

## Technical Notes

# Energy Efficiency in Chemical Reactions: A Comparative Study of Different Reaction Techniques

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### Abstract:

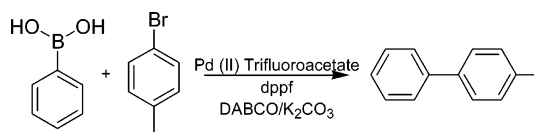
Metrics for chemists are much argued, but the energy usage of a reaction has to be one of the most simple and effective methods of comparing technologies. In this concept paper, the energy consumed in preparing one mole of a chemical compound is compared for a variety of technologies. Data are gathered for traditional oil bath, supercritical CO<sub>2</sub> (sc-CO<sub>2</sub>), and microwave reactors. Two different Suzuki couplings, a Knoevenagel condensation, and a Friedel–Crafts acylation are all compared in both the microwave and oil bath, as this is where the most noticeable differences were observed. The most notable result was an 85-fold reduction in energy demand on switching from oil bath to microwave reactor for a Suzuki reaction.

### Introduction

The subject of metrics is becoming increasingly important in green chemistry. Numerous papers have been published concerning the measurement of “greenness” within reactions,<sup>1</sup> however the majority of these seem to be only concerned with the efficiency of the chemistry of the reaction. Life cycle assessment teaches us that energy consumption should also be considered since it consumes (mainly nonrenewable) resources and produces waste. Escalating energy costs have also made energy efficiency an equally important metric in determining environmental acceptability and economic viability. Microwave-assisted chemical reactions have frequently been reported to show increased product yield, increased selectivity, and extremely short reaction times often in the absence of solvent.<sup>2</sup> These would appear to indicate good metrics, but the energy efficiency of such processes is not clear and rarely discussed. In an attempt to encourage the regular use of energy efficiency in process metrics we have compared the use of three different currently popular reaction techniques to carry out important organic reactions.

A system has been devised using a domestic six-dial electricity meter in series between the laboratory power

### Scheme 1. Suzuki coupling of phenyl boronic acid and bromotoluene



supply and reactor to measure the energy consumed during the course of the reaction. To normalise the data the energy has been calculated on the basis of moles of product formed. The experimental methods are shown in the footnotes. Assumptions are made to maintain the simple nature of the calculations, and no chemical or gas formation costs are included. As product mixtures were similar, the energy consumed in a work-up is not included as it would be identical for all crude mixtures (e.g., column then evaporation of solvent).

The homogeneous palladium-catalysed Suzuki coupling is currently a very popular reaction with the pharmaceutical and specialty chemical industries; in this example phenyl boronic acid and 4-bromotoluene are coupled to form the biaryl (Scheme 1). These reaction conditions<sup>4</sup> were selected as they are proven to work under both sc-CO<sub>2</sub> and conventional solvent conditions. Further reactions were studied with attempts made to cover a range of different chemistries. The second Suzuki coupling was selected as it is a traditionally low-yielding chloro-coupling which has been found to have excellent yields in a microwave reactor. The aluminium chloride catalysed Friedel–Crafts acetylation has been studied as an example of chemistry carried out below the “bubble point”. A Knoevenagel reaction was studied as an example of a base-catalysed reaction; furthermore, this methodology involved using a heterogeneous catalyst which the chemical industry is beginning to investigate as an alternative to homogeneous catalyst as it is simple to remove and recycle.

### Results and Discussion

Table 1 shows the results obtained for the Suzuki coupling reactions between phenyl boronic acid and bromobenzene carried out under the different reaction conditions.

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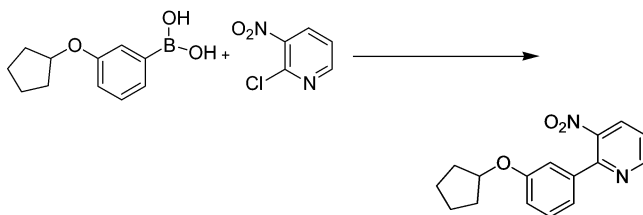
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**Table 1.** Table of results

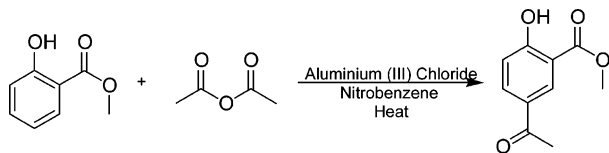
media	yield (%) <sup>a</sup>	energy (kW/mol) <sup>b</sup>
oil-bath dioxane	56.6	5830
oil-bath toluene	25.1	13541
microwave dioxane	40.7	1680
microwave toluene	0	n/a
Sc-CO <sub>2</sub> neat	11.5 (80°)	21840 (3360)

<sup>a</sup> GC yield from response factors. <sup>b</sup> Includes theoretical calculation for removal of solvent. <sup>c</sup> Literature yield.

**Scheme 2.** Suzuki coupling of cyclopentyloxybenzene boronic acid and 2-chloro-5-nitropyridine using a heterogeneous catalyst**Table 2.** Table of Results

reaction	thermal yield <sup>a</sup> / energy <sup>b</sup>	microwave yield <sup>a</sup> / energy <sup>b</sup>
heterogeneous Suzuki <sup>c</sup>	28.6/120700	77.4/1448
Friedel–Crafts acylation <sup>c</sup>	100/13.6	100/9.7
Knoevenagel <sup>d</sup>	68.2/132	18.2/37

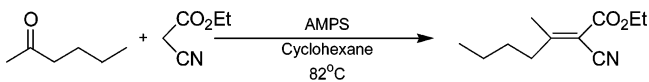
<sup>a</sup> % yield. <sup>b</sup> kW/mol. <sup>c</sup> GC yield. <sup>d</sup> GC yield corrected by *R<sub>f</sub>*.

