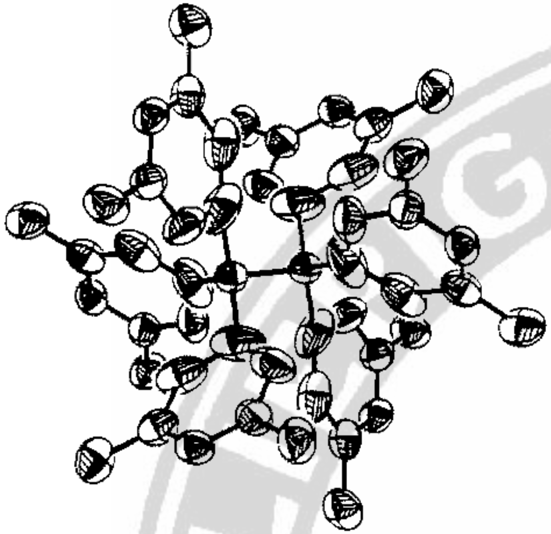
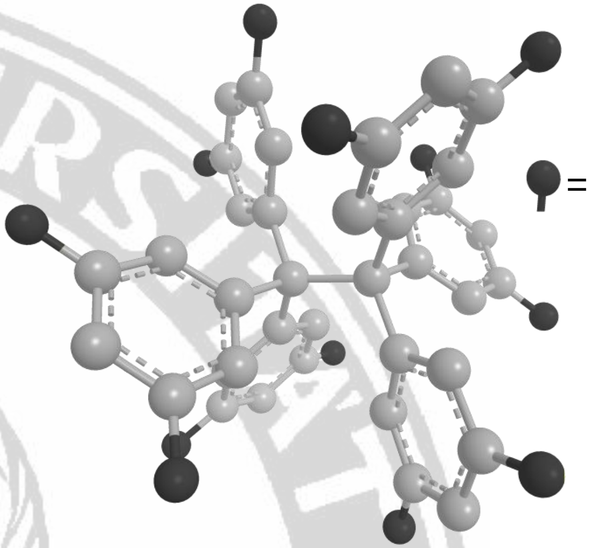




Mislow's hexaphenylethane and the approach to further derivatives

Progress Report

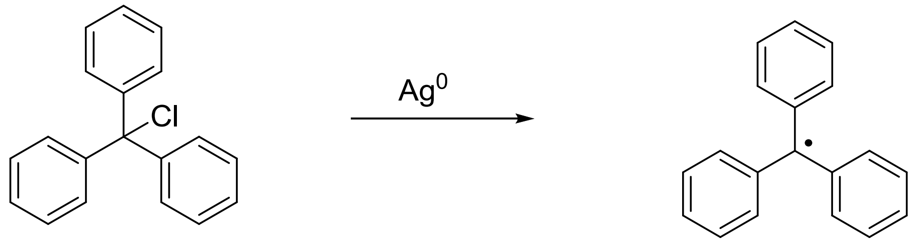
4.7.2014

Sören Rösel

AG Schreiner
Institut für Organische Chemie
Justus-Liebig-Universität
35435 Giessen, Germany

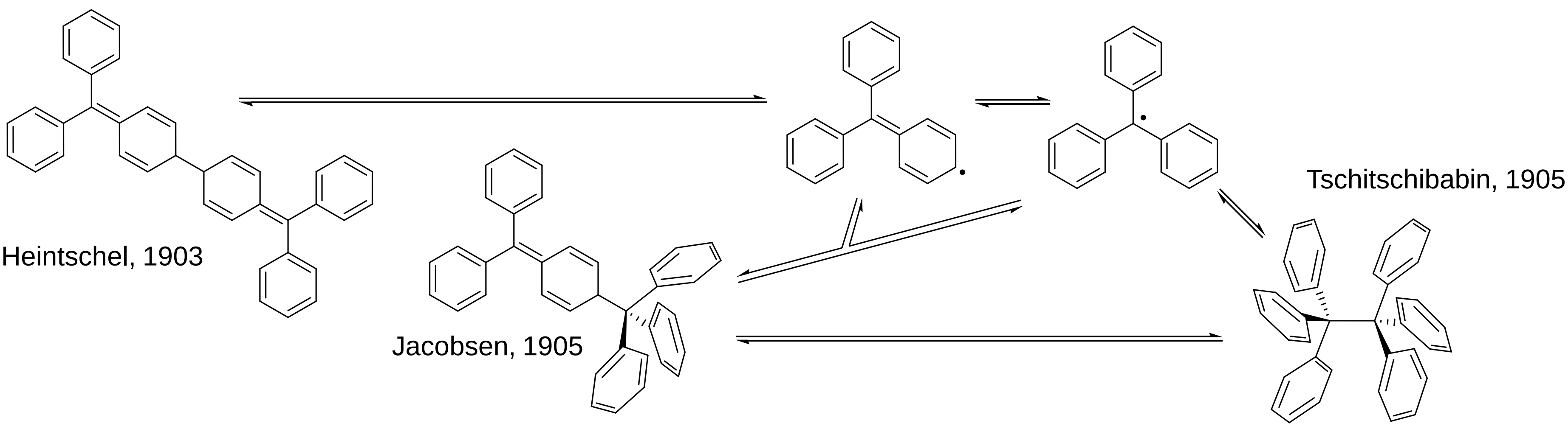
To the hexaphenylethane

1900: Gomberg



Die oben mitgetheilten experimentellen Ergebnisse zwingen mich zu der Annahme, dass in dem »ungesättigten Kohlenwasserstoff« das Radical Triphenylmethyl, $(C_6H_5)_3C$, vorliegt.

1900-1968: Discussed about the "real" structure

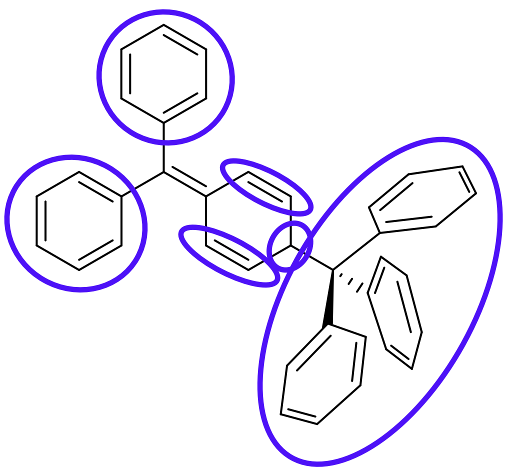


M. Gomberg, *Ber. Dtsch. Chem. Ges.*, **1900**, 33, 3150; P. Jacobsen, *Ber. Dtsch. Chem. Ges.*, **1905**, 38, 196; E. Heintschel, *Ber. Dtsch. Chem. Ges.,* **1903**, 36, 320; A. E. Tschitschibabin, *Ber. Dtsch. Chem. Ges.,* **1904**, 37, 4709; → Full overview: M. Gomberg, *J. Am. Chem. Soc.*, **1914**, 1144.

To the hexaphenylethane

1968: MacLean

NMR: signals of the protons of the phenylgroups at 6,8 - 7,4 ppm; a quartet of the olefinic protons at the 2,3,5 and 6 positions between 5,8 and 6,4 ppm and a signal of the aliphatic proton at the 4 position at 5 ppm.



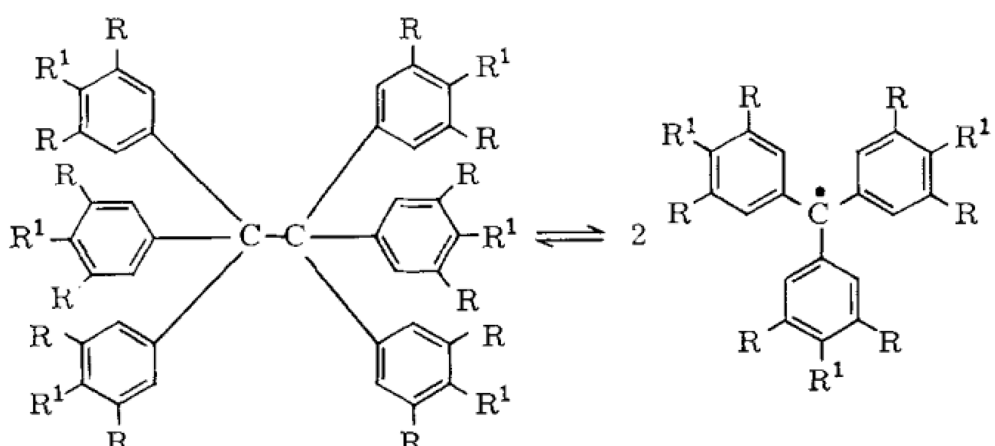
H. Lankamp, W. Th. Nauta, C. MacLean, *Tetrahedron Lett.*, **1968**, 2, 249.

To the hexaphenylethane

1978, Rieker[1]:

1) Synthesis of one or more phenyl rings in a molecule already containing the central CC bond. 2) Steric hindering of formation of the Jacobson-Nauta structure by incorporation of bulky groups R^1 and/or R; *(2)* must then either be persistent as the monomer—or dimerize (kinetically controlled) to *(1)*, which should be isolable if the dissociation equilibrium is established slowly.

In connection with our studies on the structure of twisted



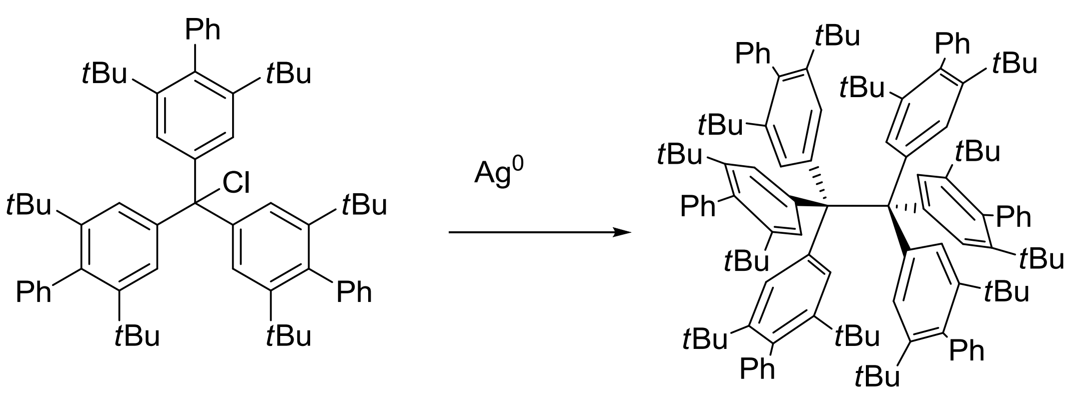
(1) *(2)*

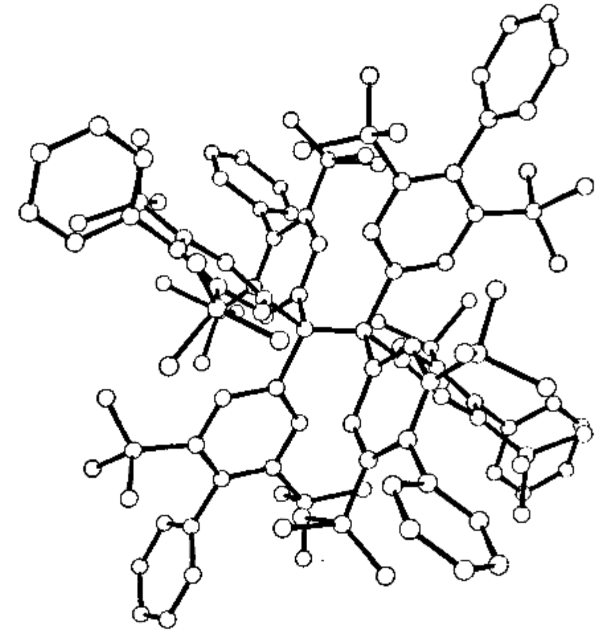
---

[1]M. Stein, W. Winter, A. Rieker, *Angew. Chem*, **1978**, 90, 9, 737.
[2]Hollemann-Wiberg “Lehrbuch der Anorg. Chemie”, 100. Auflage,**1985**, S. 133

