Polymeric Inverse-Electron-Demand Diels-Alder Reactions

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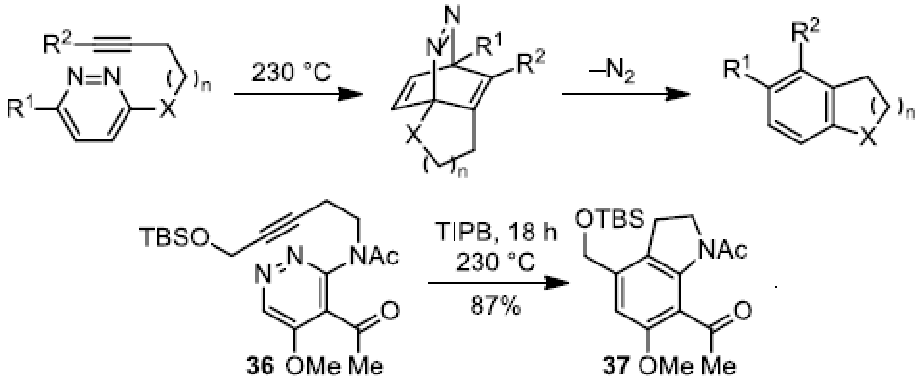
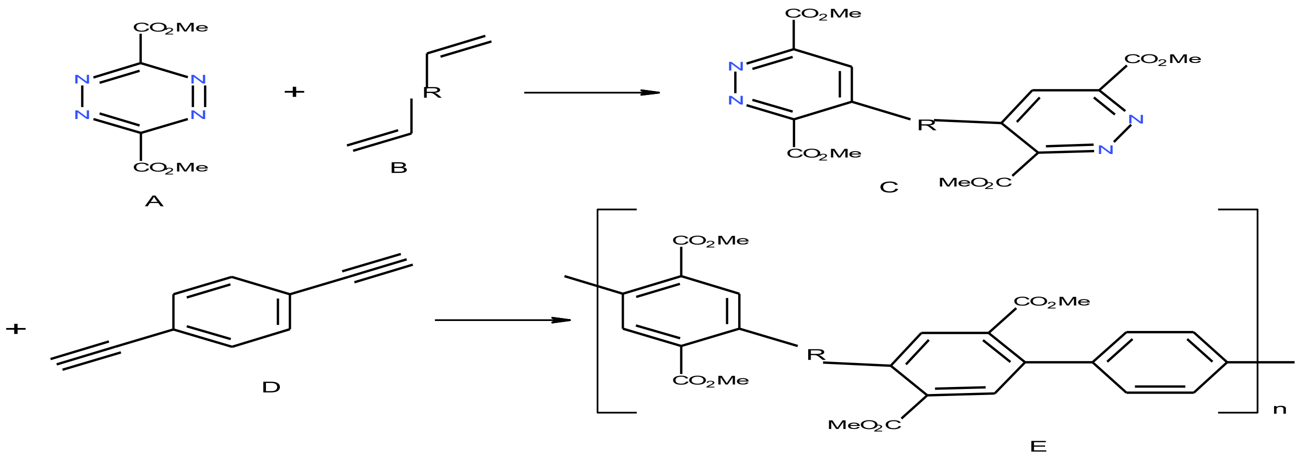
To start my discussion, two dieneophiles can react independently with a potential dienes. I base this idea on the fact that a diene can react with certain dieneophiles faster than with other less reactive dieneophiles. After the first DA reaction, with the first diene structure(s-tetrazine), a second DA reaction can occur. Boger etc. has used this idea that he and his colleagues refer to as “tandem” DA reactions.



