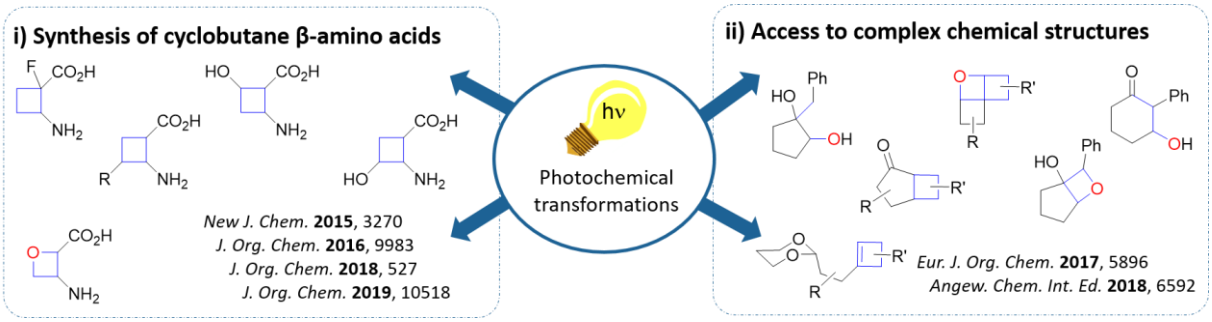
Photochemical Synthesis of Functionalized Cyclobutane Derivatives

Dr. Thomas BODDAERT

CP^{3}A Organic Synthesis group, Institut de Chimie Moléculaire et des Matériaux d'Orsay (ICMMO), UMR 8182, CNRS, Université Paris-Sud, Université Paris-Saclay,
15 rue Georges Clémenceau, 91405 Orsay Cedex France
web : https://www.icmmo.u-psud.fr/fr/perso/thomas-boddaert/
e-mail : thomas.boddaert@u-psud.fr

Cyclobutane derivatives are very versatile building blocks, thanks to the perfect balance between reactivity and stability. They can provide a source of chemical diversity due to their inherent ring strain as well as very interesting molecular scaffolds due to their specific behavior. Photochemical reactions can give an access to complex molecules that are difficult to obtain otherwise, such as our four-membered ring compounds.

This presentation will focus on our recent achievements on the development of light-initiated reactions to prepare functionalized cyclobutane β-amino acids, but also to create molecular diversity through the combination of a photochemical step with thermal transformations or other photochemical reactions.



Synthesis and reactivity of conjugated diynes and triynes: between synthetic methodology and interstellar chemistry

Yann TROLEZ

Univ Rennes, Ecole Nationale Supérieure de Chimie de Rennes, CNRS, ISCR – UMR6226, F-35000 Rennes, France

Some cyanopolyynes (R-(C≡C)$_n$-CN with R = H or Me) have been detected in the interstellar medium (ISM)[1] and on Titan for some of them.[2] For several years, our laboratory has been studying these compounds. The syntheses, chemical reactivity and photochemical reactivity of cyanopolyynes bearing two conjugated C≡C triple bonds (n = 2),[3] will be discussed. However, the synthesis of their superior counterparts (n = 3) stays elusive so far.

To solve this problem, we synthesized the bromocyanobutadiyne (Br-C≡C-C≡C-CN) and reacted it with different terminal alkynes under Cadiot-Chodkiewicz conditions.[4] Surprisingly, the corresponding cyanopolyynes were not obtained but more complex compounds, resulting from cascade reactions, were isolated. In particular, dienes were obtained stereoselectively when using monoacetylenic reactants. With triisopropylsilylbutadiyne, a functionalized benzofulvene was obtained (Figure 1). The mechanisms of formation of these unexpected products will be discussed.

Another methodology to access conjugated triynes, based on alkyne metathesis, will be discussed.[5]

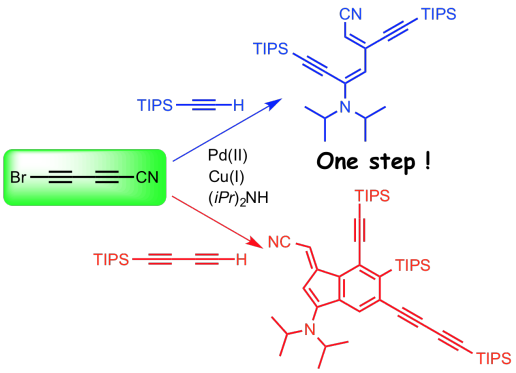


Figure 1. *Reactivity of bromocyanobutadiyne with triisopropylsilylacetylene and triisopropylsilylbutadiyne*

