Pyrrolidone Derivatized Organic Semiconductors

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Many pyrrolidone derivatives are both soluble in water and many solvents. NMP is such an example. Water soluble because it can have a significant dipole because the five membered ring is planar allowing maximum overlap of orbitals resulting in lactam resonance structures that are zwitterionic in polar solvents. Depending on the hydrophilicity of the R group attached to the lactam nitrogen or to ring carbons, can result in surface activity. Such surfactants and PVP, in the presence of large anions, the lactam oxygen can pick up a proton resulting in the nitrogen becoming cationic and forming a complex. Polyphenols are an example of acidic large anions and readily form complex's. These properties have led to numerous valuable applications. Pyrrolidones can be found in polymeric(PVP), surfactants(Surfadones), solvents(NMP) and numerous medicinals(pyrrolidone is a privileged molecule).

Gouliaev, A. H., & Senning, A. (1994). Piracetam and other structurally related nootropics. *Brain research reviews*, *19*(2), 180-222.

Caruano, J., Muccioli, G. G., & Robiette, R. (2016). Biologically active γ-lactams: synthesis and natural sources. *Organic & biomolecular chemistry*, *14*(43), 10134-10156.

Login, R. B. (1995). Pyrrolidone-based surfactants (a literature review). *Journal of the American Oil Chemists' Society*, *72*(7), 759-771.

Login, R. B. (2002). N-Vinylamide Polymers. *Encyclopedia of Polymer Science and Technology*.

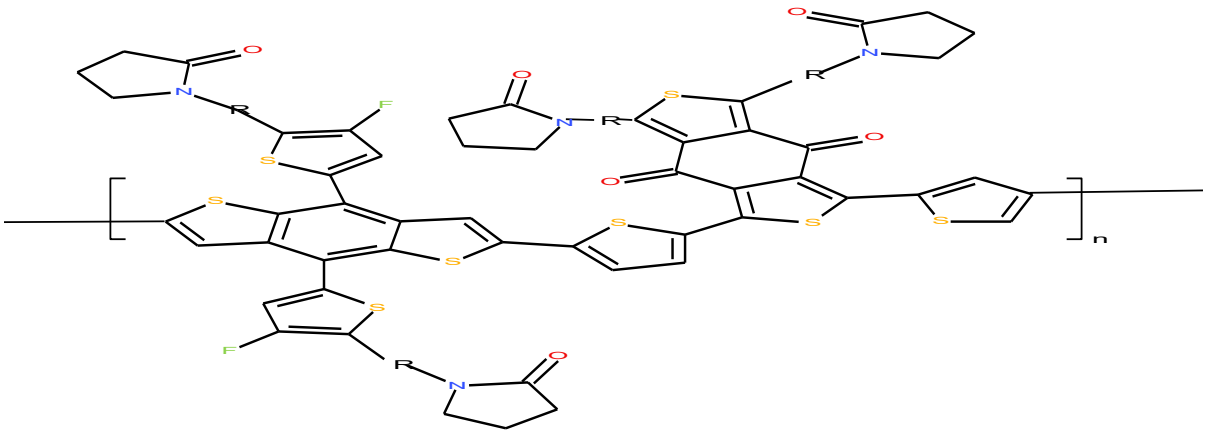
Previous methods to acquire aqueous solubility:

Aqueous applications of ionic or polyglycol derivatives of organic semiconductors have generated a significant literature. Conjugated polyelectrolytes or CPE's contain tethered cationic, anionic or zwitterionic groups that render them water/polar solvent soluble. They have been proposed or employed in a variety of applications, the most interesting are biological.

