Perfluorocyclohexene bridges in inverse DiArylEthenes: synthesis through Pd-catalysed C-H bond activation, experimental and theoretical studies on their photoreactivity.

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Perfluorocyclohexene Bridge in Inverse DiArylEthenes: One Step Synthesis through Pd-Catalysed C-H bond Activation, Joint Experimental and Theoretical Studies on Their Photoreactivity

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The palladium-catalysed direct di-heteroarylation of 1,2-dichloroperfluorocyclohexene with a variety of heteroarenes gives rise in one step to a new family of 1,2-di(heteroaryl) perfluorocyclohexenes. These derivatives do not exhibit any photoreactivity and this unexpected outcome is explained by theoretical calculations demonstrating the lack of reactive isomers.

Photochromic compounds have attracted considerable interest for optical data storage. Among them, much attention has been focused on DiArylEthene (DAE) derivatives due to their thermal stability and fatigue resistance.[1] The photochromic reactivity depends on several factors: conformation of the open-ring isomer, electron-donor/acceptor substituents, conjugation length of the heteroaryl groups, and the architecture and also varies between *normal* (N-type)[2] versus *inverse* (I-type)[3,4] DAE (see Scheme 1). In addition, the nature of the ethene bridge can be diversely modified. Beside the ubiquitous cyclopentene, perfluorinated or not, various heterocycles have been successfully employed and most of them contains a C=C bond within a five-membered ring.[5] The photochromic properties in which the ethene bridge is incorporated into a *six*-membered ring have been also demonstrated for several *normal* C6-DAE.[6] In contrast, the use of *inverse* DAE is less explored, and to the best of our knowledge, no example of *inverse* C6-DAE (2-thienyl/5-thiazolyl) species has been reported yet. This communication fills this gap.
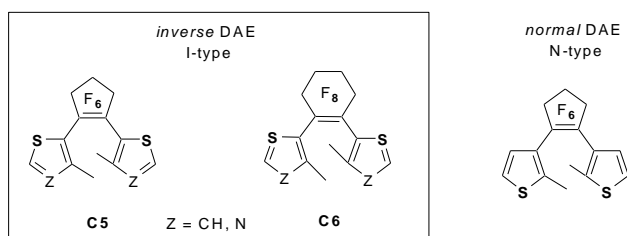
**Scheme 1.** Chemical structures of DAE derivatives: *normal* (N-type) and *inverse* (I-type) incorporating a five- (**C5**) and six membered-ring (**C6**) as central ethene bridge

We have been investigating the chemistry and the photochromic behavior of *normal* and *inverse* C5-DAE derivatives and we have studied their geometric and electronic structures by theoretical calculations.[7] Some of us also recently demonstrated that Pd-catalysed coupling of 1,2-dichlorohexafluoro*cyclopentene* with heteroarenes via C-H bond activation[8,9] is an efficient method to prepare *inverse* diarylperfluorocyclopentenes (C5-DAE).[10] As an extension of these works, and with the aim of understanding the factors that control the photoreactivity, we decided to study for the first time the impact of the *six*-membered ring, perfluorocyclohexene, as the ethene bridge in *inverse* C6-DAE.

Herein, we describe i) the one step access to I-type C6-DAE species through Pd-catalysed C-H bond activation of thiophene and thiazole derivatives,[11-13] ii) their photoreactivity, and, iii) theoretical studies rationalizing their photochemical behaviour.