[1] P. Thaddeus, M. C. McCarthy, M. J. Travers, C. A. Gottlieb, W. Chen, *Faraday Discuss.* **1998**, *109*, 121

[2] a) A. Coustenis, T. Encrenaz, B. Bézard, B. Bjoraker, G. Graner, G. Dang-Nhu, E. Arié, *Icarus*, **1993**, *102*, 240; b) V. Vuitton, R. V. Yelle, V. G. Anicich, *Astrophys. J.* **2006**, *647*, L175

[3] a) Y. Trolez, J.-C. Guillemin, *Angew. Chem. Int. Ed.* **2005**, *44*, 7224; b) N. Kerisit, L. Toupet, Y. Trolez, J.-C. Guillemin, *Chem. Eur. J.* **2013**, *19,* 17683; c) N. Kerisit, C. Rouxel, S. Colombel-Rouen, L. Toupet, J.-C. Guillemin, Y. Trolez, *J. Org. Chem.* **2016**, *81*, 3560

[4] a) N. Kerisit, L. Toupet, P. Larini, L. Perrin, J.-C. Guillemin, Y. Trolez, *Chem. Eur. J.* **2015**, *21*, 6042; b) N. Kerisit, R. Ligny, E. S. Gauthier, J.-P. Guégan, L. Toupet, J.-C. Guillemin, Y. Trolez, *Helv. Chim. Acta* **2019**, *102*, e1800232

[5] I. Curbet, S. Colombel-Rouen, R. Manguin, A. Clermont, A. Quelhas, D. S. Müller, T. Roisnel, O. Baslé, Y. Trolez, M. Mauduit, *ChemRXiv.* **2019**, DOI: 10.26434/chemrxiv.8342534.vi

Dr. Thomas BODDAERT

UMR 8182 ICMMO (Institut de Chimie Moléculaire et des Matériaux d'Orsay)
Equipe CP^{3}A (Chimie Peptidomimétique, Photochimie et Procédés Alternatifs)

Université Paris-Sud / Université Paris-Saclay
15 Rue Georges Clemenceau
91405 Orsay Cedex

Tel : +33. (0)1.69.15.32.35
mail : thomas.boddaert@u-psud.fr

Parcours Professionnel :

Sept. 2012- **Maître de Conférences** à l'ICMMO (Institut de Chimie Moléculaire et des Matériaux d'Orsay) dans l'équipe CP3A (Chimie Peptidomimétique, photochimie et Procédés Alternatifs) avec le Pr. David AITKEN.
Développement de réactions photochimiques, synthèse d'aminoacides non-naturels et analyses conformationnelle des oligomères résultants, étude de la réactivité d'hydroxycyclobutanones : ***13 Publications, 1 article de vulgarisation et 1 article pédagogique***

2010-2012 **Stage Postdoctoral** au sein de l'IRCOF (Institut de Recherche en Chimie Organique Fine de Rouen) dans l'équipe Organométalliques et Ultra-Hautes Pressions, sous la direction du Dr. Jacques MADDALUNO et du Dr. Muriel DURANDETTI.
Etude et application d'un réarrangement anionique pour la synthèse de nouveaux hétérocycles silylés et germanilés: ***3 Publications***

2009-2010 **Stage Postdoctoral** dans le laboratoire du Pr. Jonathan CLAYDEN à l'université de Manchester.
Synthèse de peptides avec contrôle du sens d'hélicité et transfert de chiralité longue distance: ***4 Publications***

2006-2009 **Doctorat** (Bourse MENRT) au sein de l'ISM2 (Institut des Sciences Moléculaires de Marseille) dans l'équipe Stéréo à l'université d'Aix-Marseille III sous la direction du Pr. Jean RODRIGUEZ et du Dr. Yoann COQUEREL.
Développement de méthodologies de recherche impliquant des réactions consécutives et domino dans le domaine de l'organocatalyse et applications en synthèse de produits naturels: ***8 Publications et 1 chapitre de livre***

2000-2006 Ecole Supérieure de Chimie Organique et Minérale de Cergy-Pontoise (**ESCOM**) option recherche et développement. Parcours universitaire réalisé en parallèle jusqu'à l'obtention avec mention Bien du **Master 2 Recherche** option chimie fine de l'université de Cergy-Pontoise.

