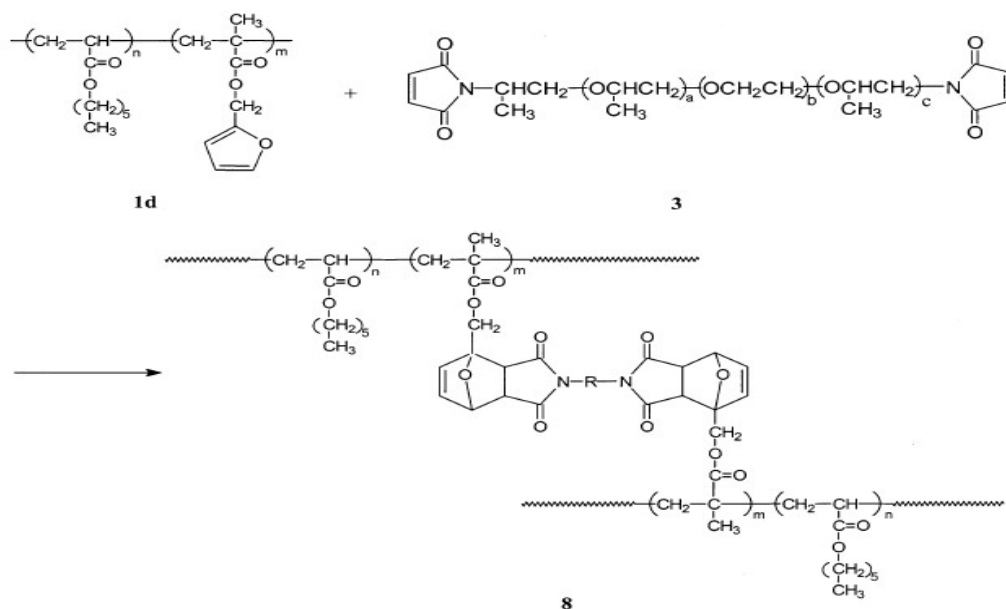


Diels-Alder Reactions of Furan

By: Robert B. Login rloginconsulting.com

Reversible DA Reactions:

DA reversible reactions of furans and maleimides are a type of “click” reaction that can proceed at some lower temperature only to be reversed at a higher temperature. This DA reaction can be applied to a variety of applications for example reversible hair fixatives. Lets review several of these furan-maleimide approaches: (The oldest reference for this reaction is Craven, James M. "Cross-linked thermally reversible polymers produced from condensation polymers with pendant furan groups cross-linked with maleimides." U.S. Patent No. 3,435,003. 25 Mar. 1969.)



Scheme 4. Cross-Linking Diels-Alder Reaction of Copolymers 4 with the Difuran Compound 5 as the Cross-Linking Agent

(1)

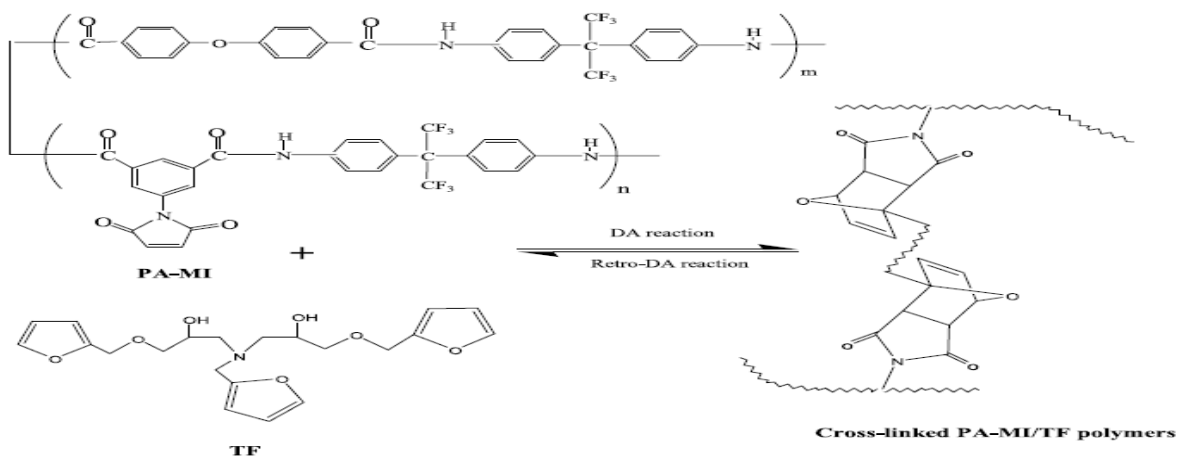


Fig. 1. Preparation of thermally-reversible polyamides.

(2)

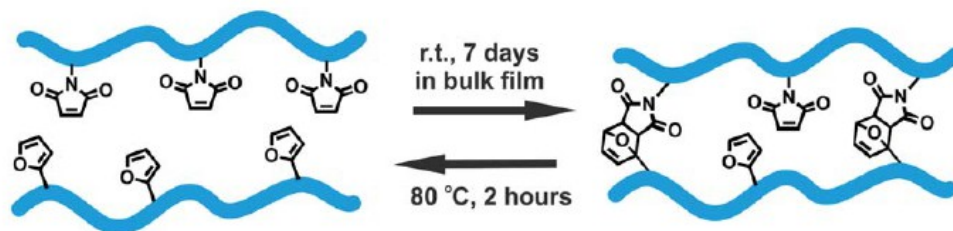
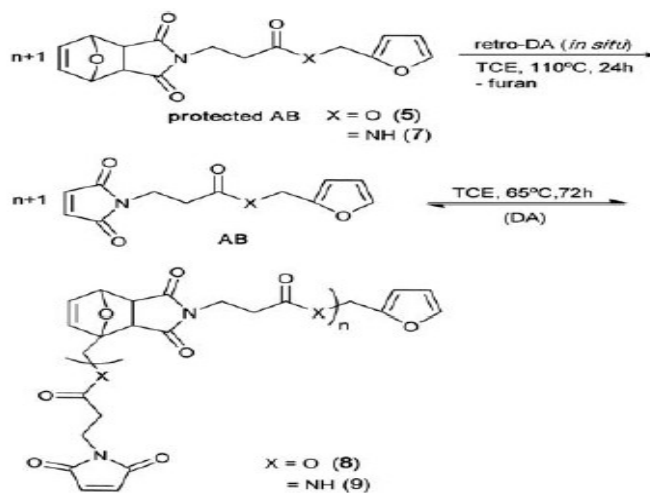


