Enantioselective synthesis of fluorinated dihydropyrans

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Heterocycles based on fluorinated dihydropyrans occur in various biologically active compounds. [4+2] Cycloadditions represent a good approach to these heterocyclic structures. In our work, we focused on the study of the enantioselective synthesis of the asymmetric oxa-Diels-Alder reaction of fluorinated β,γ-unsaturated ketones, and α-ketoesters through the dienolate formation. By [4+2] cycloaddition reaction, under the conditions of mechanical activation in a ball mill, we prepared various derivatives of fluorinated dihydropyrans with three new stereogenic centers and with potential biological activity. Liquid-assisted grinding in combination with a suitable organocatalyst represents an efficient method of obtaining dihydropyrans in a short time, in high yields (up to 99%), with high diastereo- (>4:1) and enantiomeric purity up to 94 % ee. The biological activity of the prepared products will be tested in the near future.

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