The new C6-DAE **1-5** were prepared by Pd-catalysed C-H bond activation/vinylation using the appropriate heterocycles with the commercially available 1,2-dichlorooctafluorocyclohexene used as the coupling partner (Scheme 2). The catalytic system Pd(OAc)$_2$ associated to PCy$_3$ in the presence of KOAc in CMPE[14,15] allows the regioselective C5 functionalization of 2-ethyl-4-methylthiazole giving rise to the formation in one step of compound **1** in 46% yield. The use of 3-methylbenzothiophene led to the formation of **2** in a similar yield of 40%. Then, the three thiophene-based derivatives **3-5** were obtained in 45-80% yields using PdCl(C$_3$H$_5$)(dppb) or Pd(OAc)$_2$ / PCy$_3$ as catalysts. The high yield in **5** is certainly due to the presence of a bromo substituent at C3. 3-Bromothiophenes are known to be very reactive for Pd-catalysed direct arylations.[12d] It should be noted that no cleavage of the C-Cl and C-Br bonds of the thiophene derivative was observed in the course of the synthesis of **4** and **5**, allowing further transformations. In all cases, no significant amount of the *mono*-heteroarylated octafluorocyclohexene was detected by GC/MS analysis. To our knowledge, these couplings represent the first examples of direct heteroarylations of a dichlorocyclohexene.
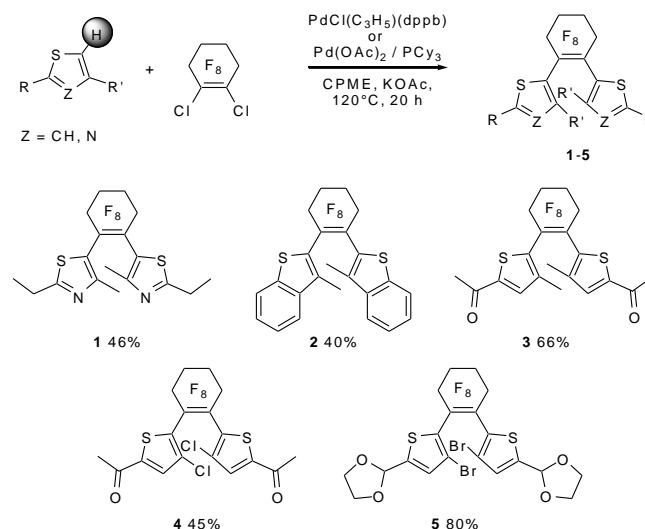
Scheme 2. One step access to I-type C6-DAE derivatives through Pd-catalysed C-H bond activation

Surprisingly, these derivatives do not exhibit any photoreactivity. The electronic spectra (CH$_2$Cl$_2$, 298 K) of compounds **1-5** in their open forms exhibit an intense absorption band at λ 300-350 nm which are ascribed to intraligand (IL) π→π* transitions of the thiophene/thiazole rings (See ESI, Table S1, Figures S2 and S3). UV irradiation (λ = 350 nm, CH$_2$Cl$_2$) of all synthesized compounds **1-5** does not induce any photochromic

response, that is we could not observe changes of the UV-vis nor ^{1}H NMR spectra irrespective of the irradiation time. For **2** that absorbs at rather short wavelength, we have tested that a more energetic irradiation (λ = 325 nm) does not yield photochromic response. These observations are certainly puzzling compared with the results reported for DAE having an azulene bridge that are photochromic only for 4-thiazolyl and not for 3-thienyl groups,[16] as a result of steric repulsion. As expected for non-photochromic DAE, we could observe fluorescence and the emission data are listed in Table S1 in ESI. Several factors have been considered to rationalize the peculiar non-photochromic behavior of *inverse* C6 DAE.[1,7,17] In particular, we show below that the ground-state conformation has a dramatic effect on the photocyclization reaction, consistently with previous works.[17]