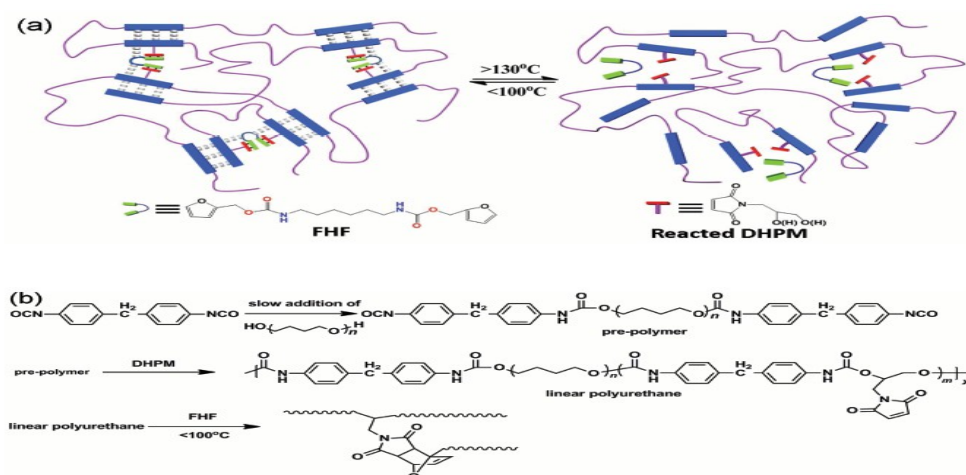
Fig. 11 Example of a re-mendable network with furan and maleimide pendant end groups *via* DA cycloaddition reactions.

(3)



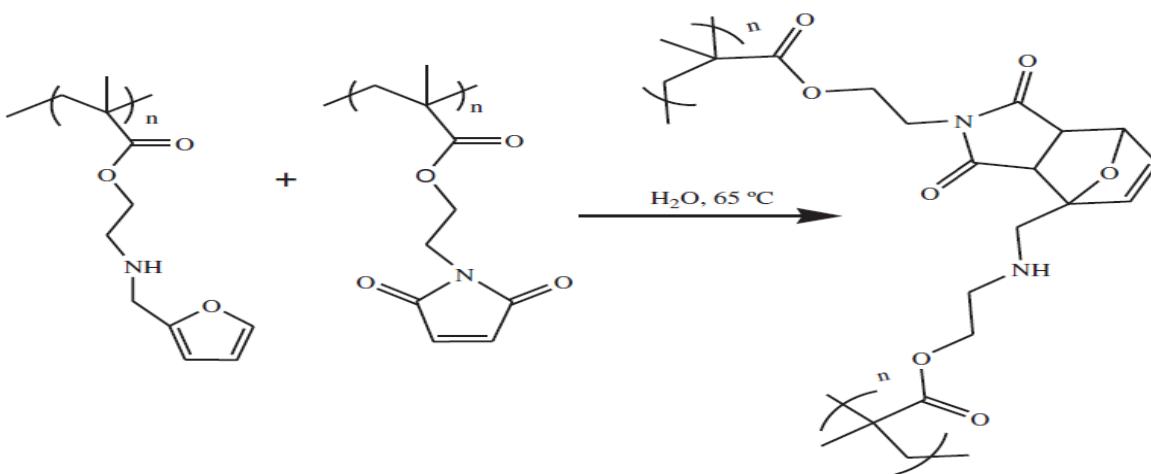
Scheme 3 Deprotection of the AB monomers and their DA polymerization.

(4)



Scheme 1. (a) Schematic view of reversible covalent cross-linked network formed by DA reaction between H-bonding hard segments to enhance network mechanical properties. (b) Synthesis pathway of recyclable cross-linked polymers (DAPUs)

(5)



