

Cyclodehydrogenation of Arenes (Scholl Reaction)

By: Chris Johnson

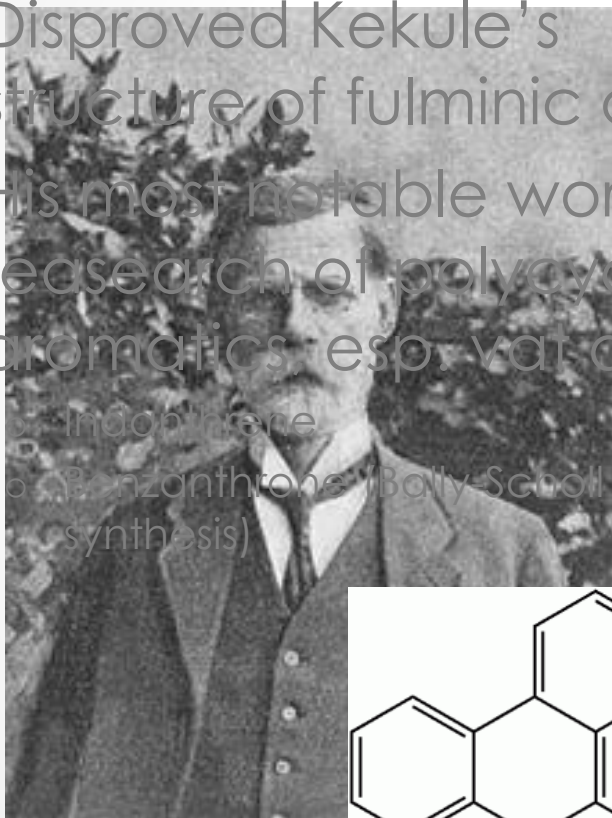
4/17/2013

Overview

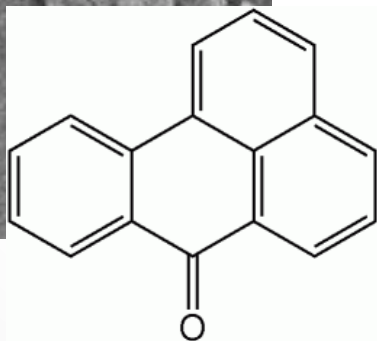
- History
 - The Man
 - The Reaction
 - Related Variatons
- Mechanism
 - Radical Cation or Arenium intermediates?
 - Controlling regioselectivity
- Applications
 - Interesting Examples
- Summary
- Questions???

Roland Heinrich Scholl

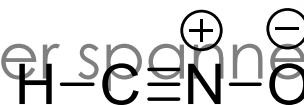
- Disproved Kekule's structure of fulminic acid.
- His most notable work was research of polycyclic aromatics, esp. vat dyes.



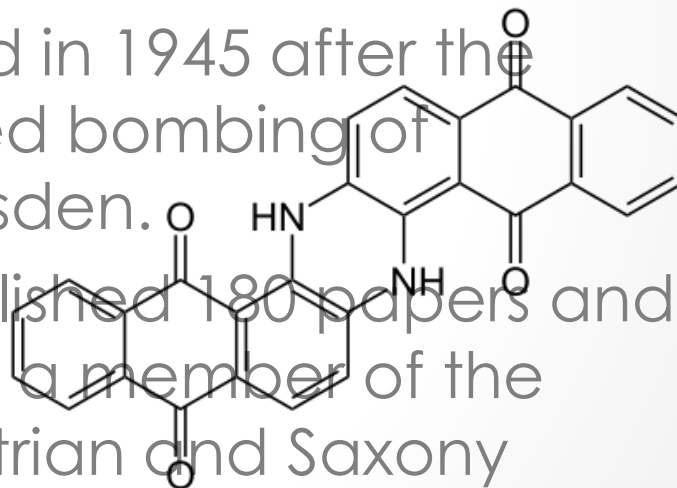
Indanthrene
Benzanthrone (Baly-Scholl synthesis)



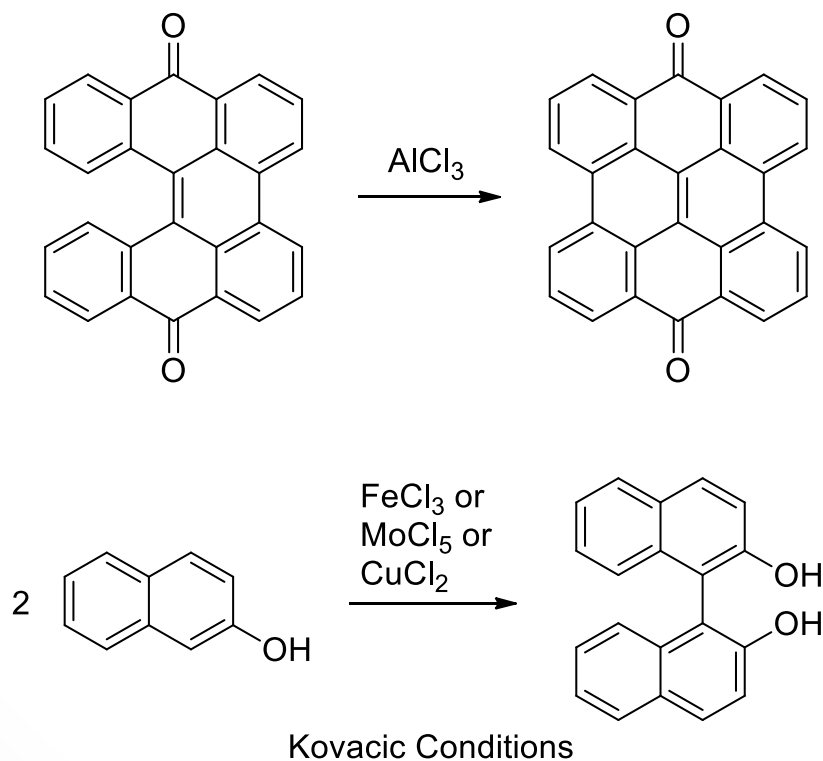
- Born in Switzerland in 1865. His Career spanned 5 universities around Europe and 2 World Wars.



- Died in 1945 after the Allied bombing of Dresden.
- Published 180 papers and was a member of the Austrian and Saxony Academy of Sciences.



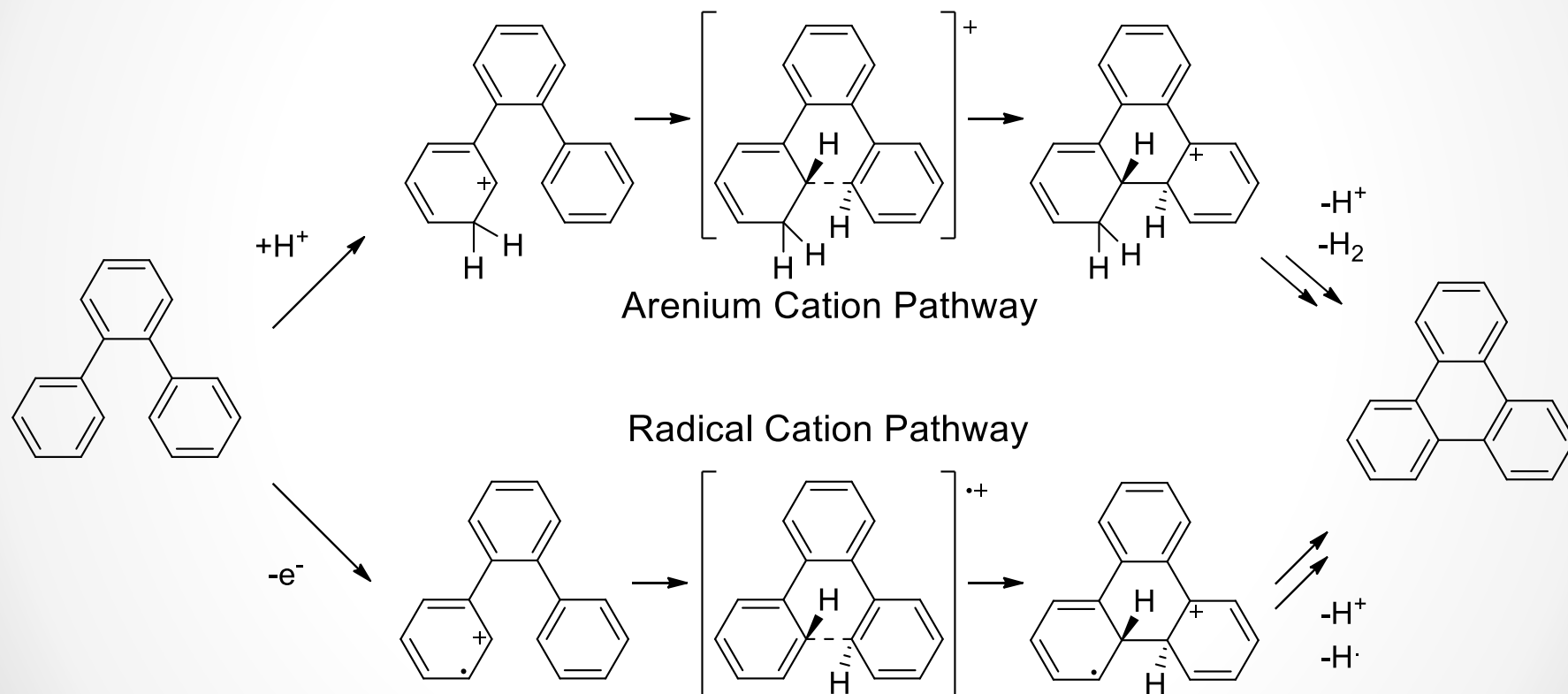
Scholl Reaction



Scholl, R.; Mansfeld, J. *Ber. Dtsch. Chem. Ges.* **1910**, *43*, 1734-1746.

Pummerer, R.; Prell, E.; Rieche, A. *Ber. Dtsch. Chem. Ges.* **1926**, *59*, 2159-2161.