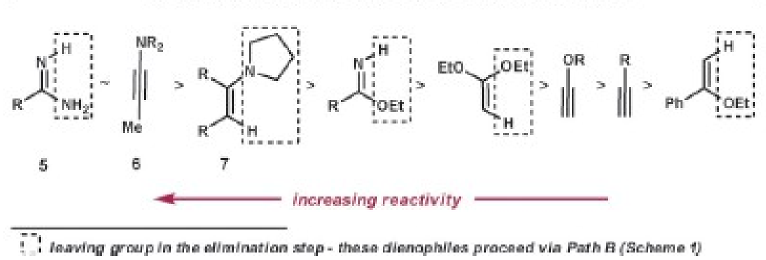
Zhang, J., Shukla, V., & Boger, D. L. (2019). Inverse Electron Demand Diels–Alder Reactions of Heterocyclic Azadienes, 1-Aza-1, 3-Butadienes, Cyclopropenone Ketals, and Related Systems. A Retrospective. *The Journal of organic chemistry*, *84*(15), 9397-9445.

The pyridazine was prepared from an s-tetrazine and hence the idea of two DA or tamdom reactions. However there is nothing in this reference about preparing polymers by tandom iEDDA's. For example:



Scheme 1: a general polymer synthesis idea(oxidation step is assumed). So if R is aromatic then the resulting polymer would be polyaromatic. Other s-tetrazines can also be used but those with electron withdrawing groups are more reactive.

Its possible, I believe, that both of the above dieneophiles can be present at the same time with the faster one reacting first followed by the less reactive as the temperature is raised. Hence orthogonal dieneophiles.



Foster, R. A., & Willis, M. C. (2013). Tandem inverse-electron-demand hetero-/retro-Diels–Alder reactions for aromatic nitrogen heterocycle synthesis. *Chemical Society Reviews*, *42*(1), 63-76.

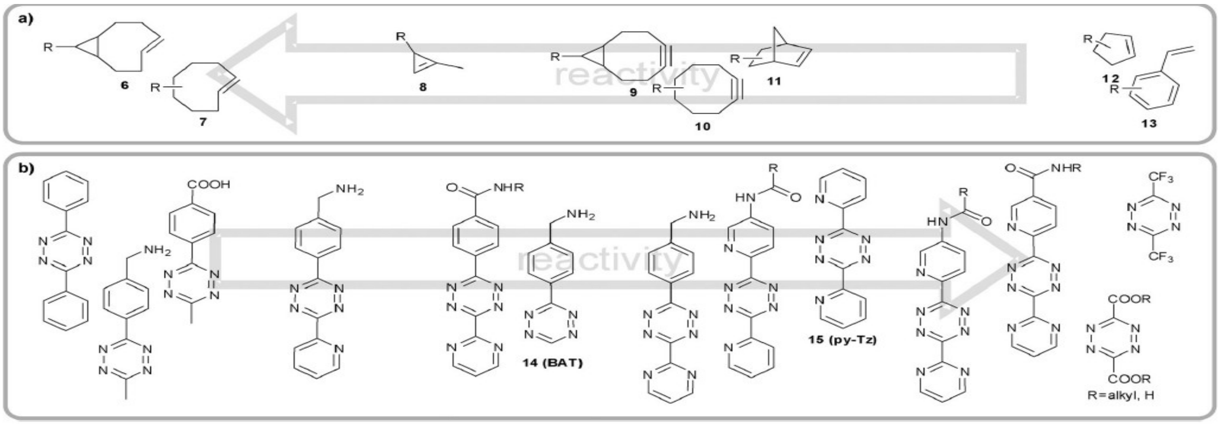
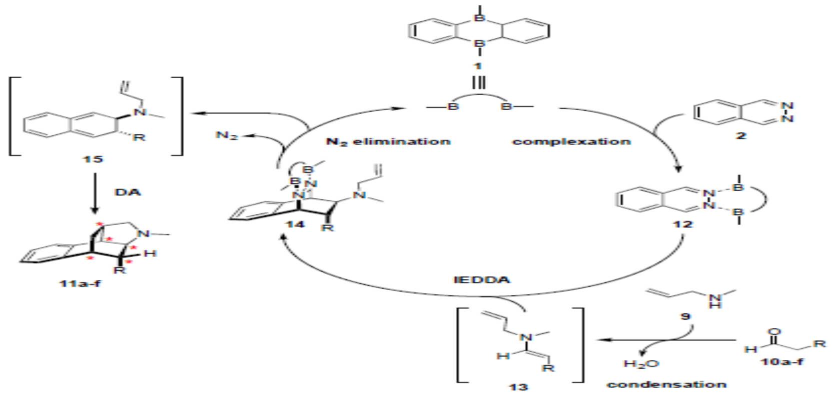