(Année de césure en Angleterre : 2004-2005)

Prix et Distinctions :

2019 Thieme Chemistry Journal Award
2009 Prix de thèse de la région PACA

Communications :

Conférences & Séminaires
- 3 conférences et séminaires invités
- 6 conférences dans des congrès nationaux et internationaux

Articles scientifique
- 28 articles scientifiques (h-index : 11, IF moyen : 5.05, citation : 461)
- 1 article de vulgarisation
- 1 chapitre de livre
- 1 article pédagogique

Encadrements et Enseignements

Encadrements 4 Masters II, 2 Doctorants diplômés Paris-sud co-encadrés, 2 Doctorants diplômés étrangers (pour une période de 6 et 9 mois), 1 Postdoctorant et autres stagiaires de courte durée.

Enseignements
- TD de Chimie Organique en M1 de Chimie (43.5h eqTD)
- TP de Modélisation Moléculaire en M1 de Chimie (12h eqTD)
- CM, TD et TP de Photochimie Organique en L3 de Chimie (16.75h eqTD)
- TD de Chimie Organique en L2 (26h eqTD)
- CM, TD et TP de Chimie Organique dans des UEs pluridisciplinaires sur les trois niveaux de Licence au sein de l'institut Villebon – *Georges Charpak* (79.375h eqTD)
- CM et TD de Chimie en DAEU (Diplôme d'Accès aux Etudes Universitaires) (37.5h eqTD)

6 Publications majeures :

6. *Stereocontrolled Preparation of Diversely Tri-Functionalized Cyclobutanes*: Z. Chang, R. Guillot, T. Boddaert, D. J. Aitken, *J. Org. Chem*. **2019**, *84*, 10518-10525.

5. *Preparation of cyclobutene acetals and tricyclic oxetanes via photochemical tandem and cascade reactions:* J. Buendia, Z. Chang, H. Eijsberg, R. Guillot, J. Xie, A. Frongia, F. Secci, S. Robin, T. Boddaert, D. J. Aitken, *Angew. Chem. Int. Ed.*, **2018**, *57*, 6592-6596.

4. *Cooperative 5- and 10-membered ring interactions in the 10-helix folding of oxetin homo-oligomers:* S. S. Ragab, A. F. Kassir, R. Guillot, M.-C. Scherrmann, T. Boddaert, D. J. Aitken, *Chem. Commun*., **2018**, *54*, 1968-1971.

3. *Acid-catalyzed synthesis of functionalized arylthiocyclopropane carbaldehydes and ketones:* S. Porcu, A. Luridiana, A. Martis, A. Frongia, G. Sarais, D. J. Aitken, T. Boddaert, R. Guillot, F. Secci, *Chem. Commun*. **2018**, *54*, 13547-13550.

2. *Stereoselective and Regioselective Pinacol-Type Rearrangement of a Fused Bicyclic Oxetanol Scaffold:* N. Melis, A. Luridiana, R. Guillot, F. Secci, A. Frongia, T. Boddaert, D. J. Aitken, Eur. *J. Org. Chem*., **2017**, 5896-5902.

1. *Synthetic access to all four stereoisomers of oxetin:* A. F. Kassir, S. S. Ragab, T. A. M. Nguyen, F. Charnay-Pouget, R. Guillot, M.-C. Scherrmann, T. Boddaert, D. J. Aitken, *J. Org. Chem.* **2016**, *81*, 9983-9991.

CURRICULUM VITAE

Yann TROLEZ
Ecole Nationale Supérieure de Chimie de Rennes
CNRS, UMR 6226, CORINT team
11, allée de Beaulieu
CS 50837
35708 Rennes Cedex 7
France
yann.trolez@ensc-rennes.fr
02.23.23.80.69

PROFESSIONAL EXPERIENCE

2015-2016	Half-time researcher at the "Université de Lorraine", UMR CNRS 7565 SRSMC under the direction of Philippe Gros
Since 2011	Assistant professor at the "Ecole Nationale Supérieure de Chimie de Rennes", research team: COrInt (ISCR).
2010-2011	Post-doctoral fellow - Laboratory of Organic Chemistry (ETH Zürich). Direction: François Diederich
2007-2010	PhD thesis at the "Laboratoire de Chimie Organo-Minérale". Supervision: Jean-Pierre Sauvage and Jean-Paul Collin (Strasbourg). Teaching at the University of Strasbourg.

