DPP analogs based on Alpha-Amino Ketones

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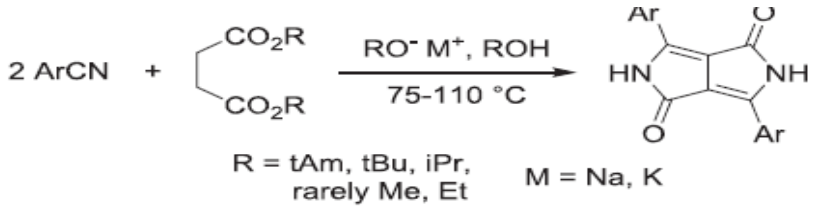
Provisional Patent 62573092

DPP (diketopyrrolopyrroles) are a very successful family of dyes and their derivatives are used extensively in a wide variety of end uses. Probably the most important application is as components of organic semiconductor compounds.

"Currently, about 150 scientific papers and more than 200 patents are published annually on topics related to DPPs. Most of these reports concern the use of DPP derivatives in semiconductor electronic devices, such as organic field effect transistors (OFETs) or solar cells and organic light-emitting diodes (OLEDs)."



Scheme 6. Succinic method of DPP synthesis.

Grzybowski, Marek, and Daniel T. Gryko. Diketopyrrolopyrroles: Synthesis, reactivity, and optical properties."*Advanced Optical Materials",* 3.3 (2015): 280-320.

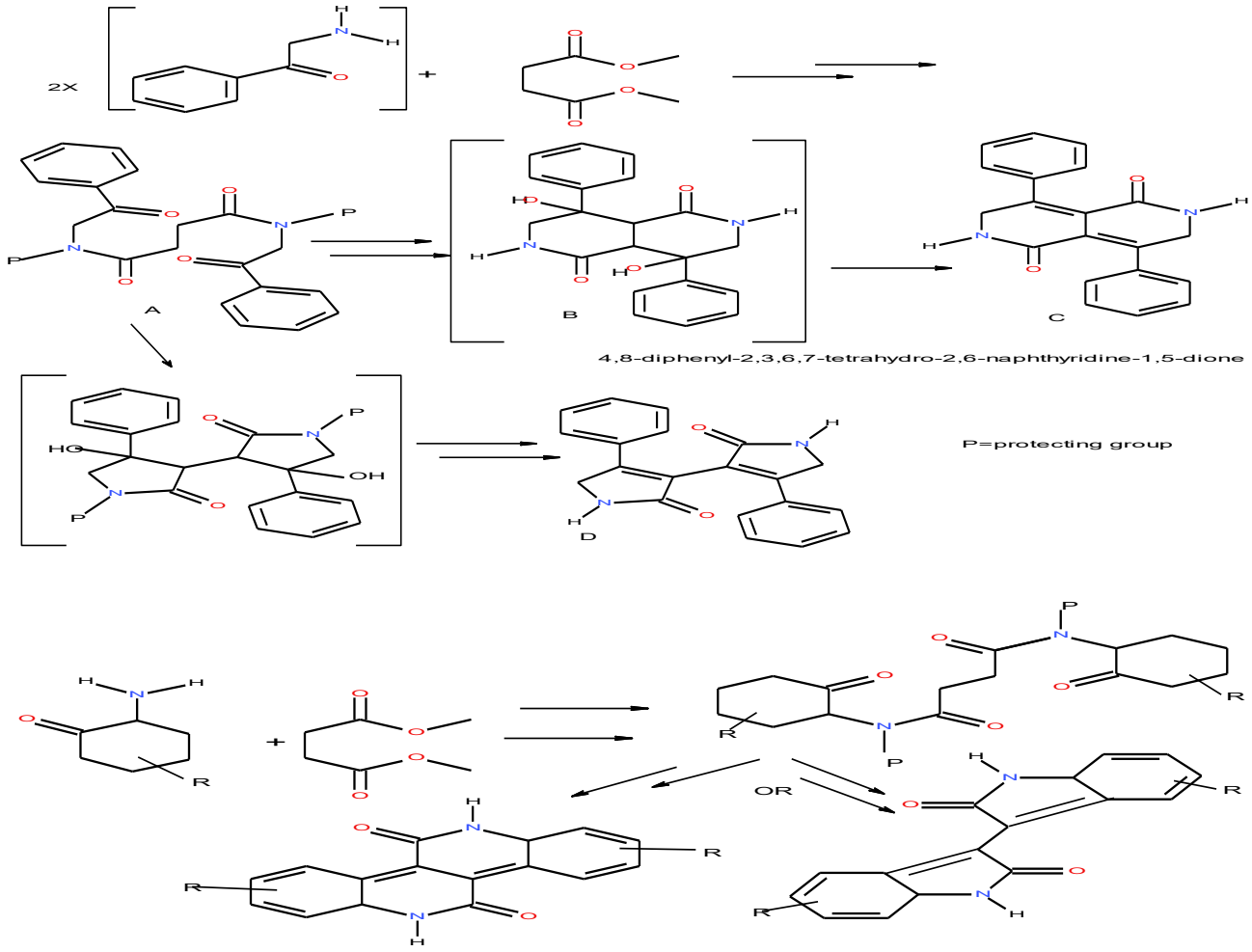
DPP synthesis is remarkably simple as indicated in the above reference.