To the hexaphenylethane

1978, Rieker[1]**:** First synthesised derivative/
Central CC Bond Length **shortened(!)** : **1.47Å** (Common[2]: 1.54Å)





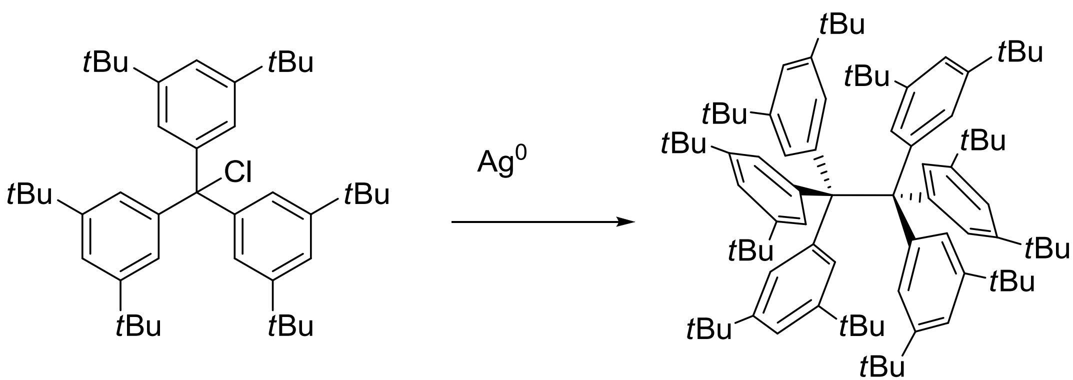
(R=0.13)
(mp. 276°C)

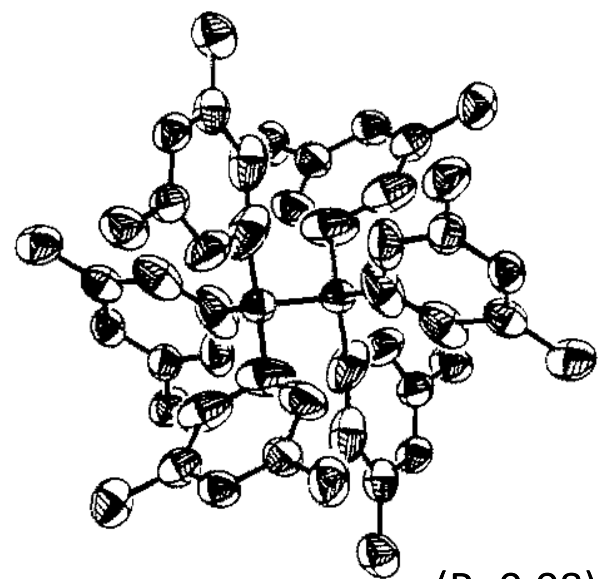
Due to the poor quality of the crystals, the bond lengths quoted in the text are to be regarded as preliminary values.

[1]M. Stein, W. Winter, A. Rieker, *Angew. Chem*, **1978**, 90, 9, 737.
[2]Hollemann-Wiberg “Lehrbuch der Anorg. Chemie”, 100. Auflage,**1985**, S. 133

To the hexaphenylethane

1986, Mislow: Showed that the only relevant groups are the *meta-tert*-Bu groups/
Central CC Bond Length **elongated**: **1.67Å**



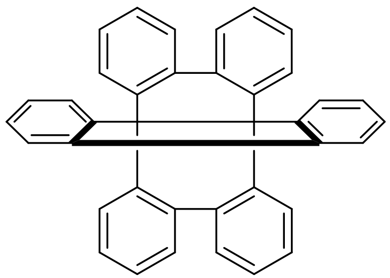


(R=0.08)
(mp. 214°C)

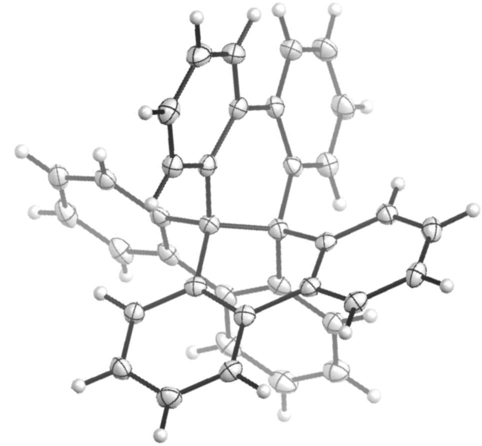
B. Kahr, D. Van Engen, K. Mislow, *J. Am. Chem. Soc.,* **1988**, 108, 8305

To the hexaphenylethane

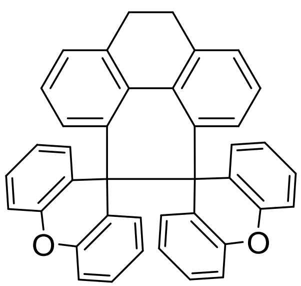
Only one fully charactarised bridged pure hydrocarbon example found jet



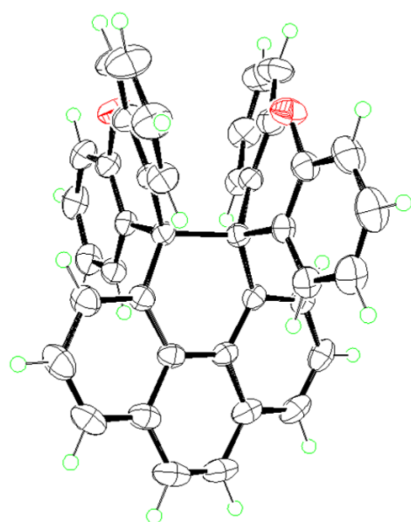
Rathore, 2007
mp. 472°C

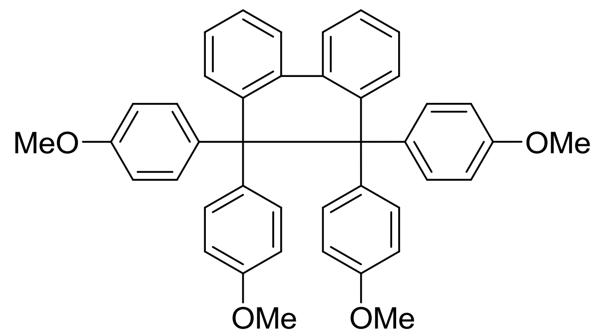


Other fully charactarised bridged heteroatom containing example

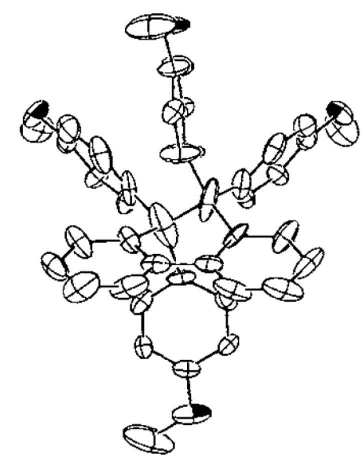


Fujiwara, 2007
mp. 274°C





Tsuji, 1997
mp. 270°C decomp.



P. Debroy , S. V. Lindeman , R. Rathore, *Org. Lett.,* **2007**, 9 ,21, 4091.
T. Suzuki, S. Tanaka, H. Higuchi, H. Kawai, K. Fujiwara, *Tetrahedron Lett*., **2004**, 45, 8563.
T. Suzuki, J. Nishida, T. Tsuji, Angew. Chem. Int. Ed. **1997**, 36, 12, 1329.

On the other hand:

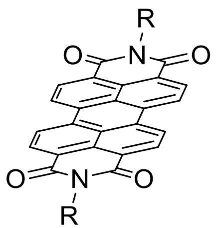
Is the stability explained of Mislow’s HPE only due to the sterically hindrance?

Forces in chemistry

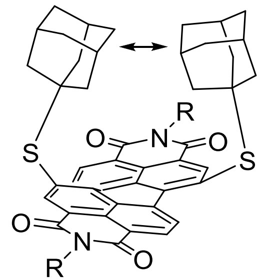
-Homopolar bondings
-Coulumb interaction
-Dipole-dipole interaction
-Hydrogen bondings
-London dispersion interaction

Underestimated dispersion?

Examples for strong dispersion interactions

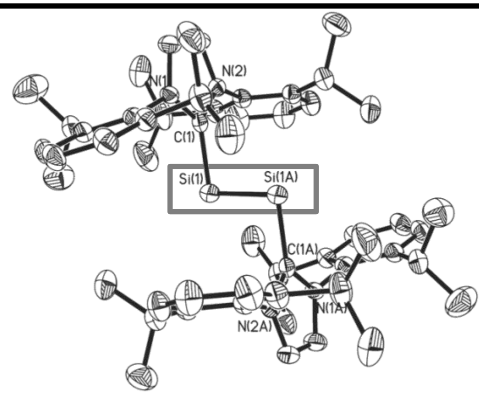


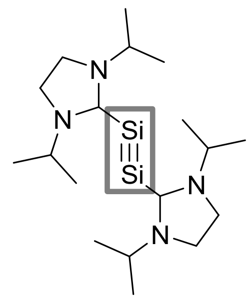
plane



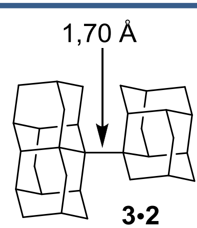
twisted

Bending of plane structures

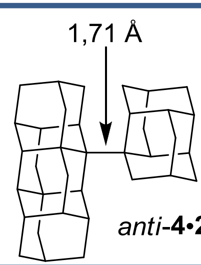




Stabilization by steric crowding



3•2



anti-**4•2**

Thermal stable very stretched C-C-bonds

A.G. Slater, E. S. Davies, S. P. Argent, W. Lewis, A. J. Blake, J. McMaster, N. R. Champness, *J. Org. Chem.*, **2013**, 78, 2853.
Wang, YZ, Xie, YM, Wei, PR, King, RB, Schaefer, HF, Schleyer, PV, Robinson, GH, *Science*, **2008**, 321, 1069.
A. A. Fokin, L. V. Chernish, P. A. Gunchenko, E. Y. Tikhonchuk,, H. Hausmann, M. Serafin, J. E. P. Dahl, R. M. K. Carlson, P. R. Schreiner, *J. Am. Chem. Soc.*, **2012**, 134, 13641.