Mechanism

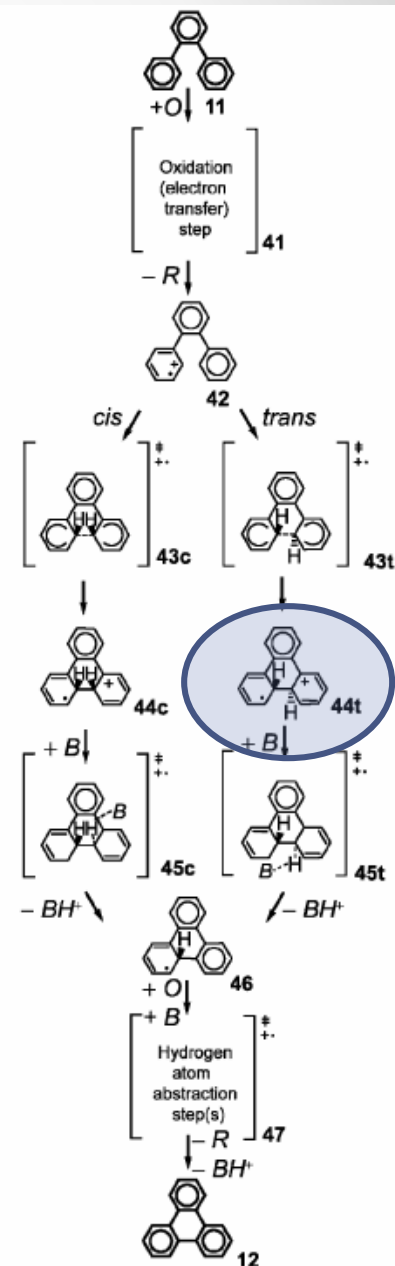
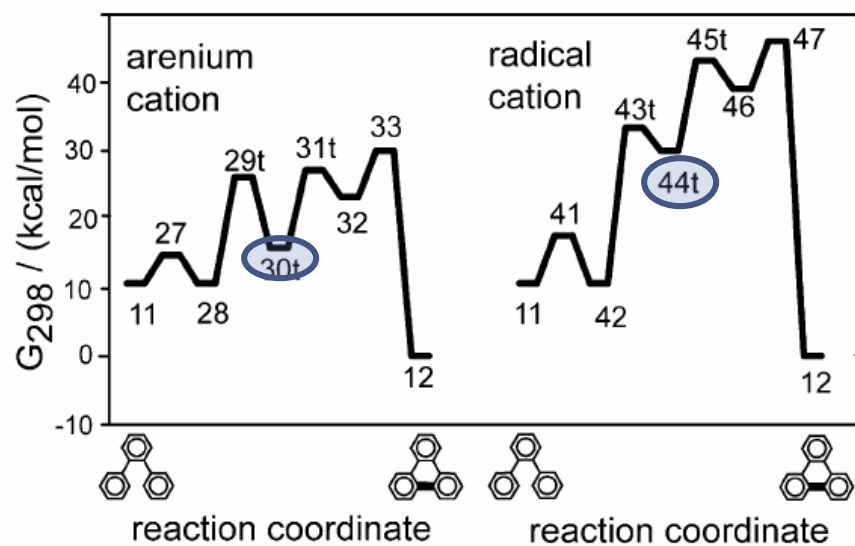
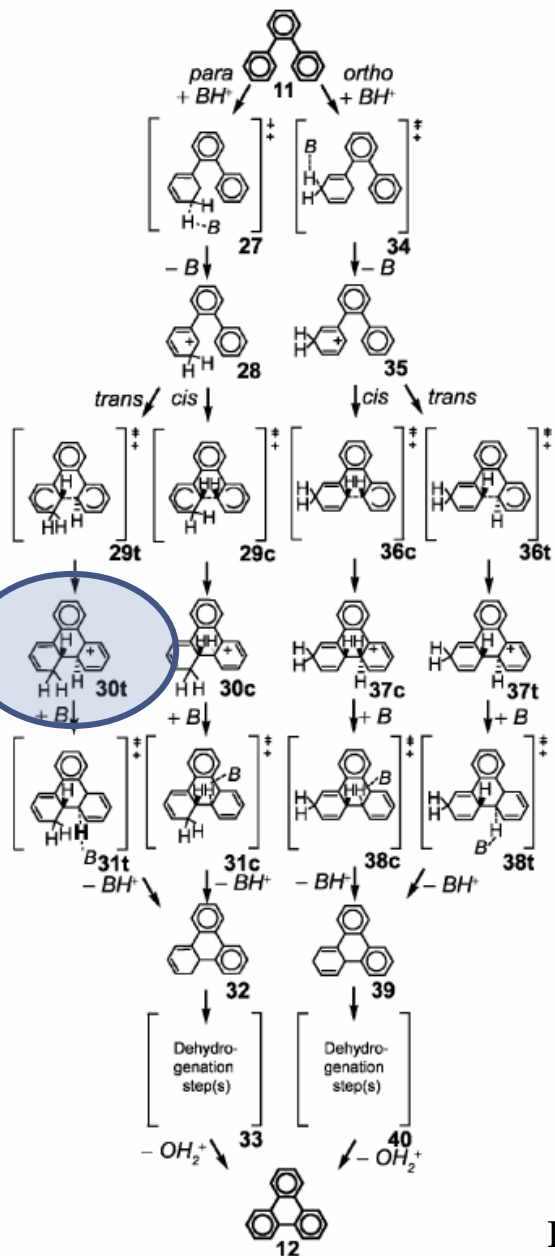


Rempala, P.; Kroulik, J.; King, B.T. *JACS* **2004**, *126*, 15002-15003.

Rempala, P.; Kroulik, J.; King, B.T. *JOC* **2006**, *71*, 5067-5081.

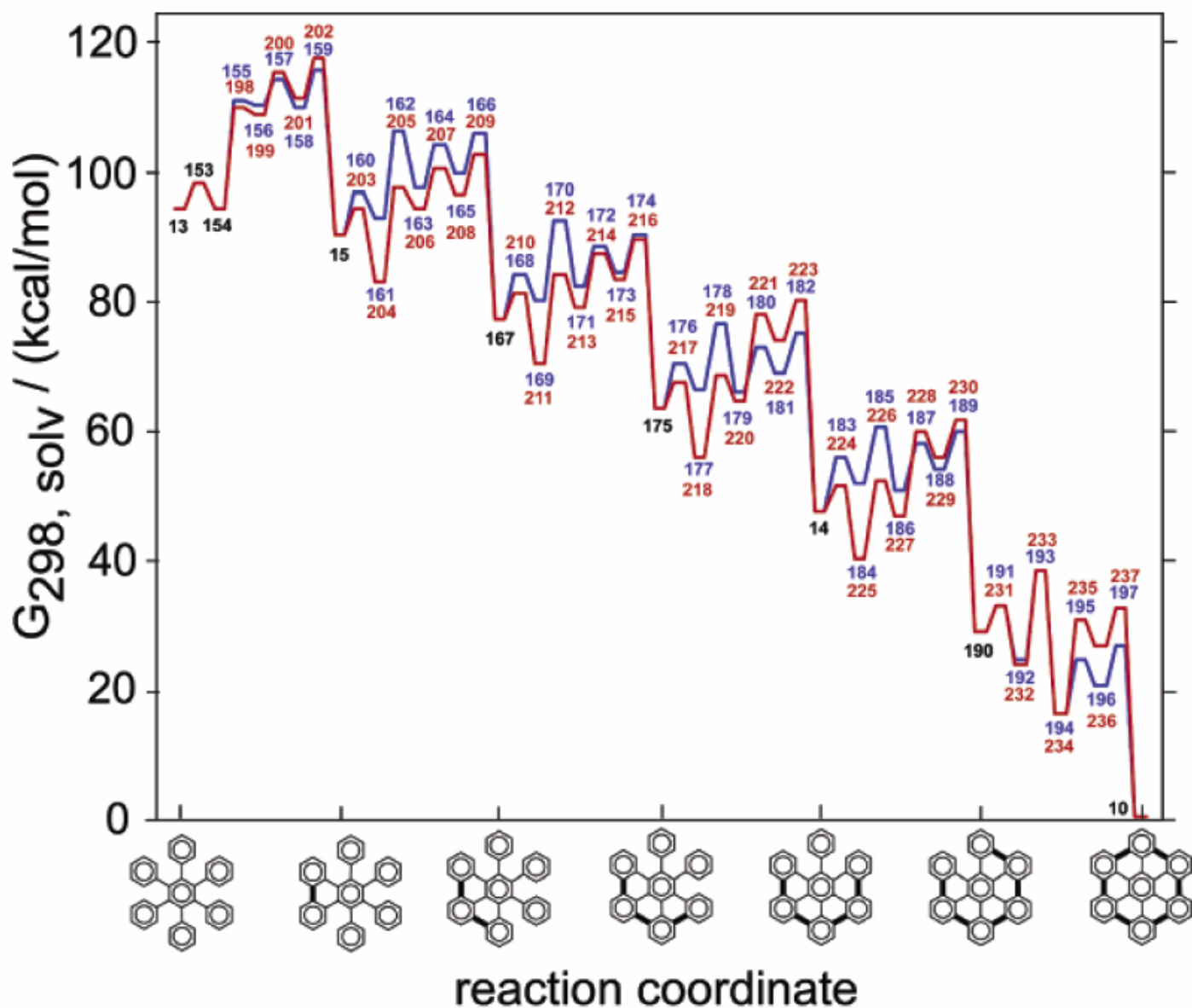
Zhai, L.; Shukla, R.; Wadumethrige, S.H.; Rathore, R. *JOC* **2010**, *75*, 4748-4760.

Arenium Cation Support

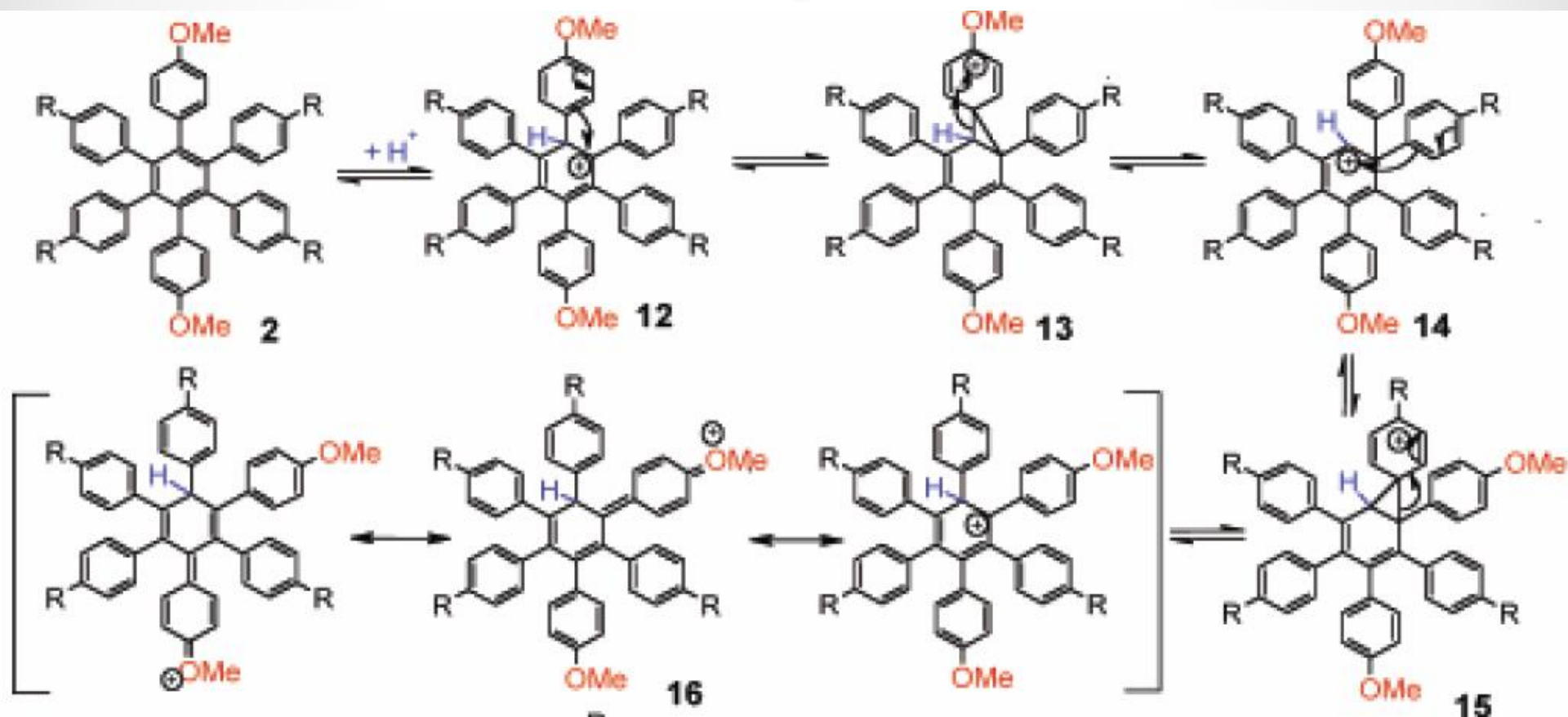


- DFT with Gaussian 03 and 98. B3LYP functional with standard 6-31G(d) basis set was used.
- CuCl_2 in CS_2
- Transition states involving radical cations were higher in energy than with arenium cations

