.* 2002, *124*, 3959–3965; b) S. M. Goldup, D. a Leigh, P. J. Lusby, R. T. McBurney, A. M. Z. Slawin, *Angew. Chem. Int. Ed.* **2008**, *47*, 6999–7003; c) R. J. Puddephatt, *J. Organomet. Chem.* **2014**, *792*, 13–24.

[14] The design of the phosphine thread is based on "clickphine" ligands developed by Reek and Maarseveen, and others. For representative examples see: a) R. J. Detz, S. A. Heras, R. De Gelder, P. W. N. M. Van Leeuwen, H. Hiemstra, J. N. H. Reek, J. H. Van Maarseveen, *Org. Lett.* **2006**, *8*, 3227–3230; b) E. M. Schuster, M. Botoshansky, M. Gandelman, *Angew. Chem. Int. Ed.* **2008**, *47*, 4555–4558.

[15] H. Lahlali, K. Jobe, M. Watkinson, S. M. Goldup, *Angew. Chem. Int. Ed.* 2011, *50*, 4151–4155.

[16] C. W. Tornøe, C. Christensen, M. Meldal, *J. Org. Chem.* **2002**, *67*, 3057–3064; b) V. V Rostovtsev, L. G. Green, V. V Fokin, K. B. Sharpless, *Angew. Chem., Int. Ed.* 2002, *41*, 2596–2599.

[17] V. Aucagne, K. D. Hänni, D. A. Leigh, P. J. Lusby, D. B. Walker, *J. Am. Chem. Soc.* 2006, *128*, 2186–218.

[18] The asymmetric unit of [**4**AuCl] is complex with four independent rotaxanes, one of which is shown in Fig 1. See supporting information for details

[19] K. Miki, K. Ohe, S. Uemura, *J. Org. Chem.* **2003**, *68*, 8505–8513.

[20] a) M. J. Johansson, D. J. Gorin, S. T. Staben, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 18002–18003; b) C. Bartolomé, D. García-Cuadrado, Z. Ramiro, P. Espinet, *Inorg. Chem.* **2010**, *49*, 9758–9764; c) J. Petuškova, H. Bruns, M. Alcarazo, *Angew. Chem. Int. Ed.* **2011**, *50*, 3799–3802; d) E. Gross, J. H.-C. Liu, F. D. Toste, G. A. Somorjai, *Nat. Chem.* **2012**, *4*, 947–952.

[21] J. H. Teles, S. Brode, M. Chabanas, *Angew. Chem. Int. Ed.* **1998**, *37*, 1415–1418;

[22] For recent reports on the inhibition of Au catalysts by Lewis basic species see: a) M. Kumar, G. B. Hammond, B. Xu, *Org. Lett.* **2014,** *16*, 3452–3455; b) P. C. Young, S. L. J. Green, G. M. Rosair, A.-L. Lee, *Dalton Trans.* **2013**, *42*, 9645–9653; c) M. Jia, M. Bandini, *ACS Catal.* **2015**, 1638–1652.

[23] For a related switchable catalyst see: G.-H. Ouyang, Y.-M. He, Y. Li, J.-F. Xiang, Q.-H. Fan, *Angew. Chem. Int. Ed.* **2015**, *54*, 4334–4337.

[24] Addition **1** to [**5**Au]$^+$ resulted in a pale red solution, presumably due to Au^0 nanoparticle formation, with a dramatic reduction in yield and selectivity observed. Although the origin of this effect is unclear, the interlocked arrangement clearly behaves very differently to a simple admixture of the two components.

[25] Bidentate diaurated phosphines such as Binap$(AuCl)_2$ typically give higher diastereoselectivity in the Au^I-mediated cyclopropanation reaction.[20] For a recent example of a hindered monodentate phosphine that delivers extremely high *de* see ref.[20c]

[26] H. Clavier, S. P. Nolan, *Chem. Commun.* **2010**, *46*, 841–861.

[27] Calculations of %V_{bur} were performed using the SambVca web application: A. Poater, B. Cosenza, A. Correa, S. Giudice, F. Ragone, V. Scarano, L. Cavallo, *Eur. J. Inorg. Chem.* **2009**, 1759–1766.

[28] G. Altenhoff, R. Goddard, C. W. Lehmann, F. Glorius, *Angew. Chem. Int. Ed.* 2003, *42*, 3690–3693.

[29] N. C. Gianneschi, S. T. Nguyen, C. A. Mirkin, *J. Am. Chem. Soc.* **2005**, *127*, 1644–1645.

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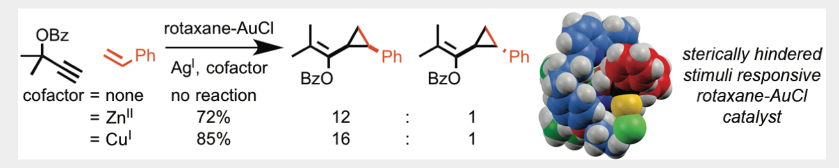

*Author(s), Corresponding Author(s)**

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Title

A group effort: We report a rotaxane-based Au catalyst and study the effect of the mechanical bond on its catalytic activity. The rotaxane requires a catalytically innocent cofactor, the identity of which significantly influences both the yield and diastereoselectivity of the reaction. Under optimised conditions Au^{I} (the catalyst), Ag^{I} (to abstract the Cl^{-} ligand) and Cu^{I} (the cofactor) combine to produce a catalyst with excellent activity and selectivity.