How to cite: *Angew. Chem. Int. Ed.* **2020**, *59*, 19905–19909
International Edition: doi.org/10.1002/anie.202008662
German Edition: doi.org/10.1002/ange.202008662

Aryl Hydrogenation

Janus Face All-*cis* 1,2,4,5-tetrakis(trifluoromethyl)- and All-*cis* 1,2,3,4,5,6-hexakis(trifluoromethyl)- Cyclohexanes

*Cihang Yu, Agnes Kütt, Gerd-Volker Röschenthaler, Tomas Lebl, David B. Cordes, Alexandra M. Z. Slawin, Michael Bühl, and David O'Hagan**

Abstract: *We report the synthesis of all-cis 1,2,4,5-tetrakis (trifluoromethyl)- and all-cis 1,2,3,4,5,6-hexakis (trifluoromethyl)- cyclohexanes by direct hydrogenation of precursor tetrakis- or hexakis- (trifluoromethyl)benzenes. The resultant cyclohexanes have a stereochemistry such that all the CF_3 groups are on the same face of the cyclohexyl ring. All-cis 1,2,3,4,5,6-hexakis(trifluoromethyl)cyclohexane is the most sterically demanding of the all-cis hexakis substituted cyclohexanes prepared to date, with a barrier (ΔG) to ring inversion calculated at 27 kcal mol^{-1}. The X-ray structure of all-cis 1,2,3,4,5,6-hexakis(trifluoromethyl)cyclohexane displays a flattened chair conformation and the electrostatic profile of this compound reveals a large diffuse negative density on the fluorine face and a focused positive density on the hydrogen face. The electropositive hydrogen face can co-ordinate chloride ($K \approx 10^3$) and to a lesser extent fluoride and iodide ions. Dehydrofluorination promoted decomposition occurs with fluoride ion acting as a base.*

The cyclohexane ring holds a special place in the history of organic chemistry. Rich narratives[1] stretch back to Baeyer's flat planar structure and through Sachse's rigid chair, its synthesis from benzene by Sabatier and then to the accepted 3D model and ring interconversion most closely associated with Hassel.[2a] Eventually the stereochemical consequences of cyclohexane containing ring systems were exemplified by Barton.[2b] The non-equivalence of the axial and equatorial conformers of monosubstituted cyclohexanes is widely used to measure and teach relative steric impacts (A-values)[3] of individual substituents and higher levels of substitution generate interconverting chair conformations which can have equivalent or non-equivalent energies, depending on relative stereochemistry. There is a certain impulse, driven largely by aesthetics to consider cyclohexanes with six identical substituents on each ring. Such compounds have nine configurational isomers (and thirteen conformational isomers),[4] but a special situation arises when all six substituents have a *syn* or *cis* stereochemistry as these isomers have the highest energy chair conformers due to steric interactions between three axial substituents. Only a small collection of such *cis*- compounds have been prepared as illustrated in Figure 1. These are where the hexa-substituents are hydroxyl **1**[5] as well as the corresponding peracetate **2**[6] and perbenzoyl **3**[7] esters, the hexa-carboxylic acid **4**[8] and its permethyl **5**[8b] and perbenzoyl **6**[9] esters, the hexamethyl **7**[10] and most recently hexafluoro cyclohexane **8**.[11] The sterically most demanding case so far is all-*cis* 1,2,3,4,5,6-hexamethyl-cyclohexane **7**,[10] where the minimum energy structure is a splayed chair. An X-ray structure of this compound reveals an average splay angle of 105.5° where the triaxial methyl groups are approximately 15.5° from parallel. The barrier (ΔG) to ring inversion was experimentally evaluated at 17.6 kcal mol^{-1} and can be compared to the significantly lower barrier for cyclohexane at ≈11.0 kcal mol^{-1}.[3a]