We have used theoretical calculations to investigate the *inverse* C6 DAE (see ESI for computational details). As the lack of photoreactivity is independent of the nature of the substituents, we have used a model **1** in which the side ethyl groups have been removed to allow the use of accurate models for determining energies (MP4, see ESI). Previous investigations have shown that three main factors can explain non-photochromic reactivity of DAE: energetic, conformational and electronic.[1d,7a] For the second aspect, it is well known that most DAE present two groups of open isomers, namely parallel (P) and anti-parallel (AP) conformers, only the latter possibly allowing the ring-closure reaction.[1] Indeed, in the parallel DAE the thiophene rings are not oriented in a way allowing electrocyclization. In most *normal* perfluorinated C5-DAE, the ratio between parallel and anti-parallel structures is close to 1/1, and this accounts for the limiting quantum yield of 50% often observed experimentally if the AP/P interconversion is slow.[1] On the contrary, in *inverse* C5-DAE, it has been shown by both NMR and theoretical studies that the ratio is in significant favour of the anti-parallel form.[7b,7c,18] In DAE there are often a large series of conformers that need to be explored,[18] and we have performed such extensive exploration of the potential energy surface for the model molecule. Eight conformers could be identified (see Figure 1): four P and four AP.
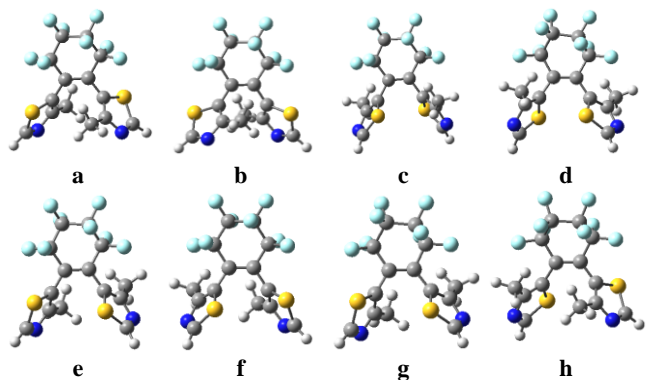

Figure 1. Representation of the eight conformers found for the model *inverse* C6 DAE.

The main features of all these eight conformers are listed in Table 1. As can be seen, both pseudo-chair and pseudo-boat conformations of the cyclohexene ring have been considered, the latter yielding much less stable structures, as expected. The only structures that would allow photochromism are conformers **a** and **b**. Indeed, in addition to presenting an AP conformation, a conformer needs to have a CC distance below the 4.2 Å threshold to allow cyclization, at least in the solid state,[19] and both **c** and **d** are significantly above this threshold. As can be seen, *inverse* C6-DAE are strongly dominated by conformers impeding cyclization: the conformational blend is strongly dominated by **c** (AP), **e** (P)

and **f** (P) all being photochromically inactive. In fact, the photoactive isomers represent less than 2.5% of the total, i.e. are present in negligible quantities in the experimental pot. In addition, their CC distances of 3.67 and 3.74 Å are significantly larger than the CC distance in the corresponding C5-DAE structure (3.59 Å at the same level of theory for the reactive AP structure) and it is known that longer CC distance in the open isomer tends to lead to smaller quantum yield of cyclization. For the *inverse* C5-DAE model (similar to **1**), the same computational protocol indicates a strong domination of a reactive AP conformer (90.0%, CC distance of 3.59 Å), an outcome consistent with previous investigations on model *inverse* C5 DAE,[7b,7c] clearly highlighting the difference between *inverse* C5 and C6 DAE.

Table 1. Relative *G* (see ESI), percentage of presence (computed at room temperature following Boltzmann equation) and distance

	Conformer		G (kcal.mol^{-1})	Ratio (%)	CC Dist. (Å)
a	AP (C_2)	Chair	2.83	0.7	3.67
b	AP (C_2)	Chair	2.30	1.6	3.74
c	AP (C_2)	Chair	0.00	79.2	4.66
d	AP (C_1)	Boat	6.29	0.0	5.13
e	P (C_1)	Chair	1.15	11.5	3.99
f	P (C_1)	Chair	1.44	7.0	3.91
g	P (C_1)	Boat	5.98	0.0	4.06
h	P (C_1)	Boat	6.15	0.0	4.00

between reactive carbon atoms for the eight conformers. The relative orientation of the two thiazole rings as well as the conformation of the perfluorocyclohexene are indicated as well. See Figure 1 for graphical representation.