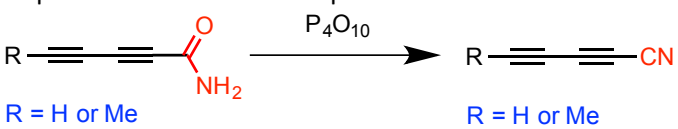
EDUCATIONAL BACKGROUND

2019	Habilitation to lead research (HDR)
2007-2010	PhD thesis at the "Laboratoire de Chimie Organo-Minérale". Supervision: Jean-Pierre Sauvage and Jean-Paul Collin, Strasbourg (France).
2006-2007	Master 2 « Chimie Moléculaire et Supramoléculaire », University of Strasbourg.
2005-2006	Studies of chemistry at the Ecole Normale Supérieure, Cachan (France). Laureate of the "agrégation" in chemistry.
2003-2005	Studies of chemistry at the Ecole Normale Supérieure, Paris (France).

CURRENT RESEARCH INTERESTS

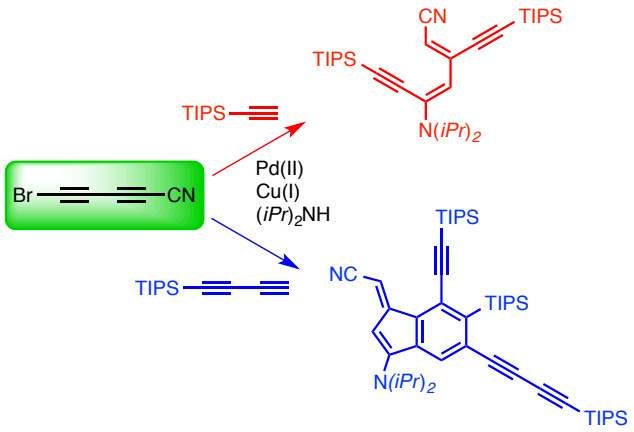
1) The interstellar organic chemistry and the origins of life

Following the idea that the main building blocks of life could have been brought on Earth from the interstellar medium (panspermy theory), we are willing to understand which kind of organic molecules are present in space, why, and what could be the relationship between them and prebiotically relevant compounds. In particular, we are interested in cyanopolyynes (H-(C≡C)$_n$-CN) and derivatives. We published new syntheses of cyanobutadiyne (*Angew. Chem. Int. Ed.* **2005**) and methylcyanobutadiyne (*Chem. Eur. J.* **2013**, *J. Org. Chem.* **2016**). We also perform photolyses experiments in the gas phase in order to understand how these molecules could be formed in the interstellar medium, and experiments in condensed phase to examine their reactivity.



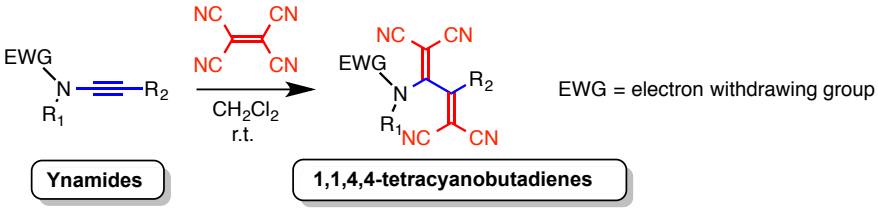
In order to synthesize the following members of this family, we synthesized the bromocyanobutadiyne (Br-C≡C-C≡C-CN) and reacted it with terminal acetylenes. Contrary to what was anticipated, the corresponding

cyanopolyynes were not obtained but other complex molecules were isolated, following an unprecedented mechanism (*Chem. Eur. J.* **2015**, *Helv. Chim. Acta* **2019**).



2) The synthesis of new 1,1,4,4-tetracyanobutadienes

We recently showed that a certain number of ynamides reacted very well with tetracyanoethylene to give 1,1,4,4-tetracyanobutadienes (TCBDs) in high yields, following a sequence of [2+2]cycloaddition-[2+2]retroelectrocyclization (*Chem. Eur. J.* **2014**; *Chem. Asian J.* **2017**). We are currently taking profit of the exceptional electron-withdrawing abilities of the TCBD group to tune the optoelectronic properties of some π-extended compounds (*Chem. Eur. J.* **2018**).



