Electronic Supplementary Material (ESI) for RSC Advances.

SUPPLEMENTAL MATERIALS

FOR

Green synthesis of (R)-3-TBDMSO glutaric acid methyl monoester using Novozym 435 in non-aqueous media

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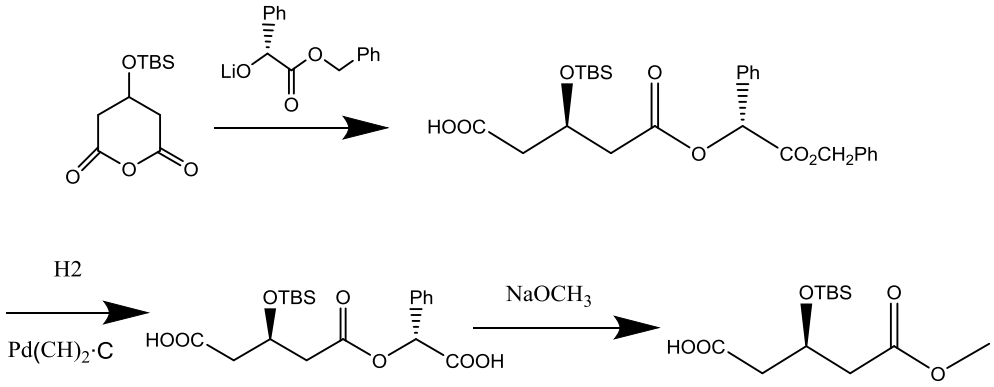
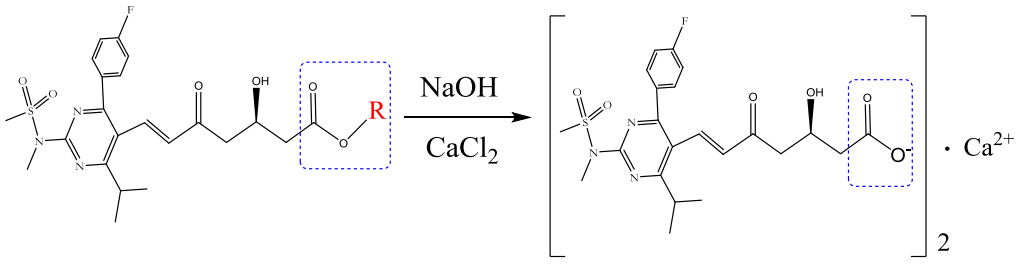
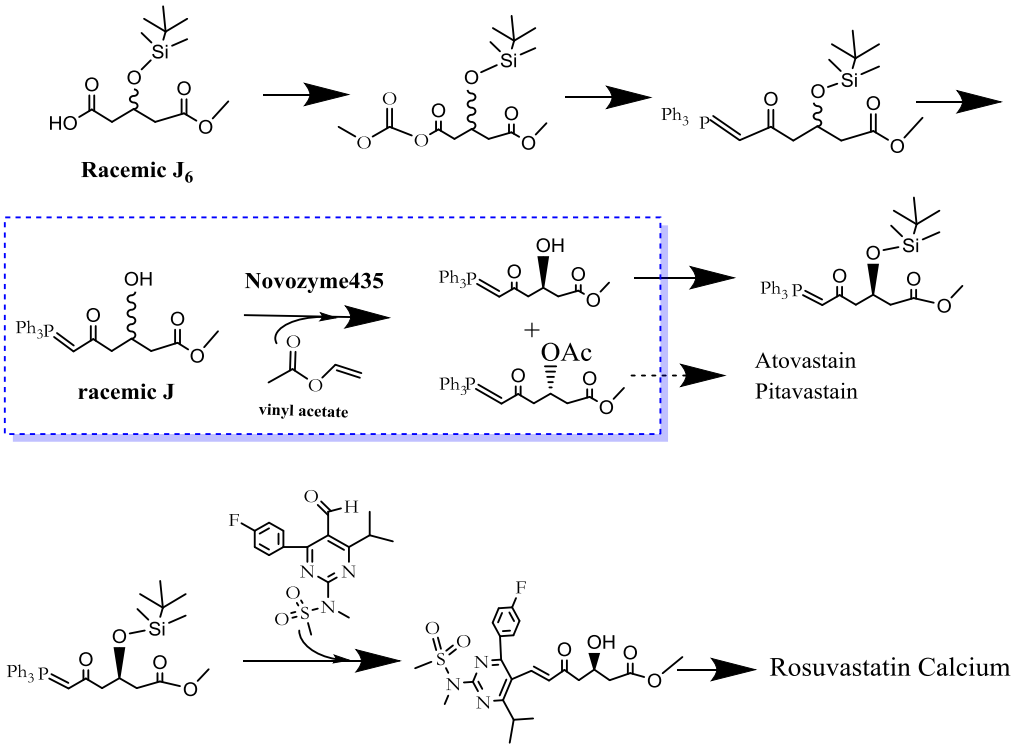