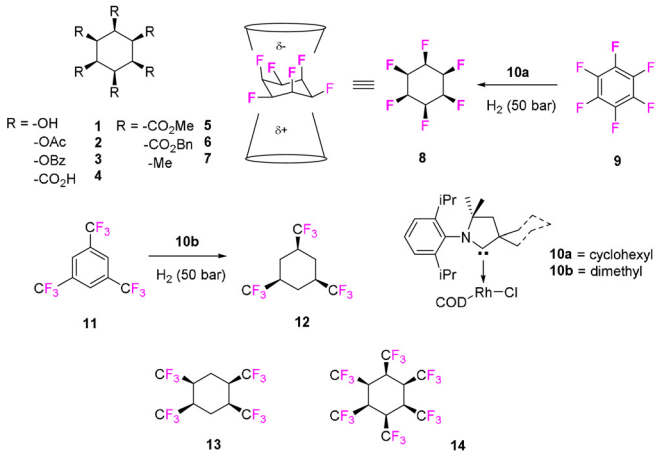

Figure 1. Structures **1**–**8** represent the known examples of all-*cis*-1,2,3,4,5,6-hexakis substituted cyclohexanes. Cyclohexane **8** is accessible by direct aryl hydrogenation with catalyst **10a**,[15] a process recently extended to the direct hydrogenation of trifluoromethyl aryls such as **11** to generate **12**.[16] Cyclohexanes **13** and **14** emerged as target compounds for this study.

[*] C. Yu, Dr. T. Lebl, Dr. D. B. Cordes, Prof. Dr. A. M. Z. Slawin, Prof. Dr. M. Bühl, Prof. Dr. D. O'Hagan
School of Chemistry, University of St Andrews
North Haugh, St Andrews, KY16 9ST (UK)
E-mail: do1@st-andrews.ac.uk
Dr. A. Kütt, Prof. Dr. G.-V. Röschenthaler
Department of Life Sciences and Chemistry, Jacobs University Bremen, gGmbH
P.O. Box 750 561, 28725 Bremen (Germany)
Dr. A. Kütt
University of Tartu, Institute of Chemistry
Ravila 14a, 50411 Tartu (Estonia)
Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under: https://doi.org/10.1002/anie.202008662.

The preparation of all *cis*-1,2,3,4,5,6-hexafluorocyclohexane **8** was reported in 2015.[11] This molecule proved to be high melting (208 °C dec) and an extraordinarily polar aliphatic with the capacity to coordinate to both cations (through the fluorine face) and anions (through the hydrogen face) in the gas phase[12] and in solution.[13] The difference in facial polarity led to the term "Janus face" rings being coined[14] for this type of ring system. The original stepwise synthesis of **8** was recently superseded by a direct heterogeneous hydrogenation approach developed by Glorius,[15] where **8** was prepared by aryl hydrogenation of hexafluorobenzene **6** under pressure (50 bar H_2) using the cyclic (alkyl)-(amino)carbene (CAAC)/Rh catalyst **10a** developed by Zeng.[16] Most recently Zeng's lab has extended[17] the approach to the preparation of aryl-CF_3 and heteroaryl-CF_3 compounds using the closely related catalyst **10b** to generate cyclohexanes and aliphatic heterocycles carrying up to three aliphatic -CF_3 substituents such as **12**, by direct hydrogenation of aryl **11**.

In light of the recent developments in direct aryl hydrogenation chemistry[15–17] we decided to explore a preparation of all-*cis* tetrakis-(trifluoromethyl)cyclohexane **13** and all-*cis* hexa-kis-(trifluoromethyl)cyclohexane **14**, by direct hydrogenation of the corresponding benzenes **15** and **16** respectively (Figure 2a and Figure 3a). These cyclohexanes are the first in the all-*cis* series that can be expected to display a "Janus face" polarity as a consequence of always possessing diaxial -CF_3 groups, if the rings adopt ground state chair conformations. This can be contrasted with tris(trifluoromethyl) cyclohexane **12** which will predominantly exist in the all equatorial conformation in the ground state. In the case of **14**, such a cyclohexane would represent the most sterically demanding member of the all-*cis* hexakis family of cyclohexanes so far and it was unclear if the steric crowding of the triaxial -CF_3 groups would allow such a stereoisomer to emerge from the hydrogenation reaction. The preparation of these cyclohexanes and an evaluation of some of their properties are reported below.