PUBLICATIONS

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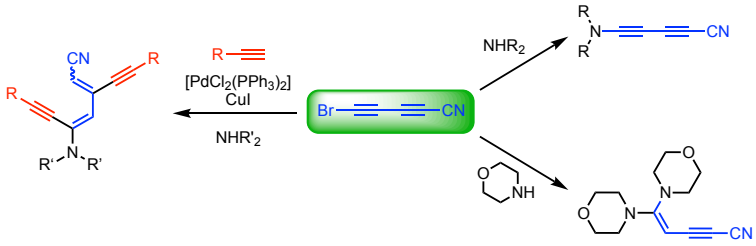
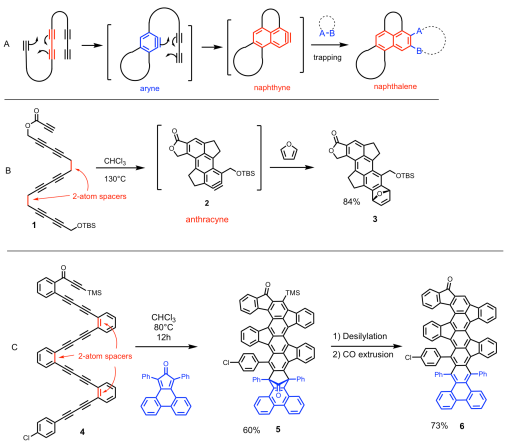
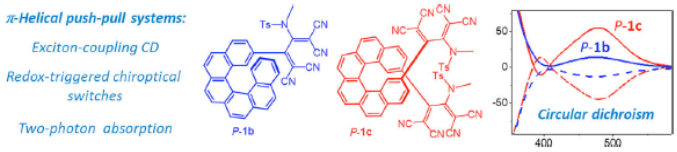
35) N. Kerisit, R. Ligny, E. S. Gauthier, J.-P. Guégan, L. Toupet, J.-C. Guillemin, Y. Trolez, "Synthesis and Reactivity of 5-Bromopenta-2,4-diynenitrile (BrC_5N): an Access to π-Conjugated Scaffolds", *Helv. Chim. Acta* **2019**, *102*, e-1800232



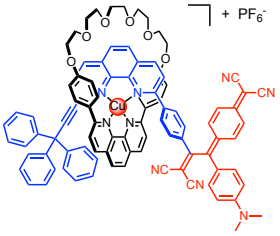
34) Y. Trolez, "The Domino Hexadehydro-Diels-Alder Reaction: An Elegant Way toward Polyacenes, *Chem* **2018**, 4, 2272-2274



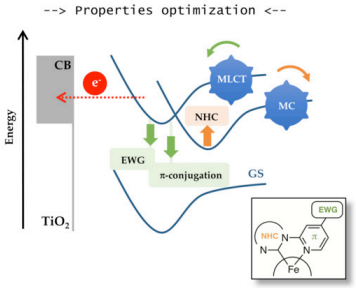
33) R. Bouvier, R. Durand, L. Favereau, M. Srebro-Hooper, V. Dorcet, T. Roisnel, N. Vanthuyne, Y. Vesga, J. Donnelly, F. Hernandez, J. Autschbach, Y. Trolez, J. Crassous, "Helicenes Grafted with 1,1,4,4-Tetracyanobutadiene Moieties: π-Helical Push–Pull Systems with Strong Electronic Circular Dichroism and Two-Photon Absorption", *Chem. Eur. J.* **2018**, 24, 14484-14494



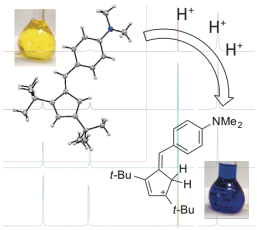
32) Y. Trolez, A. D. Finke, F. Silvestri, F. Monti, B. Ventura, C. Boudon, J.-P. Gisselbrecht, W. B. Schweizer, J.-P. Sauvage, N. Armaroli, F. Diederich, "Unconventional Synthesis of a Cu(I)-Rotaxane With a Superacceptor Stopper: Ultrafast Excited-State Dynamics and Near-Infrared Luminescence", *Chem. Eur. J.* **2018**, *24*, 10422-10433



