Towards use of Floricil-Based Molecular Batch Molecular Reactors for Conventional Free Radical Chemistry

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Abstract: Floricil (60-100nm, activated)-based Batch Molecular Reactors have been assembled and used in a variety of conventional synthetically useful free radical transformations (Hydrogen Transfer Reactions, Radical Cascade Reactions and Addition to C=C and C=N bonds). Reactions proceeded smoothly in all cases in good to excellent yields at ambient temperature in aqueous and organic media. The advantages of newly assembled setup are ease of setup, recyclability of the solid media, flexibility and scope of the transformations to be performed and ease of scale-up of methodology.

Keywords: Free radicals, batch reactors, floricil, aqueous.

Increasing emphasis has been placed on producing synthetic organic compounds faster and more efficiently using conventional methodology [1]. It has been often observed that tried and true methods for performing synthesis, work up on individual and low number of reactions do not scale up well even to modest level of parallel synthesis. In nature, however, biological machines perform tasks that enable life to proceed [2, 3]. In the pursuit of nanoscale machines, chemists are inspired to mimic nature, to produce synthetic structures that perform tasks at our discretion.

Free radicals are ubiquitous, reactive chemical entities. Free radical reactions are an important class of synthetic reactions that have been traditionally performed in organic solvents [4]. In recent years, the number of reports of free radical reactions that use water and alternative media such as supercritical CO_2, ionic liquids, fluorous solvents and solid state have been increased [5]. Radical reaction is one of the most useful and flexible methods for organic reactions in alternative media, because most of the organic radicals species are stable and not reactive with the alternative media itself.

Molecular reactors are miniature reaction vessels that control the assembly of reagents to affect the outcomes of chemical reactions at the molecular level [6]. In many ways, they are analogous to common laboratory glassware with the unique advantage that after the chemical reaction has taken place, the products are removed and the reaction vessel can be reused [6,7].

Zeolites are crystalline aluminosilicate with highly ordered crystalline structure. Cavities of a defined size are formed in the rigid, three-dimensional networks composed of SiO^{4-} and AlO^{4-} tetrahedral. The lattice contains cavities of varying diameters, depending on the type of zeolite [6, 7]. A distinction is made between large-, medium- and small pore zeolites. Several examples of zeolite catalysis in organic synthesis have been reported previously, however the application of florisil molecular reactors is unknown in radical transformations as functional reaction media [8,9]. The advantage of radical over ionic reactions lies in chemo-selectivity, tolerance of a wide range of chemical functionalities without the need for protecting groups, the general absence of solvent effect, and the kinetically controlled reaction outcomes.

In line with our continous interest in development and utilization of molecular reactors in organic synthesis, we decided to examine the performance of the florisil-filled molecular reactors under batch conditions for investigation of free radical hydrogen transfer reactions and radical cascade reaction in aqueous and organic media.

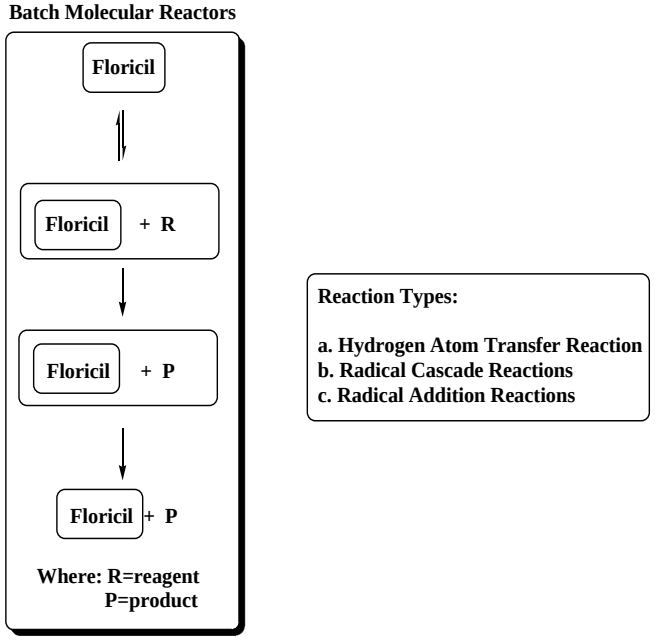

Fig. (1). Schematic representation of the prototype molecular device under investigation.