Results and Discussion: The direct hydrogenation of 1,2,4,5-tetrakis(trifluoromethyl)benzene **15** was explored with the Zeng catalyst Rh(CAAC) **10a** (H_2, 50 bar), for conversion to the resultant all-*cis* 1,2,4,5-tetrakis(trifluoromethyl)cyclohexane **13**. This proved to be a relatively straightforward transformation and the desired all-*cis* isomer **13** was isolated in a 60% yield as the only significant product. This compound was a crystalline solid (mp 73 °C) and was amenable to X-ray structure analysis. An image of the resultant structure of **13** is shown in Figure 2a. The solid state structure is a chair and this conformation dictates that there are two 1,3-diaxial, and two 1,3-diequatorial CF_3 groups. Steric and electrostatic repulsion between the two diaxial CF_3 groups is apparent from the 1,3-diaxial splay angle (CF_3^{ax}-C···C(CF_3^{ax}) = 107.5 °C) which deviates significantly from an ideal angle of 90°. A variable temperature (VT) $^{19}F\{^1H\}$-NMR study of **13** reveals an equivalence of the -CF_3 groups at 25 °C consistent with rapid ring inversion on the NMR timescale, however as the temperature is lowered to −75 °C, ring interconversion slows sufficiently to resolve the axial and equatorial -CF_3 groups.[18] This is illustrated in Figure 2b. The

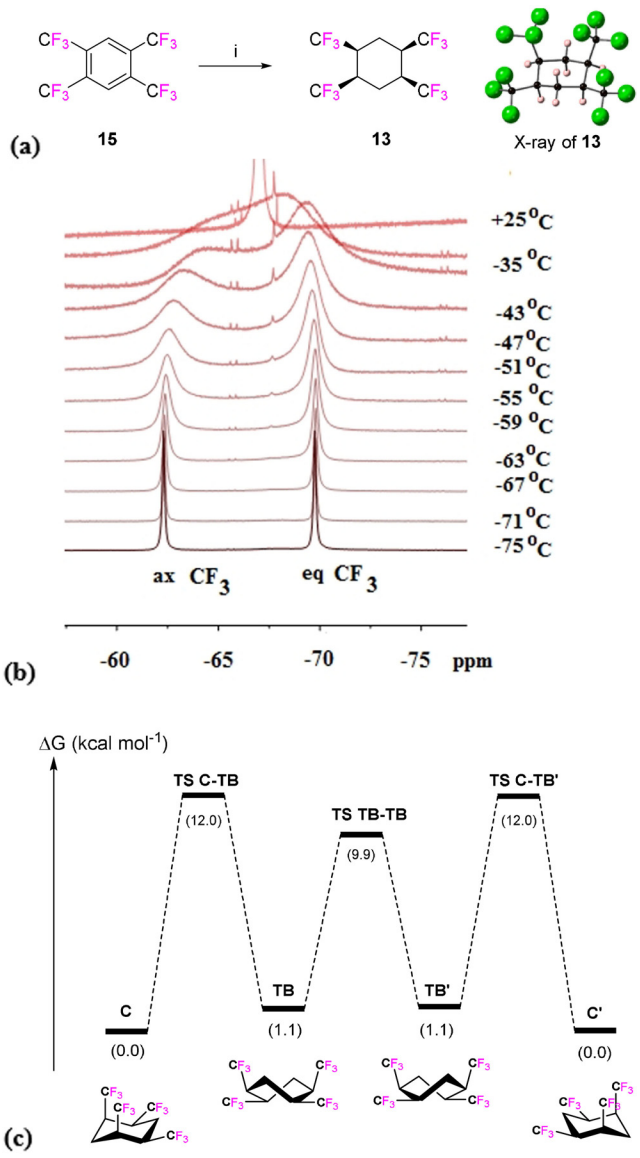

Figure 2. a) Preparation and X-ray structure of all-*cis* 1,2,4,5-tetrakis(trifluoromethyl)cyclohexane **13**. Reagents and conditions: i) Hexane, H_2 (50 bar), silica gel (7 equiv), cat **10a** (1%), 25 °C, 2 days, 60%.[23] b) Variable temperature (VT) $^{19}F\{^1H\}$-NMR of **13** showing an asymmetric signal coalescence progressing from low to high temperature. Some unidentified minor impurity(s) is visible in the base line at warmer temperatures. c) DFT (B3LYP-D3/3–311 + G**/CPCM-(CH2Cl2)//B3LYP-D3/6-31G* level) computed profile of the relative energy of intermediates for the ring interconversion of **13**.

overall barrier to ring interconversion for **13** of $\Delta G \approx 10.3$ kcal mol^{-1}, as measured by Eyring plot analysis (see Figure SI-1) of the VT-NMR data, gave a value a little lower than that for cyclohexane itself (≈ 11 kcal mol^{-1}), which was unexpected however there is complexity.[3a] The asymmetric nature of the coalescence of the axial and equatorial CF_3 peaks[18] in the $^{19}F\{^1H\}$-NMR with temperature, as shown in Figure 2b, is a notable feature of the variable temperature experiment, and suggests the presence of an additional minor (higher energy) conformer population in solution, which most probably arises from interconverting "twist boats". A com-