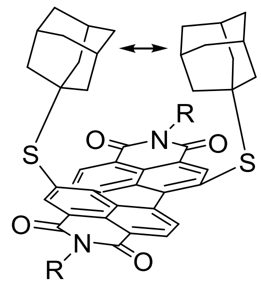
Underestimated dispersion?

interest: general usage

large nonpolar groups can be used as ***D*ispersion *E*nergy *D*onors**[1]

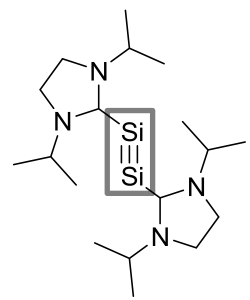
short:

„DED“

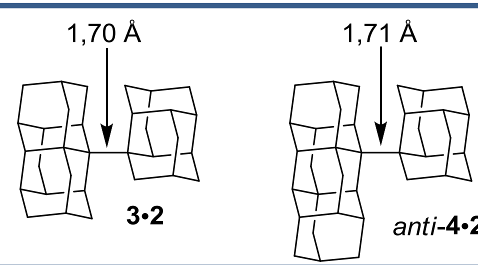


twisted

Bending of plane structures



Stabilization by steric crowding



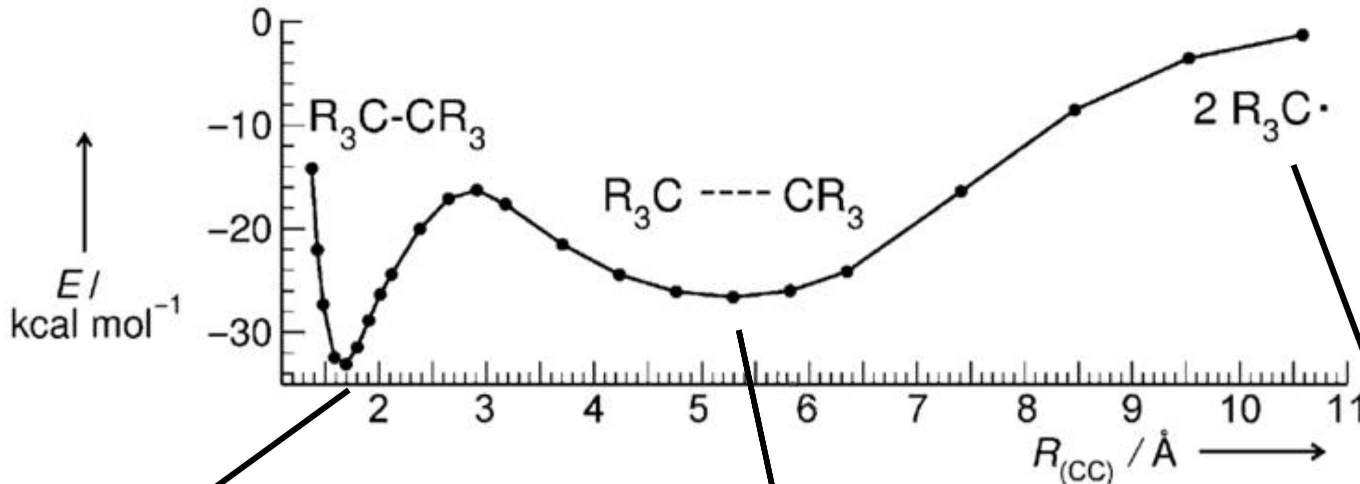
3•2 *anti*-**4•2**

Thermal stable very stretched C-C-bonds

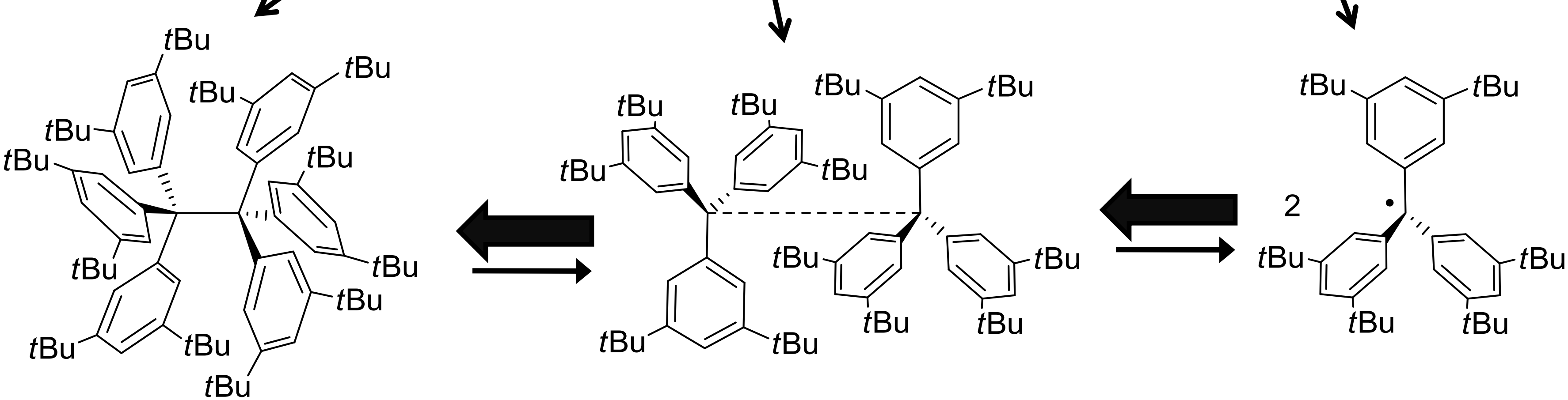
[1]S.Grimme, R. Huenerbein, S. Ehrlich, *Chem. Phys. Chem.*, **2011**, 12, 7, 1258.

Solving the hexaphenylethane riddle?

interest: uncommon bonding situations → Bond stretch isomerism



Calculated trajectory along central C-C-bond

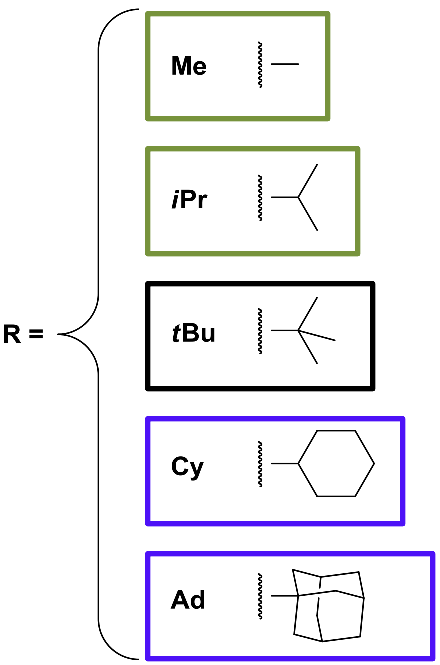


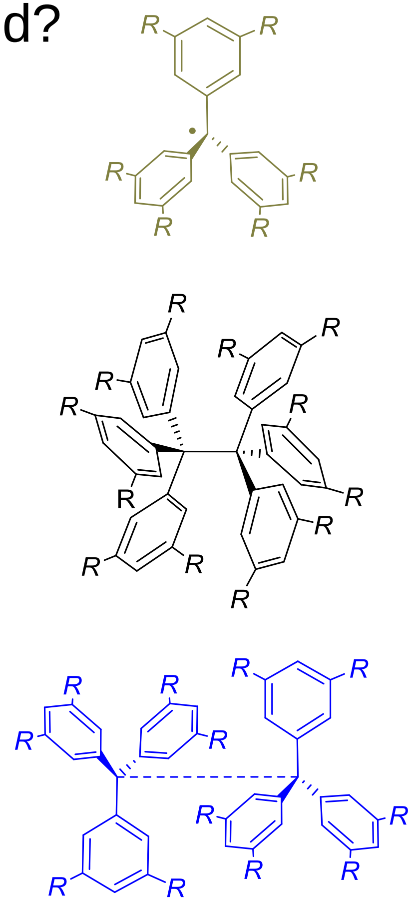
S. Grimme, P.R. Schreiner, *Angew. Chem. Int. Ed.*, **2011**, 50, 12639.

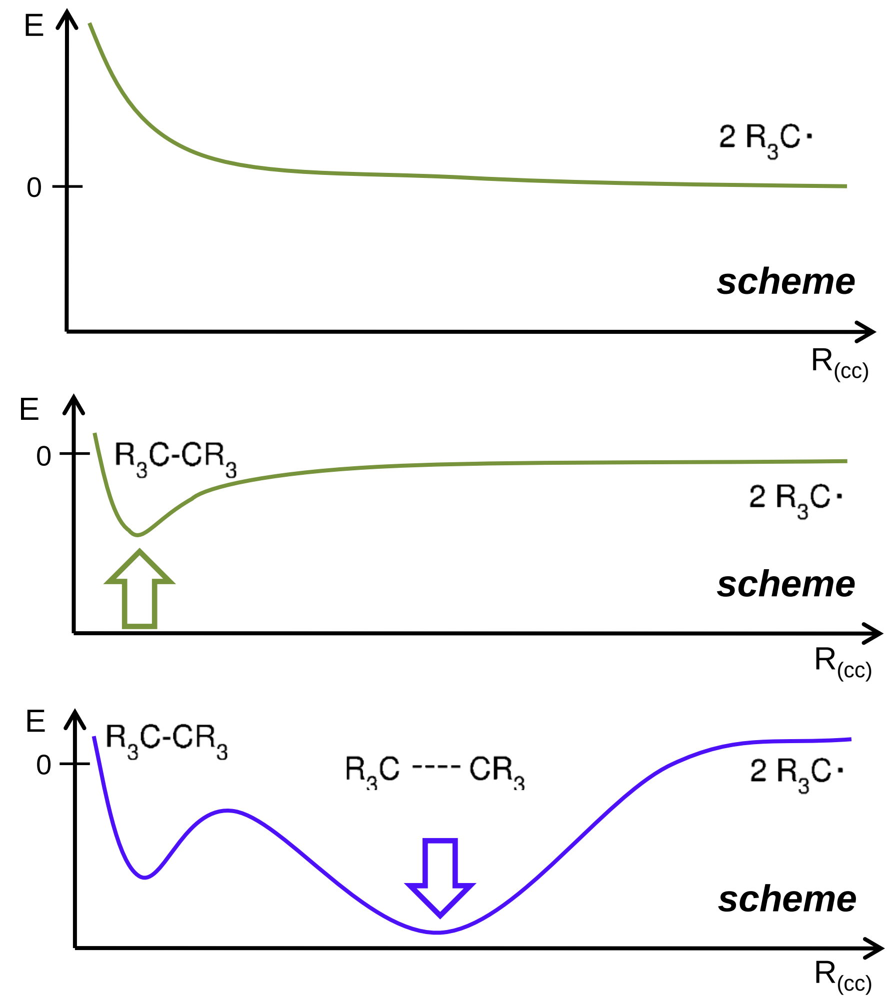
Effects of the periphery of HPE

interest: uncommon bonding situations

What will happen when the substituted is changed?