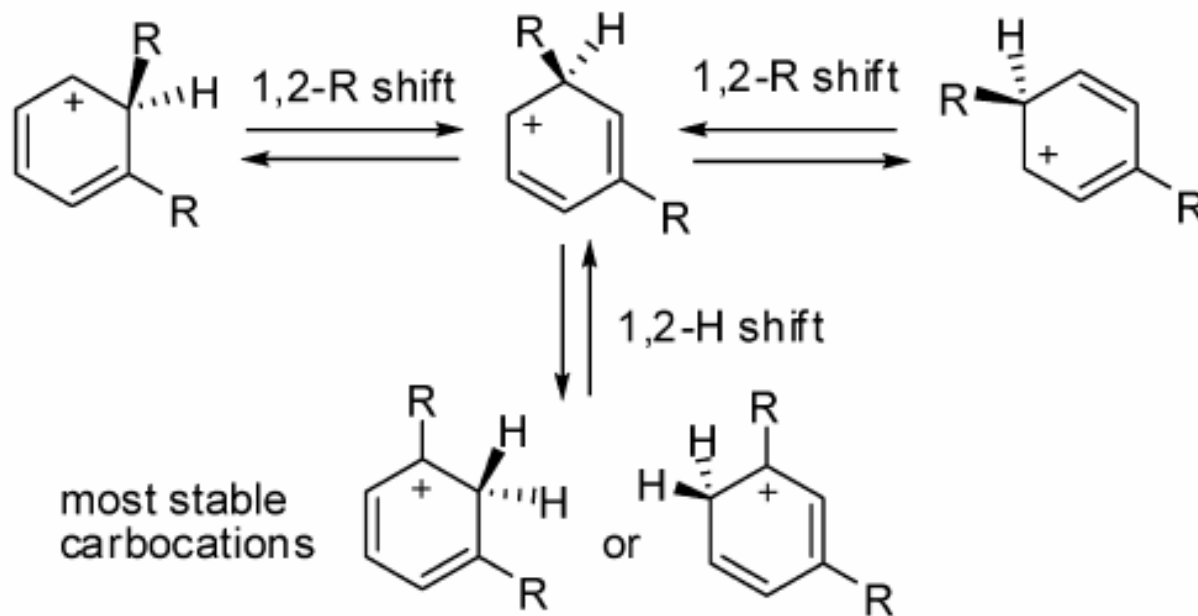
Arenium Cation Calculations



Rearrangements



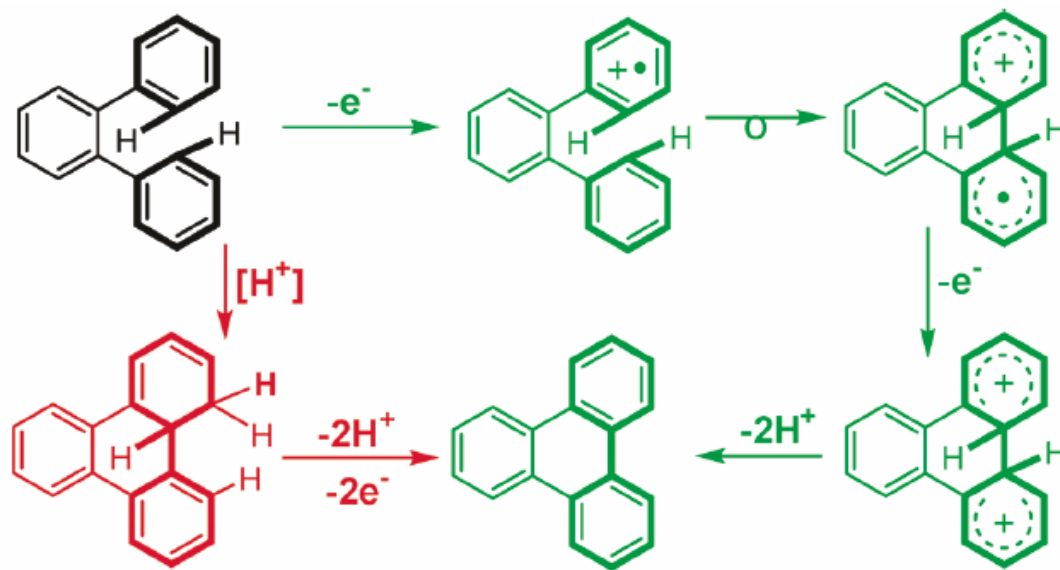
Rearrangements



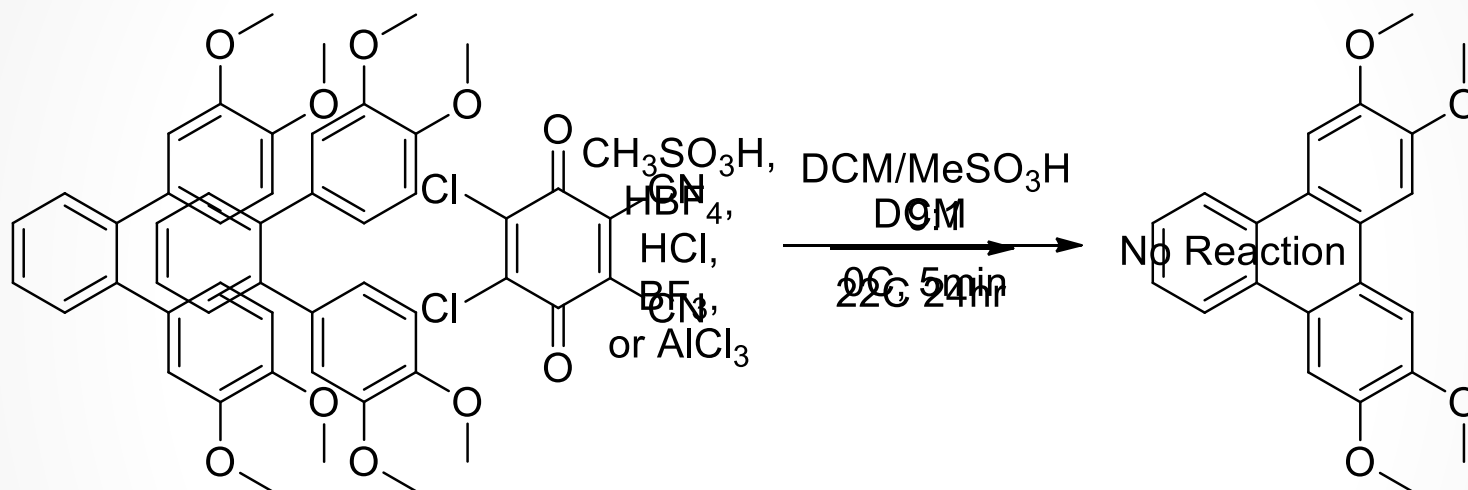
Arenium Cation Conclusions

- The arenium cation mechanism involves lower energy transition states (according to DFT studies).
- Observed rearrangement products support an arenium cation pathway.
- Although these results suggest that intermediates won't accumulate; Mullen's group was able to isolate an intermediate