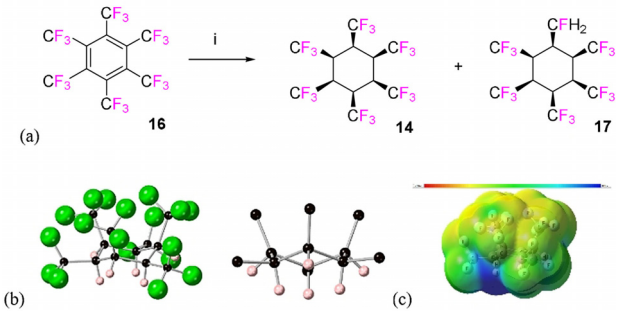

Figure 3. a) Aryl hydrogenation of **16** gave cyclohexanes **14** (13% yield) and **17** (40% yield). i) Hexane, H_2 (60 bar), silica gel (7 equiv), cat **10a** (20%), 50°C, 14 days. b) X-ray structure of all *cis*-1,2,3,4,5,6-hexakis-(trifluoromethyl)cyclohexane **14** (left) and without the fluorines (right) for clarity.[24] c) Electrostatic potential map of **14** illustrates a focused positive charge density (blue) on the hydrogen face.

putation approach was carried out to explore this further (Figure 2c). DFT (B3LYP-D3) analysis suggests a higher barrier to inversion of ≈12.0 kcal mol^{-1} but that the "chair" is close in energy (≈1.1 kcal mol^{-1}) to the "twist-boat".

The chair is observed in the crystal structure, but the small energy difference suggests that a significant population (≈13.5%) of "twist boat" will be apparent in solution under ambient conditions, consistent with the VT-NMR profile. This computational deconstruction helps rationalize the lower than expected experimental value. It is noteworthy that a theory study found that the twist boat conformation of all-*cis*-1,2,4,5-tetrakis(isopropyl)cyclohexane was more stable than the chair conformation, consistent with the general observation here that the steric influence of substituents in this 1,2,4,5- arrangement on a cyclohexane will narrow (or reverse) this energy gap.[19]

Having achieved a synthesis of **13** by direct hydrogenation, attention focussed on a preparation of all-*cis* hexakis-(trifluoromethyl)cyclohexane **14** by direct hydrogenation. The required benzene **16** was prepared by an exhaustive copper catalysed trifluoromethylation of hexaiodobenzene as previously described.[20] Substrate **16** was then exposed to direct hydrogenation with catalyst **10a** (Figure 3a). In this case the conversion was poor although some improvement was achieved with an increase in catalyst loading (20%), as well as increasing the reaction pressure (60 bar) and temperature (50°C). The production of **14** was slow and did not progress significantly after several days under these conditions. The reaction was monitored over an extended time period and in the event a sample of **14** was isolated in low yield, after 14 days. Purification required careful chromatography eluting initially with pentane, and then progressively introducing diethyl ether and then dichloromethane as the eluent. The major product (≈40% yield) from this reaction, eluting in the diethyl ether fractions is **17** with five -CF_3 groups and rather unexpectedly, one fluoromethyl (-CFH_2) moiety, but with an overall all-*cis* stereochemistry. The structure of **17** was confirmed by X-ray structure analysis[22] which shows that the fluoromethyl group is orientated axial among the sterically more congested axial -CF_3 groups (See SI). Cyclohexane **17** presumably arises after two successive exocyclic dehydrofluorinations, followed by hydrogenation to the "hydrogen" face, and directed away from the remaining -CF_3 groups. The desired all-*cis* isomer **14** (13% yield) is a white and rather amorphous material (mp 47–51°C) but was sufficiently micro-crystalline to obtain an X-ray structure, illustrations of which are shown Figure 3b, with and without (for clarity) fluorines.

The structure of **14** indicates that the cyclohexane ring adopts a shallow chair conformation due to a significant splay between the axial -CF_3 groups from the anticipated steric crowding. The diffraction data indicate that the triaxial -CF_3 groups have six splay angles (CF_3^{ax}-C···C(CF_3^{ax})) ranging between 107.9° and 113.2°, and with an average value of 110.8°. This deviates significantly from the ideal angle of 90° in cyclohexane and is wider than that observed in the X-ray structure of hexamethylcyclohexane **7** (110.8° versus 105.5°) consistent with the greater steric impact of -CF_3 over -CH_3. It is also wider than the average for these angles in **17** (108.9°) where an axial -CH_2F group replaces an axial -CF_3.

