

DIRECT ANALYSIS OF CRUDE REACTION MIXTURE OF A PHOTOCATALYTIC C-H ARYLATION REACTION VIA MOLECULAR ROTATIONAL RESONANCE SPECTROSCOPY

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Analysis of the crude reaction mixture of the arylation product of cyclohexanone with 5-bromo-2-(trifluoromethyl)pyridine was performed by molecular rotational resonance (MRR) spectroscopy. This reaction was part of a recent study to investigate the use of decatungstate photocatalysis to perform direct arylation of aliphatic C-H bonds in order to provide a single-step access to multiple pharmaceutically relevant molecules. [1] Although this approach enables a simpler approach of molecular construction, the prevalence of C-H bonds in any given molecule often results in several arylation regioisomers. For the reaction presented here, prior analysis identified the main reaction product as the 3-substituted arylation product, with the minor component being the 4-substituted arylation product. In the initial analysis, the isomers were identified using nuclear magnetic resonance (NMR) spectroscopy and separated using ultra performance liquid chromatography (UPLC) in order to determine the relative composition. The crude reaction mixture was subsequently analyzed by broadband molecular rotational resonance spectroscopy. In order to identify the reaction products in the crude reaction mixture using MRR, low energy conformers of the reaction products were identified and the MRR structural parameters were calculated. Species were identified by agreement between theoretical and experimental rotational constants. In addition to the detection of the known reaction species and starting material, several other previously unknown impurities were identified in the sample, including the 2-substituted reaction product and a solvent derived byproduct. These species were verified in the analysis by NMR and UPLC data after identification by MRR spectroscopy. Quantitation of the relative abundance of the regioisomer products by MRR was performed by comparing the line intensity of the experimental transitions to the predictions from theory. The quantitative MRR results were in good agreement with the chromatographic results. This work demonstrates the capability of MRR to perform analysis of complex mixtures, simplifying the workflow of analysis. [1] Perry, I. B.; Brewer, T. F.; Sarver, P. J.; Schultz, D. M.; DiRocco, D. A.; MacMillan, D. W. C., Direct arylation of strong aliphatic C-H bonds. *Nature* 2018, 560 (7716), 70-75.