In Figure 2, we display the frontier molecular orbitals computed for the model *inverse* C6 DAE (**b** conformer) and its C5 counterpart. The topology of these frontier orbitals are very similar for the two compounds. More specifically, both LUMO present electronic density on the reactive carbon atoms as well as a bonding character for the to-be-formed CC σ bond. Therefore, from this orbital point of view,[1d] no lack of photoreactivity could have been expected: the use of perfluorocyclohexene instead of a perfluorocyclopentene bridge is not enough to significantly pull out the electrons from the reactive five member rings.
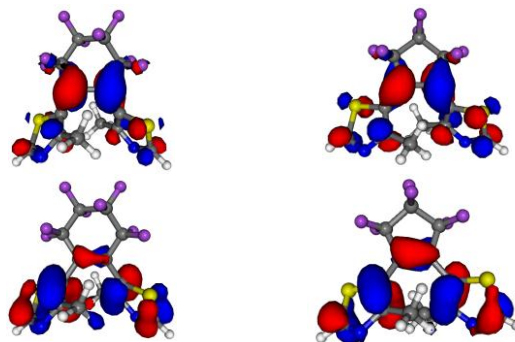

Figure 2. HOMO (bottom) and LUMO (top) of the model *inverse* C6 (left) and C5 (right) DAE. Computed with the CAM-B3LYP functional (see ESI).

In conclusion, we have demonstrated that the palladium-catalysed direct coupling of various heteroarenes with 1,2-dichloroperfluorocyclohexene offers a fast and direct access to symmetric 1,2-di-(heteroaryl)perfluorocyclohexenes. Replacing the perfluorocyclopentene by the related six-membered ring, the perfluorocyclohexene as the ethene bridge in *inverse* DAE has a dramatic effect on their photoreactivity. The suppression of the

photocyclisation process has been rationalized by theoretical calculations that demonstrate that the ratio of anti-parallel photoactive conformation is strongly lowered compared to their C5 analogs. Therefore, in the present case, steric rather than electronic factors control the photochromic behaviour, a fact also confirmed by experiment, as the substitution pattern of the thiazole rings (molecule **1**-**5**) does not impact on ethe found behaviour. These findings will help to rationally design photochromic compounds.

Notes and references

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† Electronic Supplementary Information (ESI) available: computational details, procedures; NMR data; additional absorption data and UV-visible spectra for compounds **1**-**5**. See DOI: 10.1039/b000000x/

1. (*a*) M. Irie, *Chem. Rev.*, 2000, **100**, 1685-1716; (*b*) H. Tian and S. Yang, *Chem. Soc. Rev.*, 2004, **33**, 85-97; (*c*) V. Guerchais, L. Ordronneau and H. Le Bozec, *Coord. Chem. Rev.*, 2010, **254**, 2533-2545; (*d*) A. Perrier, F. Maurel and D. Jacquemin, *Acc. Chem. Res.*, 2012, **45**, 1173-1182.

2. Normal-type DAE are the most widely used, see Ref. 1, as well as: (*a*) S.L. Gilat, S.H. Kawai and J. M. Lehn, *J. Chem. Soc., Chem. Commun.*, 1993, 1439-1442; (*b*) Higashiguchi, K. Matsuda, A. Asano, A. Murakami, S. Nakamura and M. Irie, *Eur. J. Org. Chem.*, 2005, 91-97; (*c*) S. Pu, J. Xu, L. Shen, Q. Xiao, T. Yang and G. Li, *Tetrahedron Lett.*, 2005, **46**, 871-875; (*d*) S. Yamamoto, K. Matsuda and M. Irie, *Chem. Eur. J.*, 2003, **9**, 4878-4886.

3. Inverse C5-dithienylethene derivatives, see inter alia: (*a*) K. Uchida and M. Irie, *Chem. Lett.,* 1995, 969-970; (*b*) K. Uchida, T. Matsupka, S. Kobatake, T. Yamaguchi and M. Irie, *Tetrahedron*, 2001, **57**, 4559-4565; (*c*) T. B. Norsten, A. Peters, R. McDonald, M. Wang, and N. R. Branda, *J. Am. Chem. Soc.*, 2001, **123**, 7447-7448; (*d*) T. Yamaguchi, K. Uchida and M. Irie, *Mol. Cryst. Liq. Cryst.*, 2007, **474**, 111-118; (*e*) T. Fukaminato, M. Tanaka, L. Kuroki and M. Irie, *Chem. Commun.*, 2008, 3924-3926; (*f*) Y. Tatsumi, J. Kitai, W. Uchida, K. Ogata, S. Nakamura and K. Uchida, *J. Phys. Chem. A*, 2012, **116**, 10973-10979.