Radical Cation Support

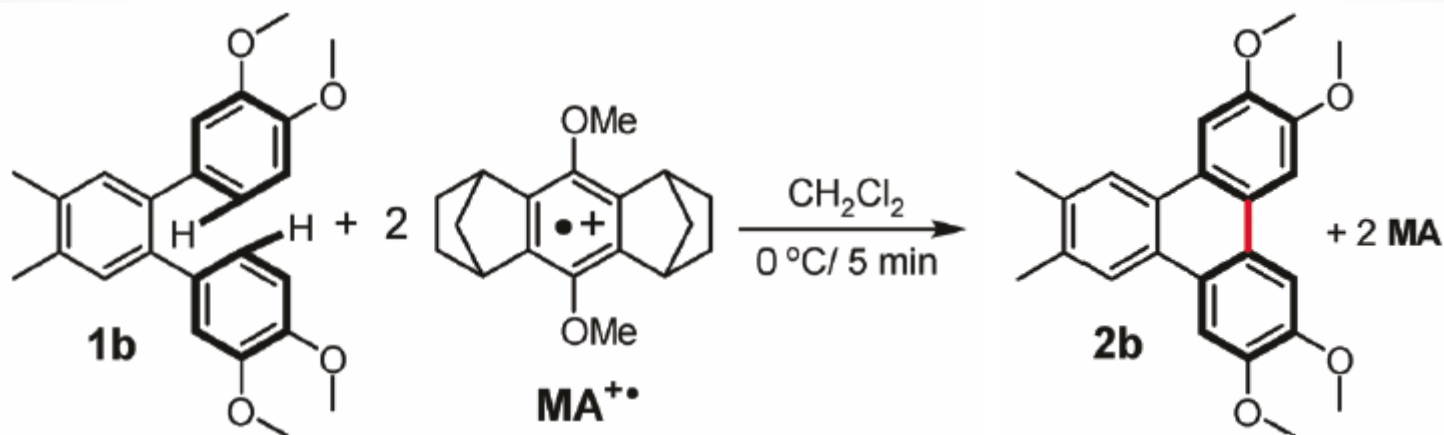


Role of Acid



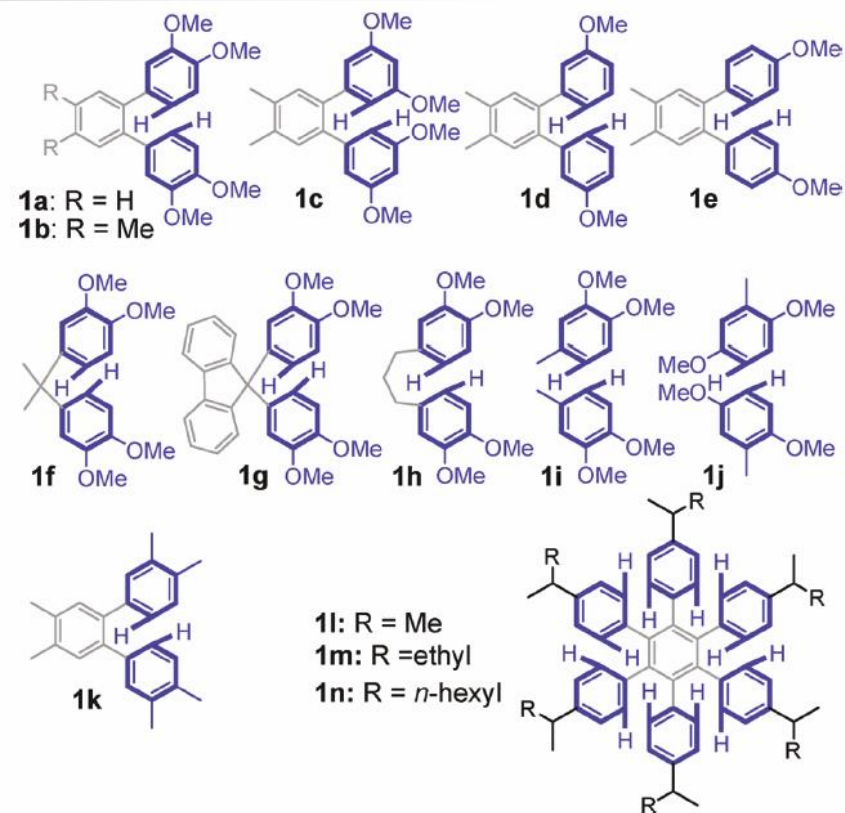
- No reaction of Scholl precursors in DCM/acid
- The same reactions worked when DDQ was added

Role of Acid



- Although acid is necessary with DDQ, it has been shown that other oxidants do not require any.

Role of Oxidant



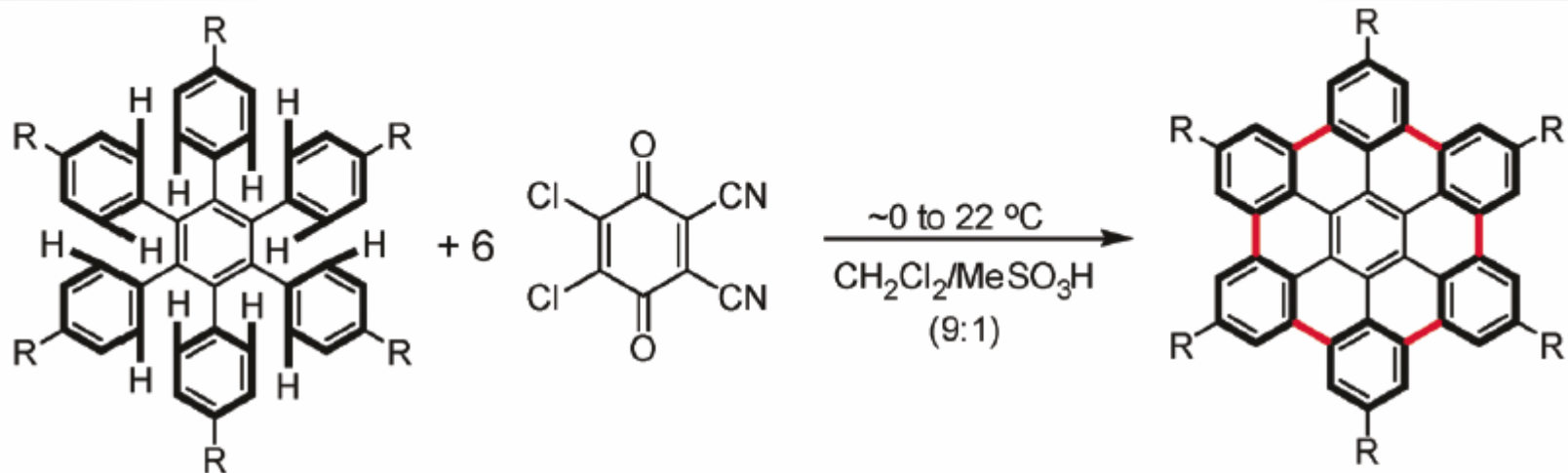
Scholl precursor	$E_{\text{ox(SP)}} \text{ V vs SCE}^b$	cyclized donor	$E_{\text{ox(CD)}} \text{ V vs SCE}^c$	$E_{\text{ox(SP)}} - E_{\text{ox(CD)}}$
1a	1.20	2a	1.15	0.05
1b	1.11	2b	1.08	0.03
1c	1.20	2c	0.89	0.31
1d	1.68	2d	1.18	0.50
1e	1.56	2e	1.28	0.28
1f	1.26	2f	0.85	0.41
1g	1.27	2g	0.86	0.41
1h	1.32	2h	1.11	0.21
1i	1.35	2i	1.24	0.11
1j	1.27	2j	1.11	0.16
1k	1.33	2k	1.41	-0.08
1l	~1.6	2l	1.00	0.48
1m	~1.6	2m	1.00	0.48
1n	~1.6	2n	1.00	0.48

^aExperimental conditions: a 1.0 mM solution of the substrate and 0.1 M *n*Bu₄NPF₆ (as the supporting electrolyte) in dichloromethane at a scan rate of 200 mV s⁻¹ and at 22 °C. ^bIrreversible cyclic voltammograms, $E_{\text{ox(SP)}}$ were determined from square-wave voltammograms. ^cReversible cyclic voltammograms.

O₂)

- Oxidants strong enough to oxidize the parent arene are necessary for the Scholl oxidation
- Zhai, L.; Shukla, R.; Wadumethrige, S.H.; Rathore, R. *JOC* **2010**, *75*, 4748-4760.

Role of Oxidant



1o: R = *tert*-butyl; E_{ox} ~ 1.6 V SCE

1p: R = Br; E_{ox} > 2.1 V SCE

1q: R = H; E_{ox} > 1.8 V SCE

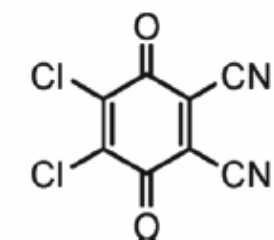
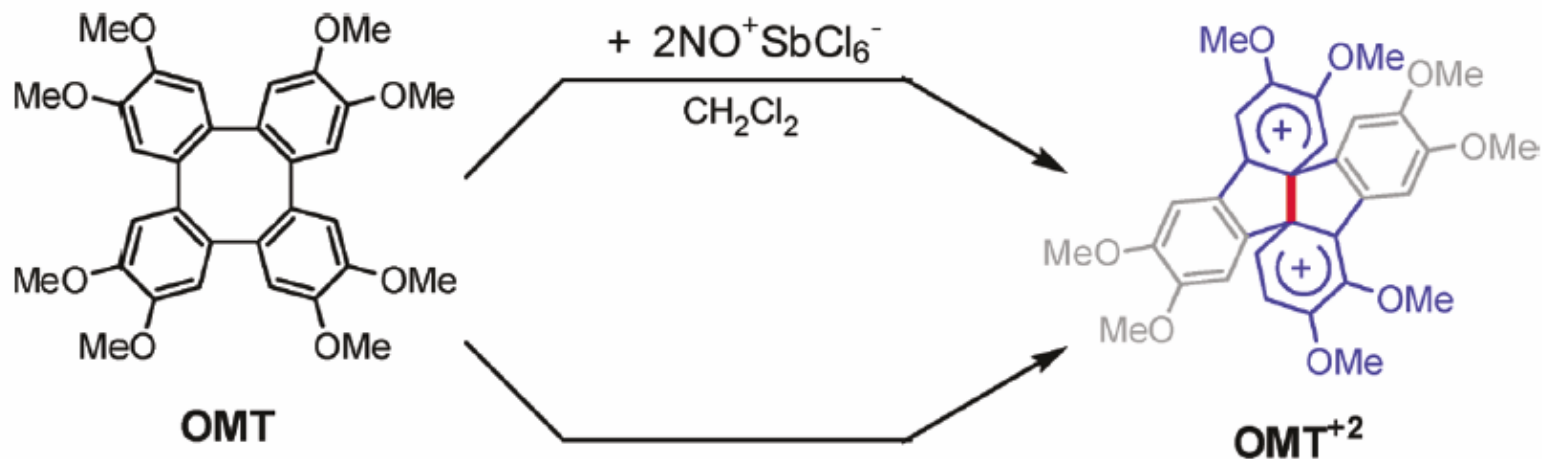
2o: R = *tert*-butyl (Y: ~99%/2h)

2p: R = Br (Y: 0%/72h)

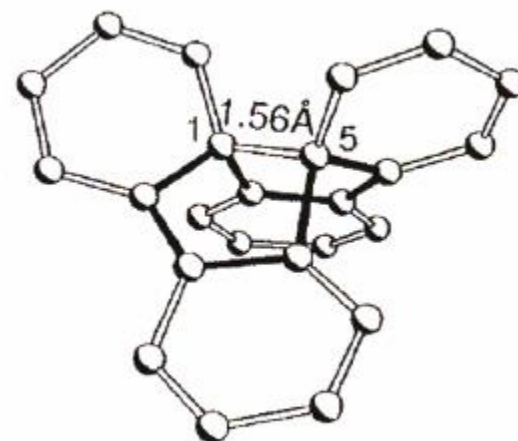
2q: R = H (Y: 0%/72h)

- Oxidants strong enough to oxidize the parent arene are necessary for the Scholl oxidation