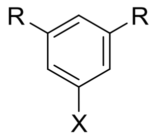






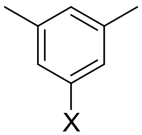
HPE derivative synthesis

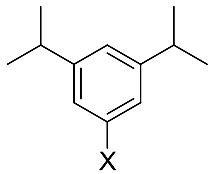
synthetically approach

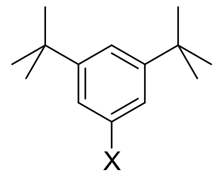


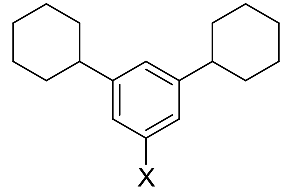
HPE derivative synthesis

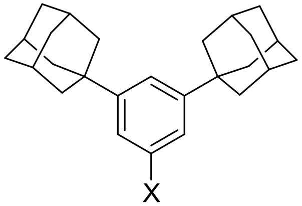
building the precursors





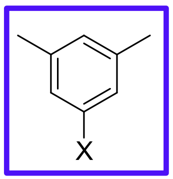


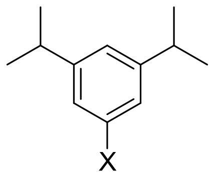


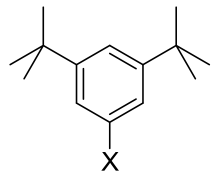


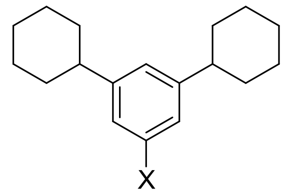
HPE derivative synthesis

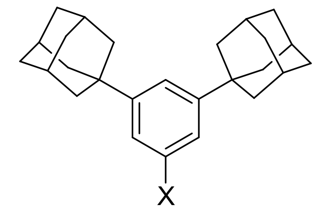
building the precursors

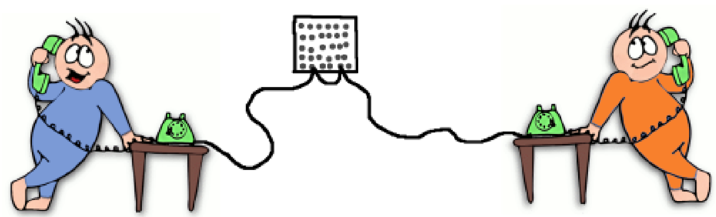




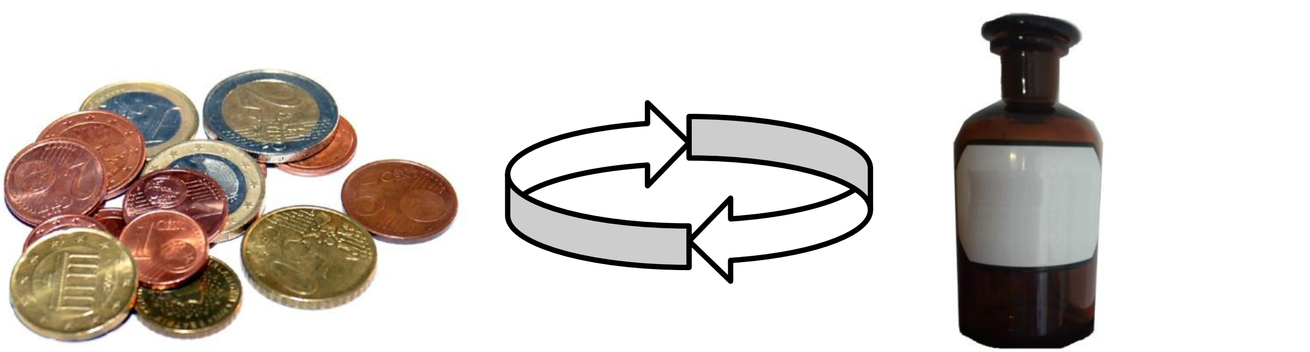








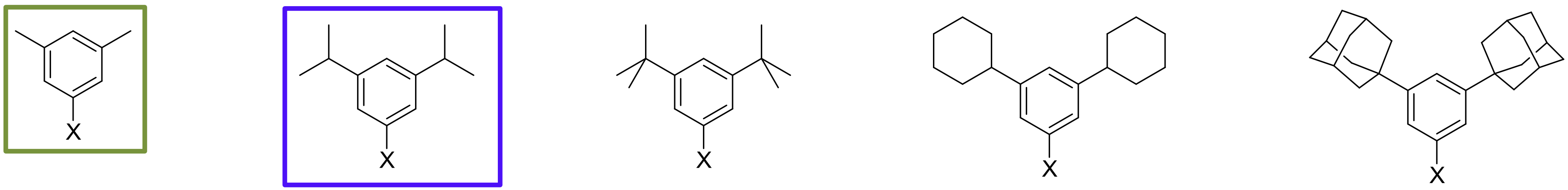
1) build stable interhuman bond

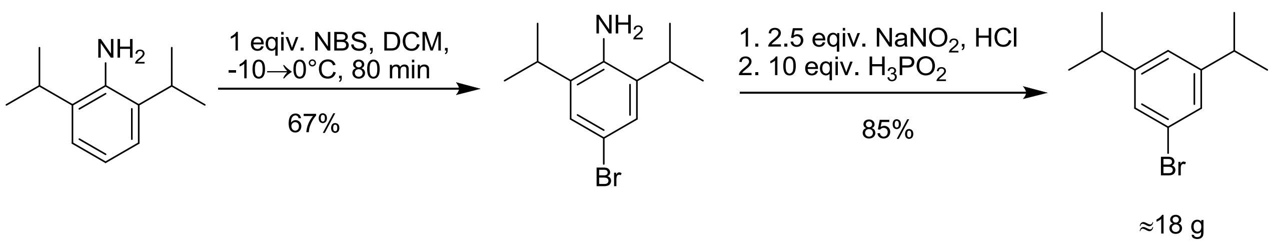


2) do proper money-to-chemical transfer

HPE derivative synthesis

building the precursors

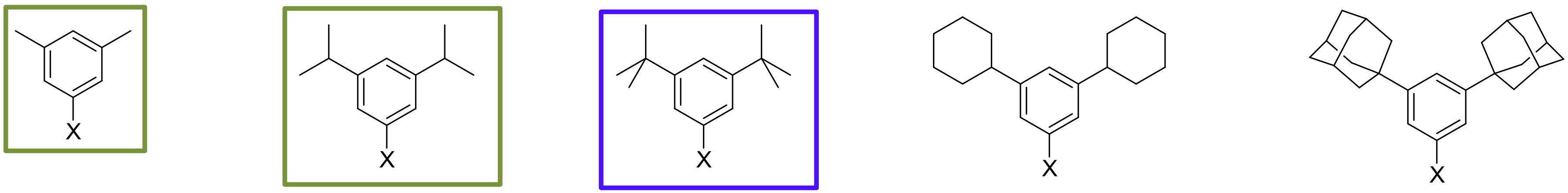


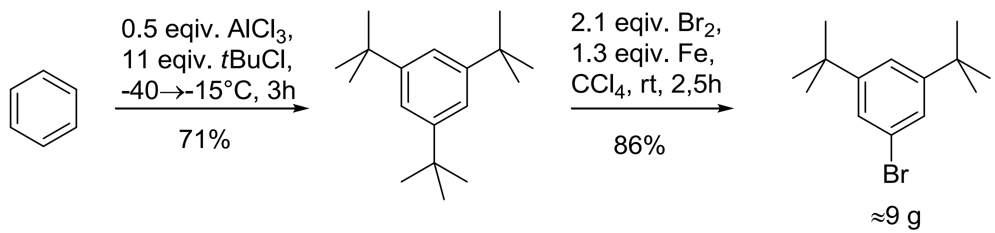


V. Diemer, H. Chaumeil, A. Defoin, A. Fort, A. Boeglin, C. Carré, *E. J. Org. Chem.,* **2006**, 2727.

HPE derivative synthesis

building the precursors

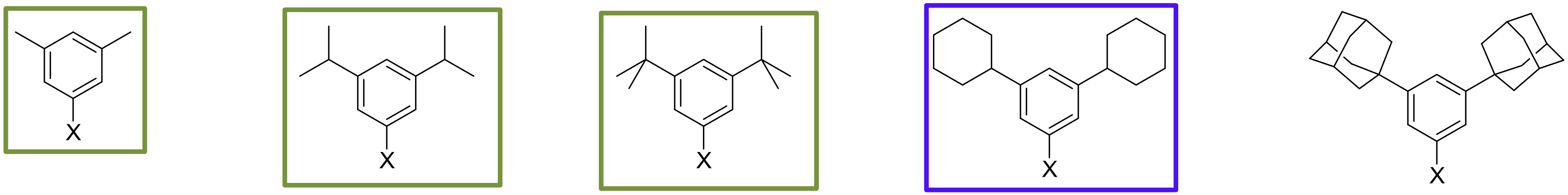


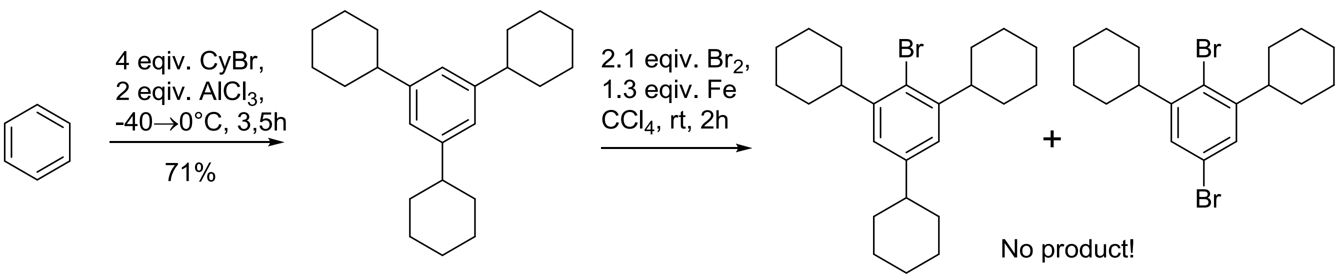


M. J. Frampton, H. Akdas, A. R. Cowley, J. E. Rogers, J. E. Slagle, P. A. Fleitz, M. Drobizhev, A. Rebane, H. L. Anderson, *Org. Lett.,* **2005**, 24, 5365.

The hexaphenylethane riddle

building the precursors

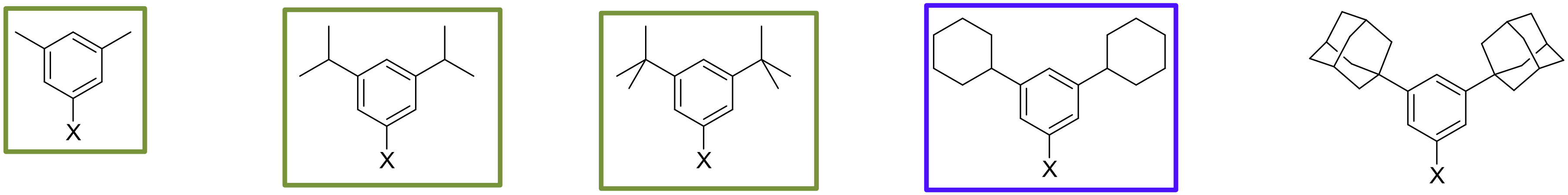


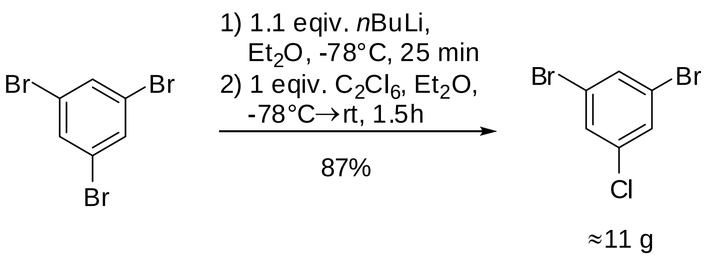


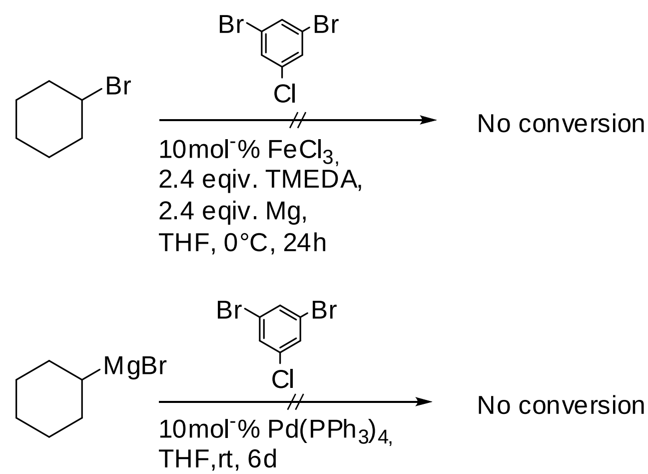
S. Torker, A. Müller, P. Chen, *Angew. Chem, Int. Ed.*, **2010**,49, 3762.