DPP of every conceivable derivatization with aromatics and aromatic heterocylics and all kinds of N-substituted derivatives have been reported. The reason is that this moiety is a strong electron acceptor(A) that can be coupled to electron donors(D) in various ways, resulting in improved performance of the resulting semiconductors.

Chandran, Deepak, and Kwang-Sup Lee. "Diketopyrrolopyrrole: A versatile building block for organic photovoltaic materials."*Macromolecular Research",* 21.3 (2013): 272-283.

Thinking about the preparation of the DPP's it occurred to me that the alpha-amino ketones that I illustrated in another proposal (see my web page) could be used for this type of chemistry (for a review of alpha-amino ketones see chap. 2 in Berkowitz, William F., and Stuart W. McCombie. "Cyclization of Vinyl and Aryl Azides into Pyrroles, Indoles, Carbazoles, and Related Fused Pyrroles."*Organic Reactions",* (2012).).

For example:



Scheme 1:I suggest that the secondary amides must be protected in order to form the amide enolates that are necessary for ring formation.

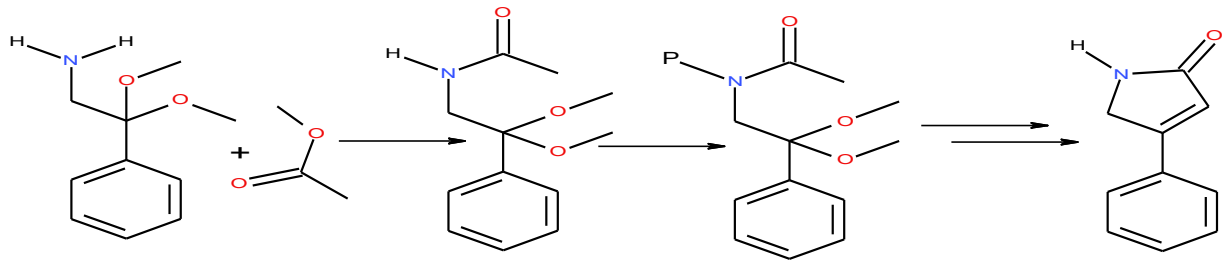
Wuts, P. G. M; Greene, T. W. *Greene's Protective Groups in Organic Synthesis*, 4th Ed; John Wiley & Sons, Inc.: Hoboken, NJ, 2007; pp 905- 906

A strong base and heat would be required for the ring closure and water elimination. A could cyclize to either C or D or a mixture of the two (spiro unlikely). C would be a six-membered analog of the DPP's but D would also be interesting as a "split" DPP. A significant variety of aromatic and heteroaromatics alpha-amino ketones could be employed in this reaction. The lactam nitrogens after removal of the protecting groups, can be derivatized with a large variety of R groups. See BASF patents for examples of what type of derivatives are used with DPP that could also be considered for the above chemistry (US 8,946,376 B2 is typical).

"The preparation of highly soluble DPP polymers is based on the use of soluble monomers, which requires substitution of the lactam NH groups of the DPP units by alkyl or other groups avoiding the strong hydrogen bonding pattern between the lactam groups.[4-7,11] Most DPP polymers

reported so far either carry *n*-hexyl,[4-9] 3,5-bis-*t*-butylbenzyl,[7] *n*-octyl,[9] or ethylhexyl[8,10] substituent groups in order to increase the solubility."

Zhang, Kai, and Bernd Tieke. "Highly luminescent polymers containing the 2, 3, 5, 6-tetraarylated pyrrolo [3, 4-c] pyrrole-1, 4-dione (N-Aryl DPP) chromophore in the main chain."*Macromolecules*", 41.20 (2008): 7287-7295.

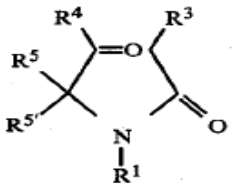


3-phenyl-1,2-dihydropyrrol-5-one

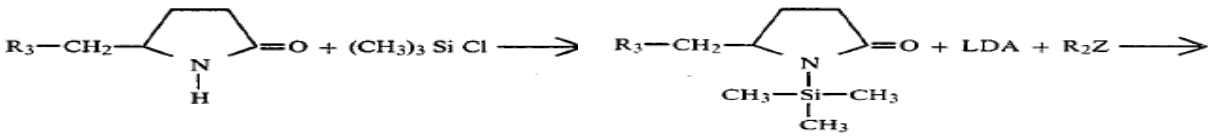
Scheme 2: This preparation is already known. Several patents describe this chemistry and the protecting group!

Hofer, Peter. "Production of 3-pyrrolin-2-ones." U.S. Patent No. 4,443,616. 17 Apr. 1984.