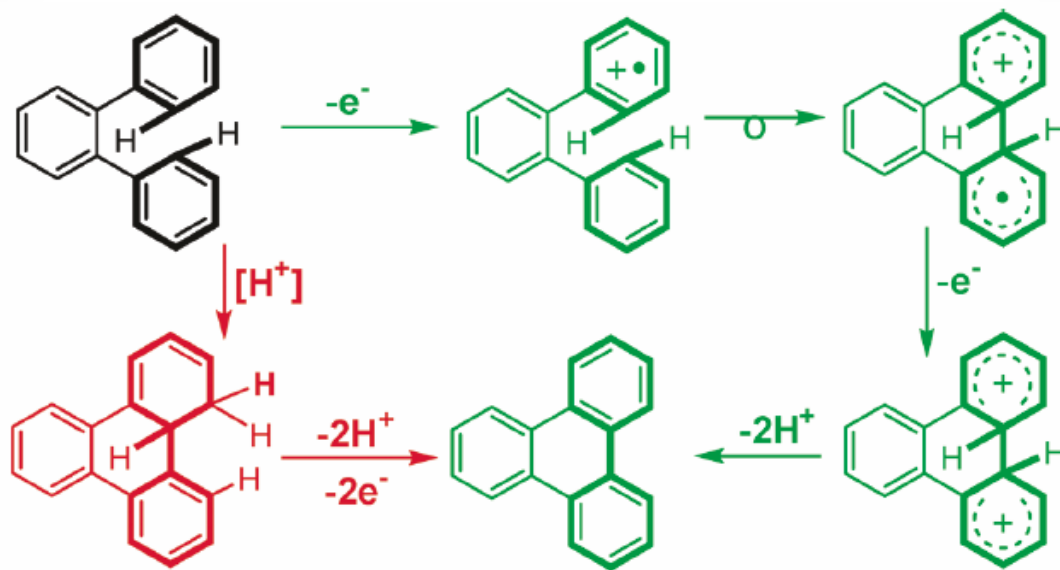
Radical Cation Dimers



Dimeric
Cation Radical

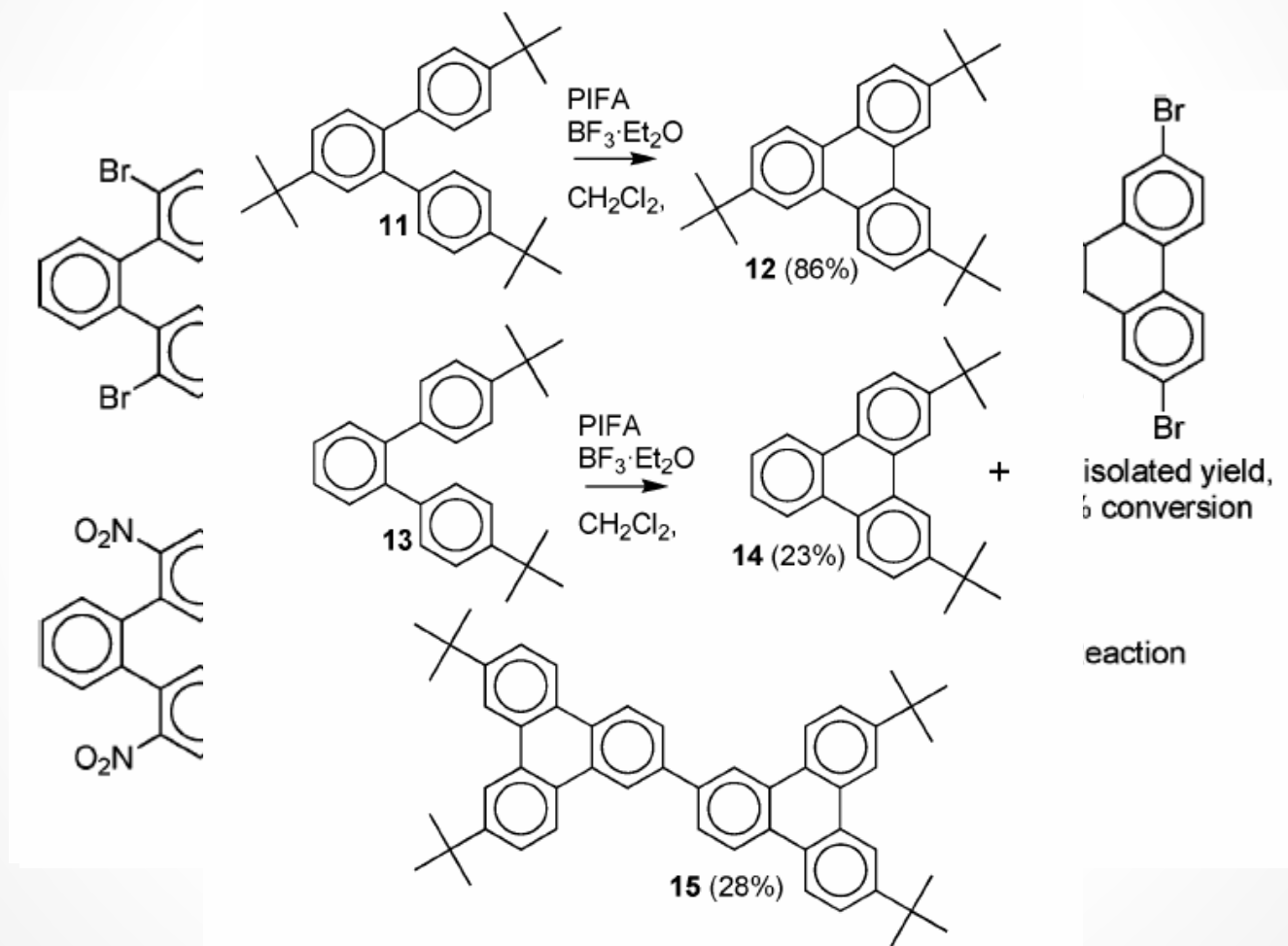


Radical Cation Summary



1. No reaction of Scholl precursors in DCM/acid
2. Powerful oxidants are necessary
3. Scholl precursors with oxidation potentials $< 1.7V$ vs SCE react when using DDQ/ H^+
4. Feasibility of the dicationic intermediate has been demonstrated

Controlling the Scholl Reaction

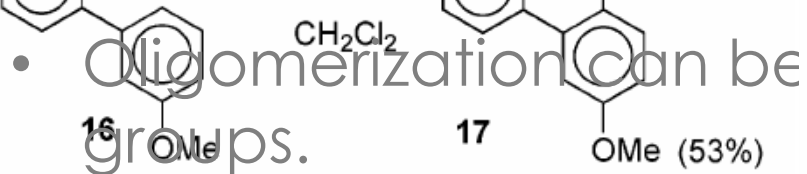


- King, B.T.; Kroulik, J.; Robertson, C.R.; Rempala, P.; Hilton, C.L.; Korinek, J. D.; Gortari, L.M. *JOC* **2007**, *72*, 2279-2288. ●

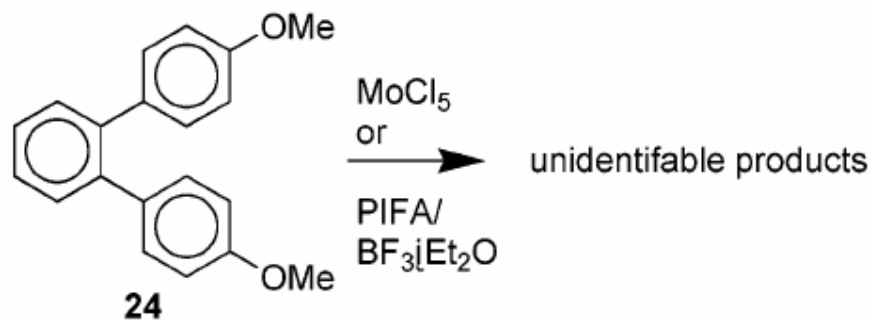
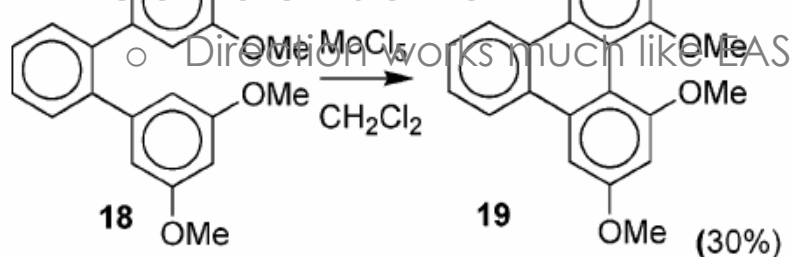
Controlling the Scholl Reaction

Conclusions

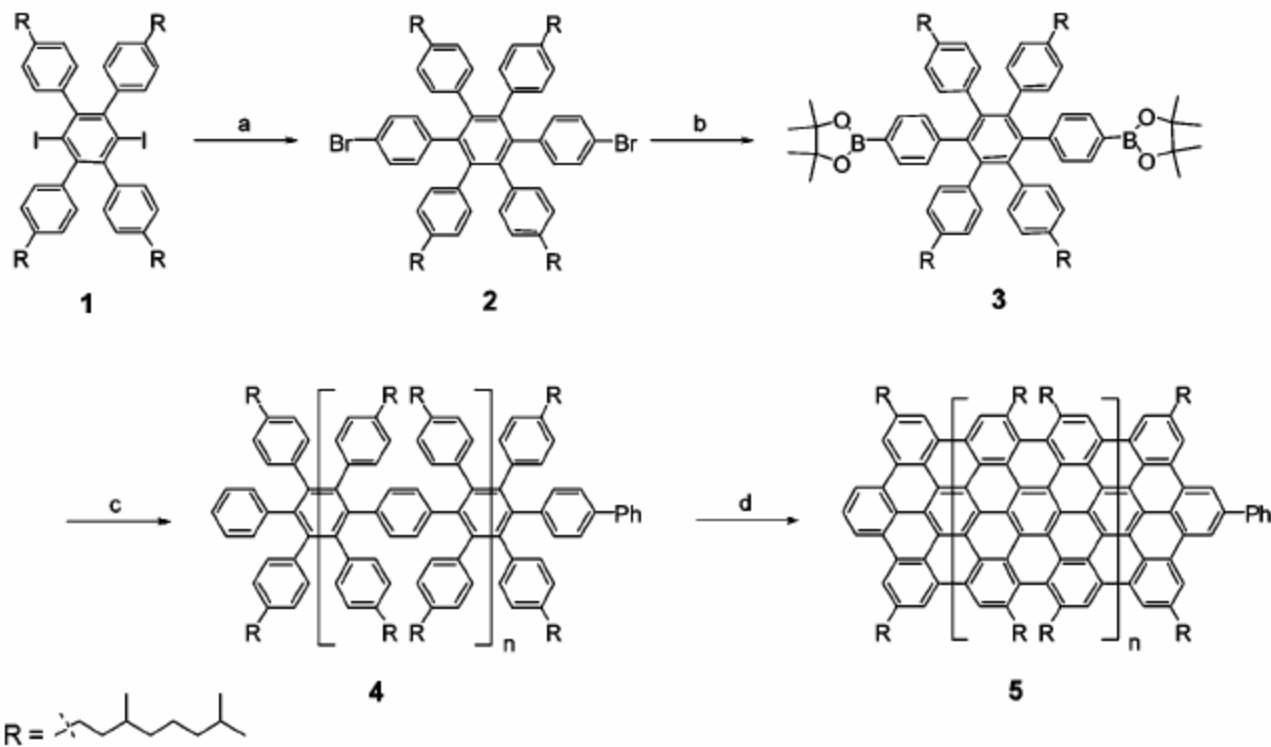
Small unfunctionalized arenes oligomerize