HPE derivative synthesis

building the precursors



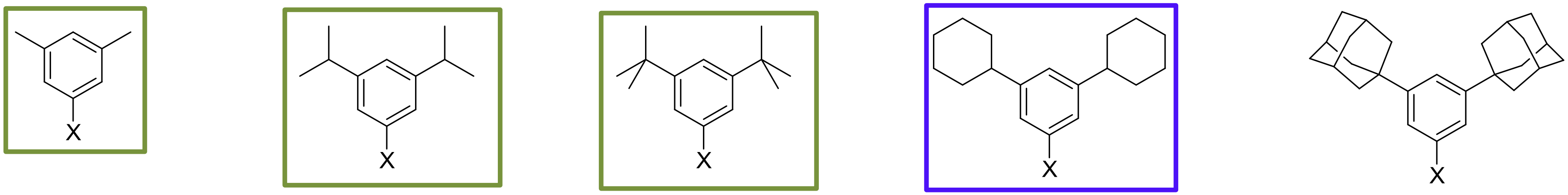


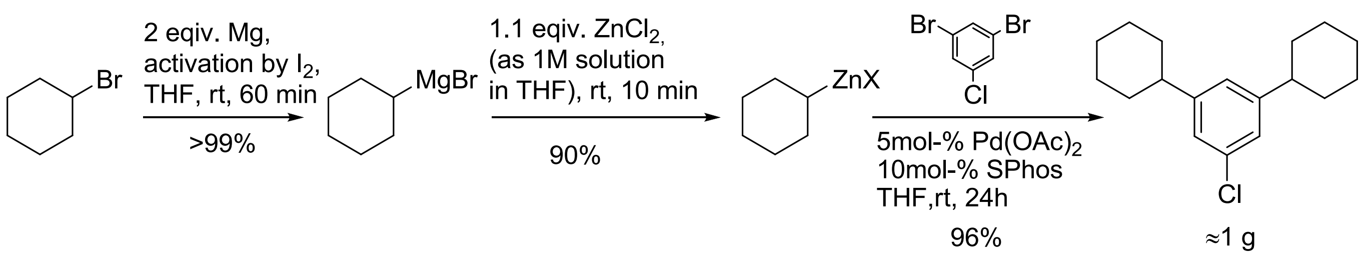


W. M. Czaplik, M. Mayer, A. J. von Wangelin, *Angew. Chem, Int. Ed.*, **2009**,48, 607.
K. R. Romines, G. A. Freeman, L. T. Schaller, J. R. Cowan, S. S. Gonzales, J. H. Tidwell, C. W. Andrews, D. K. Stammers, R. J. Hazen, R. G. Ferris, S. A. Short, J. H. Chan, L. R. Boone, *J. med. Chem.*, **2006**, 49, 2, 727.

HPE derivative synthesis

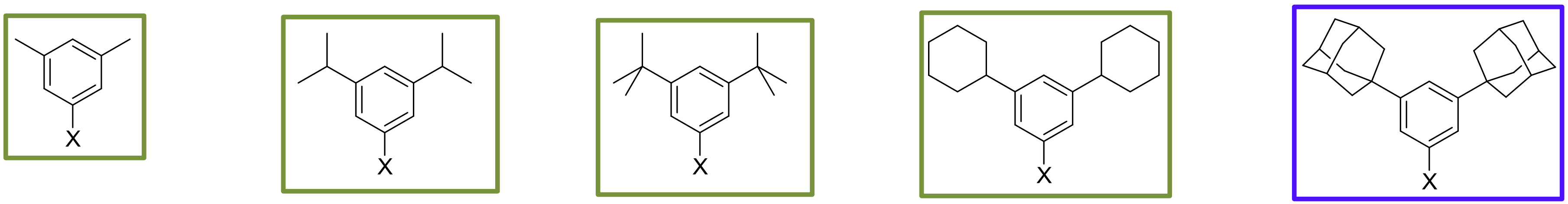
building the precursors

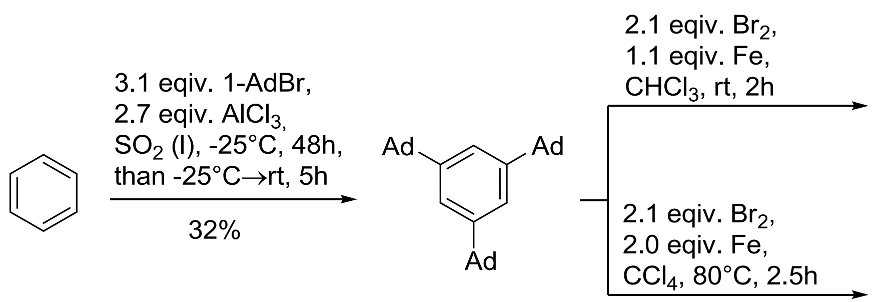




HPE derivative synthesis

building the precursors



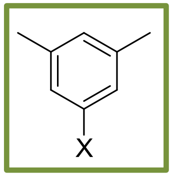


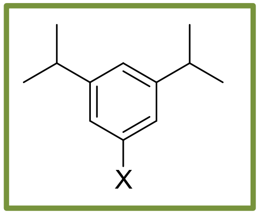
No product!

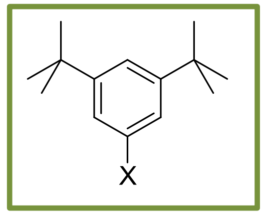
GCMS: 2-4 times Br attached,
NMR: no subtitution at the benzene

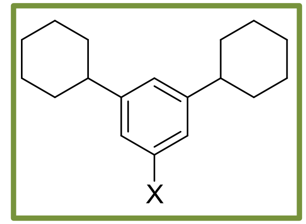
HPE derivative synthesis

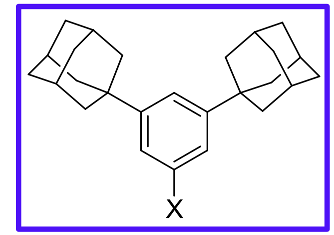
building the precursors

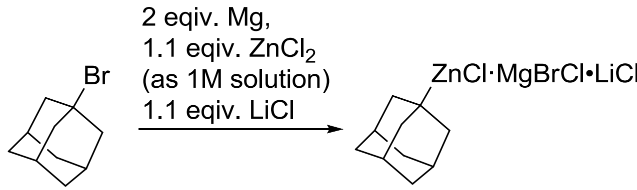












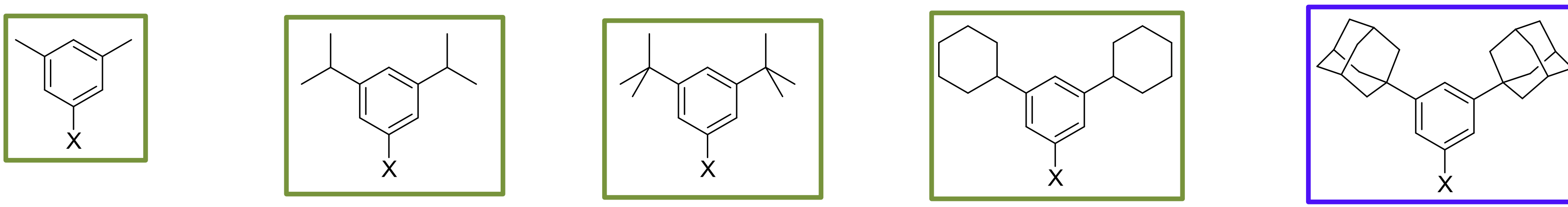
Runing Nr.	Solvent	Time	Titration		Iodolysis GCMS [%]			Comment
		[h]	[mol/l]	Ausbeute [%]	AdI ≡ AdZnX	AdBr	other (>5%)	
Literature	*THF*	*2*	*0,34*	*85*	-	-	-	*Knochel, 2014*
srs029	THF	9	0,15	37	33	28	AdH (19)	
srs029.1	THF	**2**	**0,33**	**80**	85	<1	AdH (9)	
		16	0,28	68	-	-	-	
srs029.2	THF	4	-	-	5	93	-	aborted
srs029.3	THF	21	-	-	72	1	AdH (27)	
srs029.4	THF	20	-	-	80	<1	AdH (20)	
srs029.5	THF	65	-	-	72	2	AdH (27)	weekend
srs029.6	Et_2O	21	0,15	36	35	41	AdH (2); **AdCl (23)**	
srs029.7	Et_2O	19	0,11	27	23	54	AdH (1); **AdCl (23)**	
srs029.8	THF	**1,5**	**0,33**	**80**	78	<1	AdH (16)	4 times scale up
		24	0,30	73	-	-	-	

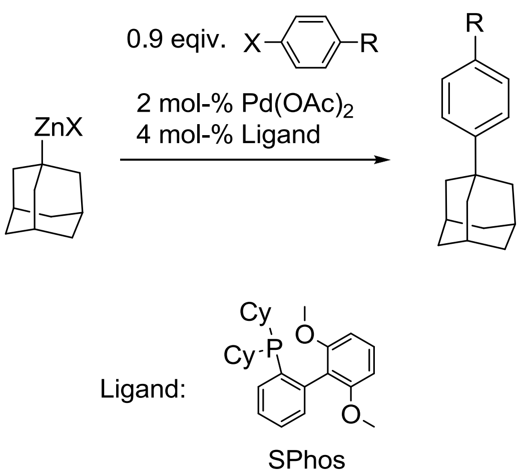
Also tried: Dioxane and tert-Butylmethylether but $ZnCl_2$ is to insoluble for the procedure

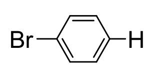
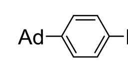
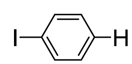
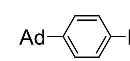
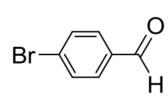
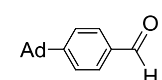
C. Sämann, V. Dhayalan, P. R. Schreiner, P. Knochel, *Org. Lett.*, **2014**, 16, 9, 2418.

