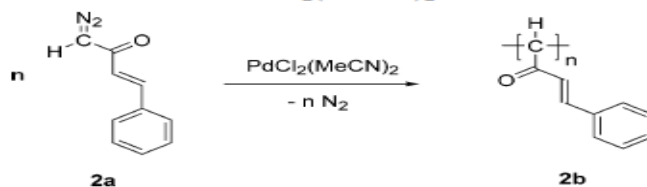


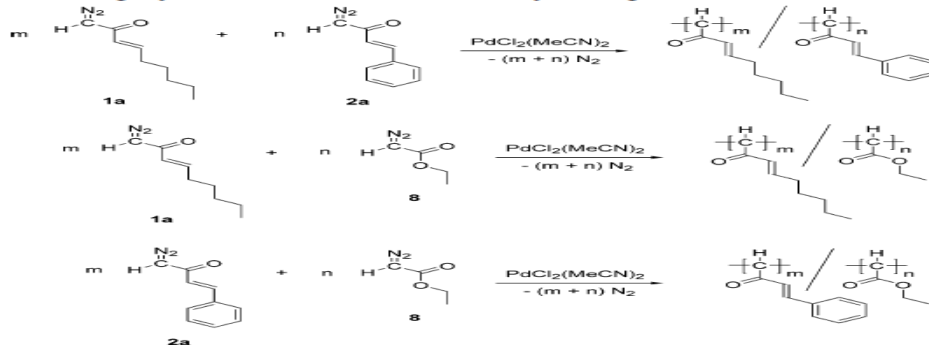
C1 Polymerization of Pyrrolidone Derivatives

Vinyl pyrrolidone, an important monomer employed in large scale commercial polymer production with applications of great pharmaceutical importance. However, since its discovery nearly 100 years ago, an improved monomer replacement has not been found. I have an interest in alternatives to vinyl pyrrolidone based polymers that might possess improved or different valuable properties and applications. In the past I have suggested alternatives to the synthesis of pyrrolidone containing polymers where the pyrrolidone is not pendant to the backbone but part of it. Alternatively, I have proposed reverse PVP where the lactam is facing away from the polymer backbone. I have also proposed a variety of new PVP derivatives. Please look at my web page rloginconsulting.com for (safe to download) pdf's that cover my ideas. Obviously I have a long term interest in this chemistry having spent years studying it as Director of R&D for GAF/ISP, a major PVP manufacturer.

Scheme 5. Polymerization of (E)-1-Diazo-4-phenyl-3-butene-2-one with PdCl₂(MeCN)₂



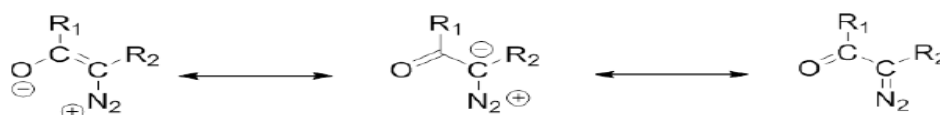
Scheme 7. Copolymerization of Diazocarbonyl Compounds with PdCl₂(MeCN)₂. I



Ihara, E., Fujioka, M., Haida, N., Itoh, T., & Inoue, K. (2005). First synthesis of poly (acylmethylene)s via palladium-mediated polymerization of diazoketones. *Macromolecules*, 38(6), 2101-2108.

Above are two schemes from this pioneering reference. They show how various diazoketones can be polymerized as homo or copolymers. The interesting thing here is that unlike vinyl polymerization, every backbone carbon has an R group. My thought is could this chemistry be applied to pyrrolidone derivatives? Could every backbone carbon R group contain a pyrrolidone derivative?

As an aside, even if this is possible, diazocarbonyl chemistry has a potential problem even though the diazocarbonyls have been employed successfully for decades with out any problem, other diazo compounds are toxic, unstable and can detonate if mis-handled. The diazocarbonyls, (ketones, carboxylates, amides) are apparently relatively safe.



Scheme 1.8.: The increased stability of diazocarbonyl compounds compared to aliphatic diazo compounds explained by mesomeric structures.

Krappitz, T. W. (2019) thesis. Functional Polymethylenes: Synthesis and Post-Polymerization Modification.