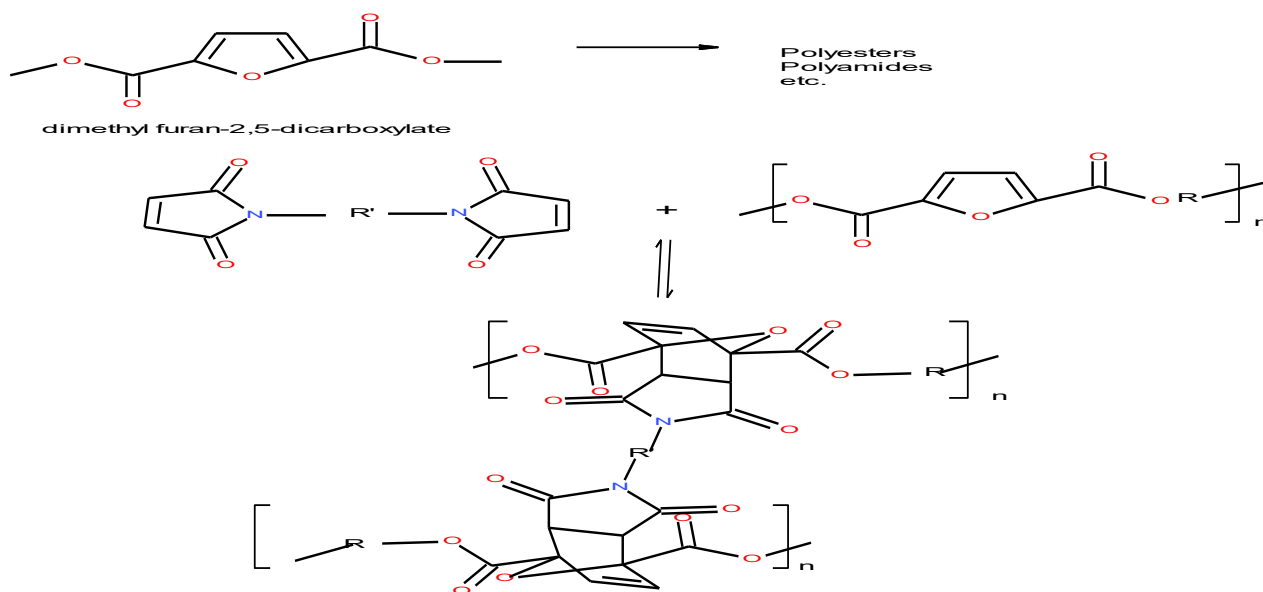
Scheme 3. Diels Alder reaction between pAEMA:furan and pAEMA:maleimide.

(6) above and others (7-18)

The above is just a sample of the extensive literature concerning reversible DA reactions.

Can this reversible DA reaction have hair care applications. As a reversible cross-linking mechanism, it would enhance fixative properties but this would be reversible with the heat of a curling iron. For example, a Gafquat type copolymer with one of these previously discussed suitable reversible DA reactions would fit this idea.

All of the above references have things in common, the Diels-Alder components are either terminal or pendant to the polymer chain. I have found only one reference where the Diels-Alder component is in the polymer backbone. This seems like an obvious idea so why only the one reference? For example:

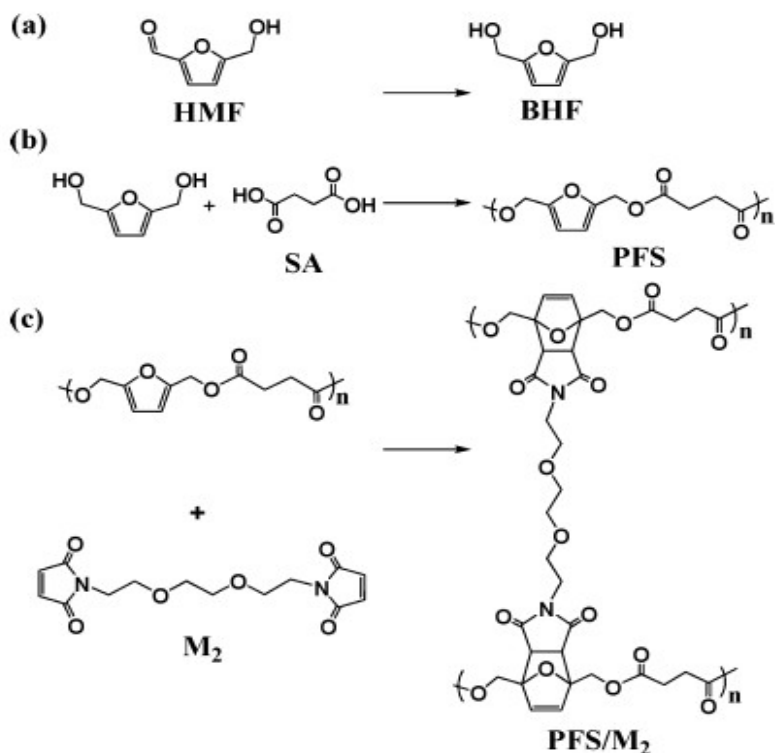


Scheme 1

Apparently the above scheme doesn't work because the carboxylic esters reduce the electron density in the furan ring making it a less attractive DA diene. DA dieneophiles can be enhanced in reactivity with transition metal derivatives. Could such enhanced dieneophiles work with the above scheme 1 furan dicarboxylates? Can the dicarboxylates be moved further away from the furan ring or can the 3,4 furan dicarboxylates react because the carboxylates are attached to carbons away from the furan ring oxygen? Actually 3,4-furan reacts very well with dieneophiles.(19-20)

As the following shows, the hydroxyl derivatives work as DA dienes.