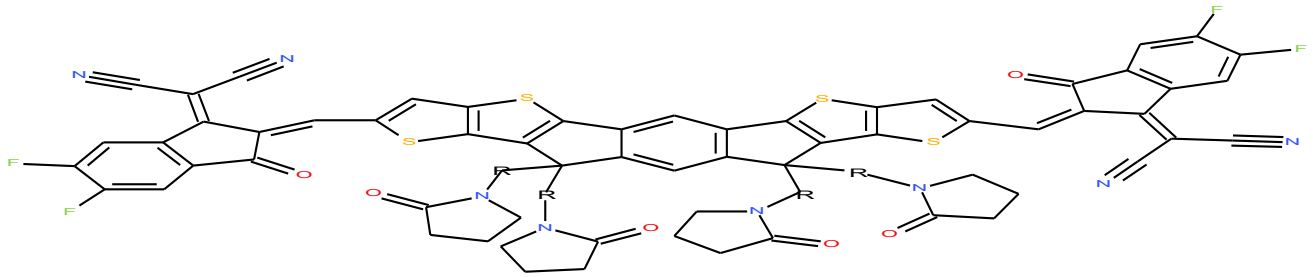
Cui, Q., & Bazan, G. C. (2017). Narrow Band Gap Conjugated Polyelectrolytes. *Accounts of chemical research*, *51*(1), 202-211.

Proposal

While water solubility can be achieved with nonionic polyethylene glycol derivatized organic semiconductors. I'm now proposing that select pyrrolidone derivatives would promote water/polar solvent solubility. NMP is considered a super solvent because it is soluble in both water and many polar solvents. What I'm suggesting is that some of the benefits of NMP can be found in said pyrrolidone organic semiconductor derivatives. For example:



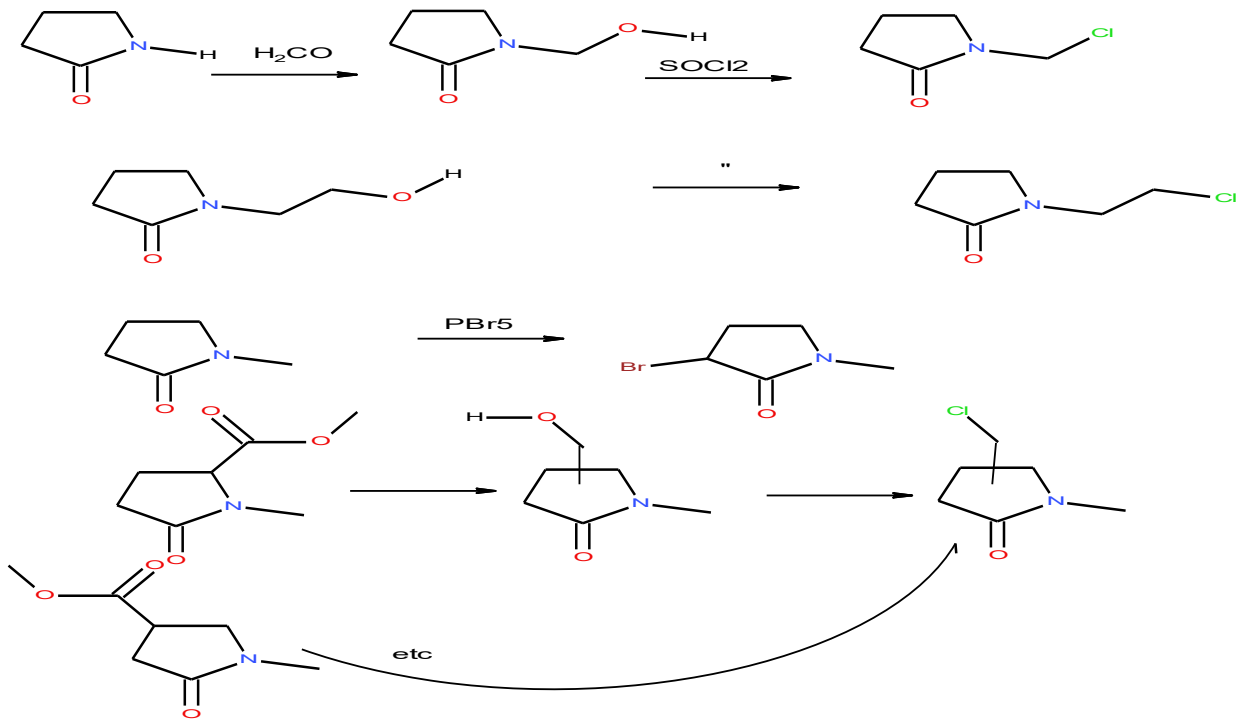
Scheme 1: Donor polymer example with several possible pyrrolidone attachment sites.