Academically, its reactions are conducted on a small or micro scale but large scale is still problematic as far as I know?

Green, S. P., Wheelhouse, K. M., Payne, A. D., Hallett, J. P., Miller, P. W., & Bull, J. A. (2019). Thermal Stability and Explosive Hazard Assessment of Diazo Compounds and Diazo Transfer Reagents. *Organic Process Research & Development*.

Xin, D., & Lu, Y. (2018). Thermal Decomposition of Ethyl Diazoacetate in Microtube Reactor: A Kinetics Study. *ACS omega*, 3(9), 10526-10533.

Burtoloso, A. C., Momo, P. B., & Novais, G. L. (2018). Traditional and New methods for the Preparation of Diazocarbonyl Compounds. *Anais da Academia Brasileira de Ciências*, 90(1), 859-893.

Don't misunderstand my pointing out potential commercial problems. For all I know there might be large scale applications now in use or being pursued?

“Carbon functionalised sulfur

ylides are synthetically not easily accessible and diazoalkanes are potentially explosive. On the other hand, a wide variety of diazoketones and diazoesters, which are much more stable than diazoalkanes (and therefore relatively safe to work with, even in large scale applications) are readily available”

Jellema, E., Jongerius, A. L., Reek, J. N., & de Bruin, B. (2010). C1 polymerisation and related C–C bond forming ‘carbene insertion’ reactions. *Chemical Society Reviews*, 39(5), 1706-1723.

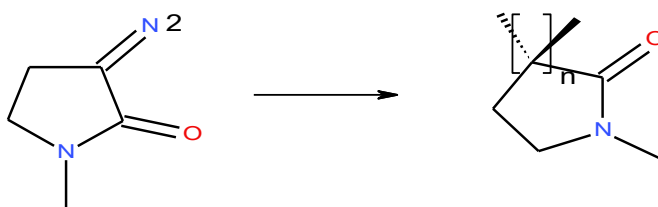
Diazocarbonyl chemistry is of substantial utility and of major interest to synthetic organic chemistry. Please look at the following monumental reviews to see the fantastic scope of their applications.

Ye, T., & McKervey, M. A. (1994). Organic synthesis with α -diazo carbonyl compounds. *Chemical reviews*, 94(4), 1091-1160.

Ford, A., Miel, H., Ring, A., Slattery, C. N., Maguire, A. R., & McKervey, M. A. (2015). Modern organic synthesis with α -diazocarbonyl compounds. *Chemical reviews*, 115(18), 9981-10080.

Arora, R., Kashyap, K., Mittal, A., & Kakkar, R. (2019). Synthesis and Reactions of Diazoketones. *Organic Preparations and Procedures International*, 51(2), 103-146.

Is the following C1 polymerization feasible?

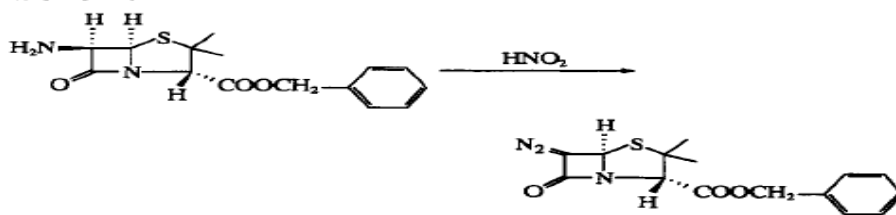
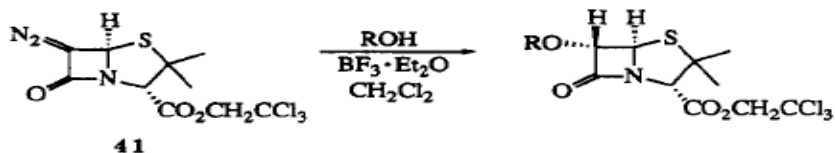


Scheme 1: This structure is in the realm of the diazocarbonyls and it should be synthensizable. Several C1 polymerisation reviews are available.

Jellema, E., Jongerius, A. L., Reek, J. N., & de Bruin, B. (2010). C1 polymerization and related C–C bond forming ‘carbene insertion’ reactions. *Chemical Society Reviews*, 39(5), 1706-1723.