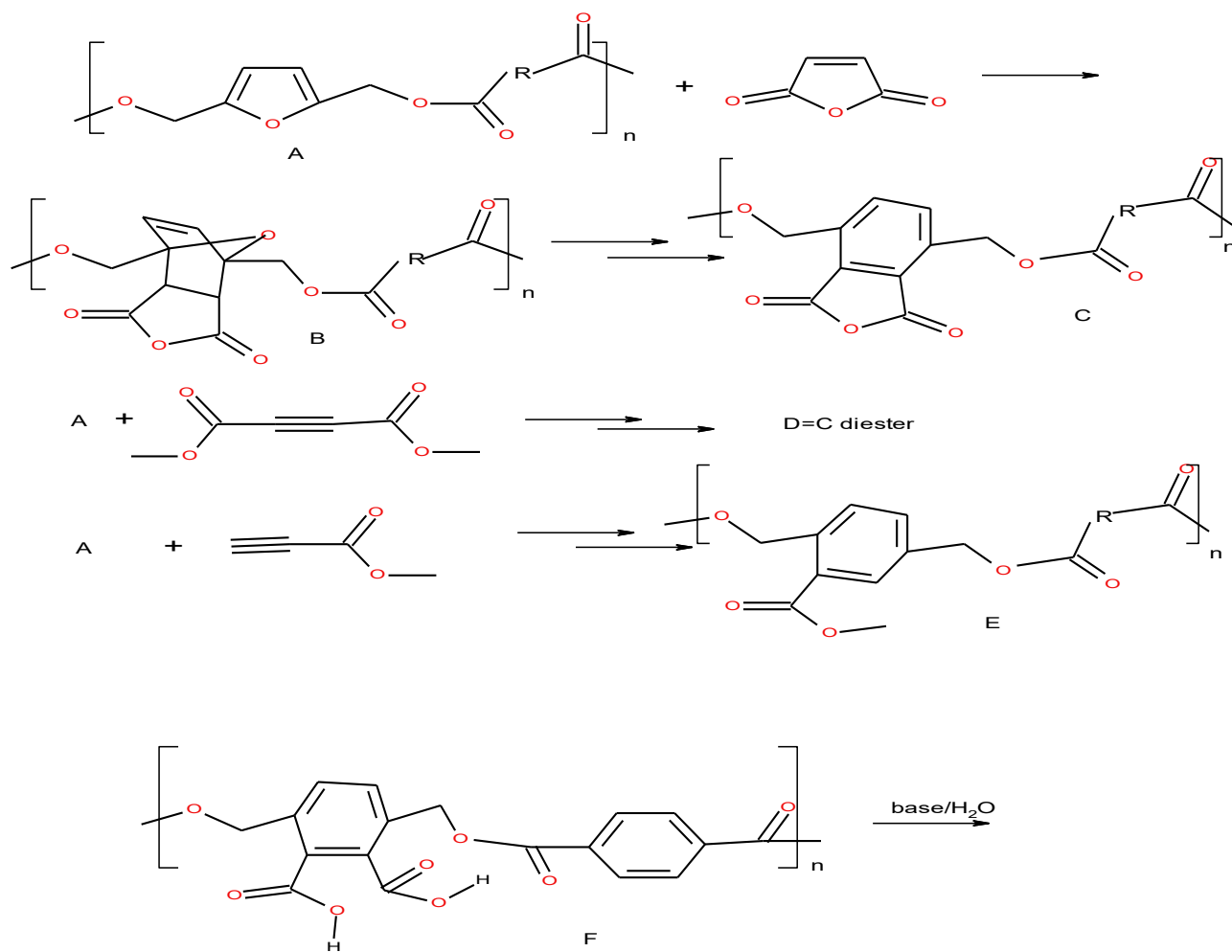
Scheme 1. Synthesis of BHF, PFS, and PFS/M₂



PFS as shown, is DA reactive.(21-22)

Maleic Anhydride and Benzene derivatives:

PFS can be employed in other DA reactions with strong dieneophiles like maleic anhydride. For example:

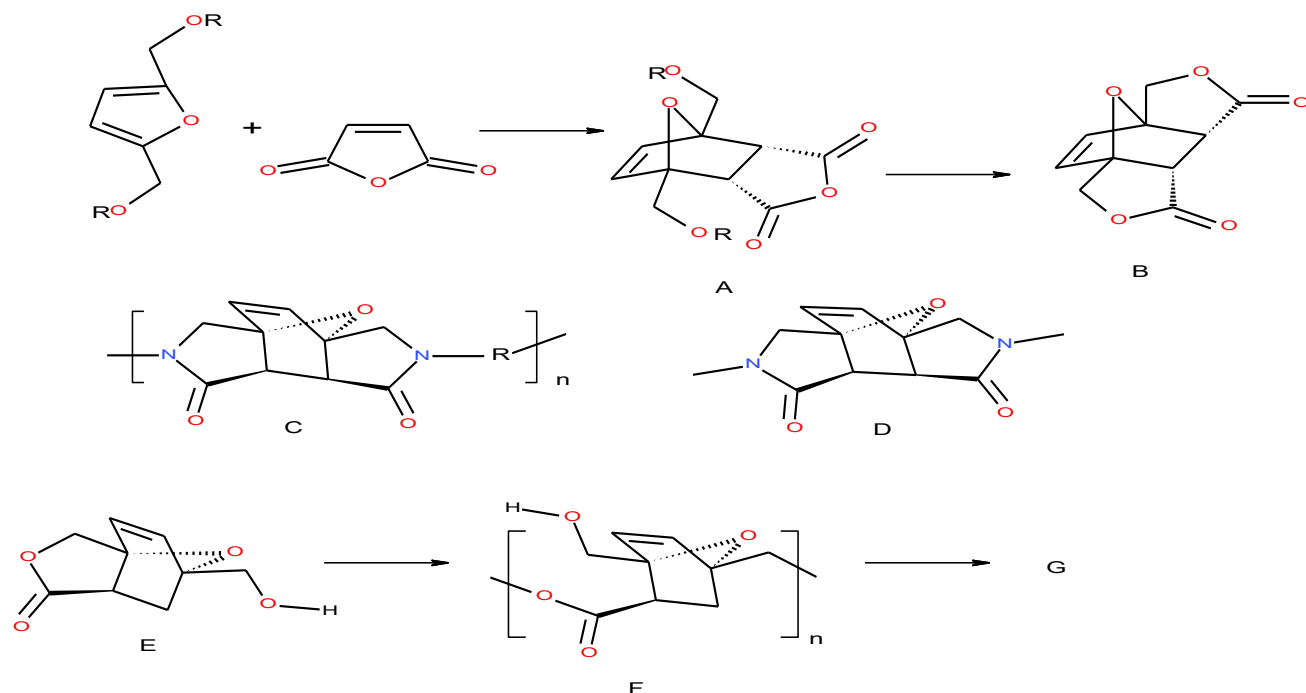


Scheme 2 Possible aromatic derivatives.