HPE derivative synthesis

building the precursors



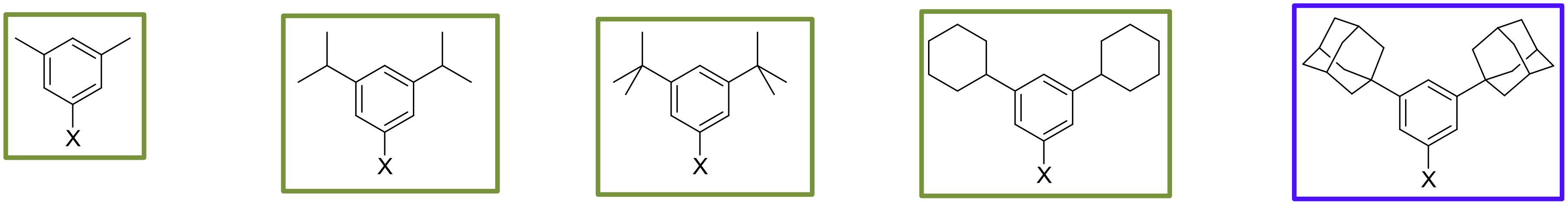


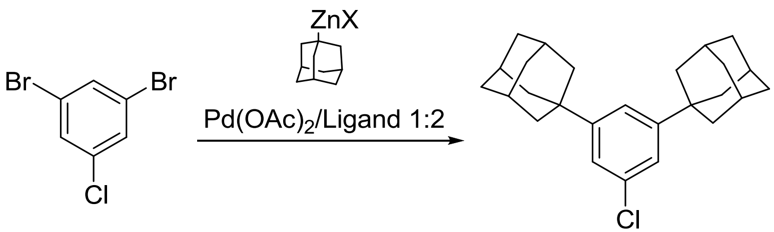
Starting Material	c(AdZnX) [mol/l]	Time [h]	Temperature [°C]	Conversion [%]	Product	Comment
	0,33	17	50	**98**		
	0,33	17	50	**98**		
	0,33	17	50	**97**		Knochel, 2014 88% (isolated)

C. Sämann, V. Dhayalan, P. R. Schreiner, P. Knochel, *Org. Lett.*, **2014**, 16, 9, 2418.

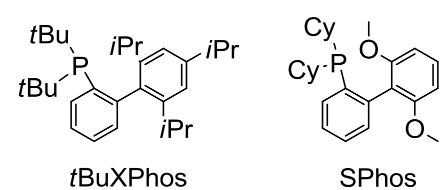
HPE derivative synthesis

building the precursors





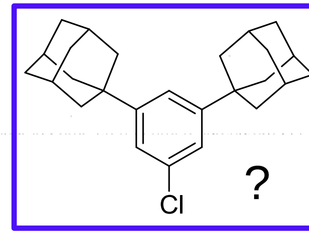
Ligands:

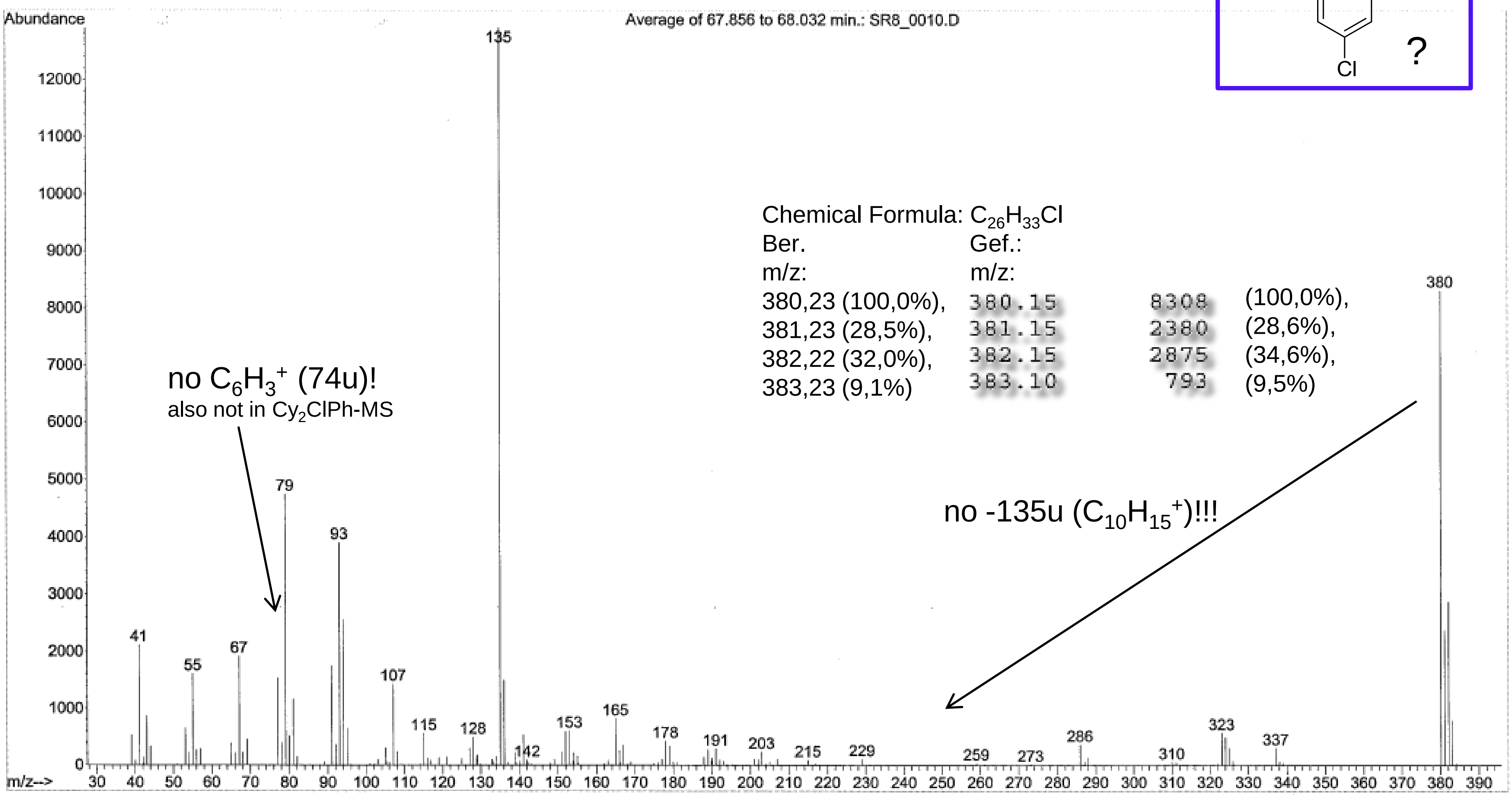


Runing Nr.	Solvent	AdZnX eqiv.	c(AdZnX) [mol/l]	Ligand	Catalyst [mol%]	Temp. [°C]	Time [h]	Product *by GCMS/ ‡by MNR	Comment
srs030	THF	1,1	0,15	*t*BuXPhos	1	rt	12	no convertion*‡	
srs030.1	THF	2,1	0,28	SPhos	5	rt	72	no convertion*‡	
srs030.2	THF	2,1	0,25	SPhos	5	50	4,5	no convertion*‡	additonal 60h at rt/ THF-Ad formed
srs030.3	Et2O	2,1	0,15	SPhos	5	Δ	16,5	no convertion*	everything as suspension
							1	≈0,4*	
srs030.4	THF	2,1	0,30	SPhos	5	50	16	≈0,6*	doubled scale; 1/3 amout of solvent; poor evidence of Product
							40	≈1,1*	

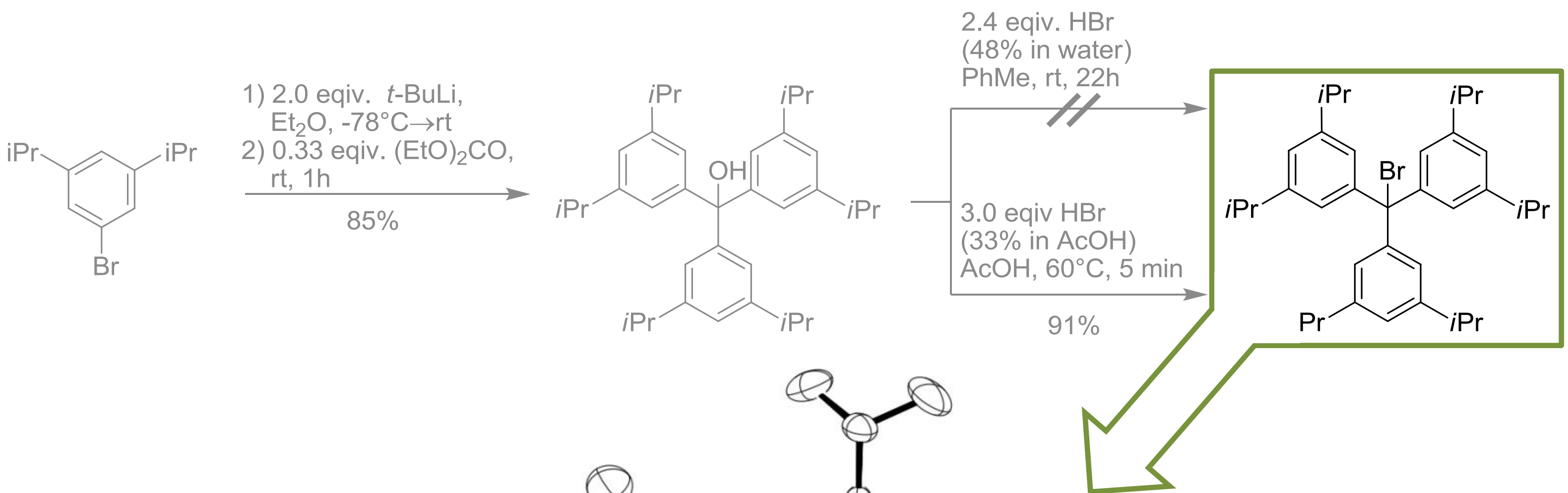
HPE derivative synthesis

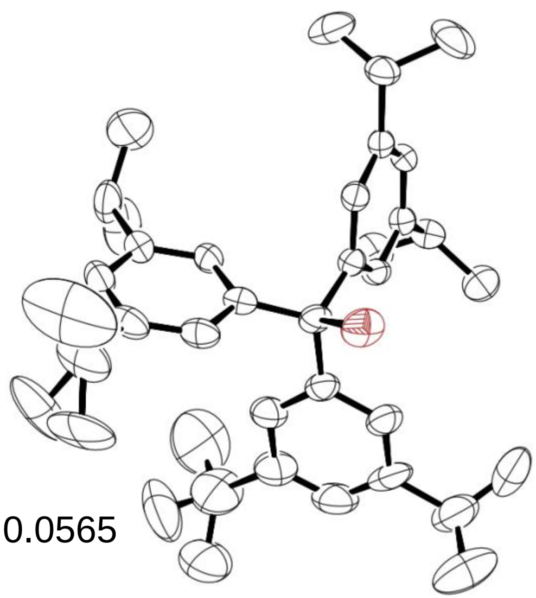

```
File        : C:\HPCHEM\1\DATA\ROESEL\SR8_0010.D
Operator    : sr
Acquired    :  3 Jul 2014    9:53     using AcqMethod S306F25L
Instrument  :   GC_MS_597
Sample Name: srs030.4 nach 40h 50°C
Misc Info   : in Et2O
Vial Number: 1
```





Hexakis(3,5-di*iso*propylphenyl)ethane





R_1 = 0.0565

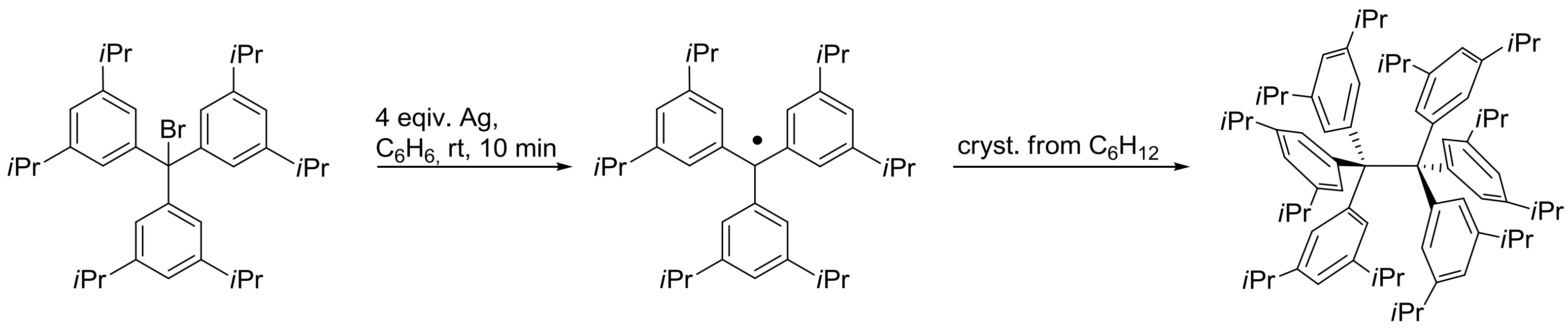
–sensitive towards air (hydrolysis)