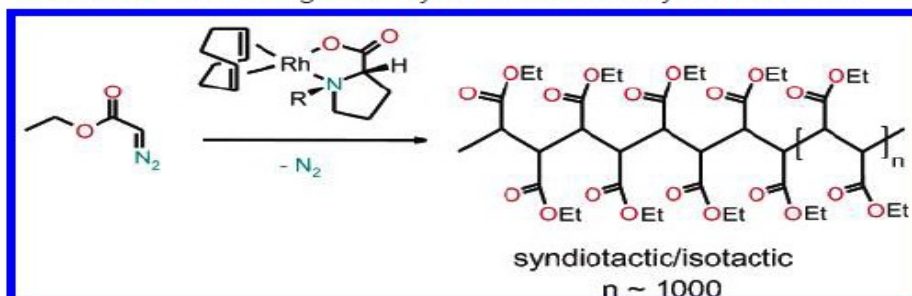
Franssen, N. M., Reek, J. N., & de Bruin, B. (2013). Synthesis of functional ‘polyolefins’: state of the art and remaining challenges. *Chemical Society Reviews*, 42(13), 5809-5832.

The following are presented to show that lactams can be converted to diazocarbonyls.

Scheme 14**Scheme 38**

Ye, T., & McKervey, M. A. (1994). Organic synthesis with alpha.-diazo carbonyl compounds. *Chemical reviews*, 94(4), 1091-1160.

The above show that diazocarbonyl are possible even with beta-lactams therefore it should also work with pyrrolidones. Scheme 38 shows an insertion reaction typical of said compounds. Polymerisation however depends on specific ruthenium or palladium catalysts.

Scheme 2. Stereoregular Polymerization of Ethyl Diazoacetate

Hetterscheid, D. G., Hendriksen, C., Dzik, W. I., Smits, J. M., van Eck, E. R., Rowan, A. E., ... & Jellema, E. (2006). Rhodium-mediated stereoselective polymerization of "carbenes". *Journal of the American Chemical Society*, 128(30), 9746-9752.

Scheme 1. Polymerization of EDA with (NHC)Pd/Borate Systems

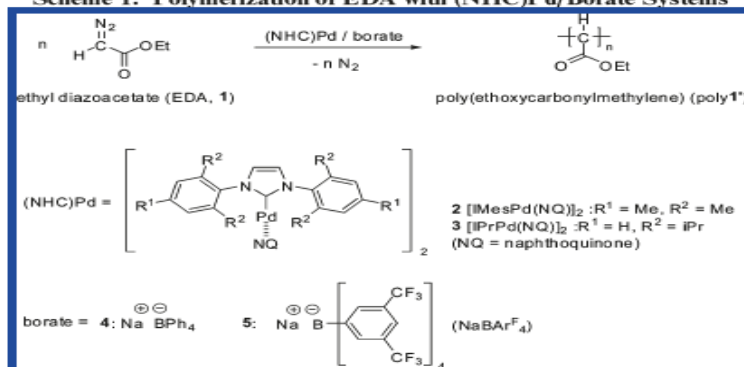
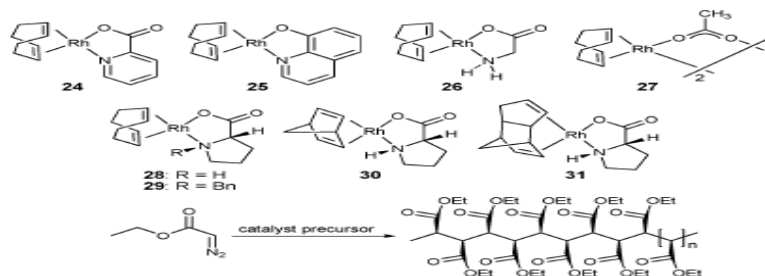