"The present invention, therefore, further contem plates general methods of producing compounds of Formula V, and this is accomplished according to the invention by ring closure of N-aroylmethyl acetamides of the formula:



to form the corresponding compound of Formula V. This ring closure is accomplished according to the in vention under basic conditions, for example in t-butanol with potassium t-butoxide as base under nitrogen fol lowed by acidifcation with a mineral acid such as HCl"



Biziere, Kathleen, Jean-Pierre Chambon, and Jean-Charles Molimard. "Pyrrolidin-2-ones and medicaments containing them." U.S. Patent No. 4,604,383. 5 Aug. 1986. (LDA is used to put R2 on carbon alpha to lactam carbonyl.)

None however show my ideas.

Obviously the right conditions would have to be developed to avoid synthesis of the pyrazine derivative formed by self condensation of the alpha-amino ketones. The succinic acid could be an acid halide or anhydride fast to react with the alpha-amino ketone before it can react with itself. Alternatively and more reliable, the ketone could be protected allowing the amine to form the amide before the ketone is released. Synthesis of the ketal of the alpha amino ketones is readily achieved.

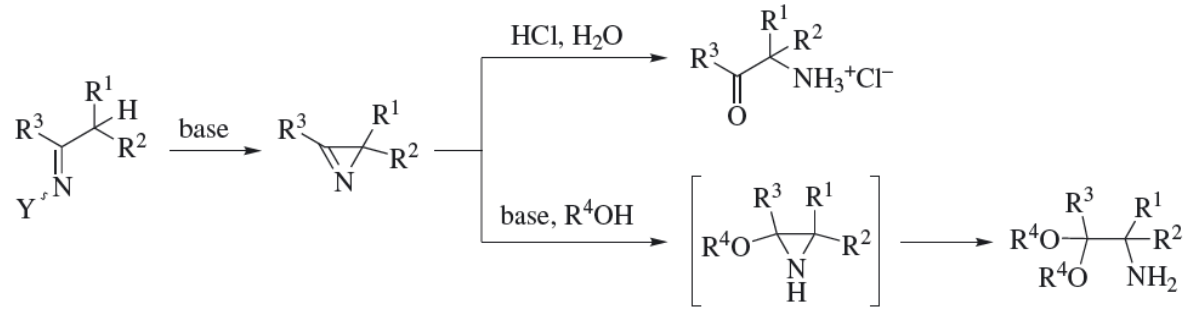
In the example (scheme 1) the aromatic could be other heteroaromatics and derivatives like bromonated phenyls or R groups commonly used in the various coupling reactions etc.

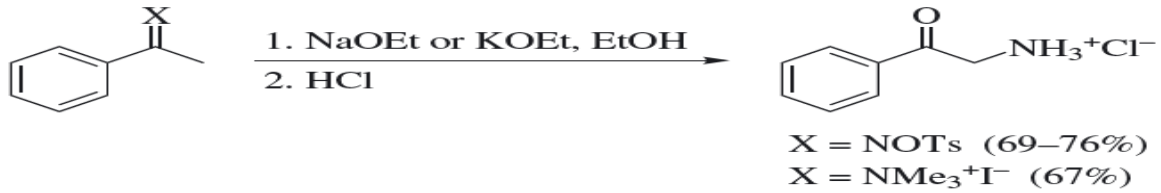
The question is if the DPP analogs will treat the polyunsaturation the same as DPP? A model of the both bis-amides indicates that both are relatively planar so I think each isomer will behave in a similar fashion to DPP.

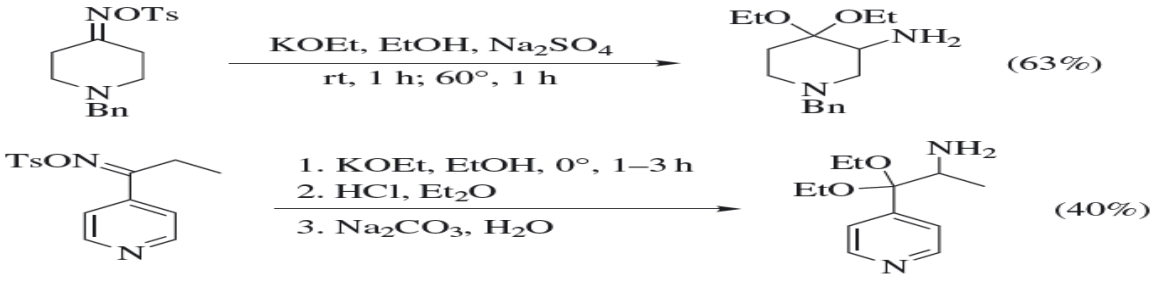
Alpha-amino Ketone Synthesis:

Berkowitz, William F., and Stuart W. McCombie. "Cyclization of Vinyl and Aryl Azides into Pyrroles, Indoles, Carbazoles, and Related Fused Pyrroles."*Organic Reactions",* (2012). Chap. 2 Neber Rearrangement.