A computed electrostatic potential map of **14** (B3LYP/6-31G*) reveals a large diffuse electronegative area associated with the -CF_3 groups on one face of the ring, with a much more concentrated electropositive area (blue) on the opposite face associated with the hydrogens (Figure 3c). In another hydrogenation reaction of benzene **16**, an adduct between **17**, the major product of the hydrogenation reaction and lactam **18** co-eluted during chromatography. This adduct was amenable to X-ray crystallography and the resultant structure shown in Figure 4, demonstrated that the amide carbonyl is coordinated to the electropositive region on the hydrogen face of this cyclohexane in the solid state. Lactam **18** was recently shown to derive from reaction of (CAAC)Rh catalyst **10a** with molecular oxygen.[21]

In order to explore the Janus face aspect of cyclohexane **14** further, ^{1}H-NMR spectra were recorded in different solvents to compare relative chemical shift changes of the H_{ax} and H_{eq} signals. Comparative spectral data are shown in Figure 5. There is a very clear upfield shift associated with each set of hydrogens in toluene, relative to DCM, a shift which is significantly larger for the axial hydrogens (H_{ax} $\Delta\delta$ = 1.25 ppm & H_{eq} $\Delta\delta$ = 0.6 ppm). This is consistent with the aromatic ring of toluene associating with the electropositive hydrogen face of cyclohexane **14** and inducing a larger anisotropic influence on the axial relative to the equatorial

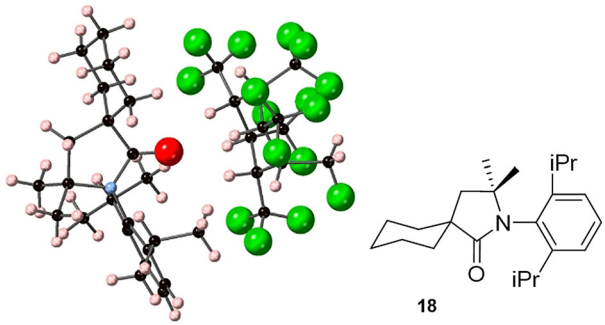

Figure 4. An X-ray structure[25] of a co-complex of **17** with catalyst derived lactam **18**.

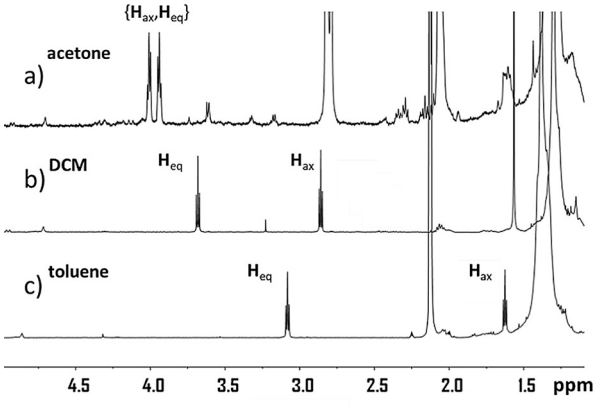

Figure 5. Comparison of $^{1}H\{^{19}F\}$-NMR spectra of **14** in a) acetone, b) dichloromethane (DCM), and c) toluene, indicates changes in the relative chemical shift values (δ^{H})of the axial (H_{ax}) and equatorial (H_{eq})hydrogens.

hydrogens. Conversely there is a very strong downfield shift, particularly for the -H_{ax} protons when the NMR is recorded in acetone, consistent with hydrogen bonding contacts between the carbonyl oxygen of solvent molecules and the electropositive hydrogens. This interaction of **14** with acetone has a model in amide coordination in the co-crystal of **17** with lactam **18** (Figure 4).