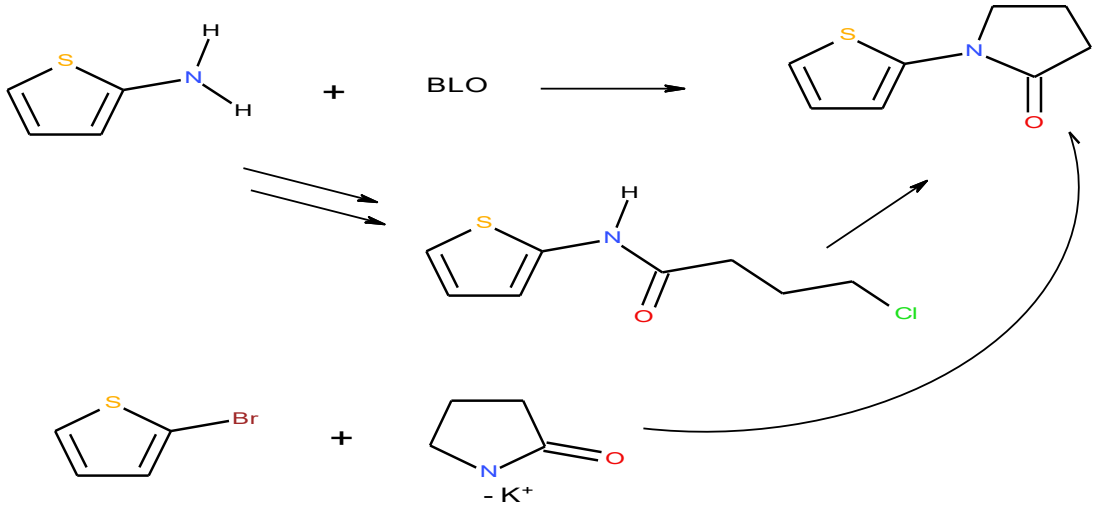
Scheme 2: NFA(non-fullerene acceptors). These structures illustrate the possible locations of pyrrolidone moieties. The R groups are alkyl chains or the pyrrolidone nitrogen or ring carbons can be connected directly to the thiophenes. Solubility of NFA's is a major issue because the solvents now used are chlorinated(toxic) and or expensive. Scheme 2 illustrates a 4 pyrrolidone derivative which is probably not water soluble but might be soluble in innocuous alcohols for example? Pyrrolidone is associated with contributing mildness and low toxicity; however, NMP does have toxicity issues because it is a super solvent.

Synthesis

Pyrrolidones can be synthesized by the condensation of BLO (buterolactone) with primary amines at some high temperature. If the starting amine can stand up to these temperatures, then this is the simplest approach. Numerous other synthetic routes are possible and pyrrolidone can be connected to an organic semiconductor at other positions on its ring, not illustrated in the above examples.



Scheme 3: Nucleophilic examples that can conceivably react with electrophilic thiophenes.



Scheme 4: 3-amino thiophene derivatives can be prepared by the Gewald reaction especially 2-amino-3cyano thiophene which can be substituted for the 2-amino-3-flouro thiophene in scheme 1. Although fluorine is the most electronegative atom, the cyano group I think is a close second.

Bozorov, K., Nie, L. F., Zhao, J., & Aisa, H. A. (2017). 2-Aminothiophene scaffolds: Diverse biological and pharmacological attributes in medicinal chemistry. *European journal of medicinal chemistry*.
Caruano, J., Muccioli, G. G., & Robiette, R. (2016). Biologically active γ-lactams: synthesis and natural sources. *Organic & biomolecular chemistry*, *14*(43), 10134-10156.