Table 1. Polymerization of Ethyl Diazoacetate (1) with (NHC)Pd/Borate Systems^a

run	(NHC)Pd	borate	[I]/[Pd] ^b	temp	yield (%)	M _n ^c	M _w /M _n ^c
1	2	4	20	r.t.	82.3	7800	1.19
2	2	4	50	r.t.	52.5	12 200	1.20
3	2	4	100	r.t.	49.3	15 100	1.36
4	2	4	200	r.t.	34.9	20 700	1.50
5	2	4	100	50 °C	52.3	16 500	1.40
6	2	4	100	0 °C	7.3	4100	1.20
7	3	4	20	r.t.	74.5	9900	1.32
8	3	4	100	r.t.	34.0	24 000	1.53
9	3	4	100	50 °C	57.3	19 800	1.70
10	3	4	100	0 °C	9.1	400	1.15
11	2	5	20	r.t.	57.5	5600	1.26
12	2	5	100	r.t.	56.6	17 600	1.67
13	3	5	20	r.t.	59.6	11 000	1.45
14	3	5	100	r.t.	40.8	20 400	1.62

^aIn THF (2 mL) for 13 h; EDA 1 = 0.30 to 1.76 mmol (1.66 to 3.33 M solution in CH₂Cl₂ or Cl₂HCCH₂Cl). ^b[Pd] = 2[(NHC)Pd(NQ)]₂. ^cM_n and M_w/M_n were obtained by GPC calibration using standard PMMAs and dibutyl sebacate in THF solution.

Ihara, E., Ishiguro, Y., Yoshida, N., Hiraren, T., Itoh, T., & Inoue, K. (2009). (N-Heterocyclic carbene) Pd/borate initiating systems for polymerization of ethyl diazoacetate. *Macromolecules*, 42(22), 8608-8610.



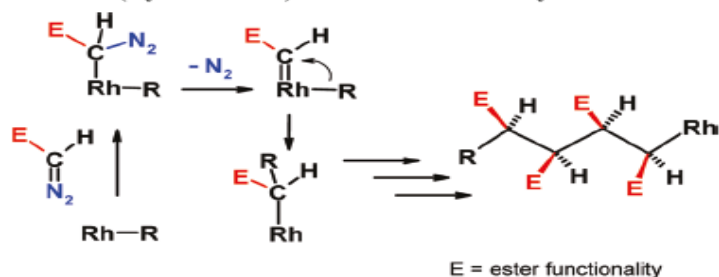
Scheme 16 Formation of high molecular weight stereoregular polymers by Rh-mediated polymerisation of EDA (showing syndiotactic poly(ethyl 2-ylidene-acetate)).

Table 3 Polymerisation of EDA with Rh-complexes 24–31

Entry	Catalyst	Yield (%)	M _w (Da)	M _w /M _n
1	24	11	130 000	3.7
2	25	11	140 000	3.7
3	26	30	150 000	3.4
4	27	15	150 000	3.7
5	28	50	150 000	3.6
6	29	25	120 000	2.9
7	30	5	350 000	15.4
8	31	30	540 000	2.0

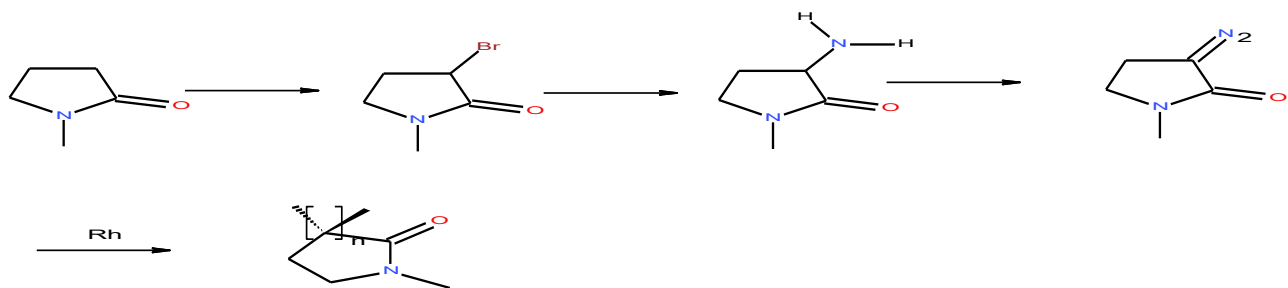
Jellema, E., Jongerius, A. L., Reek, J. N., & de Bruin, B. (2010). C1 polymerization and related C–C bond forming 'carbene insertion' reactions. *Chemical Society Reviews*, 39(5), 1706-1723.