Fig. 1 (a) Dienophiles[14] *trans*-bicyclo[6.1.0]nonene (**6**), *trans*-cyclooctene (TCO, **7**), methylcyclopropene (**8**), bicyclo[6.1.0]nonyne (**9**), cyclooctyne (**10**), norbornene (**11**), cyclopentene (**12**), styrene (**13**) and (b) tetrazines[5,13,15,16] (*e.g.* 3-(benzylamino)-tetrazine (**14**) or 3,6-di(pyridin-2-yl)-1,2,4,5-tetrazine (**15**)) used in iEDDA reactions and their (estimated) relative reactivities.

Knall, A. C., & Slugovc, C. (2013). Inverse electron demand Diels–Alder (iEDDA)-initiated conjugation: a (high) potential click chemistry scheme.*Chemical Society Reviews*, *42*(12), 5131-5142.

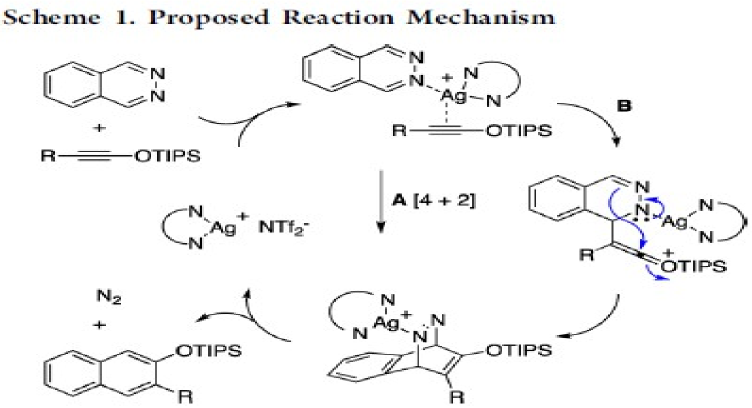
The tandem path can be enhanced by catalysts if each iEDDA is done in two separate stages with different dienophiles.

Scheme 2. Catalytic cycle of the domino reaction leading to products 11a–f.



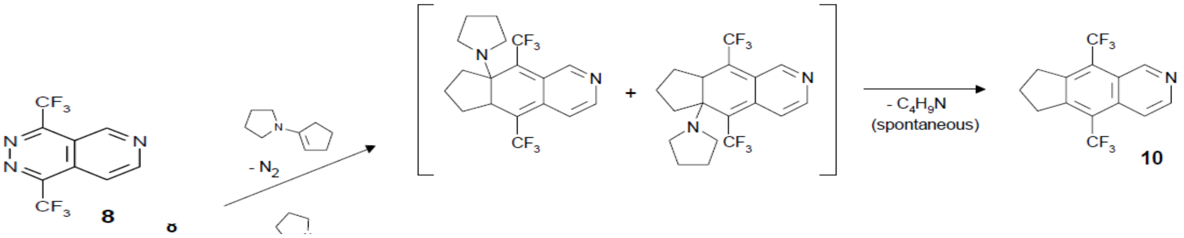
Schweighauser, L., Bodoky, I., Kessler, S. N., Häussinger, D., Donsbach, C., & Wegner, H. A. (2016). Bidentate Lewis acid catalyzed domino Diels–Alder reaction of phthalazine for the synthesis of bridged oligocyclic tetrahydronaphthalenes. *Organic letters*, *18*(6), 1330-1333.