7-Oxanorbornenes are readily converted to aromatic derivatives with acidic catalysis. Might acetylene work by itself to go more readily to the benzene derivative since many references show that even relatively unreactive ethylene reacts with furans under the right conditions and will form the benzene derivative.

Polymers E and F above should be water soluble in their carboxylate form. I would expect them to also be readily hydrolytically degradable because of the location of the carboxylate vs. the ester backbone. This could be a way to degradable PET plastics by putting enough of these repeat units in the PET backbone to do the job. When exposed to sea water for example, they would hydrolyze the anhydrides and cause polymer hydrolysis by **anchimeric assistance**.(23-26)

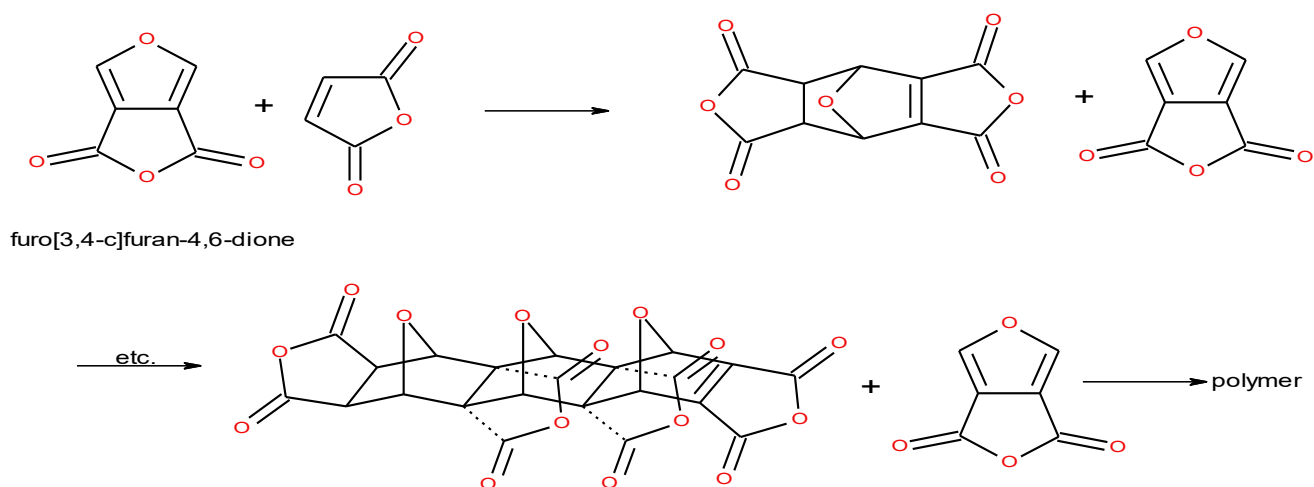
This suggests another possible synthesis:



Scheme 3: Alcohol groups would initially need to be protected. D is a monomeric bis imide. E is the adduct of acrylates.

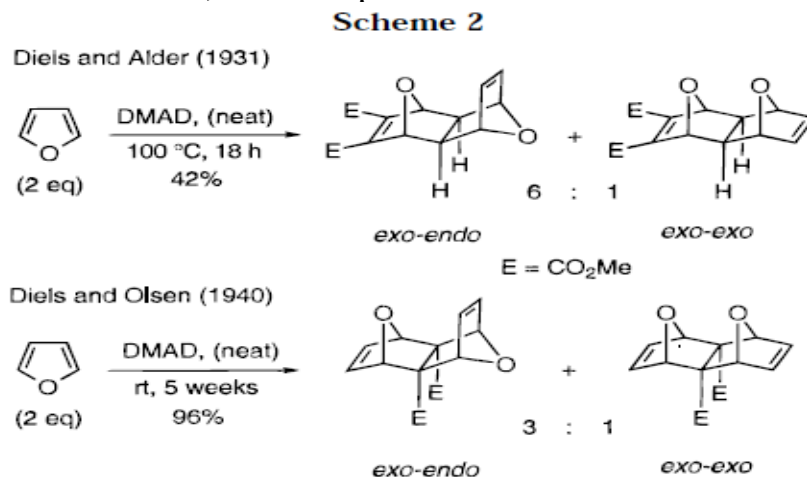
In this case, the alcohols are protected with removable R groups which when removed allow the esters or amides to form. If treated with acidic reagents, the resulting oxanorbornenes can be transformed into benzene rings. Compound B would therefore be a very versatile reactant.

Further ideas as in scheme 4 seems related to the “Pincer” DA reaction.



Scheme 4

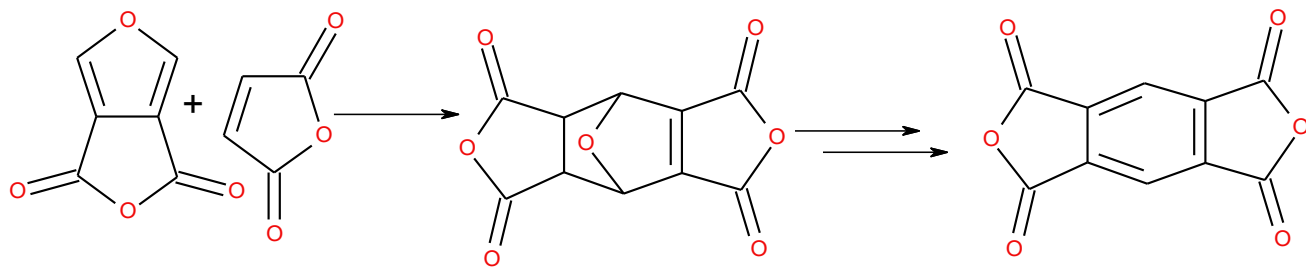
3,4 furan dicarboxylic acid is a known compound that can be converted to the anhydride. I'm suggesting that the DA reaction with maleic anhydride initiates a chain reaction to form the above polymer. MW would be controlled by the amount of maleic anhydride or other suitable dieneophile used to start the reaction. This proposed DA reaction is somewhat similar to "Pincer" DA's, for example:



(27-28)

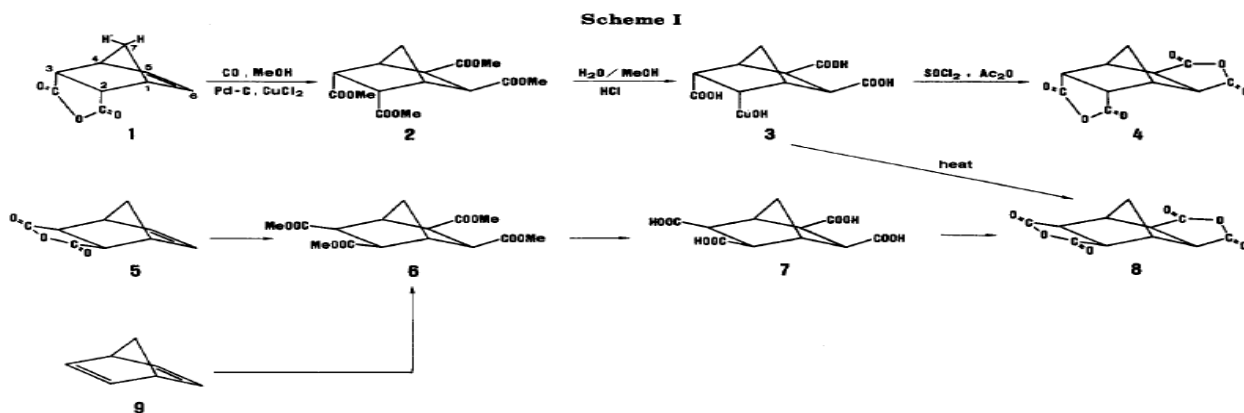
As can be seen in the above scheme, that my scheme 3 proposal might have a more complicated stereochemistry than I have proposed but the idea is the same.

The 3,4 furan dicarboxylic anhydride could also be converted to the aromatic tetracarboxylic dianhydride, a valuable polyimide component.



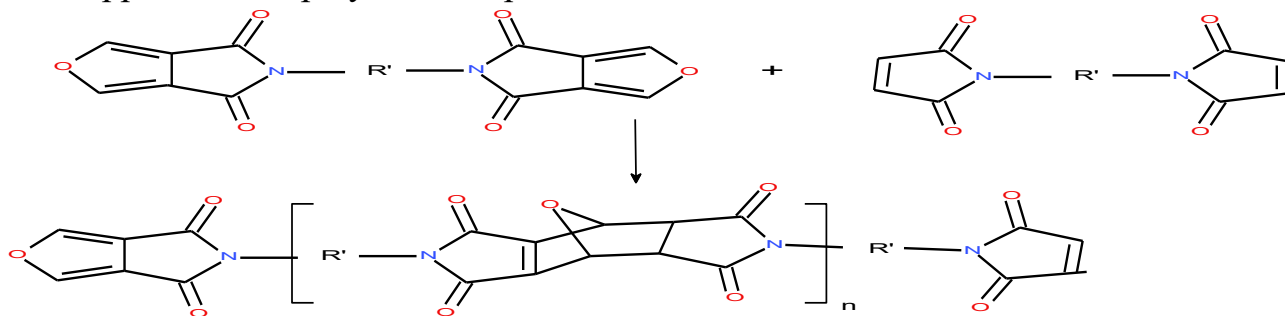
Scheme 5

Or this is a simpler approach to aliphatic bis-anhydrides vs. the following scheme?



All that would have to be done is the hydrogenation of the scheme 5 illustrated double bond.

Other approaches to polymers are possible.

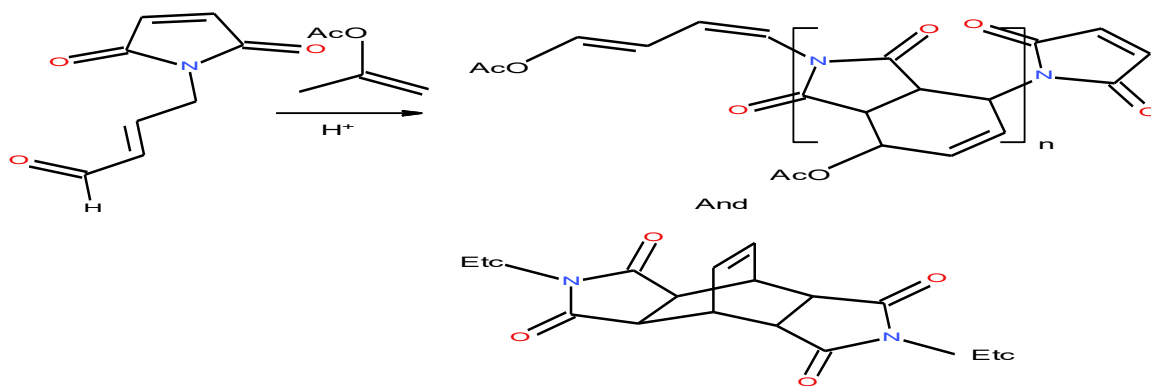


Scheme 6: The above polyimide can be post converted to the aromatic derivative, a new method of synthesizing polyimide plastics.