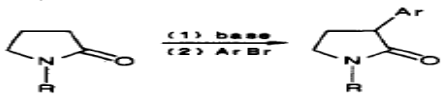
Schemes 3&4 are just examples and are not the only possibilities as thiophene chemistry

is a vast subject covered at great length in various books. Parker and Marder's book "Synthetic Methods in Organic Electronic and Photonic Materials, A Practical Guide" (RSC, 2015) is an excellent introduction.

Lactam chemistry is covered in the monumental(1000pp+) book, **Synthesis of Lactones and Lactams (1993)**John Wiley & Sons Ltd.
Author(s):Michael A. Ogliaruso and James F. Wolfe

Not up to date but a great place to start a search for their synthesis.

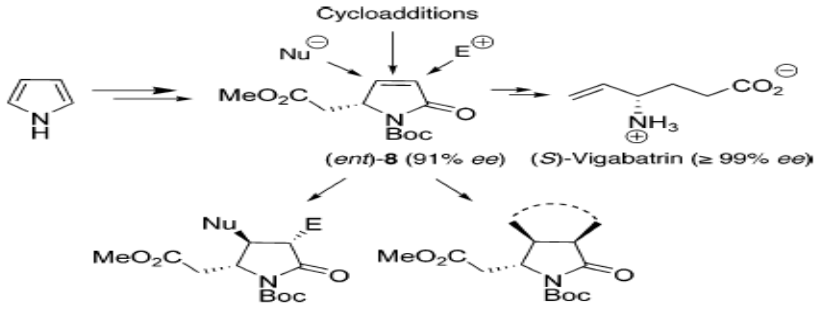
Table I. Arylation of Lactams



R[a]	base (equiv)	ArBr[b]	% yield[c]
CH_3	LICA (3.2)	BB	35–40
CH_3 (4.0)	LICA (8.0)	BV	20
CH_3	LICA (4.0)	BD	16[d]
$CH_2C_6H_5$	LICA (4.0)	BB	24–27
$CH_2C_6H_5$	LICA (4.0)	BV	35
$CH_2C_6H_5$ (4.0)	LICA (8.0)	BV	40
CH_3	LDA (3.2)	BB	18
CH_3	LTMP (3.2)	BB	35[e]
CH_3	LDCA (4.0)	BB	30
$CH_2C_6H_5$	LICA (4.0)	BD	30
CH_3	LICA (4.0)	BA	50[f]

[a] Two equivalents of lactam used (based on ArBr), unless otherwise indicated. [b] Key: BB = bromobenzene, BV = bromoveratrole, BD = 4-bromo-1,2-(methylenedioxy)benzene, BA = 4-bromoanisole. [c] Refers to pure, isolated products, except as noted. [d] Material in purified yields up to 27% darken with time. [e] 3,3-Diphenyl-NMP also formed. [f] Both meta and para products obtained in a 1:1 ratio by GC/MS analysis.

Although the yields are low, I wondered if the reaction would work better with thiophenes?



Starting from pyrrole, the novel 3,4-didehydropyrohomoglutamate **8** or (*ent*)-**8** can be efficiently synthesized in up to 91% ee, which can be utilized as a versatile building block toward functionalized pyrrolidin-2-ones. Moreover, (*ent*)-**8**

Gheorghe, A., Schulte, M., & Reiser, O. (2006). Synthesis of functionalized pyrrolidin-2-ones and (S)-Vigabatrin from pyrrole. *The Journal of organic chemistry*, *71*(5), 2173-2176.

This reference illustrates that pyrrolin-2-one itself can react at the double bond as above. A nice review as of 2014 that also has a rather complete set of references.

Ye, L. W., Shu, C., & Gagosz, F. (2014). Recent progress towards transition metal-catalyzed synthesis of γ-lactams. *Organic & biomolecular chemistry*, *12*(12), 1833-1845.

There are hundreds of references dealing with the synthesis of pyrrolidone derivatives because it is a structure that appears in numerous molecules both natural and synthetic of biological and medical significance. Some of the natural ones are very complicated and it is humbling to think that they were synthesized by lowly creatures.

Thank you for reading this proposal. Comments or corrections would be appreciated,
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