Scheme 1. Rh-Mediated Carbene Polymerization Leading to Fully Functionalized, High Molecular Weight, and Stereoregular (Syndiotactic) Carbon-Chain Polymers



Jellema, E., Jongerius, A. L., van Ekenstein, G. A., Mookhoek, S. D., Dingemans, T. J., Reingruber, E. M., ... & Reek, J. N. (2010). Rhodium-mediated stereospecific carbene polymerization: from homopolymers to random and block copolymers. *Macromolecules*, 43(21), 8892-8903.

I would think that the Rh catalyzed C1 polymerization are superior to those employing Pd because of MW and stereoselectivity.

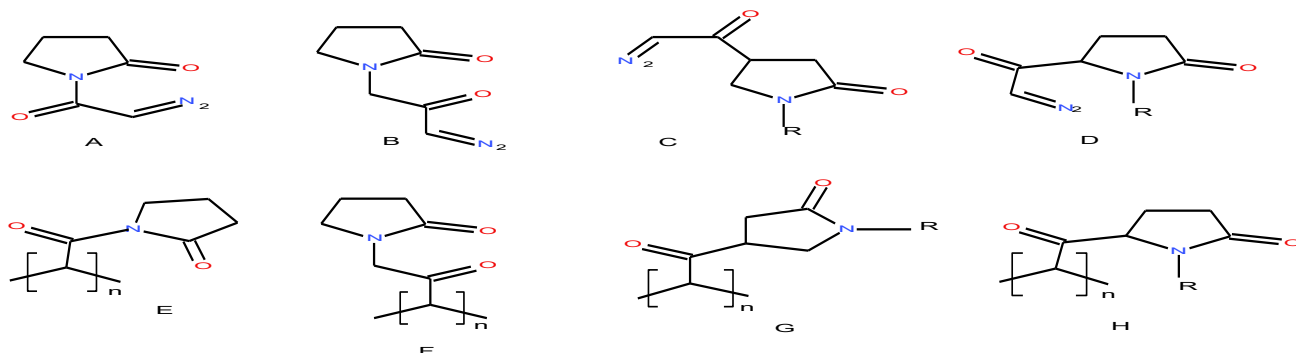


Scheme 2: Possible synthesis with readily available RM's.

So far I have not found a reference that shows a polymer like the above. Although this C1 polymerization seems possible, I'm concerned about the lack of references. Although diazoacetamide C1 polymerization is known.

Ihara, E., Hiraren, T., Itoh, T., & Inoue, K. (2008). Palladium-mediated polymerization of diazoacetamides. *Polymer journal*, 40(11), 1094-1098.

Therefore the following scheme 3 suggests more typical polymerizable diazocarbonyls.

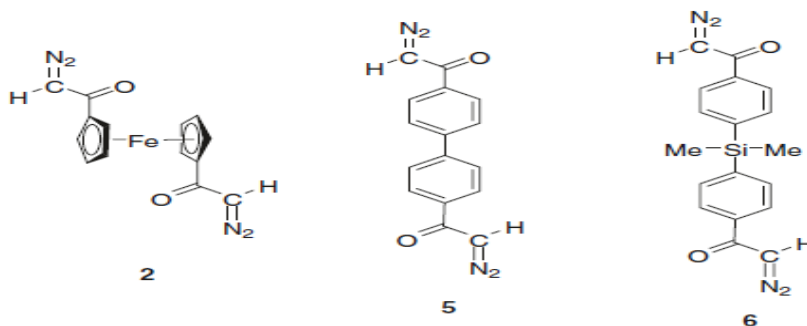


Scheme 3: More typical C1 monomers. Synthesis of the above diazocarbonyls seems straight forwardsee this reference:

Burtoloso, A. C., Momo, P. B., & Novais, G. L. (2018). Traditional and New methods for the Preparation of Diazocarbonyl Compounds. *Anais da Academia Brasileira de Ciências*, 90(1), 859-893.

C1 polymerization with appropriate Rh based catalysts would result in pyrrolidone containing polymers with a pyrrolidone moiety on every carbon. Such polymers and C1 copolymers (random or block) would exhibit unique complexing ability. Take iodine for example, its complex with PVP is of major importance as a safe biocide used daily in surgery. The C1 version having pyrrolidone on every carbon could conceivably complex more iodine than PVP resulting in superior biocidal activity. Wherever PVP or its copolymers are used a C1 version would afford interesting possibilities if not improved performance.