• Electron directing group condensation

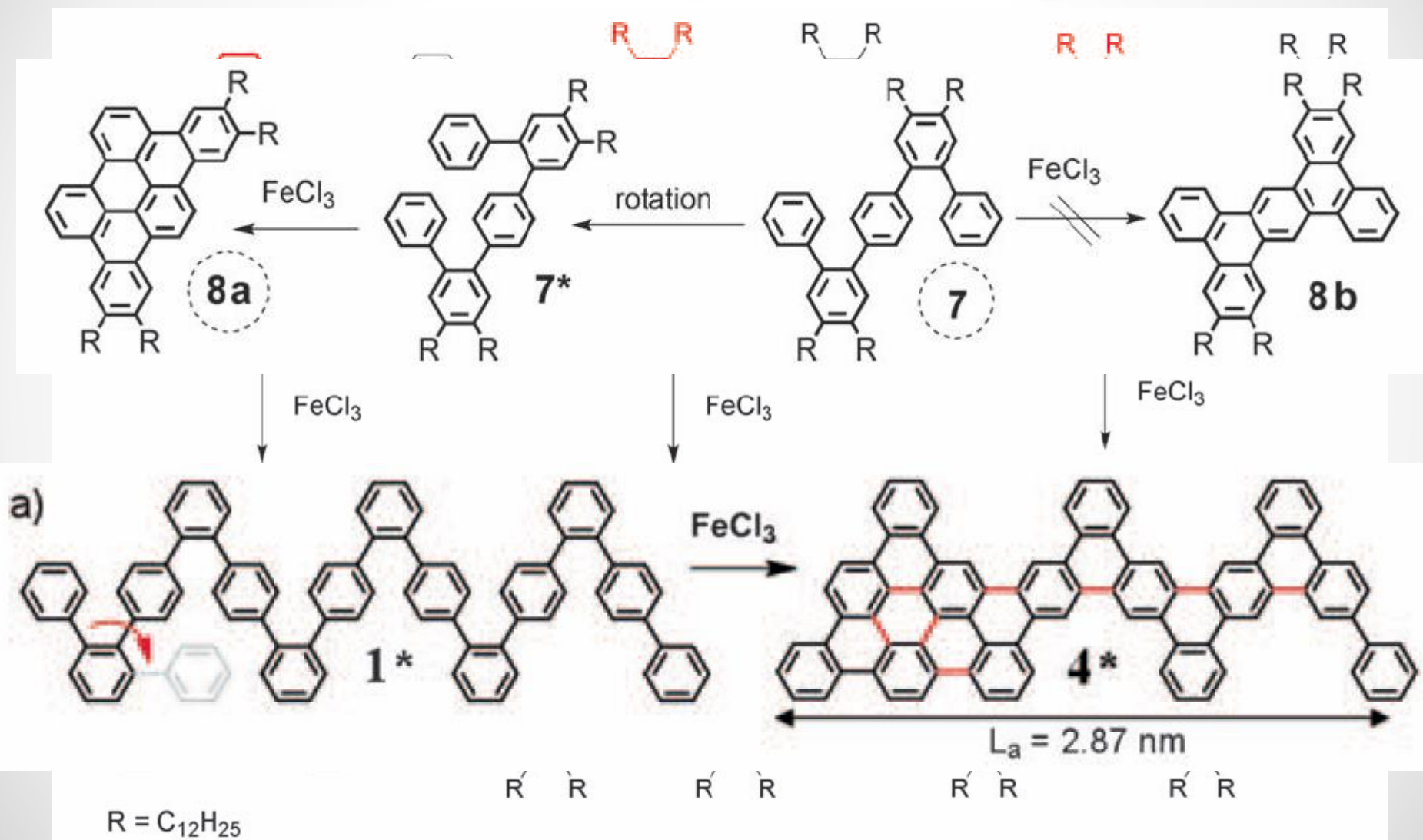


Interesting Examples



^a Reagents and conditions: (a) 4-bromophenylboronic acid, Pd(PPh₃)₄, aliquat 336, K₂CO₃, toluene, 80 °C, 24 h, 93%. (b) (i) *n*-BuLi, THF, -78 °C, 1 h; (ii) 2-isopropoxy-4,4,5,5-tetramethyl[1,3,2]dioxaborolane, rt, 2 h, 82%. (c) compound 1, Pd(PPh₃)₄, aliquat 336, K₂CO₃, toluene/H₂O, reflux, 72 h, 75%. (d) FeCl₃, CH₂Cl₂/CH₃NO₂, 25 °C, 48 h, 65%.

Interesting Examples



- Dossel, L.; Gherghel, L.; Feng, X.; Mullen, K. *Angew. Chem. Int. Ed.* **2011**, *50*, 2540-2543.

Interesting Examples

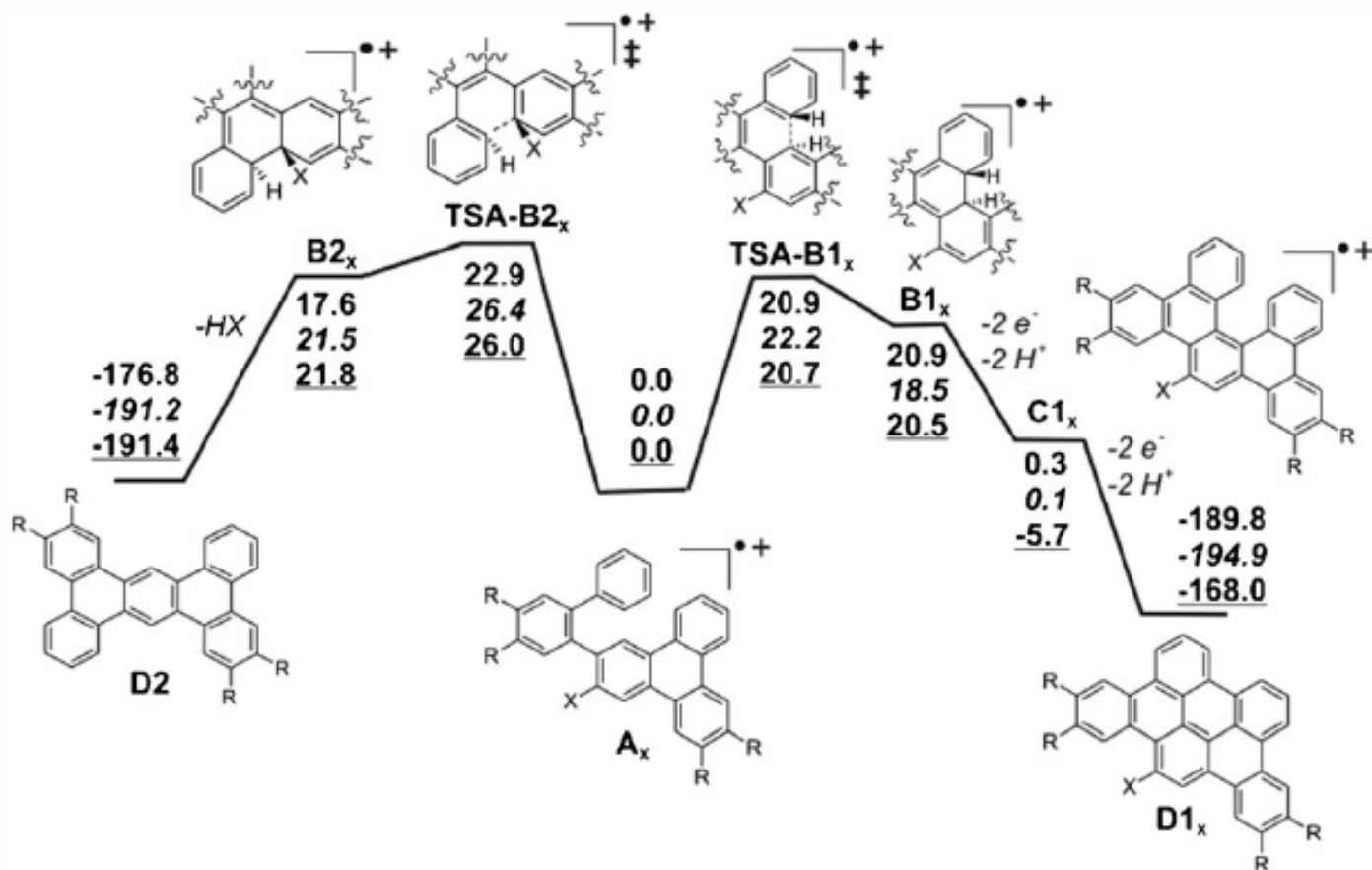
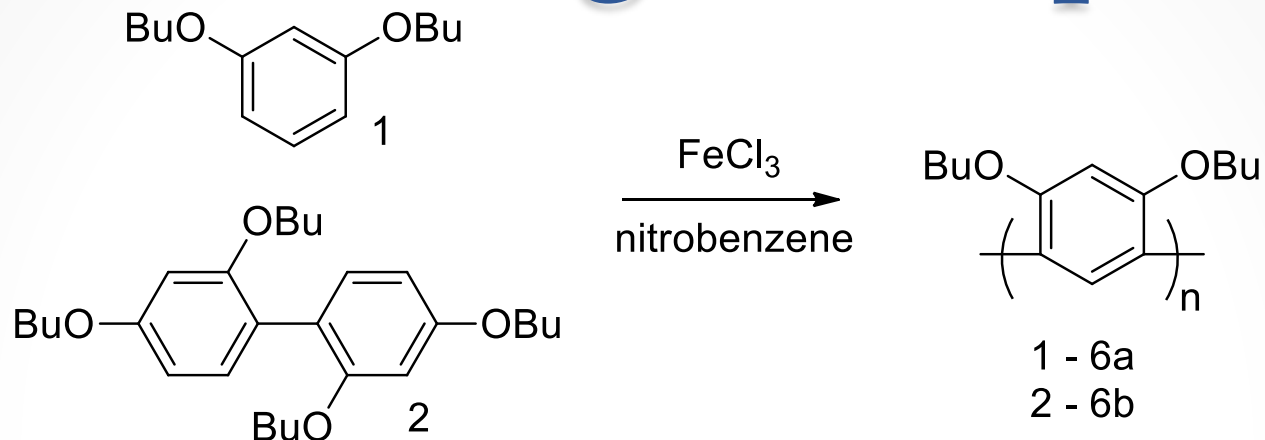


Fig. 1 Free energies ΔG (LC- ω PBE/def2-SVP) for the selectivity-determining transition states relative to A_x ($X = H, F, OMe$ (underlined values); $R = Me$).

Interesting Examples



Entry No.	Monomer	Polymer	FeCl_3 (Equiv.)	Yield (%)	M_n^b	M_w/M_n^b
1	1	6a	2	41	4,000	1.4
2	1	6a	3	70	5,000	2.8
3	1	6a	4	77	12,000	2.8
4	1	6a	5	80	15,000	3.6
5	3	6b	2	85	11,000	1.8
6	3	6b	4	89	42,000	2.1

^a Reaction condition: 1.0 mmol of monomer, Reaction time = 20 h, solvent = Nitrobenzene 2.0 mL (Entry No. 5 and 6 = 4.0 mL), room temperature, N_2 atmosphere.