A titration of **14** with chloride ion (Cl^{-}) was explored, titrating tetrabutylammonium chloride (TBACl) into a solution **14** in DCM and monitoring by ^{1}H-NMR. The titration progression is illustrated in the ^{1}H-NMR profiles in Figure 6. A very large chemical shift change, again particularly for the axial hydrogens ($\Delta\delta^{Hax} = 2.4$ ppm) is observed up to the addition of approximately two equivalents of Cl^{-}, and then the chemical shifts of both the H_{ax} and H_{eq} hydrogens remain much more stable. An association constant for chloride ion was evaluated at $K \approx 10^{3}$ (Figure SI-17). A similar ^{1}H-NMR titration analysis for fluoride indicated a lower affinity ($K \approx 10^{2}$) and this reduced further for the softer iodide. When the tetrabutylammonium fluoride (TBAF) titration of **14** was monitored by ^{19}F-NMR, it could be observed that decomposition occurred after 2 equivalents of TBAF was added (see Figs SI-13 & SI-14), consistent with fluoride ion acting as a base to promote exocyclic dehydrohalogenations. Endocyclic dehydrohalogenation decomposition was previously observed when hexafluorocyclohexane **8** was titrated with fluoride.[13]

In an effort to explore the barrier to cyclohexane ring inversion for **14**, VT-NMR experiments were conducted between +80 °C to −80 °C, however there were no significant changes in chemical shifts in the ^{1}H-NMR or $^{19}F\{^{1}H\}$-NMR spectra over this temperature range and no polarisation transfer could be detected between the ^{1}H- or ^{19}F-NMR nuclei in exchange correlation (EXSY) NMR experiments, even at the higher temperatures. This indicated that the barrier to ring inversion for **14** is high and that the rate is slow on the NMR timescale. To complement these findings, DFT calculations were performed at the B3LYP-D3 level, and this located transition states (TSs) that are likely to be involved in connecting the minima. The lowest of these TSs is a boat structure involved in connecting two enantiomeric twist boat (**TB**) minima, with a $\Delta G^{\ddagger}$ relative to the twist-boat intermediate of 5.9 kcal mol^{-1} at RT. Chair and twist-boat minima are indicated to interconvert via a half-chair or envelope-like structure with a large computed barrier of $\Delta G^{\ddagger} = 27.1$ kcal mol^{-1} at room temperature as illustrated in Figure 7 (and Figure SI-23). At the highest theory level explored, including a continuum model for the solvent (DCM), the **TB** conformer of **14** is computed to be significantly higher in energy than the chair (**C**) conformer, with a value of $\Delta G^{0} = 10.2$ kcal mol^{-1} at room temperature. The complete pathway for chair inversion was not traced due to complexity involved in deconvoluting several additional intermediates and transition states which arise due to the interlocking -CF_3 groups. It is clear, however,

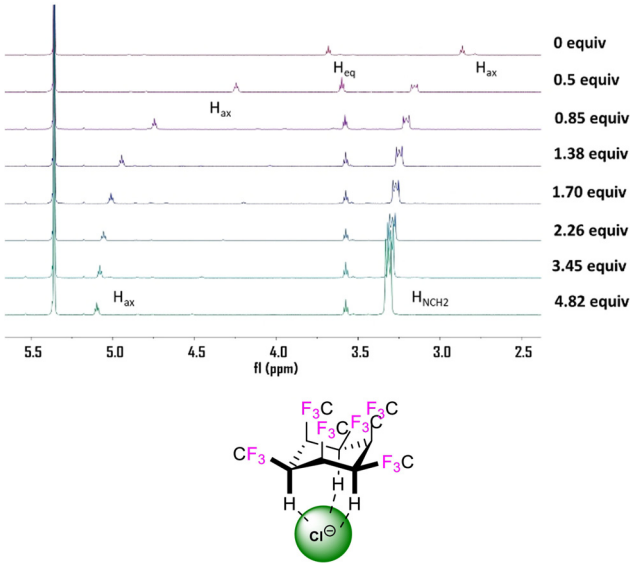

Figure 6. Chloride ion (TBAC) titration of cyclohexane **14** followed by ^{1}H-NMR (CD_2Cl_2) with a schematic of the Cl^{-}:**14** complex.

