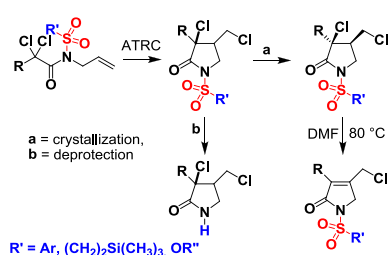
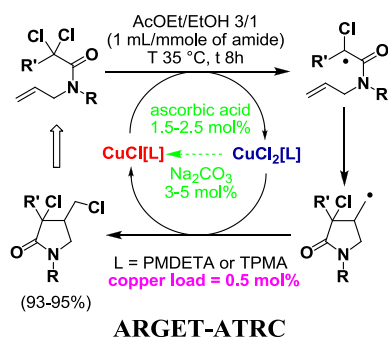
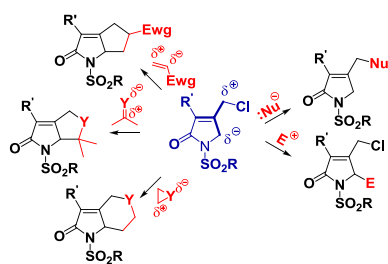


Atom Transfer Radical Cyclizations

Franco Bellesia, Franco Ghelfi, Fabrizio Roncaglia

Deprotection and dehydrohalogenation of *N*-sulfonyl- γ -lactamsSome hypothetical uses of the unsaturated γ -lactams

CONTACTS

Prof. Franco Ghelfi

franco.ghelfi@unimore.it

Tel. +39 059 205 5049

Sito web del gruppo

RESEARCH TOPIC

Synthesis of polychloro γ -lactams, by copper catalysed atom transfer radical cyclization (ATRC) of *N*-substituted-*N*-allyl- α -polychloroamides, and their transformation in valuable intermediates.

External collaborations:

Prof. Armando Gennaro e Dott. Abdirisak Ahmed Isse (Dipartimento di Scienze Chimiche, Università degli Studi di Padova),

Prof. Andrew J. Clark (Department of Chemistry, University of Warwick, UK).

Techniques and instrumentation:

reactions under controlled atmosphere, radical reactions, transition metal catalysis, electrochemical methods, analytical and preparative chromatography, GC-MS, HRMS, NMR, mini-pilot plant.

The most popular transition metal catalysed atom transfer radical cyclization (ATRC) is the cyclo-isomerization of *N*-allyl- α -haloamides.¹ Owing to its practical advantages, it has become one of the leading methods to prepare γ -lactams, important target structures in organic chemistry.¹⁻³ Not only a number of interesting products, natural and not, were obtained thanks to this method,¹ but useful domino processes, involving ATRC, were also developed.^{1,4-6} Typical catalysts for these reactions are Cu^{I} complexes with polydentate nitrogen ligands.¹ The metal complex, in its reduced state ($\text{Cu}^{\text{I}}\text{L}_m$) abstracts (reversibly) a halogen atom from the halo-precursor, generating a radical species and increasing its oxidation state by one unit ($\text{Cu}^{\text{II}}\text{L}_m\text{Cl}$). The radical intermediate then adds to the olefinic moiety yielding a new radical, which is quenched by halogen transfer from the oxidized complex $\text{Cu}^{\text{II}}\text{L}_m\text{Cl}$, regenerating the active form of the catalyst ($\text{Cu}^{\text{I}}\text{L}_m$) and affording the reaction product. The atom transfers to and from the metal complex follow a concerted mechanism, via an inner-sphere electron transfer process.³

Our current research in the field points to:

- decrease the mol% of metal through the regeneration of the complex active form by chemical reduction (“activator regenerated by electron transfer” or ARGET-technique)⁷ or by using a cathodic current (electrochemical regeneration);
- establish the kinetic constants which characterize the ATRC process;
- develop semicontinuous batch processes, where the catalyst is supported on a coated magnetic nanoparticles (MNP, e.g. Fe_3O_4), and can thus be easily excluded from the reaction mixture by an external magnetic field;⁸
- characterize sulfonyl protections, which are “easily” removable and make the cycloisomerizations more stereoselective;
- expand the synthetic potential of the downstream ATRC products, *N*-sulfonyl 4-chloromethyl-1*H*-pyrrol-2(5*H*)-ones.

Bibliography

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