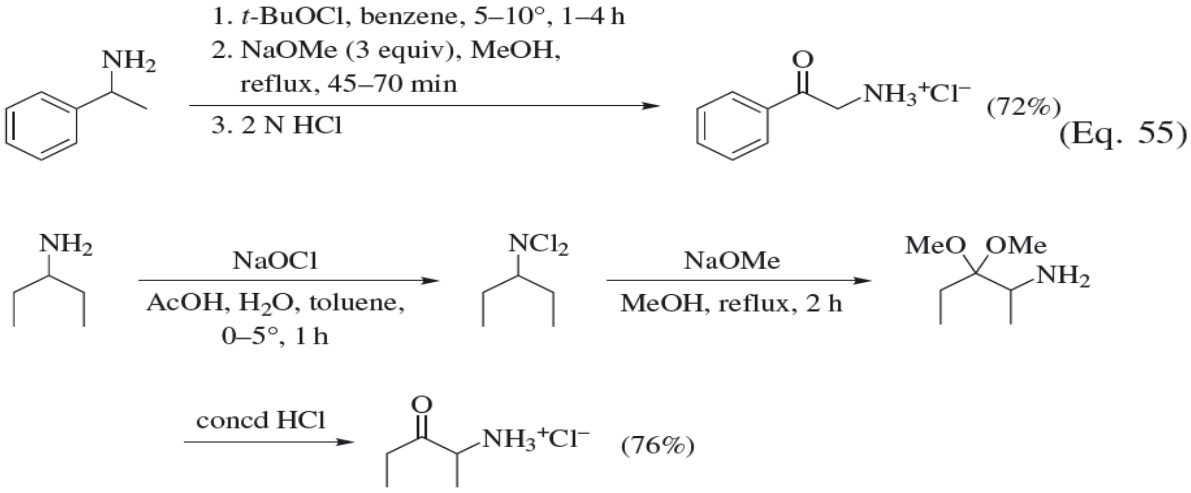
The above reference covers every aspect of the **Neber Rearrangement**, one of the most important reactions leading to alpha-amino ketones and also reviews every other worthwhile alternative synthetic method. For example:







Baumgarten Rearrangement:



Of the above routes to alpha-amino ketones, my idea revolves around the ketal derivatives because the ketone is protected while the primary amine is free to react with esters resulting in amides that can reveal the ketone moieties upon hydrolysis.

The Knorr pyrrole synthesis depends on alpha-amino carbonyl compounds either as is or generated in-situ.

“It is the most widely used method for pyrrole synthesis. α-Aminocarbonyl compounds will readily dimerize to dihydropyrazines, one way to avoid this dimerization is to prepare and use them in the form of salts to be liberated for reaction by the base present in the reaction mixture. An alternative way was reported by L. Knorr where the oximino precursor was converted to amino *in-situ.”*

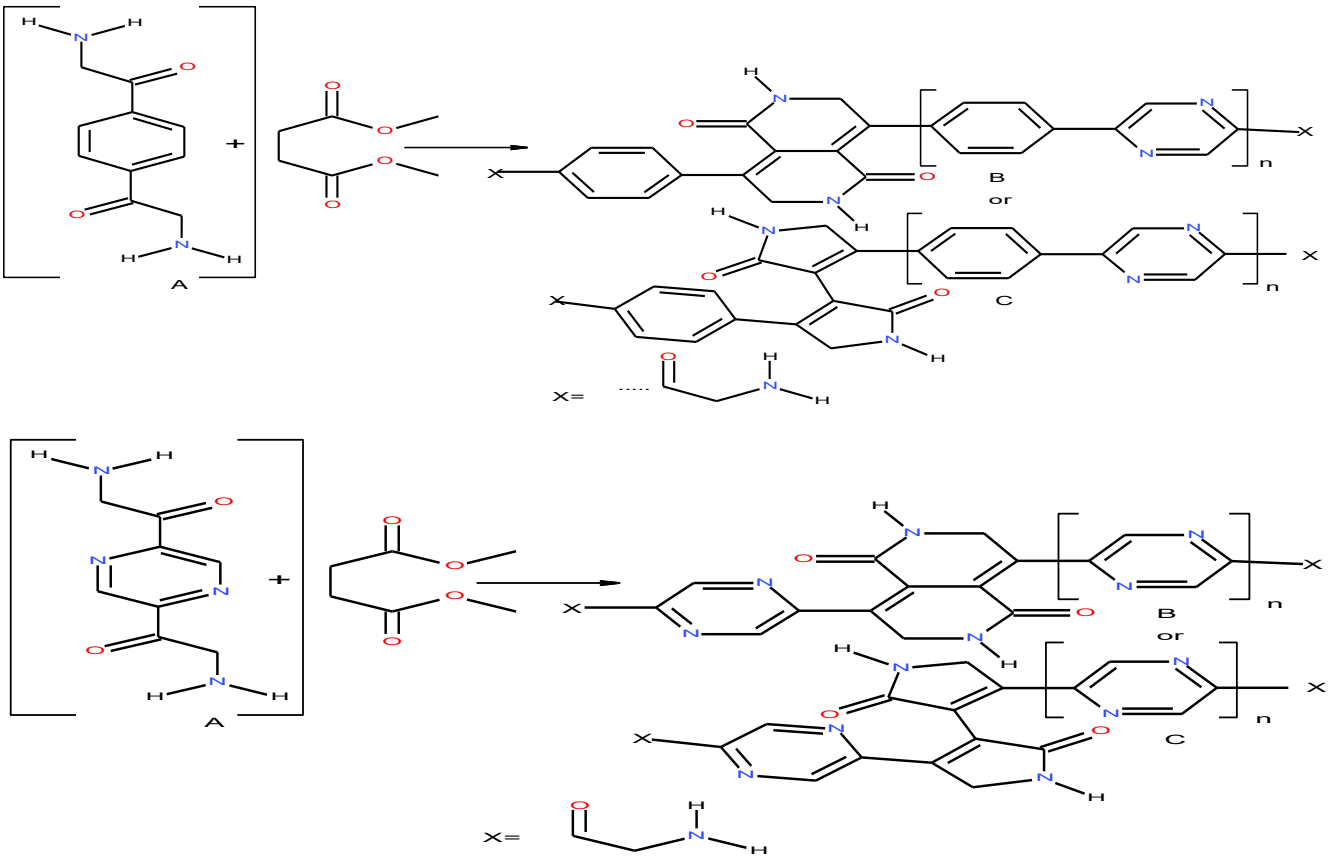
Mohamed, Mosaad S., Rania H. Abd El-Hameed, and Amira I. Sayed. "Synthesis Strategies and Biological Value of Pyrrole and Pyrrolopyrimidine." (2017)
Yurovskaya, M. A., and R. S. Alekseyev. "New Perspectives on Classical Heterocyclic