–turns from colorless to brown in 4h under Ar

–purification by recrystallisation from dry Hexane leads to back reaction

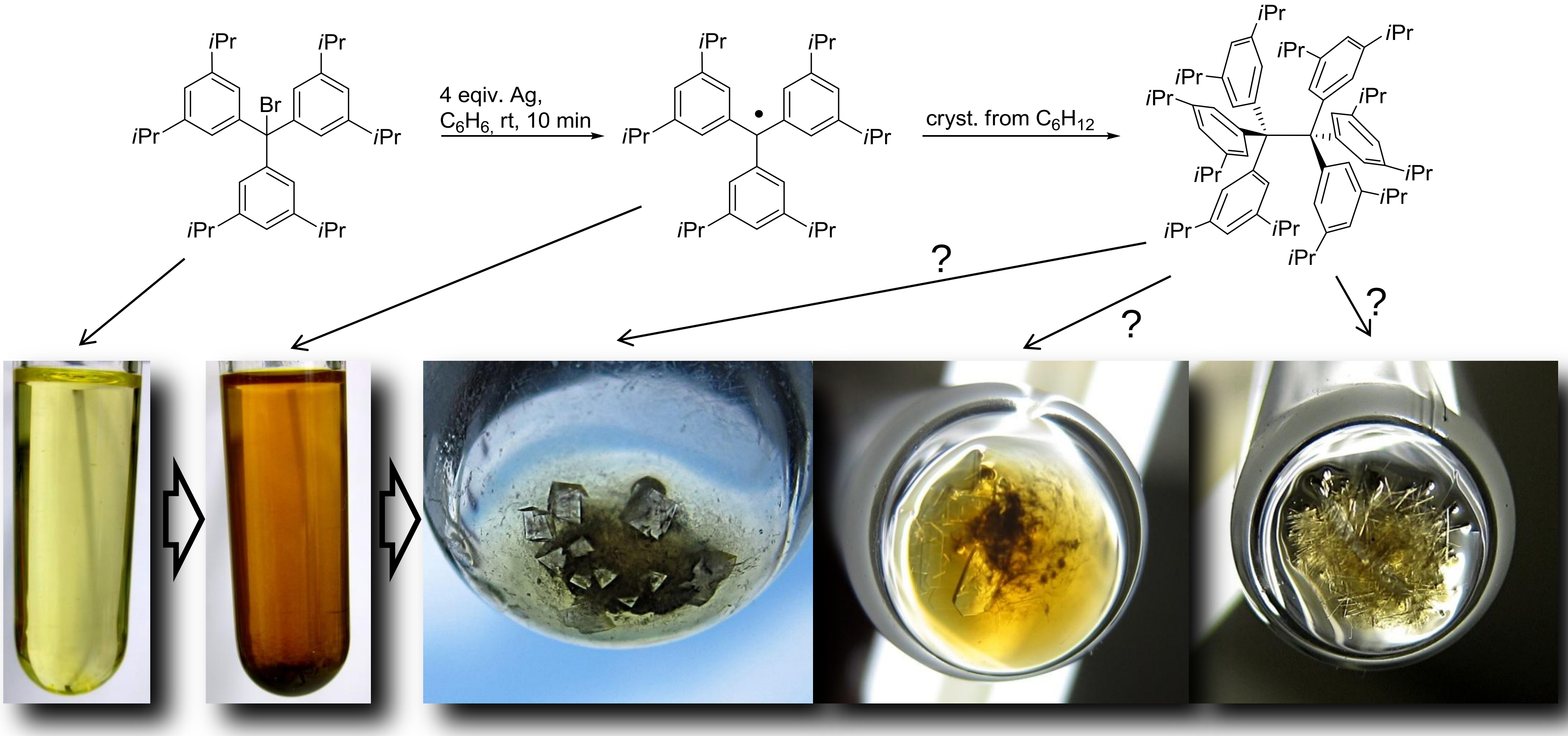
W. Zhang, H. Yamamoto, *J. Am. Chem. Soc.*, **2007**, 129, 286 SI.

Hexakis(3,5-di*iso*propylphenyl)ethane



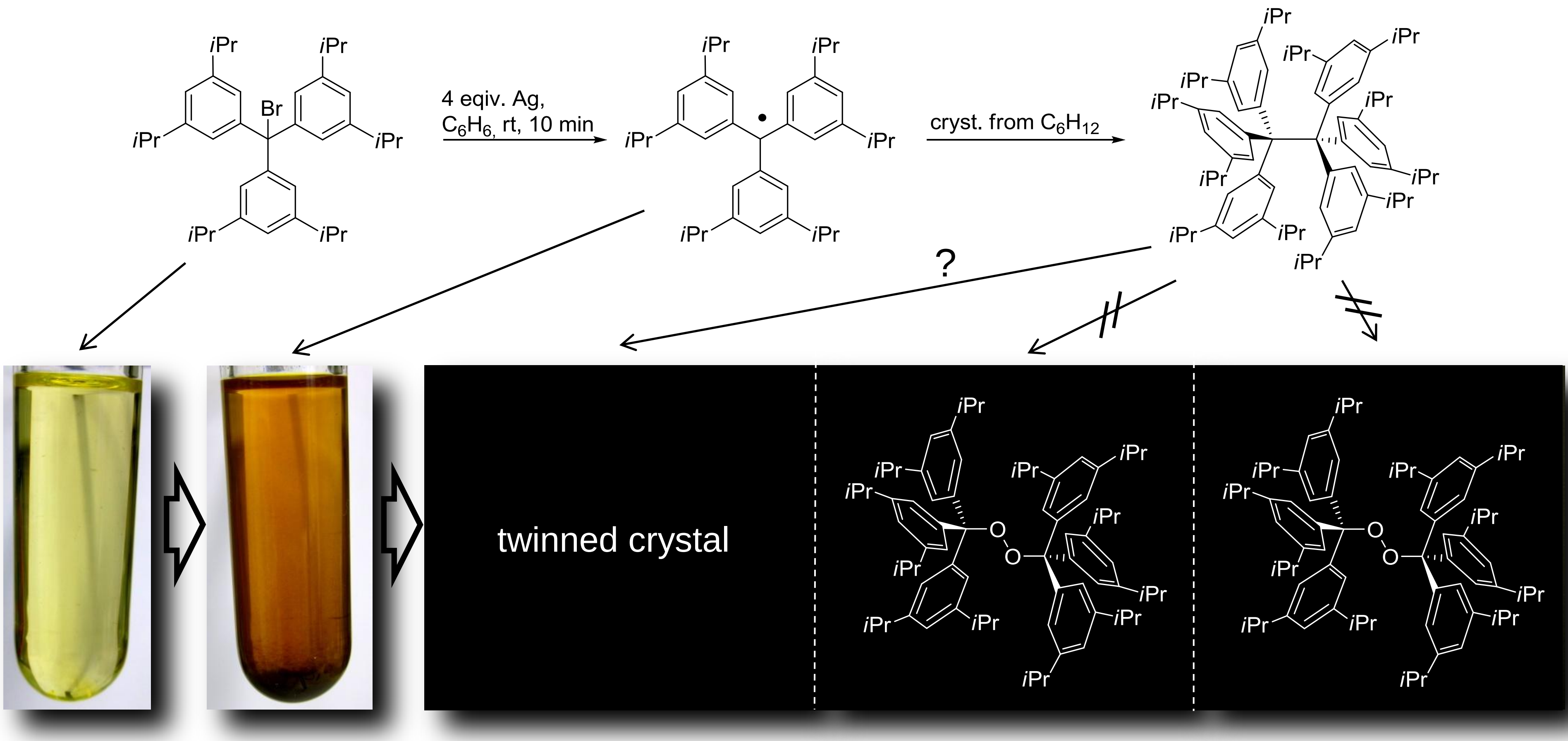
B. Kahr, D. Van Engen, K. Mislow, *J. Am. Chem. Soc.,* **1988**, 108, 8305