4. For some examples of I-type C5-dithiazolylethene derivatives, see: (*a*) S. Iwata, Y. Ishihara, C.-P. Qian and K. Tanaka, *J. Org. Chem.*, 1992, **57**, 3726-3727; (*b*) K. Uchida, T. Ishikawa, M. Takeshita, and M. Irie, *Tetrahedron*, 1998, **54**, 6627-6638; (*c*) M. Giraud, A. Léaustic, M.-F. Charlot, P. Yu, M. Césario, C. Philouze, R. Pansu, K. Nakatani and E. Ishow, *New J. Chem.*, 2005, **29**, 439-446;

5. Examples using heterocycle bridges: (*a*) H. Miyasaka, T. Nobuto, M. Murakami, A. Itaya, N. Tamai, and M. Irie, *J. Phys. Chem. A,* 2002, **106**, 8096-8102; (*b*) M. Ohsumi, M. Hazama, T. Fukaminato and M. Irie, *Chem. Commun.*, 2008, 3281-3283; (*c*) C.-H. Chan, W. H. Lam, H. L. Wong, N. Zhu, W.-T. Wong and V. W.-W. Yam, *J. Am. Chem. Soc.*, 2011, **133**, 12690-12705; (*d*) B. M. Neilson, V. M. Lynch and C. W. Bielawski, *Angew. Chem. Int. Ed*., 2011, **50**, 10322-10326; (*e*) S. Chen, L.-J. Chen, H.-B. Yang, H. Tian and W. Zhu, *J. Am. Chem. Soc.*, 2012, **134**, 13596-13599; (*f*) H.-H. Liu and Y. Chen, *J. Mater. Chem.*, 2011, **21**, 1246-1249.

6. (*a*) M. Hanazawa, R. Sumiya, Y. Horikawa and M. Irie, *Chem. Commun.*, 1992, 206-207; (*b*) V. W.-W. Yam, C.-C. Ko and N. Zhu, *J. Am. Chem. Soc.,* 2004, **126**, 12734-12735; (*c*) M. Walko and B. L. Feringa, *Chem. Commun.*, 2007, 1745-1747; (*d*) W. Zhu, Y. Yang, R. Métivier, Q. Zhang, R. Guillot, Y. Xie, H. Tian and K. Nakatani, *Angew. Chem. Int. Ed.*, 2011, **50**, 10986-10990; (*e*) K. Suzuki, T. Ubukata and Y. Yokoyama, *Chem. Commun.*, 2012, **48**, 765-767; (*f*) V. Lemieux and N. R. Branda, *Org. Lett.*, 2005, **7**, 2969-2972; (*g*) W. Zhu, L. Song, Y. Yang and H. Tian, *Chem. Eur. J.*, 2012, **18**, 13388-13394; (*h*) M. Kose, C. Y. Sekerci, K. Suzuki and Y. Yokoyama, *J. Photochem. Photobiol. A*, 2011, **219**, 58-61; (*i*) Example of C7-DAE: J. Kitai, T. Kobayashi, W. Uchida, M. Hatakeyama, S. Yokojima, S. Nakamura and K. Uchida, *J. Org. Chem.*, 2012, **77**, 3270-3276.

7. (*a*) A. Perrier, F. Maurel and D. Jacquemin, *J. Phys. Chem. C*, 2011, **115**, 9193-9203; (*b*) S. Aloïse, M. Silwa, G. Buntinx, S. Delbaere, A. Perrier, F. Maurel, D. Jacquemin and M. Takeshita *Phys. Chem. Chem. Phys.*, 2013, **5**, 6226-6234; (*c*) A. Perrier, S. Aloïse, M. Olivucci and D. Jacquemin, *J. Phys. Chem. Lett.*, 2013, **4**, 2190-2196.