^b Measured by GPC on standard PST.

- Okada, T.; Fujiwara, N.; Ogata, T.; Haba, O.; Ueda, M. *J. Polym. Sci. A*. **1997**, 2259.

Interesting Examples

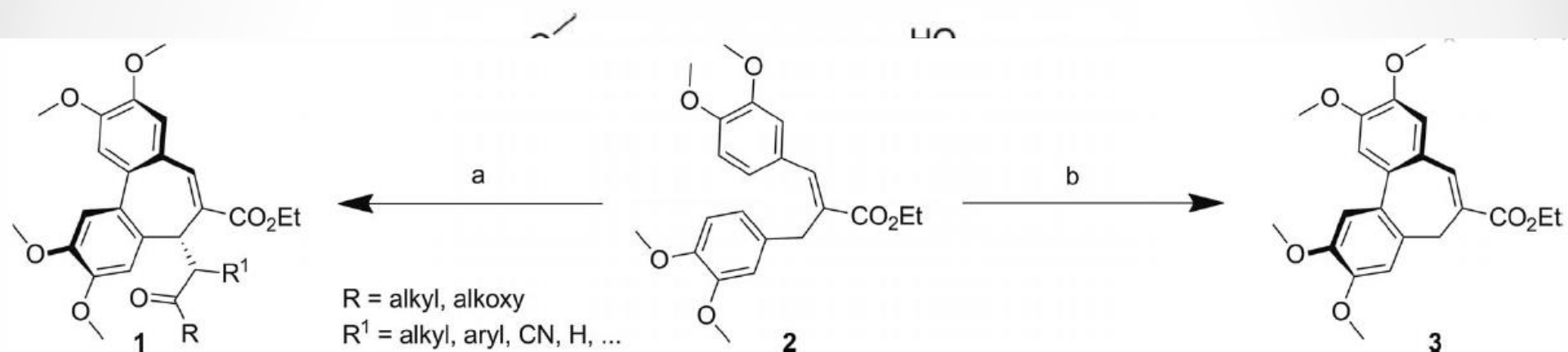


Figure 1. Oxidant-dependant reaction pathway: (a) MoCl₅, TiCl₄ then R¹CH₂COR, NEt₃; (b) PIFA, BF₃·OEt₂.
 (aR,7S)-alcolchicine metasequinin-B

Summary

- Long history, since 1910, but most applications have been during the last decade.
- The mechanism is controversial
 - Radical Cation Vs. Arenium Cation
 - Support for both
 - Rearrangement is possible for intermediates
- Scholl reactions have been used in polymerizations, synthesis of graphene nanoribbons, and the formation of a natural product core structure

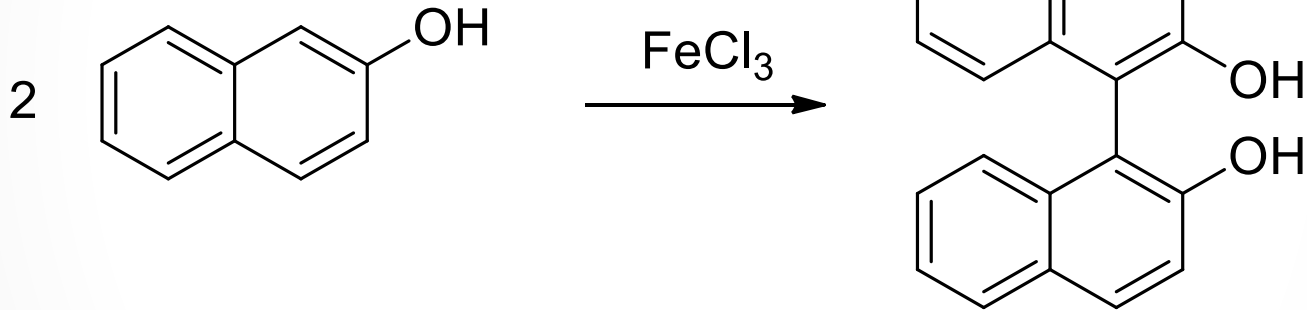
THANKS!!!



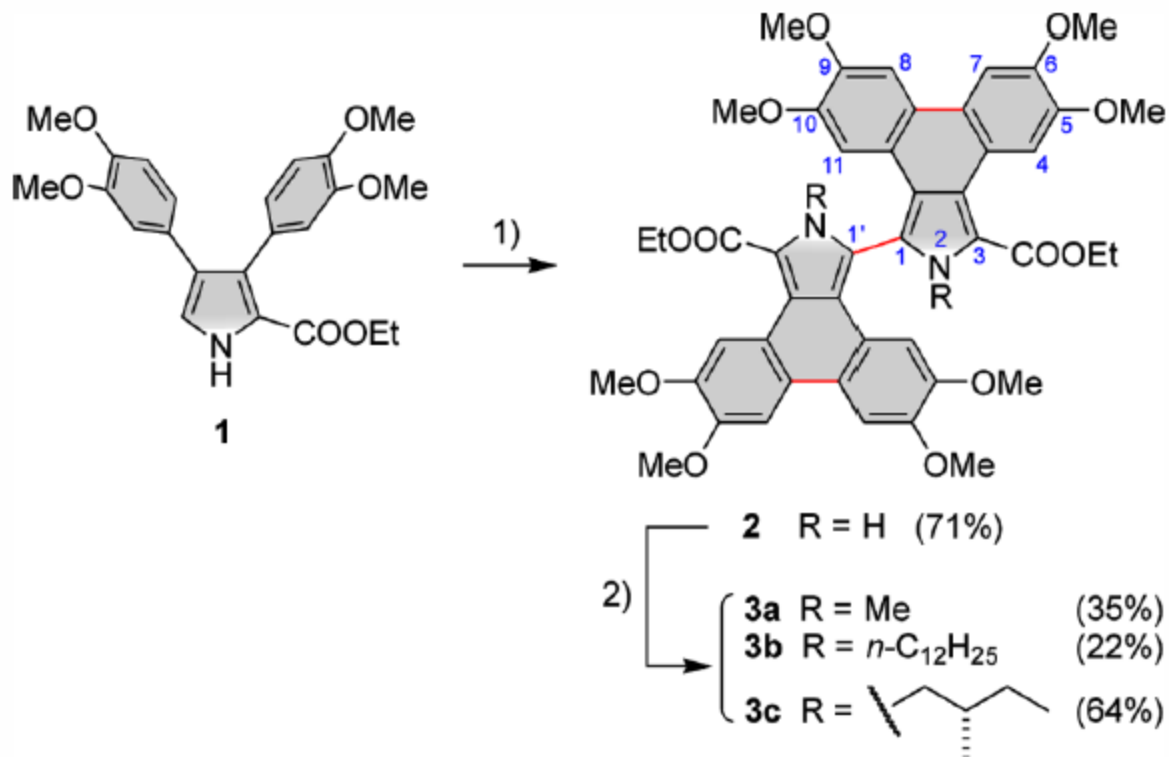
Question Time

Volunteers???