Reactions Involving Pyrrole Derivatives."*Chemistry of Heterocyclic Compounds”,* 49.10

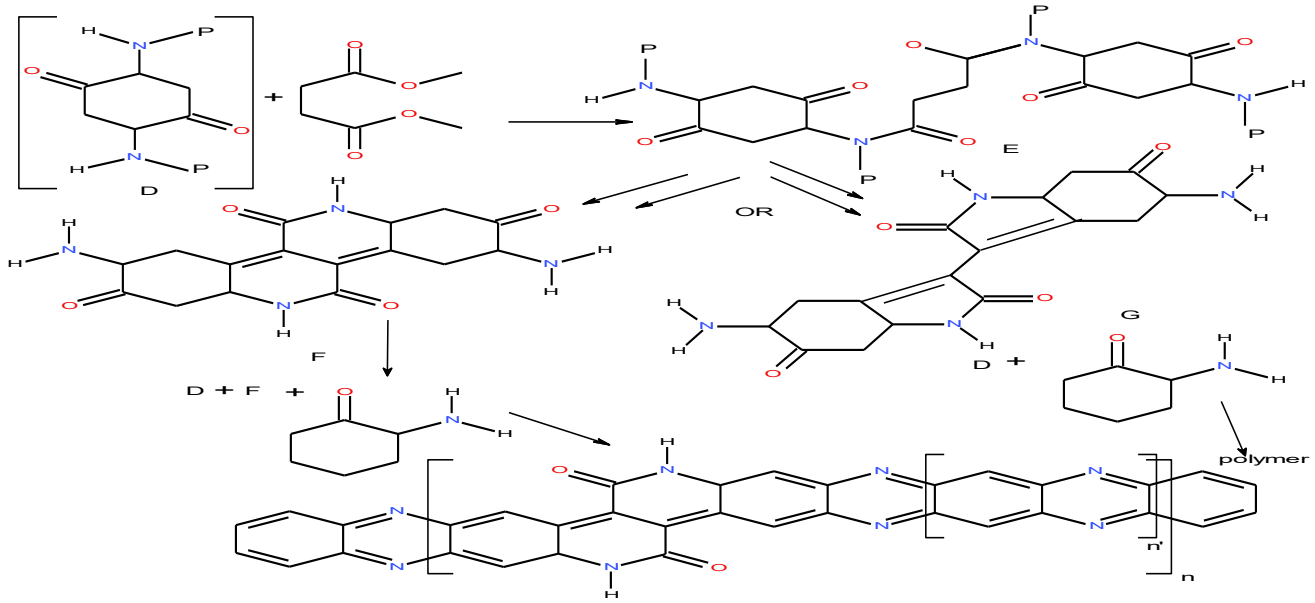
(2014): 1400-1425.
Both references cover many routes to alpha-amino carbonyls, which might work with said ideas. Also Jones's book has many examples:

Jones, Richard Alan. *Pyrroles: The synthesis and the physical and chemical aspects of the pyrrole ring*. Vol. 1 Wiley-Interscience, 1990.