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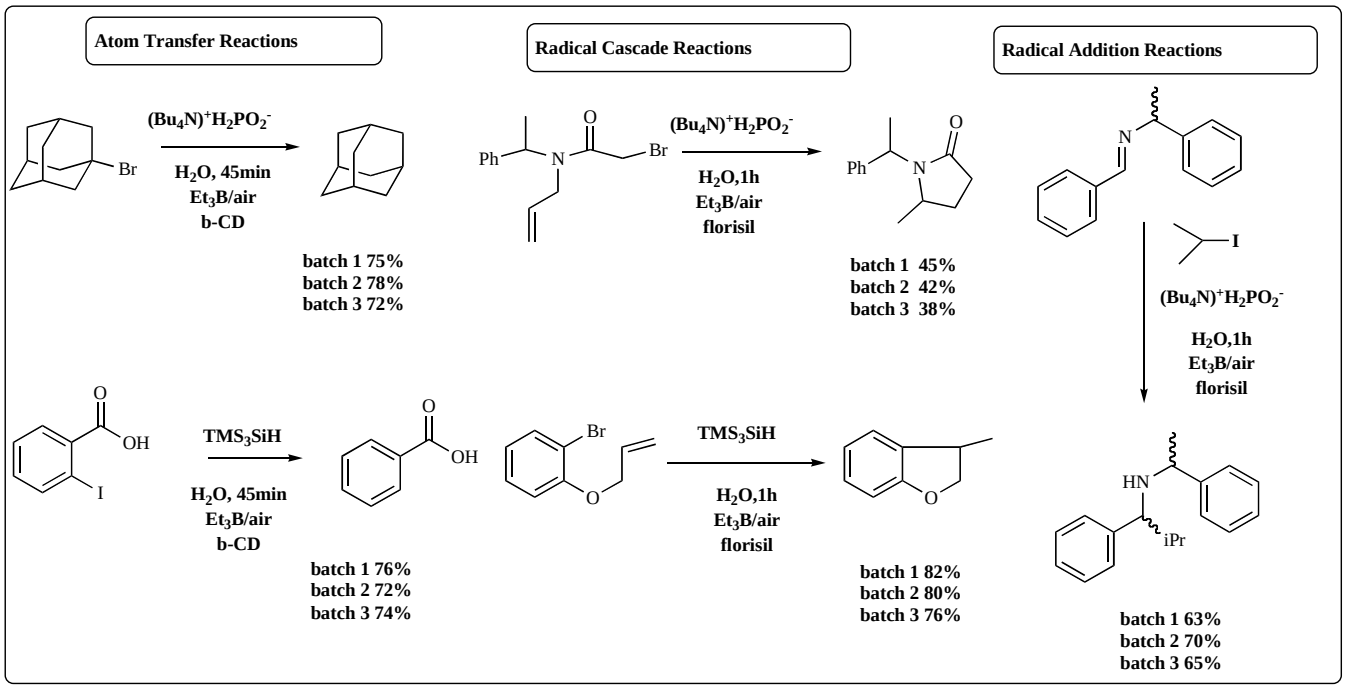

Scheme 1. Selected Free Radical Transformations performed in the floricil batched molecular reactors.

CONVENTIONAL FREE RADICAL CHEMISTRY FLORICIL AS MOLECULAR BATCH REACTOR

We chose to investigate the 3 types of synthetically useful free radical transformations: hydrogen transfer reaction and carbon-carbon bond formations *via* radical cascade reaction and radical addition to C=C and C=N bonds. All reactions were performed in aqueous and organic media in order to expand the applicability of the proposed methodology and results of the investigations are summarized in Scheme **1**.

Floricil (60-80nm) activated have shown to be a powerful experimental set-up as a molecular batch reactor suitable for the range of synthetically useful transformations, such as atom transfer reactions, radical cascade reactions and additions to C=C and C=N double bonds reported in Scheme **1** with the following advantages being observed in broad scope of fundamental synthetic transformations with added advantage of a homogeneous distribution of substrate, reactants and products over the molecular reactor, reliable operation and recyclability for 2-3 cycles at present and stable conditions under substrate-limiting conditions as well as unexplored and novel aspects of the transformations. In parallel, transformations were repeated in organic media (benzene and cyclohexane, for comparison) in order to provide comparison of the system performance in organic and aqueous media, with isolated yields being excellent in both solvent systems. The floricil was recycled and reused after thorough washing with hexane/ethyl acetate (50:50) mixture and drying, performance of zeolite was not altered. These outcomes demonstrate for the first time successful application of natural floricil as a functional molecular reaction media which is suitable for the use as a molecular batch reactor, which is commercially available, cheap and in some instances recyclable and undoubtedly will lead to further exciting developments and applications and further uses in chemically important transformations.

CONCLUSION

In this short communication we have demonstrated for the first time, excellent performance of the floricil-based molecular reactors under batch conditions in organic and aqueous media to expand the scope and application of conventional free radical chemistry in modern, potentially high-throughput conditions suitable to broad range of applications and future developments.

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