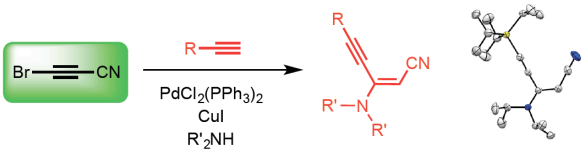
31) T. Duchanois, L. Liu, M. Pastore, A. Monari, C. Cebrián, Y. Trolez, M. Darari, K. Magra, A. Francés-Monerris, E. Domenichini, M. Beley, X. Assfeld, S. Haacke, P. C. Gros, "NHC-Based Iron Sensitizers for DSSCs" *Inorganics* **2018**, *6*, 63



30) S. Haberland, A. D. Finke, N. Kerisit, C. Katan, Y. Trolez, P. Gawel, I. Leito, M. Lokov, R. Järviste, K. Kaupmees, N. Trapp, L. Ruhlmann, C. Boudon, D. Himmel, F. Diederich, "Enhancement of Push–Pull Properties of Pentafulvene and Pentafulvalene Derivatives by Protonation at Carbon", *Eur. J. Org. Chem.* **2018**, 739-749



29) R. Ligny, E. S. Gauthier, M. Yáñez, T. Roisnel, J.-C. Guillemin, Y. Trolez, "One-step synthesis of conjugated enynenitriles from bromocyanoacetylene", *Org. Biomol. Chem.* **2017**, *15*, 6050-6056



28) M. Betou, R. J. Durand, A. Sallustrau, C. Gousset, E. Le Coz, Y. R. Leroux, L. Toupet, E. Trzop, T. Roisnel, Y. Trolez, "Reactivity of Functionalized Ynamides with Tetracyanoethylene: Scope, Limitations and Optoelectronic Properties of the Adducts", *Chem. Asian J.* **2017**, *12*, 1338-1346

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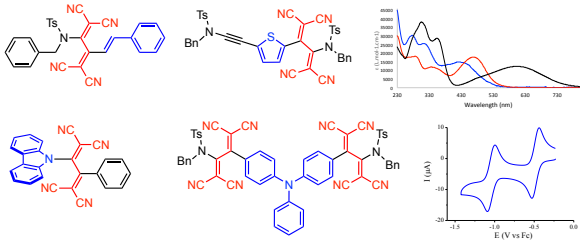
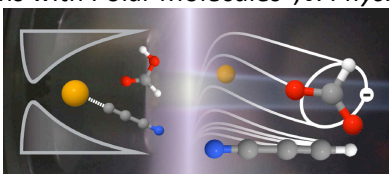
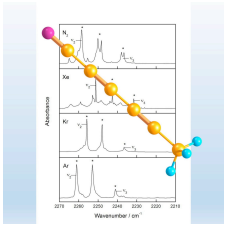


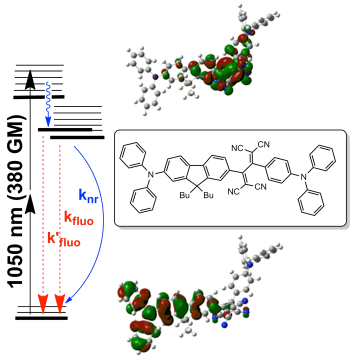
27) B. Joalland, N. Jamal-Eddine, J. Klos, F. Lique, Y. Trolez, J.-C. Guillemin, S. Carles, L. Biennier, "On the Low-Temperature Reactivity of C2*n*+1N- Anions with Polar Molecules", *J. Phys. Chem. Lett.* **2016**, *7*, 2957-2961



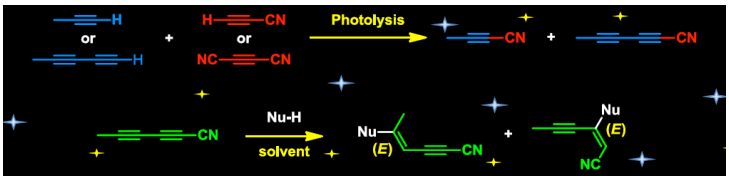
26) U. Szczepaniak, M. Turowski, T. Custer, M. Gronowski, N. Kerisit, Y. Trolez, R. Kołos, "Infrared and Raman spectroscopy of methylcyanodiacetylene (CH_3C_5N), *ChemPhysChem* **2016**, *17*, 3047-3054