Carbene Dimerization

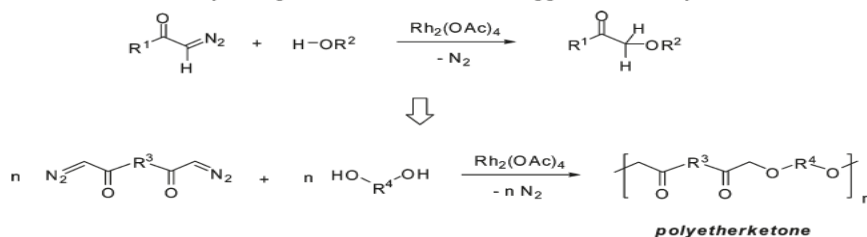


Scheme 1. Bifunctional diazocarbonyl compounds employed in this study.

These bis-diazocarbonyls 5&6 led to cross-linked polymers as each diazocarbonyl afforded a C1 polymeric incorporation while 2 formed a cyclic product. Apparently some -N=N- was also observed.

Ihara, E., Goto, Y., Itoh, T., & Inoue, K. (2009). Palladium-Mediated Polymerization of Bifunctional Diazocarbonyl Compounds: Preparation of Crosslinked Polymers by Copolymerization of Bi- and Monofunctional Diazocarbonyl Compounds. *Polymer journal*, 41(12), 1117-1123.

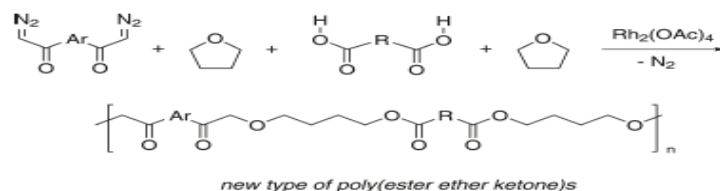
Scheme 1. O–H Insertion of Diazocarbonyl Compound with Alcohol and its Application to Polycondensation Affording Polyetherketone



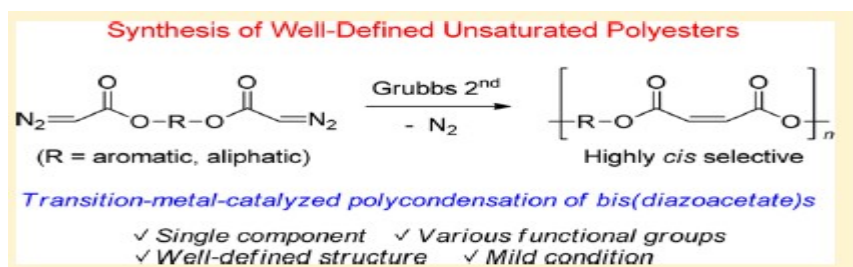
Ihara, E., Saiki, K., Goto, Y., Itoh, T., & Inoue, K. (2010). Polycondensation of bis (diazocarbonyl) compounds with aromatic diols and cyclic ethers: synthesis of new type of polyetherketones. *Macromolecules*, 43(10), 4589-4598.

These pioneers show how the carbene insertion reaction can be used to prepare polymers.

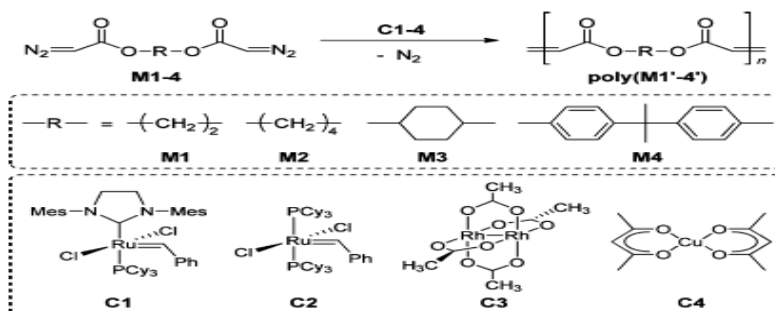
Scheme 2. Three-Component Polycondensation of Bis-(diazoketone) with Dicarboxylic Acid and THF



Ihara, E., Hara, Y., Itoh, T., & Inoue, K. (2011). Three-component polycondensation of bis (diazoketone) with dicarboxylic acids and cyclic ethers: synthesis of new types of poly (ester ether ketone) s. *Macromolecules*, 44(15), 5955-5960. This reference continues to illustrate the flexibility of the insertion reactions.