Polymeric possibilities:



Scheme 3: The intermediate bis-amide must be protected so that the amide enolate forms...not shown. The above polymers have their reactive alpha-amino ketone end groups and under the reaction conditions would be expected to continue polymerizing with more “A” and/or the alpha-amino ketone terminals. In the above examples stiochiometry is such that one succinate reacts with multiple alpha-amino ketones. It could also be one to one resulting a different repeat unit than the one shown with multiple bis-amides. MW could be controlled with the use of capping monofunctional alpha-amino ketones of which a cyclohexyl example is shown in scheme 4. F and G would continue to condense eventually to pyrazine ladder chains. Oxidation could result in the pyrazine chains, generated even by air(O2) oxidation.



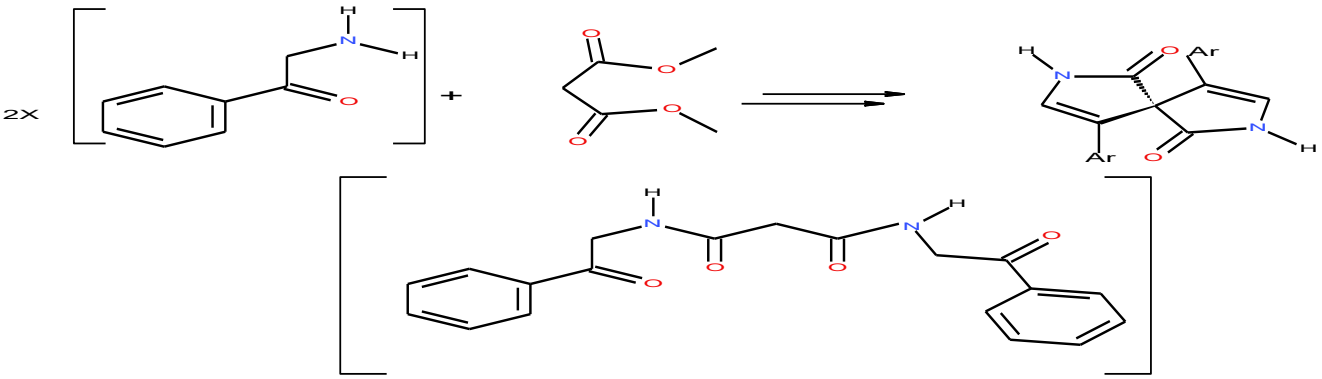
Scheme 4: Only one version of the two possibilities is shown as a finished polymer. If only one mole of succinate is used and one mole each of the other ingredients then n=1 and n'=0.

The terminal cyclohexanes could also be oxidize to aromaticity and this polymer would then have no aromatic sextet and according to Clar's rules, it would have labile electrons that are associated with enhance semiconductor performance.

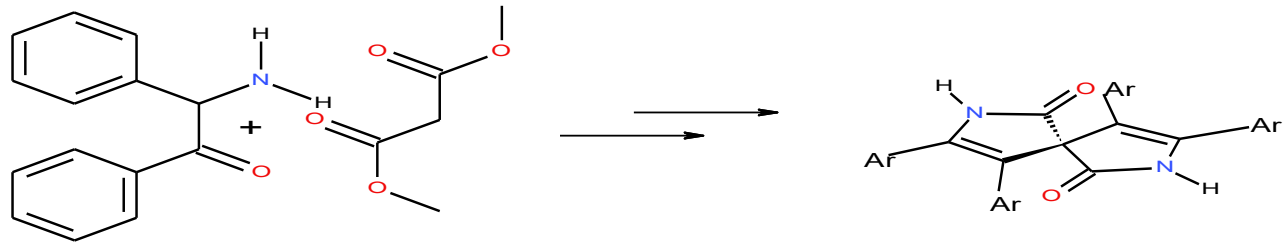
Misra, Anirban, D. J. Klein, and T. Morikawa. "Clar theory for molecular benzenoids.", *The Journal of Physical Chemistry A*113.6 (2009): 1151-1158.

Portella, Guillem, Jordi Poater, and Miquel Sola. "Assessment of Clar's aromatic π-sextet rule by means of PDI, NICS and HOMA indicators of local aromaticity."*Journal of physical organic chemistry",* 18.8 (2005): 785-791.