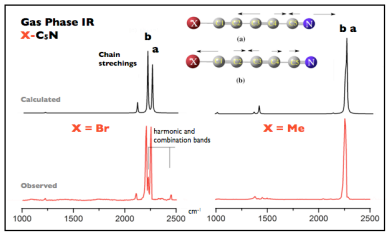
25) Z. Pokladek, N. Ripoche, M. Betou, Y. Trolez, O. Mongin, J. Olesiak-Banska, K. Matczyszyn, M. Samoc, M. G. Humphrey, M. Blanchard-Desce, F. Paul, "Linear Optical and Third-Order Nonlinear Optical Properties of Some Fluorenyl- and Triarylamine-Containing Tetracyano-butadiene Derivatives", *Chem. Eur. J.* **2016**, *22*, 10155-10167



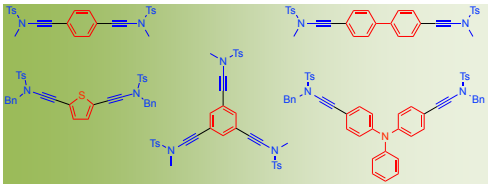
24) N. Kerisit, C. Rouxel, S. Colombel-Rouen, L. Toupet, J.-C. Guillemin, Y. Trolez, "Synthesis, Chemistry, and Photochemistry of Methylcyanobutadiyne in the Context of Space Science", *J. Org. Chem.* **2016**, *81*, 3560-3567.



23) M. M. Montero-Campillo, O. Mó, M. Yáñez, A. Benidar, C. Rouxel, N. Kerisit, Y. Trolez, J.-C. Guillemin, "Gas Phase Infrared Spectroscopy of Substituted Cyanobutadiynes. The Role Played by Bromine Atom and Methyl Group as Substituents.", *ChemPhysChem* **2016**, *17*, 1018-1024



22) M. Betou, A. Sallustrau, L. Toupet, Y. Trolez, "Synthesis of conjugated multi-ynamides by copper-catalyzed reaction", *Tetrahedron Lett.* **2015**, *56*, 4627-4630



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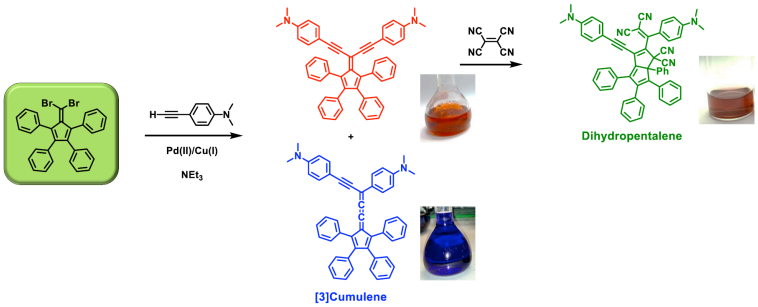

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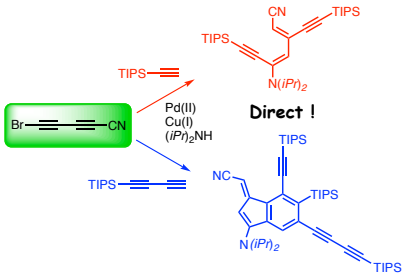

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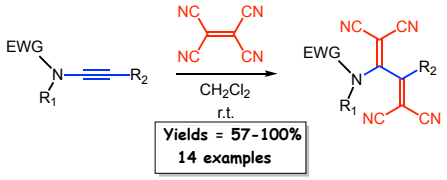

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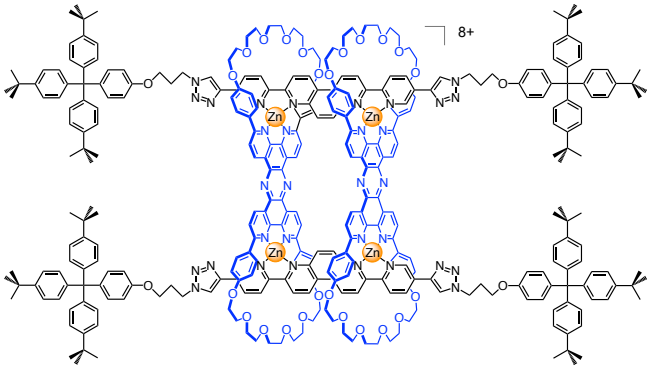

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