In conclusion, derivatives of Oxabicyclo[2.2.1]heptane are a significant area of organic chemistry; therefore, I would think that furan, a readily available RM from biomass should inspire new possibilities.(29-30)

The following idea is based on chemistry that Prof. Wolinsky and I developed in the 1960's.(31-32)

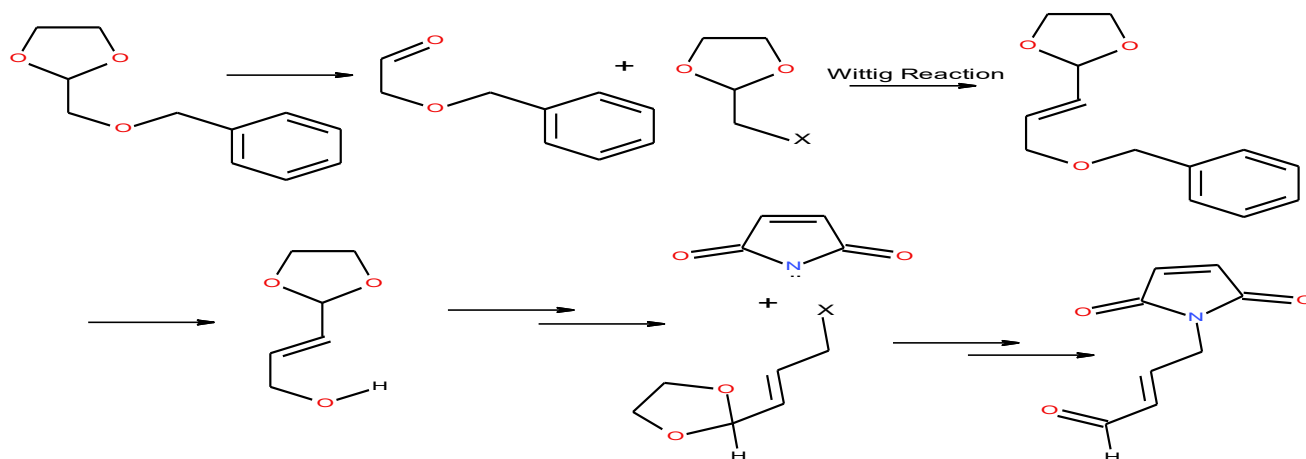
It is based on the reaction of the in-situ formation of a diene from an unsaturated carbonyl compound and isopropenyl acetate catalyzed by acid.



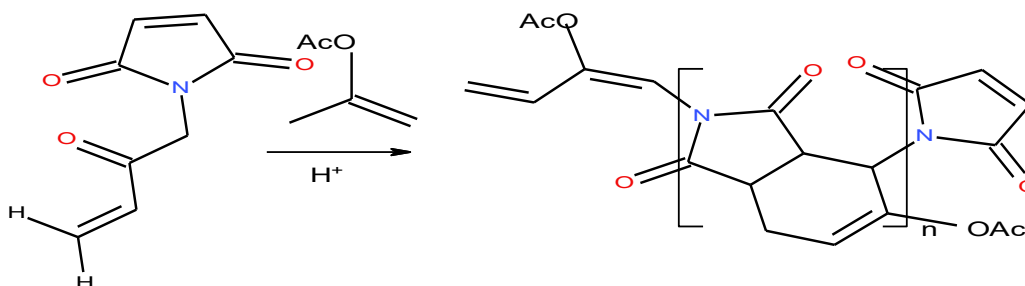
Scheme 7

The in-situ formed diene attached to the maleimide dieneophile results in a polymer that since the acetoxy cyclohexene can with heat lose acetic acid resulting in a cyclohexadiene that can also react to form a bicyclooctane cross-link. These DA reactions should be reversible forming “healable” polymers.

Scheme 8 is one suggested outline synthesis of the starting RM.



Scheme 8



Scheme 9

Alternative polymerization with the unsaturated ketone.

References:

1. Gheneim, Rana, Catalina Perez-Berumen, and Alessandro Gandini. "Diels–Alder reactions with novel polymeric dienes and dienophiles: synthesis of reversibly cross-linked elastomers." *Macromolecules*, 35.19 (2002): 7246-7253.
2. Liu, Ying-Ling, Chia-Yun Hsieh, and Yi-Wen Chen. "Thermally reversible cross-linked polyamides and thermo-responsive gels by means of Diels–Alder reaction." *Polymer*, 47.8 (2006): 2581-2586.
3. Tasdelen, Mehmet Atilla. "Diels–Alder “click” reactions: recent applications in polymer and material science." *Polymer Chemistry*, 2.10 (2011): 2133-2145.
4. Gandini, Alessandro, Armando JD Silvestre, and Dora Coelho. "Reversible click chemistry at the service of macromolecular materials." *Polymer Chemistry*, 2.8 (2011): 1713-1719.
5. Yu, Shen, et al. "Bio-Inspired High-Performance and Recyclable Cross-Linked Polymers." *Advanced Materials*, 25.35 (2013): 4912-4917.
6. García-Astrain, C., et al. "Green chemistry for the synthesis of methacrylate-based hydrogels crosslinked through Diels–Alder reaction." *European Polymer Journal*, 49.12 (2013): 3998-4007.
7. Bai, Nan, George P. Simon, and Kei Saito. "Investigation of the thermal self-healing mechanism in a cross-linked epoxy system." *RSC Advances*, 3.43 (2013): 20699-20707.
8. Du, Pengfei, et al. "Synthesis and characterization of linear self-healing polyurethane based on thermally reversible Diels–Alder reaction." *RSC Advances*, 3.35 (2013): 15475-15482.
9. Berg, Gayla J., et al. "A dual-cure, solid-state photoresist combining a thermoreversible Diels–Alder network and a chain growth acrylate network." *Macromolecules*, 47.10 (2014): 3473-3482.
10. García-Astrain, C., et al. "Diels–Alder “click” chemistry for the cross-linking of furfuryl-gelatin-polyetheramine hydrogels." *RSC Advances*, 4.67 (2014): 35578-35587.
11. Du, Pengfei, et al. "Diels–Alder-based crosslinked self-healing polyurethane/urea from polymeric methylene diphenyl diisocyanate." *Journal of Applied Polymer Science*, 131.9 (2014).
12. Rivero, Guadalupe, et al. "One-pot thermo-remendable shape memory polyurethanes." *Macromolecules*, 47.6 (2014): 2010-2018.
13. Chen, Shengli, et al. "A Single Molecular Diels–Alder Crosslinker for Achieving Recyclable Cross-Linked Polymers." *Macromolecular rapid communications*, 36.18 (2015): 1687-1692.
14. Roy, Nabarun, Bernd Bruchmann, and Jean-Marie Lehn. "DYNAMERS: dynamic polymers as self-healing materials." *Chemical Society Reviews*, 44.11 (2015): 3786-3807.
- Li, Jinhui, et al. "Thermally reversible and self-healing novolac epoxy resins based on Diels–Alder chemistry." *Journal of Applied Polymer Science*, 132.26 (2015).
15. Pramanik, Nabendu B., and Nikhil K. Singha. "Amphiphilic functional block copolymers bearing a reactive furfuryl group via RAFT polymerization; reversible core cross-linked micelles via a Diels–Alder “click reaction”." *RSC*