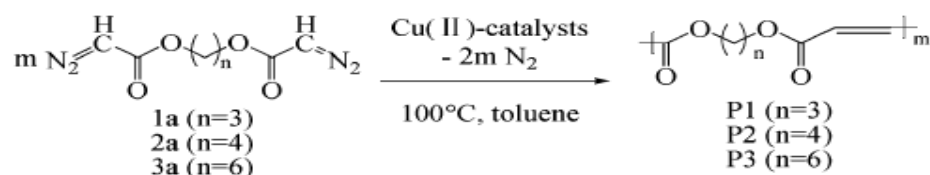
Scheme 2. Synthesis of Unsaturated Polyesters by Polycondensation of Bis(diazoacetate)s (M1–4) Using Transition-Metal Catalysts (C1–4)



Shimomoto, H., Hara, Y., Itoh, T., & Ihara, E. (2013). Synthesis of well-defined unsaturated polyesters by transition-metal-catalyzed polycondensation of Bis (diazoacetate) s. *Macromolecules*, 46(14), 5483-5487.

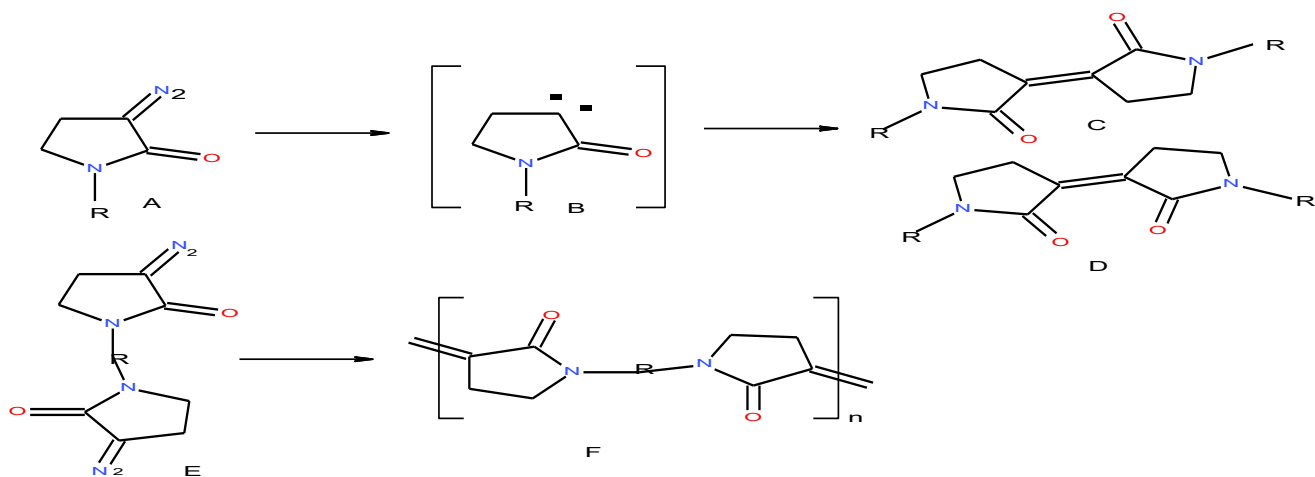
This is the first reference I found useful for my ideas for carbene alkene dimerization polymerizations.

Another example:



Scheme 1 Denitrogen alkene/coupling polymerization of bisdiazo compounds by copper-catalysts.

Xiao, L., Li, Y., Liao, L., & Liu, L. (2013). Denitrogen alkene polymerization of bisdiazo compounds by copper (II) catalysts. *New Journal of Chemistry*, 37(7), 1874-1877.



Scheme 4: Unsaturation pyrrolidone dimers and polymers. The pyrrolidones starting compounds can be coupled together with aldehydes or prepared from BLO and primary diamines. Preparation of the diazocarbonyl moieties is by one of the standard methods. From the above references, an appropriate catalyst can be chosen.

Thank you for reading these proposals!

Dr. Robert B. Login rloginconsulting.com