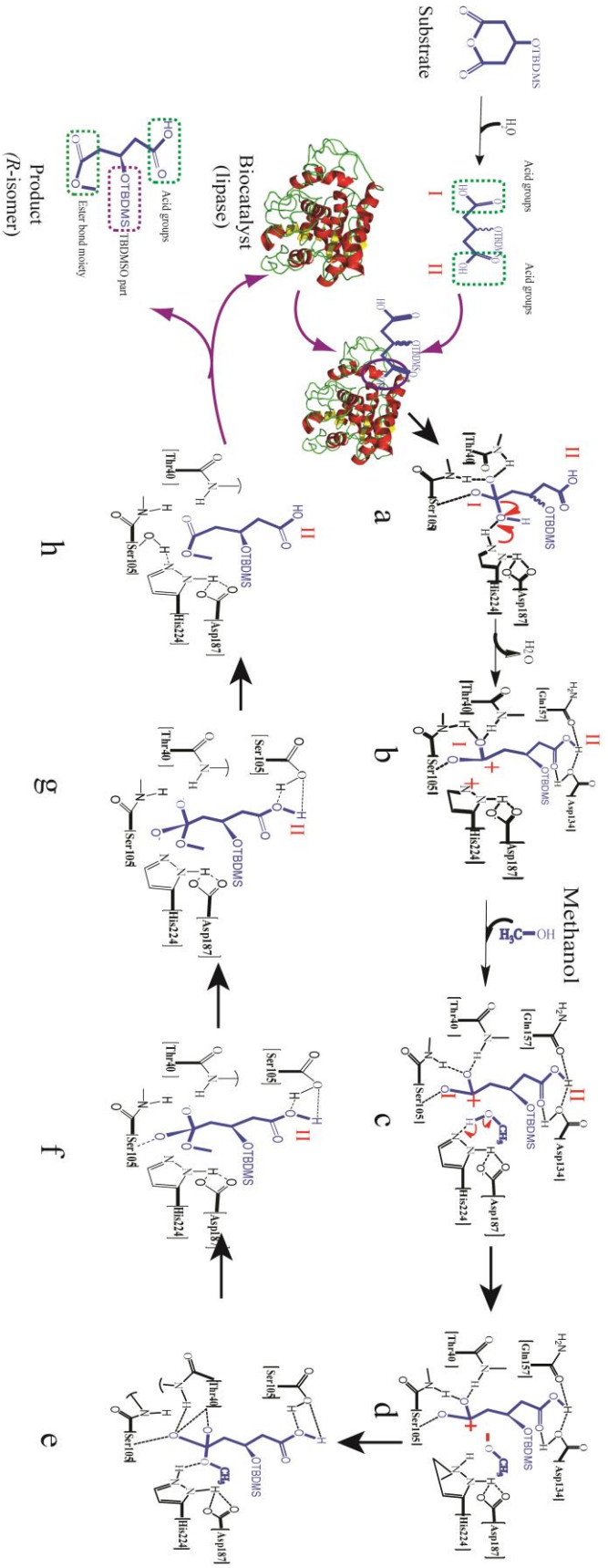
Scheme S1. Preparation of *R*-J$_6$ by chemical synthesis.



Scheme S2. Preparation of rosuvastatin calcium by chemical synthesis.



Scheme S3. The follow-up process from racemic J$_6$ to rosuvastatin calcium by Novozym 435. The optical purification of *R*-J$_6$ by enzymatic kinetic resolution is shown in the blue dashed box.



Scheme S4. The proposed mechanism for enzymatic synthesis of *R*-J$_6$ by CALB based on molecular docking and molecular dynamics. 3-TBDMSO glutaric acid is generated from 3-TBDMSO glutaric anhydride in the presence of trace water before participating at the active centre of CALB (Scheme 2a). Firstly, one of the carboxylic acids (I) coordinates with the lipase while the other (II), away from the catalytic center, is coordinated by Asp^{134} and Gln^{157}, providing a stable molecular conformation of the substrate in the catalytic site (Scheme 2b). Ser^{105} then attacks the carboxylic acid (I) to form a tetrahedral intermediate from which a water molecule is eliminated (Scheme 2b), leaving a positive charge at (I) .After binding of methanol to the catalytic site, the hydroxyl (–OH) is deprotonated by His^{224} to generate a negatively charged methoxy group (CH_3-O^-) (Scheme 2d). A C–O bond is then formed between the positively charged carbon of the carboxylic acid (I) and the negatively charged oxygen of the methoxy group (Scheme 2e). After the ester-bond formation, the free-energy of the transition state is at its minimum, the carboxylic acid group (II) is fixed by the Ser^{105} residue and the TBDMS substituent points out of the active site. Collapse of this intermediate releases *R*-J$_6$ (Scheme 2h).

Table S1. Enzymatic desymmetrization by hydrolysis of diethyl 3-hydroxyglutarate (a) and dimethyl 3-hydroxyglutarate (b).

Substrate	Enzyme	Activity	$[\alpha]_D^{20}$	Configuration
a	CALB	7 PLU/mg	+ 1.8 (c 11.5, acetone)	*S*
a	CALA		+ 1.8 (c 11.5, acetone)	*S*
a	CLEC-CALB	17 U/mg		*S*
a	HLL			*S*
a	RML	60 U/g		*S*
a	PLE	15 U/mg	+ 0.2 (c 11.5, acetone)	*S*
a	*A. lwoffii*	(cell cult.)		*S*
a	α -Chymotrypsin	70 U/mg		*R*
b	PLE			*S*
b	MCL	cell prep.		*S*