Hong, L., Ahles, S., Heindl, A. H., Tiétcha, G., Petrov, A., Lu, Z., ... & Wegner, H. A. (2018). An air-stable bisboron complex: a practical bidentate Lewis acid catalyst. *Beilstein journal of organic chemistry*, *14*(1), 618-625.



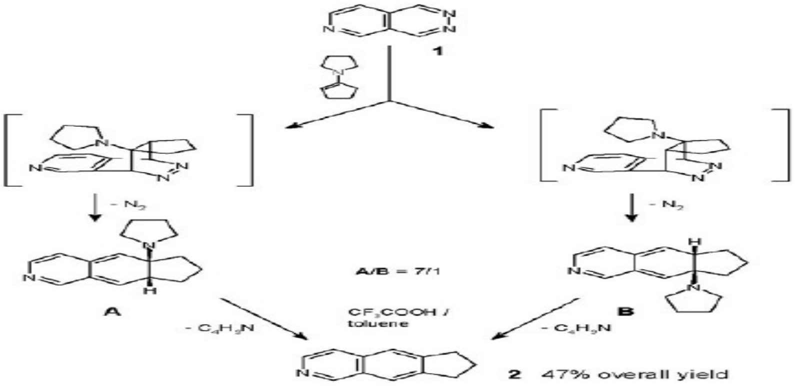
Türkmen, Y. E., Montavon, T. J., Kozmin, S. A., & Rawal, V. H. (2012). Silver-Catalyzed Formal Inverse Electron-Demand Diels–Alder Reaction of 1, 2-Diazines and Siloxy Alkynes. *Journal of the American Chemical Society*, *134*(22), 9062-9065.

In addition, the following dieneophiles will act as leaving groups resulting in formation of aromatics.

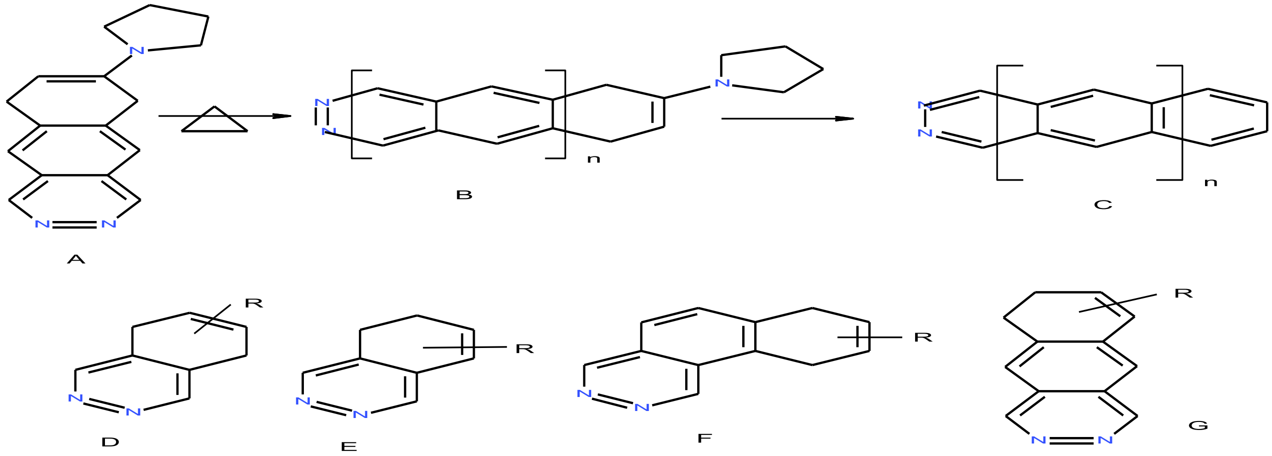


Haider, N., Merelter, K., & Wanko, R. (1994). Inverse-Electron-Demand Diels-Alder Reactions of Condensed Pyridazines. 4. Synthesis and Cycloaddition Reactions of 1, 4-Bis (trifluoromethyl) pyrido (3, 4-a) pyridazine. *Heterocycles-Sendai Institute of Heterocyclic Chemistry*, *38*(8), 1845-1858.