Question 1

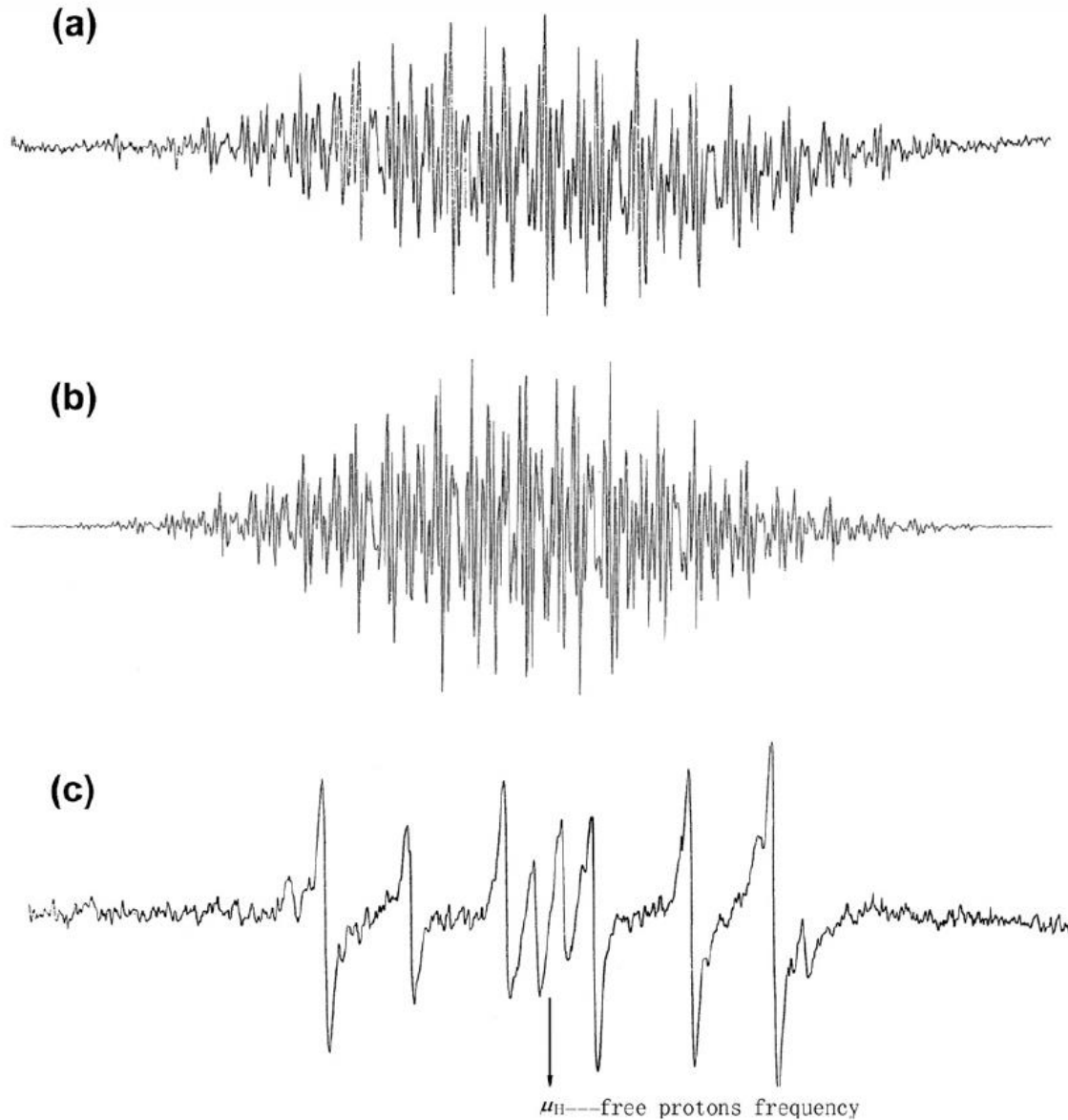


Question 2



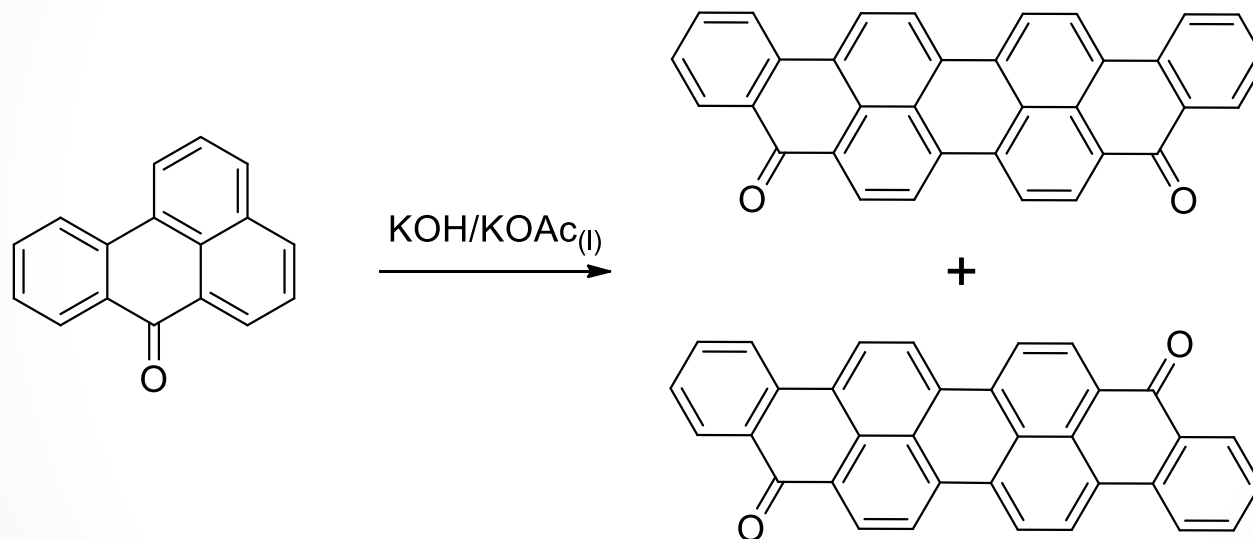
^aReagents and conditions: (1) FeCl_3 (4 equiv), CH_2Cl_2 , 22 h, 71%; (2) RBr (**3b**) or RI (**3a**, **3c**), K_2CO_3 , 18-crown-6, 22–63%.

Question 3

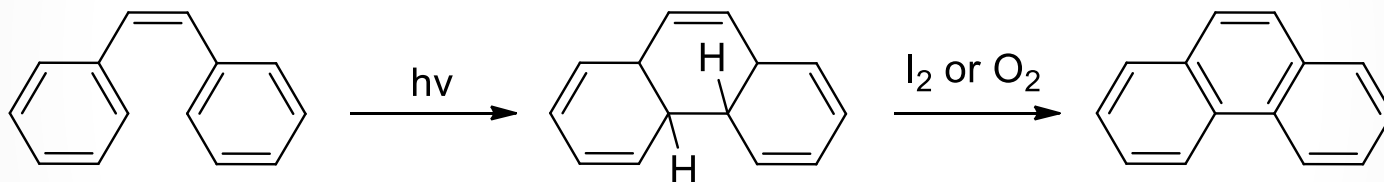


g. 1. (a) Experimental EPR spectrum of $\text{R1}^{\bullet+}$. (b) Simulated spectrum, using the EXP parameters reported in Table 3. (c) Experimental ENDOR spectrum of $\text{R1}^{\bullet+}$.

Related Reactions

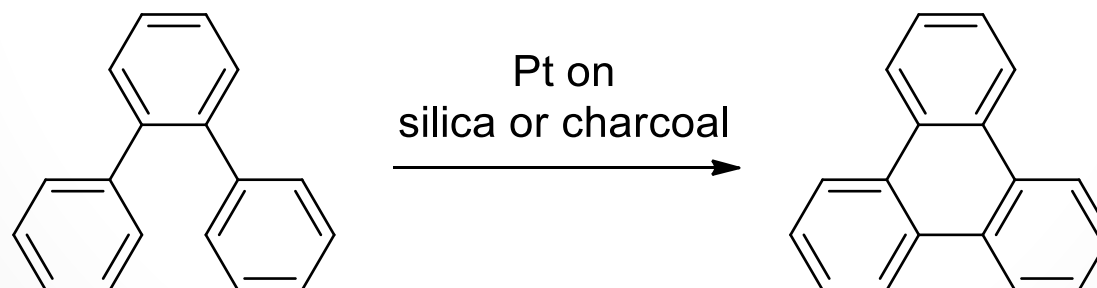
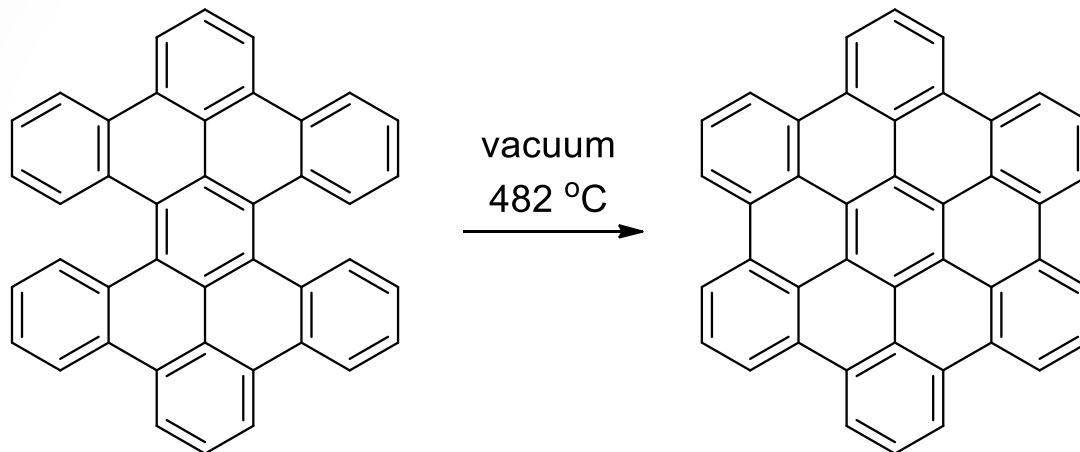


Related Reactions



- Mallory, F. B.; Wood, C. S.; Gordon, J. T.; Lindquist, L. C.; Savitz, M. L. *J. Am. Chem. Soc.* **1962**, *84*, 4361-4362. ●

Related Reactions



Clar, E.; Ironside, C. T.; Zander, M. J. *Chem. Soc.* **1959**, 142-148.

Copeland, P. G.; Dean, R. E.; McNeil, D. J. *Chem. Soc.* **1960**, 1687-1689.

Hansch, C.; Geiger, C. F. *J. Org. Chem.* **1958**, 23, 477-478.

Arenium Cation Calculations

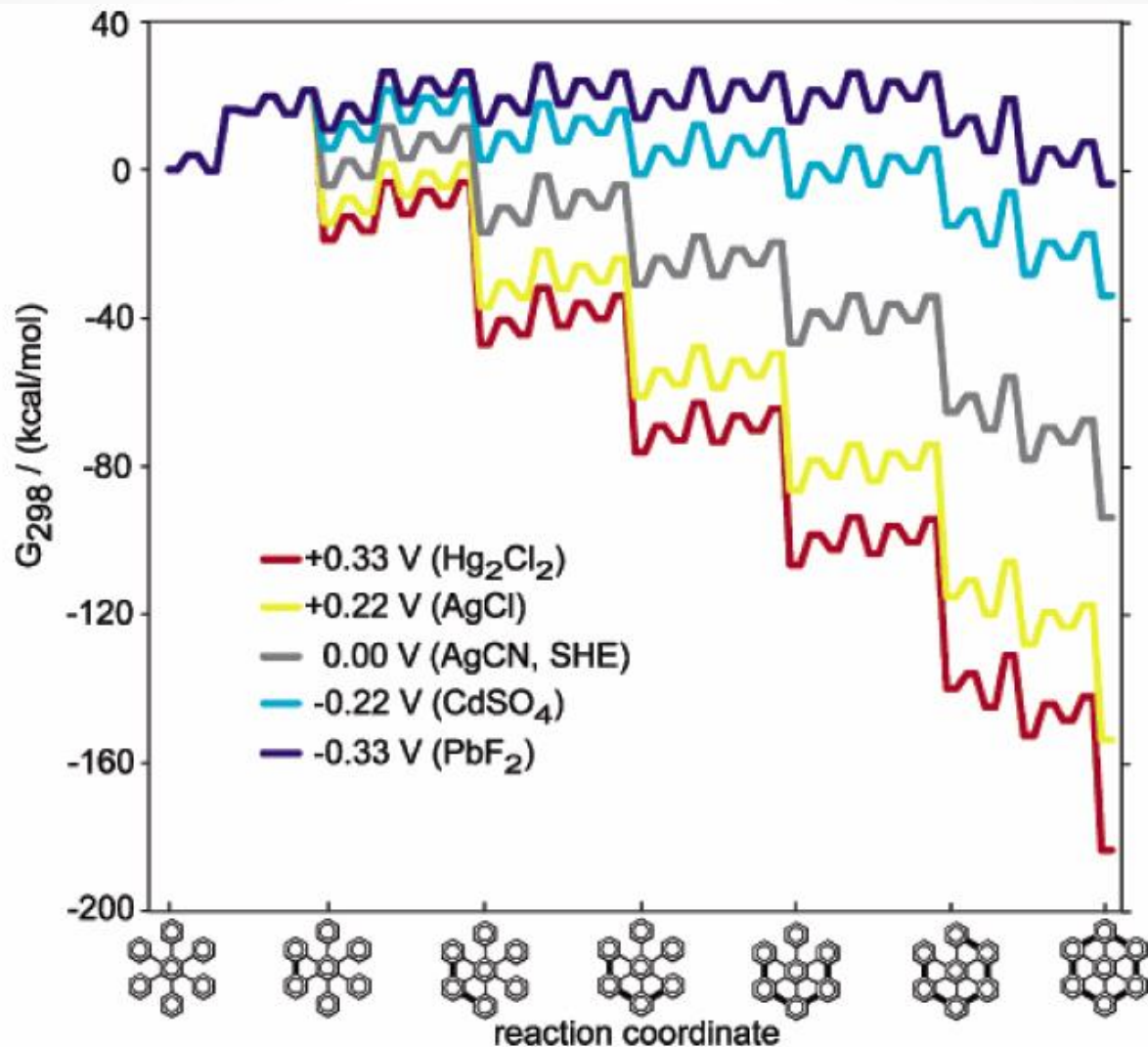


FIGURE 6. Influence of the oxidant strength (defined as $\Delta_r G(O_{(\text{sol})} + \text{H}_{2(\text{sol})} \rightarrow \text{OH}_{2(\text{sol})})$).