

APPLICATION OF MICROWAVE ENERGY TO ORGANIC SYNTHESIS:  
IMPROVED TECHNOLOGY

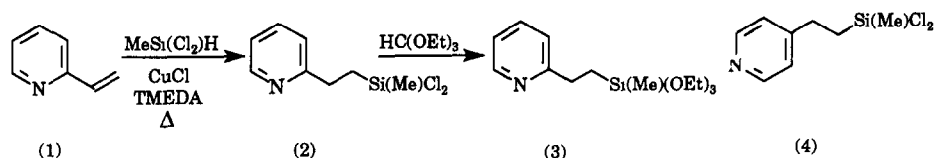
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**Abstract:** The application of microwave energy to the sulfonation of naphthalene and anthraquinone, to the amination of *p*-chloronitrobenzene, and to the hydrosilylation of 2- and 4-vinylpyridine has been studied. Though faster (5 - 360-fold) reactions were observed problems were encountered with the available microwave technology. These were overcome by using a microwave oven equipped with stirring facility and both temperature and pressure control.

The application of microwave energy to effect a variety of chemical processes has blossomed rapidly in the past few years. From its use in moisture analysis<sup>1</sup> and wet ashing of biological and geological materials<sup>2</sup> it has been applied to base-catalyzed hydrolysis of esters,<sup>3</sup> to S<sub>N</sub>2 reactions,<sup>3</sup> to Diels Alder reactions,<sup>4</sup> to the synthesis of short-lived pharmaceuticals,<sup>5</sup> applications for dry organic reactions,<sup>6</sup> the synthesis of intercalation compounds,<sup>7</sup> and to polymerization and curing of polymers,<sup>8</sup> (all in sealed Teflon or glass vessels). Reports are now appearing of much faster reactions carried out in open glass vessels.<sup>4b, 9, 10</sup>

We found<sup>11</sup> that the hydrosilylation of 2-vinylpyridine (**1**) with methylchlorosilane and CuCl in the presence of TMEDA (18h at 180°C) (with or without Et<sub>3</sub>N) was, as reported<sup>12a</sup> a very dirty reaction whose extremely tedious workup produced a low yield (5%) of the desired (**2**).<sup>12b</sup> The same reaction in a PARR 23 ml microwave bomb in a Sears microwave oven (750W) (six 30 sec bursts of energy at full power, separated by 30 min cooling down periods, followed by workup and isolation of the product as the diethoxysilane derivative (**3**)) led to a very clean reaction whose workup was very facile, and to a good yield (75%) of product.<sup>11</sup> This represents a dramatic 360-fold decrease in reaction time and a considerable improvement in yield and workup. 4-Vinylpyridine gives (**4**) (71%, 10m, microwave oven), as opposed to a 50% yield after 16 hr of conventional heating.<sup>13</sup>



We examined some applications of microwave energy to reactions of interest to industry. Amination of *p*-chloronitrobenzene to *p*-nitroaniline with aq. ammonia occurs in a Teflon bomb, but at the high (180°C) internal temperatures and pressures necessary the Teflon was gradually destroyed and the bombs leaked (the internal temperatures were determined by long, tedious calibrations using a series of compounds in sealed mp tubes<sup>4a</sup> for every reaction mixture, volume, power setting and heating time). The reaction was then carried out in sealed thick-walled Pyrex tubes, with microwave irradiation at low power for 2-2.5 min followed by a cooling period, and then repeating the process 15-20 times. Even then the tubes exploded occasionally. Using a Cu<sub>2</sub>O catalyst the reactions go faster and more safely, and a 93.2% yield of product could be obtained after a total heating time of 1 h, compared with 95% after 10 h of conventional heating<sup>10</sup> (10-fold decrease in reaction time). This procedure is still not practical and the technology of heating and temperature (or pressure) control in sealed glass vessels will have to be developed.

The industrially important sulfonation of naphthalene to naphthalene-1- and -2-sulfonic acids with conc. H<sub>2</sub>SO<sub>4</sub> takes place in good yields (78%) at 163°C (4 h).<sup>15</sup> Using conventional microwave bombs, temperature control was difficult. Pressure control (CEM Corp. model MDS-81D microwave bomb) could not be used, since conc. H<sub>2</sub>SO<sub>4</sub> has a negligible vapor pressure at those temperatures. Sulfonation of anthraquinone with fuming sulfuric acid (18% SO<sub>3</sub> at 135°C for 3 h and then 66% SO<sub>3</sub> at 110°C for 4h) takes place conventionally and gives 49% of anthraquinone-2-sulfonic acid.<sup>16</sup> Pressure control of microwave power should be possible but as SO<sub>3</sub> is consumed, the pressure drops, and the internal temperature rises so as to restore the desired pressure, and disulfonation now predominates.

CEM Corp. modified their model MDS-81D microwave oven for us to incorporate some rudimentary stirring capability and an internal temperature monitor/controller. Sulfonations

could now be effected efficiently. Naphthalene and 98% H<sub>2</sub>SO<sub>4</sub> at 160°C (3 min) gave a 92.5% yield of sulfonic acids ( $\beta$ -: $\alpha$ - = 87.7:4.7; isomer ratio most conveniently determined by integration (300 MHz NMR): $\delta$  7.6(s) for C<sub>1</sub>-H ( $\beta$ -isomer), 7.9(d) for C<sub>8</sub>-H ( $\alpha$ -isomer)) (after 3 min heating in an oil bath the  $\beta/\alpha$  ratio was 2.1 1; after 5.55 min it was 10:1). Anthraquinone-2-sulfonic acid (53.9%) was formed in 6 min with 30% fuming H<sub>2</sub>SO<sub>4</sub> at 170°C.

Some comments about the wide variation in rate enhancements observed with microwave energy as compared with conventional forms of heating is appropriate. Rate increase ranging from 2 to 1240-fold have been reported by various authors. Apparently,<sup>17</sup> microwave and conventional heating effect hydrolysis of adenosine triphosphate at pH 6.8 at the same rate, and an earlier 25-fold rate acceleration reported with microwave heating is probably accounted for either by erroneous temperature readings or by a strong temperature gradient in the sample. That this is not the case in general is suggested by the sulfonation of anthraquinone, where the temperature is monitored and controlled inside the vessel and the solution is stirred (no temperature gradients -- though localized superheating possible). On the other hand, the rate increases observed in these cases are modest compared to, say, hydrosilylation (no solvent) or the reactions on Montmorillonite. We suggest that if the microwave energy is absorbed by the solvent (e.g. H<sub>2</sub>SO<sub>4</sub>) and not by the substrate only modest rate increases (if any) will result over conventional heating. If, on the other hand, the microwave energy is absorbed by a reactant (vinylpyridine or its copper complex) or by a complex or an intermediate on the way to the rate-determining transition state then large rate increases will result. We plan to test this hypothesis soon.

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