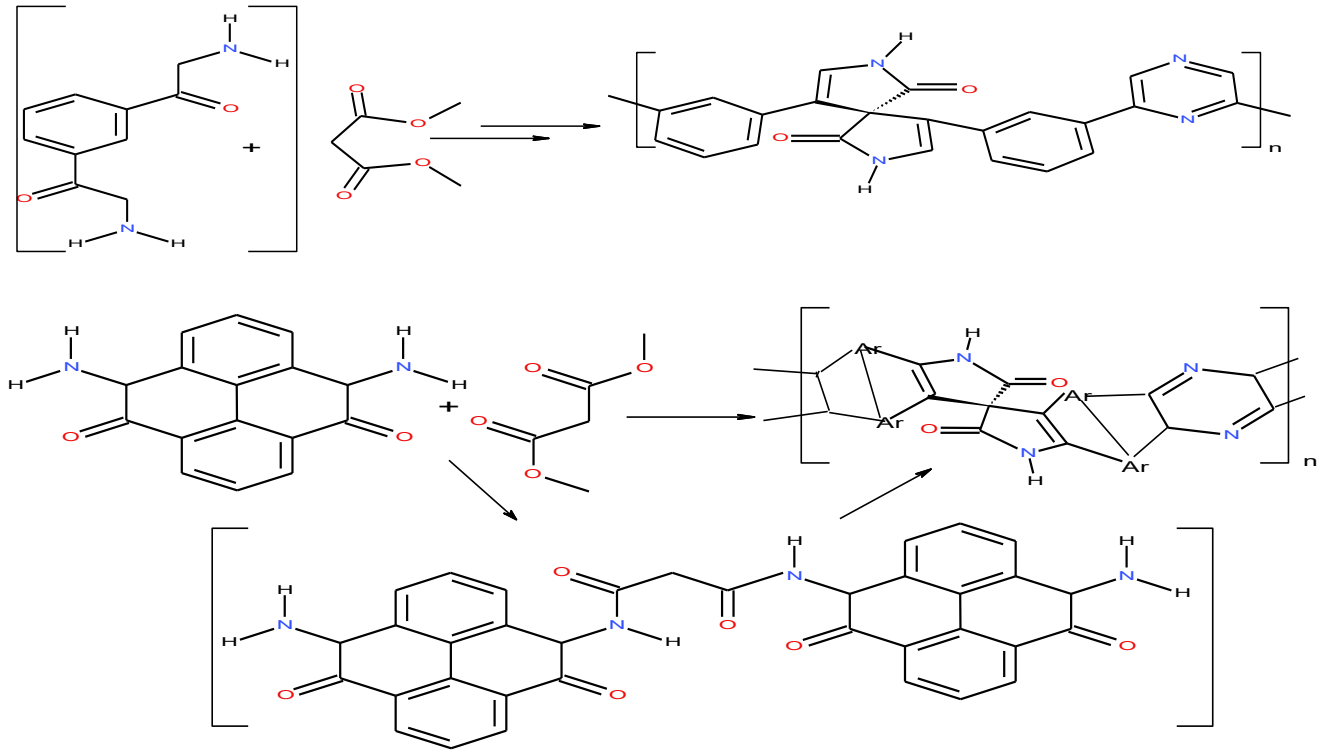
Spirolactams:
With a three carbon diester you obtain a spiro unconjugated dilactam.



Scheme 5: The malonamides methylene maybe acidic enough to not need amide protection?
However, if the alpha-amino ketone is di-substituted then this might be possible:



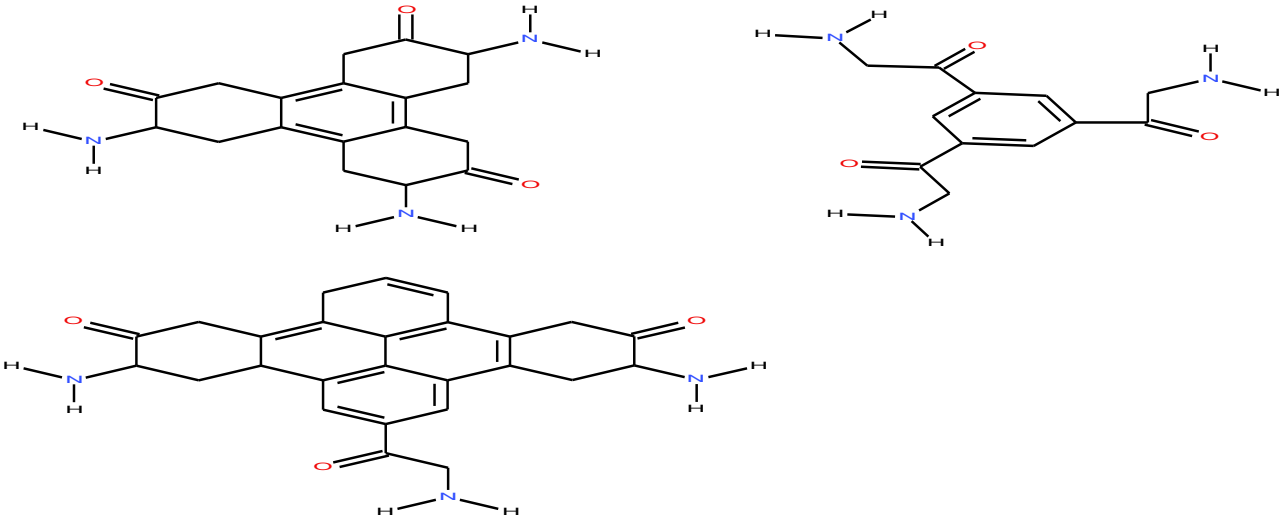
Scheme 6: Ar groups are illustrated but many other unsaturated moieties can be visualized that would then be conjugated with the spirolactams double bond and each other.