Hexakis(3,5-di*iso*propylphenyl)ethane



B. Kahr, D. Van Engen, K. Mislow, *J. Am. Chem. Soc.,* **1988**, 108, 8305

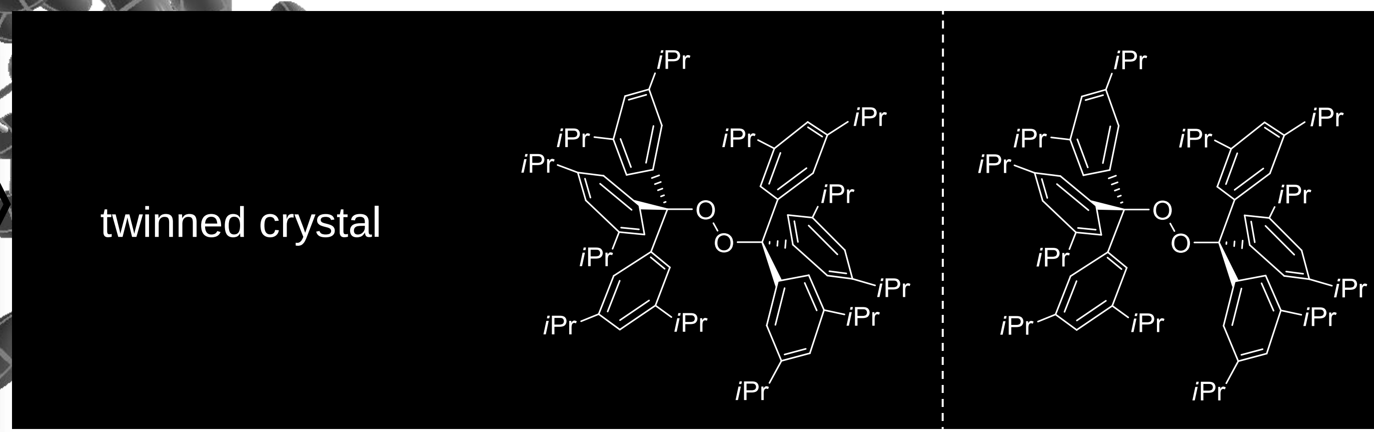
Hexakis(3,5-di*iso*propylphenyl)ethane



B. Kahr, D. Van Engen, K. Mislow, *J. Am. Chem. Soc.,* **1988**, 108, 8305

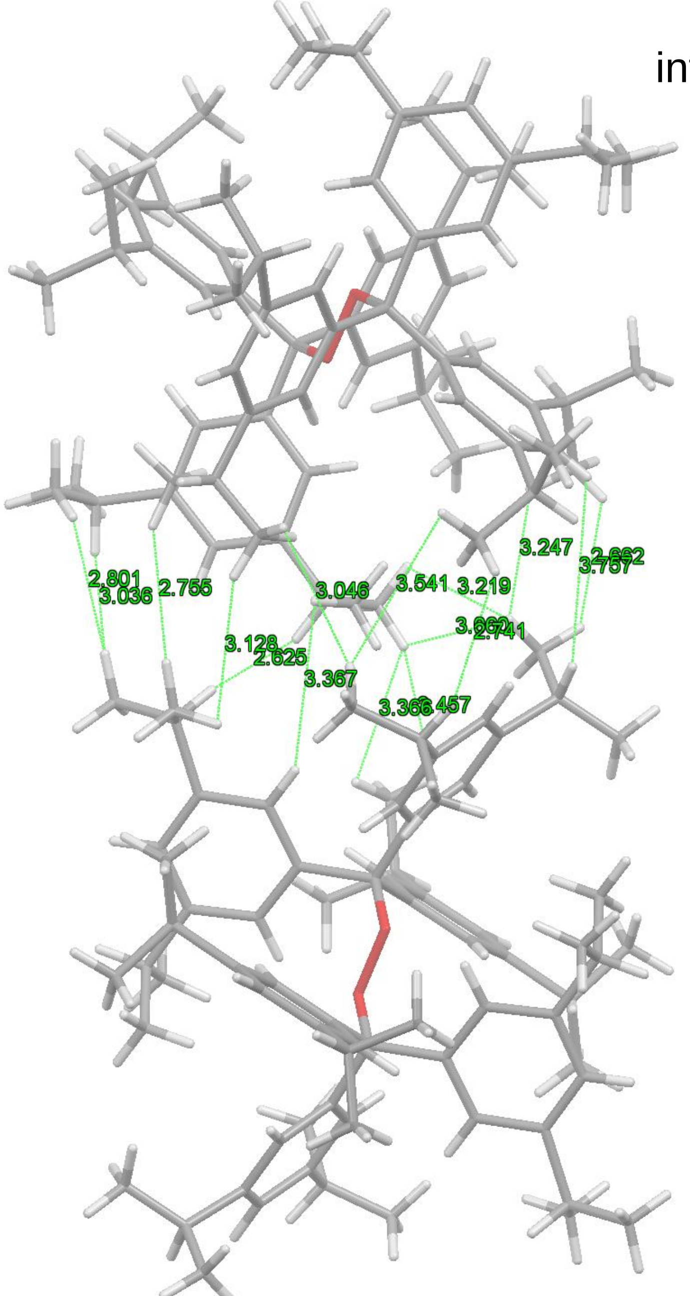
*all-meta iso*Propyl tritylperoxide

	HOOH (Levy 1965)	*t*BuOO*t*Bu (Blaschette 1977)	TrOOTr (Sheldrick 1979)	*all-meta i*Pr TrOOTr (this work)
Distances [Å]				
C-O	0,99	1,46	1,46	1,46
O-O	1,45	1,48	1,48	1,48
C(Ar)-C	-	1,52	1,53	1,53
C-C‘	-	3,58	3,65	3,65
Angles [°]				
C(Ar)CO	-	n/a	100; 110; 111	97; 110; 110
COO‘	102	103,9	107,5	107,3
COO‘C‘	90,2	165,8	180	180

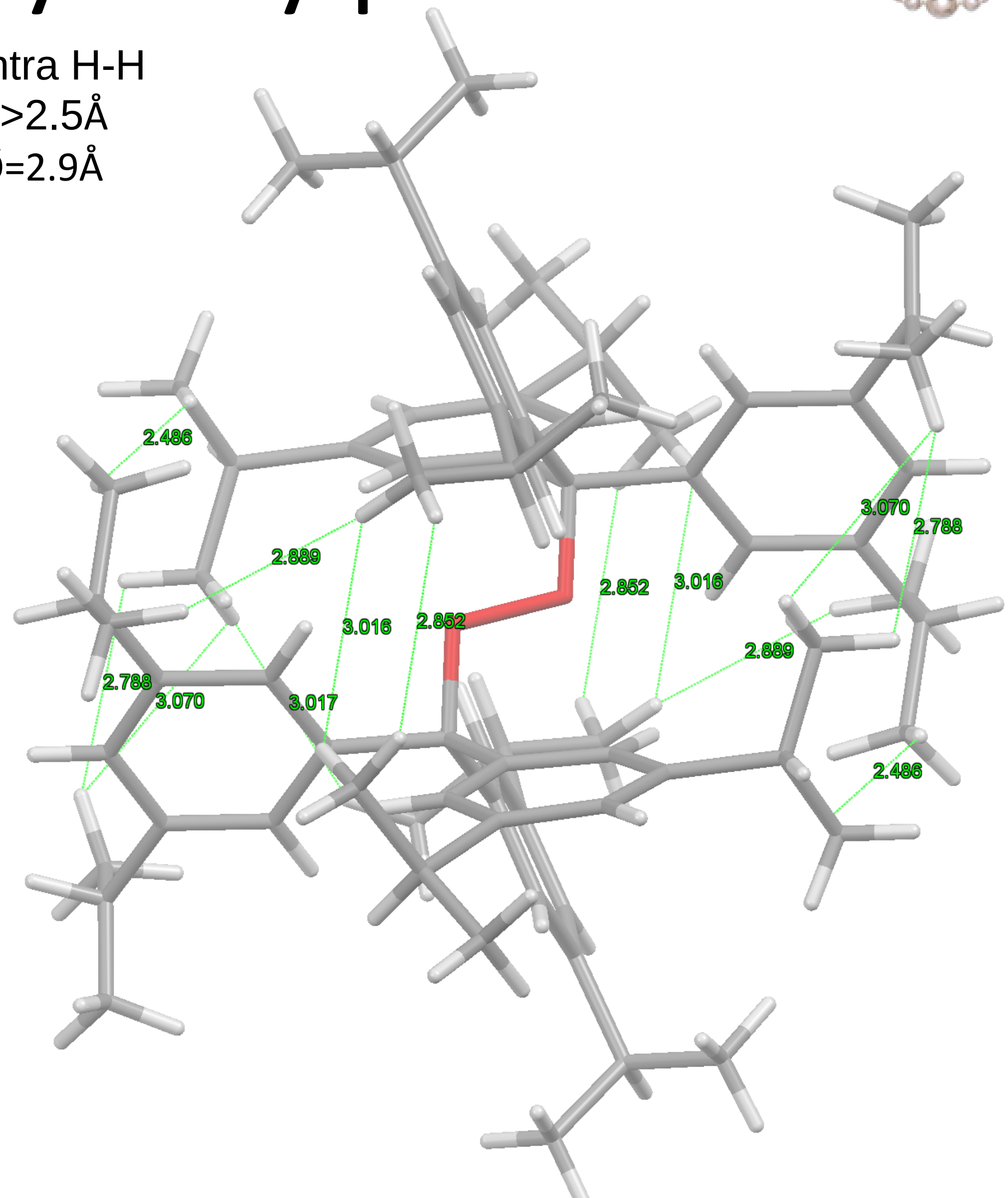


C. Glidewell, D. C. Liles, D. J. Walton, G. M. Sheldrick, *Acta Cryst.*, **1979**, B35, 500.
W. R. Busing, H. A. Levy, *J. Chem. Phys.*, **1965**, 42, 3054.
D. Käss, H. Oberhammer, D. Brandes, A. Blaschette, *J. Mol. Struct*. **1977**, 40, 65.

*all-meta iso*Propyl tritylperoxide

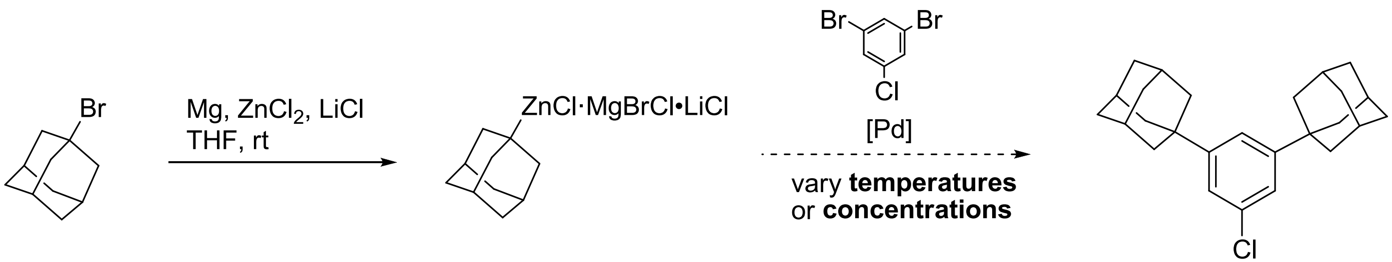


inter H-H	intra H-H
d>2.6Å	d>2.5Å
Ø=3.1Å	Ø=2.9Å

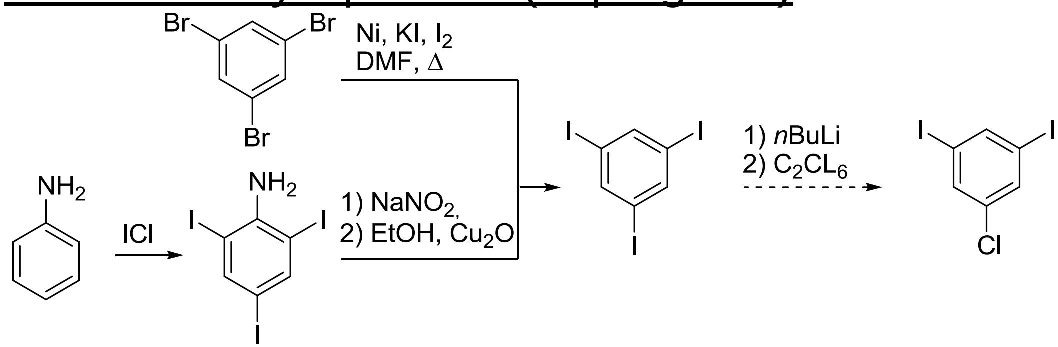


Outlook

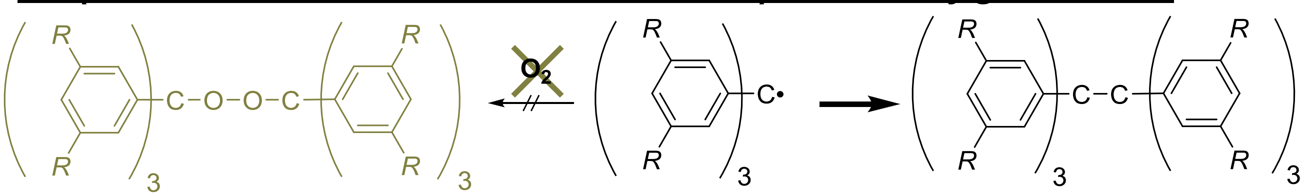
Synthesize Precursor to Adamantylderivative.



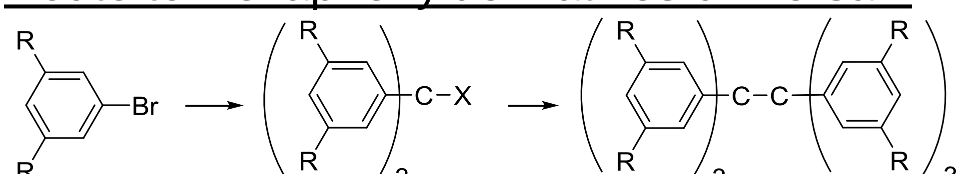
Use other Aryl species? (In progress)



Reproduce Mislow‘s HPE. Work *superoir* oxygen free!



Route to Hexaphenylderivatives universal?



Crystals? **Elonged bonds? Bond-stretch-isomerism? BDE?**