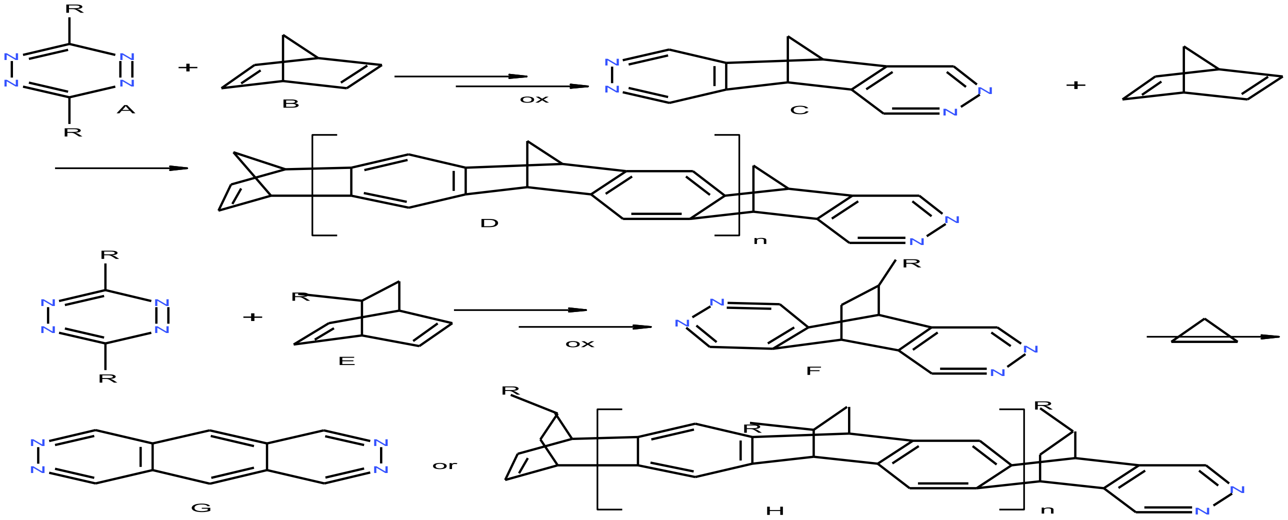
OISHI, E., TAIDO, N., IwAMoTo, K. I., MIYASHITA, A., & HIGASHINO, T. (1990). Phthalazines. XV. Ring Transformation of Phthalazines into Naphthalenes by Means of Inverse-Electron-Demand Diels-Alder Reaction. *Chemical and pharmaceutical bulletin*, *38*(12), 3268-3272.



Abdel-Rehem, E., & Haider, N. (2001). Unsubstituted pyrido [3, 4-d] pyridazine as an electron-deficient azadiene in [4+ 2] cycloaddition reactions: a short route to g-fused isoquinolines. *ARKIVOC*, *2*, 21-27.



Scheme 2: My proposal is that azadienes such as A, D-G can take part in iEDDA polymerizations(any required oxidation is assumed). I have not shown additional R groups at other ring positions for clarity. Such additional R groups can increase the reactivity of the azadienes in this type of reaction. Other amine type leaving groups are well known in these reactions and could be substituted for the above leaving group.



Scheme 3: Another polymer idea. If R=H then H above is possible. If R is a stabilizing group like an ester then a rDA can produce intermediate G. B & E are bicyclics but could be separated dienes that would also work like the above. Note: the tetrazine R

groups are undefined for clarity but those that can increase reactivity would be beneficial.

Thanks for reading the above proposals.

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