Scheme 7: Difunctional examples of cyclohexane type. Because of the spiro carbon, the unsaturation is not conjugated; however, the spiro structure would prevent close chain to chain interaction which is supposedly a benefit to semiconductor performance.

Marco, A. Belen, et al. "Twisted Aromatic Frameworks: Readily Exfoliable and Solution-Processable Two-Dimensional Conjugated Microporous Polymers."*Angewandte Chemie International Edition",* (2017).

Tri-functional and multi-functional alpha-amino ketones would the form branched polymers. Synthesis of a possible intermediate that could work, for example:



Scheme 8: Polyfunctional monomers
Also the following reference illustrates a possible intermediate.

Mueller, Felix, Anke Karwe, and Jochen Mattay. "A new synthesis of porphyrin systems by four sequential [3+ 2] cycloadditions of an alkyne with azaallenyl radical cations." *The Journal of Organic Chemistry,* 57.22 (1992): 6080-6082.

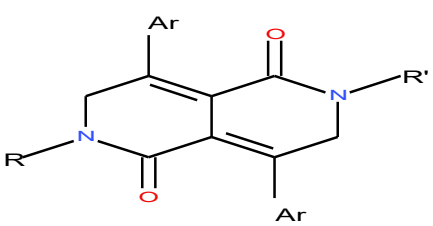
General Comments:
As previously mentioned, protecting groups could be required to conduct these reactions. For example the (alpha amino) ketones might need to be protected so that the amines can form succinamides in high yields with less chance of side reactions. The resulting secondary amides would need protecting groups to effect amide enolate ring closure. Many details of the proposed chemistry would need to be worked out experimentally; however, if the basic ideas are sound, then this chemistry would result in valuable compounds and polymers.

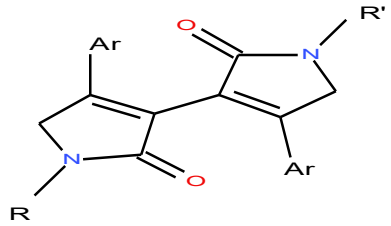
The idea of using alpha-amino ketones and succinates just touches the surface of this chemistry as numerous suitable derivatives of said reagents can be visualized. Reading Grzybowski, Marek, and Daniel T. Gryko excellent review suggests that whatever you can do with DPP chemistry you can probably do with my idea. I think most of the DPP derivatives can be reproduced with these ideas.

Thank you for reading this proposal. I would be happy to receive feedback.
Dr. Robert B. Login robertblogin@gmail.com

Claims: (examples of possible claims, not meant to be limiting)

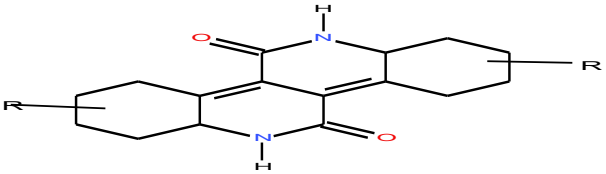
1. Compounds of the following structure;

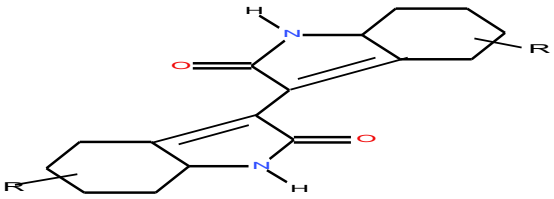




wherein; Ar stands for an aromatic moiety or a chain of aromatic moieties such as illustrated in USP 8,946,376 (included as a reference in its entirety). R and R' maybe the same or different and can be long chain aliphatics, substituted as explained in said patent reference.

2. Compounds of the following structures wherein the lactam nitrogen hydrogen can be





substituted as described in claim 1 and the R group can be one of the well known coupling moieties and the cyclohexane groups can be an aromatic ladders.

3. Compounds of claim 2 wherein the cyclohexyl groups can be oxidized to aromaticity.
4. Polymers prepared from di or polyfunctional alpha-amino ketones and succinate esters.
5. The polymers of claim 4 wherein said ketone is protected as a ketal before reaction of the amines with the succinate esters.
6. The polymers of claim 4 wherein said amine is a primary amine.
7. The polymers of claim 4 wherein the ketal is converted to the ketone after the formation of the succinamides.

8. The reaction of said secondary succinamides with protecting groups in order to facilitate amide enolate formation and ring closure.
9. The reaction of malonate esters with said ketal primary amines to form malonamides.
10. The reaction of the malonamides of claim 9 wherein the secondary amides are converted to tertiary amides with easily removed protecting groups.
11. The protected ketomalonamides of claim 10 converted to spirolactams by the reaction with a strong base.
12. The polymeric spirolactams when the reactants of claim 9 are polyamino ketones.