8. For reviews on C-H bond functionalisation: (*a*) D. Alberico, M. E. Scott and M. Lautens, *Chem. Rev.*, 2007, **107**, 174-238; (*b*) F. Bellina and R. Rossi, *Tetrahedron*, 2009, **65**, 10269-10310; (*c*) L. Ackermann, R. Vicente and A. Kapdi, *Angew. Chem. Int. Ed.,* 2009, **48**, 9792-9826; (*d*) J. Roger, A. L. Gottumukkala and H. Doucet, *ChemCatChem*, 2010, **2**, 20-40; (*e*) J. Wencel-Delord and F. Glorius, *Nature Chem.* 2013, **5**, 369-375.

9. For selected recent examples of palladium-catalysed direct arylation from our laboratory: (*a*) K. Beydoun, M. Zaarour, J. A. G. Williams, H. Doucet and V. Guerchais *Chem. Commun.* 2012, **48**, 1260-1262; (*b*) K. Beydoun, J. Boixel, V. Guerchais and H. Doucet, *Catal. Sci. Technol.* 2012, **2**, 1242-1248.

10. K. Beydoun, J. Roger, J. Boixel, H. Le Bozec, V. Guerchais and H. Doucet, *Chem. Commun.*, 2012, **48**, 11951-11953.

11. For selected examples of palladium-catalysed direct arylation of thiazoles: (*a*) K. Masui, A. Mori, K. Okano, K. Takamura, M. Kinoshita and T. Ikeda, *Org. Lett.,*2004, **6,** 2011-2014; (*b*) L.-C. Campeau, M. Bertrand-Laperle, J.-P. Leclerc, E. Villemure, S. Gorelsky and K. Fagnou, *J. Am. Chem. Soc.,* 2008, **130**, 3276-3277; (c) J. Roger, F. Pozgan and H. Doucet, *J. Org. Chem.,* 2009, **74**, 1179-1186.

12. For selected examples of palladium-catalysed direct arylation of thiophenes: (*a*) M. Nakano, H. Tsurugi, T. Satoh and M. Miura, *Org. Lett.*, 2008, **10**, 1851-1854; (*b*) B. Liegault, D. Lapointe, L. Caron, A. Vlassova and K. Fagnou, *J. Org. Chem.*, 2009, **7**, 1826-1834; (*c*) J. J. Dong, J. Roger, C. Verrier, T. Martin, R. Le Goff, C. Hoarau and H. Doucet, *Green Chem.*, 2010, **12**, 2053-2063; *(d)* O. René, F. Fagnou *Org. Lett.*, 2010, **12**, 2116-2119.

13. For examples of palladium-catalysed direct couplings of vinyl halides with heteroarenes: (*a*) A. L. Gottumukkala, F. Derridj, S. Djebbar and H. Doucet, *Tetrahedron Lett.* 2008, **49**, 2926-2930; (*b*) C. Verrier, C. Hoarau and F. Marsais, *Org. Biomol. Chem.* 2009, **7**, 647-650; (*c*) S. Sahnoun, S. Messaoudi, J.-D. Brion and M. Alami, *Eur. J. Org. Chem.* 2010, 6097-6102; (*d*) R. Vabre, F. Chevot, M. Legraverend and S. Pigel, *J. Org. Chem.* 2011, **76**, 9542-9547.

14. K. Beydoun and H. Doucet, *ChemSusChem*, 2011, **4**, 526-534.

15. K. Watanabe, N. Yamagiwa and Y. Torisawa, *Org. Proc. Res. Dev.*, 2007, **11**, 251-258.

16 J. Kitai, T. Kobayashi, W. Uchida, M. Hatakeyama, S. Yokojima, S. Nakamura and K. Uchida, *J. Org. Chem.*, 2012, **77**, 3270-3276.

17 S. Fukumoto, T. Nakashima and T. Kawai, *Angew. Chem. Int. Ed.,* 2011, **50**, 1565-1568.

18 N. Tanaka, C. Okabe, K. Sakota, T. Fukaminato, T. Kawai, M. Irie, A. Goldberg, S. Nakamura and H. Sekiya, *J. Mol. Struct.*, 2002, **616**, 113-118.

19 S. Kobatake, K.Uchida, E. Tsuchida and M. Irie, *Chem. Commun.*, 2002, 2804-2805.