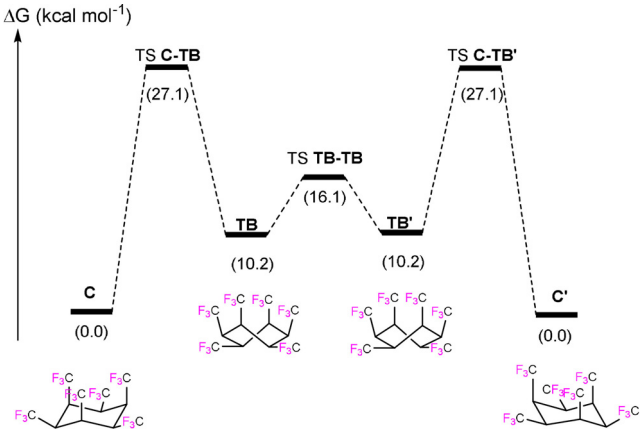

Figure 7. Profile of relative energies (kcal mol^{-1}) of intermediates and transition states for the interconversion of cyclohexane **14** between chair (**C**) and twist-boat (**TB**) conformers, with their mirror images (**C′** and **TB′**, respectively—note that **TB** and **TB′** are enantiomers. Free energies at 298 K (in kcal mol^{-1}) at the B3LYP-D3/3–311 + G(d,p)/CPCM(CH_2Cl_2)//B3LYP-D3/6-31G(d) level.

that much higher barriers for this process are required than the hexamethyl- or hexafluoro- cyclohexanes **7** and **8** respectively, and thus **14** emerges as the most sterically demanding example of an all-*cis* hexakis substituted cyclohexane prepared to date.

In summary we have prepared all-*cis* substituted cyclohexanes with four **13** and six **14** trifluoromethyl (-CF_3) groups on one hemisphere of the ring. The ground state conformation in each case is a chair although for all-*cis* 1,2,4,5-tetrakis(trifluoromethyl)cyclohexane **13** DFT computation indicated that the chair and twist boat conformers are close in energy and that the twist boat should be relevant in solution, consistent with the observed VT-NMR profiling. All-*cis* 1,2,3,4,5,6-hexakis(trifluoromethyl)cyclohexane **14** has the highest barrier ($\Delta G^{\ddagger} = 27.1\ \mathrm{kcal\,mol^{-1}}$) to ring inversion of the small family of all-*cis* hexakis substituted cyclohexanes (**1**–**8**, **14**) prepared so far. The stereochemical arrangement of the -CF_3 groups in **14** leads to a large diffuse electronegative fluorine face and a much more concentrated electropositive area associated with the hydrogens on the opposite face. The molecule has polarity and displays some affinity to acetone through carbonyl coordination and a modest affinity ($K \approx 10^3$) for chloride ion is demonstrated indicating another example of a Janus face cyclohexane following from the preparation and demonstrated properties of **8**.

Acknowledgements

We thank the Engineering and Physical Sciences Research Council (EPSRC) for funding and the Chinese Scholarship Council for a studentship (C.Y.). Calculations were performed on a local computer cluster maintained by Dr H. Früchtl.

Conflict of interest

The authors declare no conflict of interest.

Keywords: aryl hydrogenation · cyclohexanes · Janus face · triaxial orientations · trifluoromethyl groups