Advances", 6.3 (2016): 2455-2463.

16. Kuang, Xiao, et al. "Triple-shape memory epoxy based on Diels–Alder adduct molecular switch." *Polymer*", 84 (2016): 1-9.

17. Buonerba, Antonio, et al. "A Comprehensive Depiction of the Furan-Maleimide Coupling via Kinetic and Thermodynamic Investigations of the Diels-Alder Reaction of Poly (styrene–co-2-vinylfuran) with Maleimides." *ChemistrySelect*", 2.4 (2017): 1605-1612.

18. Polgar, Lorenzo Massimo, et al. "Thermoreversible Cross-Linking of Furan-Containing Ethylene/Vinyl Acetate Rubber with Bismaleimide." *Polymers*", 9.3 (2017): 81.

19. Weis, C. D. "Diene and Retrodiene Reactions of Electronegatively 3, 4-Disubstituted Furans." *The Journal of Organic Chemistry*", 27.10 (1962): 3520-3524.

20. Vogel, Pierre. "Combinatorial Diels-Alder approach to the synthesis of anti-tumor anthracyclines and analogues." *Current Organic Chemistry*", 2.LGSA-ARTICLE-1998-004 (1998): 255-280.

21. Zeng, Chao, et al. "Bio-based furan polymers with self-healing ability." *Macromolecules*", 46.5 (2013): 1794-1802.

22. Gandini, Alessandro. "Furans as offspring of sugars and polysaccharides and progenitors of a family of remarkable polymers: a review of recent progress." *Polymer Chemistry*", 1.3 (2010): 245-251.

23. Koehle, Maura, et al. "Production of p-Methylstyrene and p-Divinylbenzene from Furanic Compounds." *ChemSusChem*", 10.1 (2017): 91-98.

24. Patet, Ryan E., et al. "Kinetic regime change in the tandem dehydrative aromatization of furan Diels–Alder products." *ACS Catalysis*", 5.4 (2015): 2367-2375.

25. Padwa, Albert, et al. "Diels–Alder Reaction of 2-Amino-Substituted Furans as a Method for Preparing Substituted Anilines." *The Journal of Organic Chemistry*", 62.12 (1997): 4088-4096.

26. Mahmoud, Eyas, et al. "Diels–Alder and Dehydration Reactions of Biomass-Derived Furan and Acrylic Acid for the Synthesis of Benzoic Acid." *ACS Catalysis*", 5.11 (2015): 6946-6955.

27. Lautens, Mark, and Eric Fillion. "An expedient route for the stereoselective construction of bridged polyheterocyclic ring systems using the tandem "pincer" Diels–Alder reaction." *The Journal of organic chemistry*", 62.13 (1997): 4418-4427.

28. Danishefsky, S., and T. Kitahra. "Diels-Alder route to cis-fused. DELTA. 1-3-octalones." *The Journal of Organic Chemistry*", 40.4 (1975): 538-539.

29. Vogel, Pierre, et al. "Derivatives of 7-oxabicyclo [2.2. 1] heptane in nature and as useful synthetic intermediates." *Tetrahedron*", 55.48 (1999): 13521-13642.

30. Puerto Galvis, Carlos E., Leonor Y. Vargas Méndez, and Vladimir V. Kouznetsov. "Cantharidin-Based Small Molecules as Potential Therapeutic Agents." *Chemical biology & drug design*", 82.5 (2013): 477-499.

31. Wolinsky, Joseph, and Robert B. Login. "Novel route to bicyclo [2.2. 2] octenetetracarboxylic acid dianhydrides." *The Journal of Organic Chemistry*", 37.1 (1972): 121-125.

32. Wolinsky, Joseph, and Robert B. Login. "Diels-Alder reaction of acetoxy-1, 3-dienes with dimethyl acetylenedicarboxylate and chloromaleic anhydride. Synthesis of benzene derivatives." *The Journal of Organic Chemistry*, 35.10 (1970): 3205-3207.

Thank you for reading these proposals.
Dr. Robert B. Login rloginconsulting.com