**Scheme 3.** Friedel–Crafts acylation of methyl salicylate

The supercritical reaction has been reported to give 80% yield,<sup>4</sup> which would equate to an energy usage of around 3360 kW/mol. This is still considerably higher than the microwave reaction but is twice as energy efficient as the traditional thermal method.

In the next reaction selected for the microwave (Scheme 2) the Suzuki coupling of 2-chloro-5-nitropyridine with the boronic acid over Si Cat1,<sup>5</sup> a 77% yield was obtained in 4 min which corresponds to an energy usage of 1500 kW/mol—nearly 2 orders of magnitude less than that of the oil bath (Table 2).<sup>7</sup> The low yields under the conventional thermal conditions make the energy consumption per gram extremely high compared to that calculated in the microwave. However, even taking this into account, there is a huge energy saving in using microwaves.

The aluminium chloride-catalysed Friedel–Crafts acetylation of methyl salicylate was studied (Scheme 3/Table 2) as another example of a reaction highly important in many

**Scheme 4.** Knoevenagel reaction

chemical manufacturing processes. The energy efficiency of the microwave method is again higher than the thermal reaction although this time the difference is less due to the lower temperature and short reaction times required.

The heterogeneous aminopropyl silica-catalysed Knoevenagel reaction was selected as a base-catalysed reaction for comparison (Scheme 4/Table 2). When powered in the microwave, the yield could not be pushed above 18.6%; this is probably partially due to water being formed in the reaction system. Under thermal conditions a Dean–Stark water-collecting system was employed to azeotropically remove the water produced during the reaction, since according to the literature this boosts the yield.<sup>6</sup> Additionally, the reaction is conducted in cyclohexane which is not a good microwave absorbing solvent; hence, these conditions reduced the rate of reaction during microwave heating. The good yield along with the low boiling point of the solvent and short reaction time make the Knoevenagel thermal reaction relatively low in terms of energy usage.

The results indicate a significant gain in energy efficiency using microwave activation. Microwave activation provides highly focused energy, enabling rapid reaction and more efficient energy consumption. This is in addition to any actual microwave effect causing specific bond activation. We did use typical laboratory equipment in terms of type and size, and oil-bath reactions were not lagged. With low-boiling solvents and comparatively short reaction times the oil bath becomes more energy efficient. Continuation of this study into flow systems versus batch and semi-batch processes would be interesting; continuous processing should increase the energy efficiency of the system further. Application of this methodology to other systems would allow for quantification of the energy savings offered by process intensification. The supercritical reactors shared similar energy efficiency to oil baths—when the work-up of the product is considered, large energy savings may be possible using the supercritical method.

We hope that this preliminary study will encourage others to develop this concept and report other and more thorough calculations of the energy demands of reactions carried out under fundamentally different conditions. In this way we can seek to move towards a more proper consideration of energy consumption in green chemical process metrics.<sup>8</sup>

## Experimental Methods

**Suzuki 1.** Palladium (II) trifluoroacetate (5.00 mol %), bis(diphenylphosphino)ferrocene (dppf) (10.0 mol %), DABCO/K<sub>2</sub>CO<sub>3</sub> (1.49 mol equiv), benzenboronic acid (1.10 mol equiv), and bromobenzene (1.00 mol equiv) were added to an appropriate vessel. For thermal and microwave reactions toluene or 1,4-dioxane were used as solvents.<sup>4</sup> Microwave conditions were 300 W for 1 h with simultaneous air-cooling

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under autogenous pressure (maximum temperature 180 °C). Thermal reactions were carried out under reflux conditions at atmospheric pressure for 24 h. The supercritical rig was pressurised to 600 psi at room temperature, heated to 100 °C and pressurised to 2500 psi.

**Suzuki 2.** 2-Chloro-5-nitropyridine (1 mol equiv), boronic acid (1.1 mol equiv), K<sub>2</sub>CO<sub>3</sub> (2 mol equiv), Si-Cat1<sup>5</sup> (0.05 mol equiv Pd) in xylene were mixed in an appropriate vessel and stirred at 120 °C for 8 h at atmospheric pressure or microwaved at 300 W 4 min.

**Friedel–Crafts Acylation.** Methyl salicylate (1 mol equiv), acetic anhydride (1.1 mol equiv), aluminium chloride (3 mol equiv) were stirred in nitrobenzene in an appropriate vessel at 60 °C for 4 h at atmospheric pressure or with a microwave programmed to ramp for 2 min to 120 °C, then ramp to 180 °C over 2 min, then hold for 4 min under autogenous pressure.

**Knoevenagel.** As by Macquarrie et al., see ref 6.<sup>6</sup>

**Hardware.** Heidolf MB 3003 stirrer hotplate, CEM Discover microwave reactor, supercritical extraction rig SFT-150 SFE system with Julabo F12 cooler, and a Varian 3800 GC with autosampler. No computer control systems were included in the energy calculation, only the reaction hardware. On the supercritical extraction rig the cooling system was only switched on when pressurising the vessel to minimise energy wastage. No energy was added for the compression of the CO<sub>2</sub> into the cylinder and compressed air used for simultaneous cooling of the microwave.

#### Acknowledgment

We thank GSK for support for this project.

Received for review November 1, 2004.

OP0498060