[1] a) H. Sachse, *Chem. Ber.* **1890**, *23*, 1363 – 1370; b) E. W. Warnhoff, *J. Chem. Educ.* **1996**, *73*, 494 – 497; c) P. Sabatier, J. B. Senderens, *C. R. Hebd. Seances Acad. Sci.* **1901**, *132*, 210 – 212.
[2] a) O. Hassel, B. Ottar, *Acta Chem. Scand.* **1947**, *1*, 929 – 943; b) D. H. R. Barton, *J. Chem. Soc.* **1953**, 1027 – 1040.
[3] a) E. L. Eliel, S. H. Wilen, *Stereochemistry of organic compounds*, Wiley, New York, **1994**; b) S. Winstein, N. J. Holness, *J. Am. Chem. Soc.* **1955**, *77*, 5562 – 5578.
[4] a) V. Umadevi, N. Santhanamoorthi, L. Senthilkumar, *Comput. Theor. Chem.* **2014**, *1049*, 55 – 61; b) Q. Luo, K. R. Randall, H. F. Schaefer, *RSC Adv.* **2013**, *3*, 6572 – 6585.
[5] a) H. C. Freeman, D. A. Langs, C. E. Nockolds, Y. L. Oh, *Aust. J. Chem.* **1996**, *49*, 413 – 424; b) S. J. Angyal, D. J. McHugh, *J. Chem. Soc.* **1957**, 3682 – 3691.
[6] S. Brownstein, *Can. J. Chem.* **1962**, *40*, 870 – 874.
[7] S.-K. Chung, Y.-U. Kwon, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2135 – 2140.
[8] a) S. Brückner, L. M. Giunchi, G. Di Silvestro, M. Grassi, *Acta Crystallogr. Sect. B* **1981**, *37*, 586 – 590; b) M. Farina, M. Grassi, G. Di Silvestro, *J. Am. Chem. Soc.* **1985**, *107*, 5100 – 5104.
[9] M. E. Furrow, A. G. Myers, *J. Am. Chem. Soc.* **2004**, *126*, 12222 – 12223.
[10] a) H. Van Koningsveld, J. M. A. Baas, B. Van de Graaf, M. A. Hoefnagel, *Cryst. Struct. Commun.* **1982**, *11*, 1065 – 1071; b) H. Werner, G. Mann, M. Mühlstädt, H. J. Köhler, *Tetrahedron Lett.* **1970**, *11*, 3563 – 3566.
[11] N. S. Keddie, A. M. Z. Slawin, T. Lebl, D. Philp, D. O'Hagan, *Nat. Chem.* **2015**, *7*, 483 – 488.
[12] a) M. J. Lecours, R. A. Marta, V. Steinmetz, N. S. Keddie, E. Fillion, D. O'Hagan, T. B. McMahon, W. S. Hopkins, *J. Phys. Chem. Lett.* **2017**, *8*, 109 – 113; b) B. E. Ziegler, M. Lecours, R. A. Marta, J. Featherstone, E. Fillion, W. S. Hopkins, V. Steinmetz, N. S. Keddie, D. O'Hagan, T. B. McMahon, *J. Am. Chem. Soc.* **2016**, *138*, 7460 – 7463; c) R. Cormanich, N. S. Keddie, R. Rittner, D. O'Hagan, M. Bühl, *Phys. Chem. Chem. Phys.* **2015**, *17*, 29475 – 29478.
[13] O. Shyshov, K. A. Siewerth, M. von Delius, *Chem. Commun.* **2018**, *54*, 4353 – 4355.
[14] N. Santschi, R. Gilmour, *Nat. Chem.* **2015**, *7*, 467 – 468.
[15] a) D. Moock, M. P. Wiesenfeldt, M. Freitag, S. Muratsugu, S. Ikemoto, R. Knitsch, J. Schneidewind, W. Baumann, A. H. Schäfer, A. Timmer, M. Tada, M. R. Hansen, F. Glorius, *ACS Catal.* **2020**, *10*, 6309 – 6317; b) M. P. Wiesenfeldt, T. Knecht, C. Schlepphorst, F. Glorius, *Angew. Chem. Int. Ed.* **2018**, *57*, 8297 – 8300; *Angew. Chem.* **2018**, *130*, 8429 – 8432; c) M. P. Wiesenfeldt, Z. Nairoukh, W. Li, F. Glorius, *Science* **2017**, *357*, 908 – 912.
[16] Y. Wei, B. Rao, X. Cong, X. Zeng, *J. Am. Chem. Soc.* **2015**, *137*, 9250 – 9253.
[17] X. Zhang, L. Ling, M. Luo, X. Zeng, *Angew. Chem. Int. Ed.* **2019**, *58*, 16785 – 16789; *Angew. Chem.* **2019**, *131*, 16941 – 16945.
[18] ^{19}F-NMR Chemical shift assignments for the CF_3 signals follow precedents which consistantly place equatorial CF_3 upfield of axial CF_3. Eg see E. W. Della, *J. Am. Chem. Soc.* **1967**, *89*, 5221 – 5224.
[19] J. Weiser, O. Golan, L. Fitjer, S. E. Biali, *J. Org. Chem.* **1996**, *61*, 8277 – 8284.
[20] A. Kűtt, V. Movchun, T. Rodima, T. Dansauer, E. B. Rusanov, I. Leito, I. Kaljurand, J. Koppel, V. Pihl, I. Koppel, G. Ovsjannikov, L. Toom, M. Mishima, M. Medebielle, E. Lork, G.-V. Röschenthaler, I. A. Koppel, A. Kolomeitsev, *J. Org. Chem.* **2008**, *73*, 2607 – 2620.
[21] J. Tang, X. J. Gao, H. Tang, X. Zeng, *Chem. Commun.* **2019**, *55*, 1584 – 1587.
[22] CCDC 2008659 (**17**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.
[23] CCDC 2008657 (**13**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.
[24] CCDC 2008658 (**14**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.
[25] CCDC 2008660 (**17-18** complex) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

Manuscript received: June 19, 2020
Accepted manuscript online: July 21, 2020
Version of record online: September 1, 2020

