[P17] Predicting reaction conditions for Michael reactions

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In order to identify the structural reaction patterns describing different sub-types of reactions, partial derivative QSPR technology 3 and Condensed Graph of Reaction approach have been applied.

One can distinguish different types of Michael β-addition reactions, which proceed under different combinations of solvent (e.g., hydrophobic, aprotic polar, protic) and catalyst (e.g., Brønsted acid, Lewis acid, Lewis base, “no catalyst”). The question arises: which reaction conditions – particular solvent and catalyst – are the most favorable to carry out a given reaction? To answer this question, a number of 2-classes classification models have been built on a set of 198 Michael reactions retrieved from literature. Different machine-learning methods (SVM, Naïve Bayes and Random Forest) in combination with different types of descriptors (ISIDA fragments[1] issued from Condensed Graphs of Reactions[2], MOLMAP[3], EED, CDK[4]) have been used. Obtained models have a reasonable predictive performance in 3 times 3-fold cross-validation: Balance Accuracy varies from 0.7 to 1.

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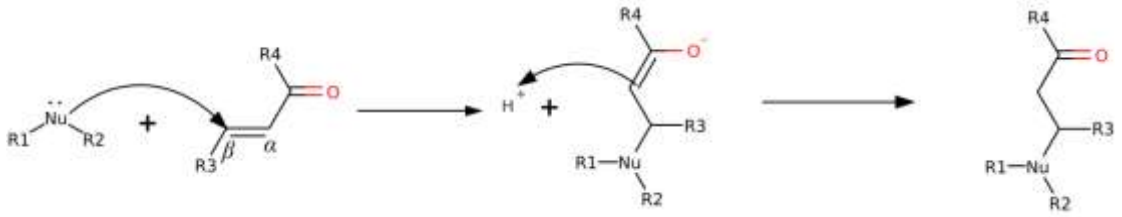

Figure 1. Michael β-addition reaction: optimal reaction conditions (solvent, catalyst) depend on nucleophile type (N or S) and the substituents R1, R2, R3 and R4.

[1] A. Varnek, D. Fourches, D. Horvath, O. Klimchuk, C. Gaudin, P. Vayer, V. Solov’ev, F. Hoonakker, I. V. Tetko, G. Marcou *Current Computer-Aided Drug Design*, 2008, **4** (3), 191-198.
[2] A. Varnek In: "*Chemoinformatics and Computational Chemical Biology*", J. Bajorath, Ed., Springer, 2010
[3] Q.-Y. Zhang, J. Aires-de-Sousa, *J. Chem. Inf. Model.*, 2005, **45**(6), 1775-1783.
[4] CDK Descriptor Calculator, version 1.1.1. http://cdk.sourceforge.net/ . Steinbeck, C.; Hoppe, C.; Kuhn, S.; Floris, M.; Guha, R.; Willighagen, E. L., *Curr. Pharm. Des.*, 2006, **12**, 2111.
[5] G. Marcou, D. Horvath, V. Solov'ev, A. Arrault, P. Vayer, A. Varnek, *Mol. Informatics*, 2012, **31**(9), 639–642