Green microwave nitration as an undergraduate organic chemistry lab procedure

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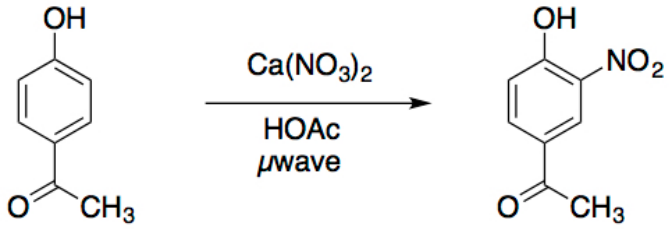
ABSTRACT: The purpose of this research is to modify a recent method from the literature [1] to design an undergraduate organic chemistry lab that utilizes the "12 Principles of Green Chemistry" and that is significant in the curriculum. In this procedure, 4-hydroxyacetophenone is nitrated with calcium nitrate and acetic acid to create 4-hydroxy-3-nitroacetophenone. The transformation occurs smoothly, at high yield, with microwave irradiation at low power for under 10 minutes. This procedure is efficient, feasible in a three-hour lab period, and uses much safer conditions than the usual approach with nitric acid and sulfuric acid.



As the field of green chemistry advances, the adoption and development of new, greener undergraduate lab curricula that can teach students about the "Twelve Principles of Green Chemistry" become increasingly more important. The nitration of phenols, a classic organic synthesis performed to demonstrate electrophilic aromatic substitution, is a synthesis that typically uses reagents that are both not green; instead, they are toxic and hazardous.

Since phenolic nitrations teach important organic processes but also are common to many different industries, such as the pharmaceutical, agricultural, and food industries, it is vital to find ways to make this type of reaction more green and more accessible to undergraduate institutions. Recently, many methods have been published that use safer nitrating reagents, *e.g.* $Ca(NO_3)_2$ or $Cu(NO_3)_2$, as replacements for the usual approach that uses nitric acid and sulfuric acid and carry out the reaction with a domestic microwave. We chose to modify a recently published method that uses $Ca(NO_3)_2$ and glacial acetic acid, basing our decision off of the safety profiles of many different electrophilic reagents and choosing to work with $Ca(NO_3)_2$ as we saw that it posed the least safety concerns. The method was modified by using a microwave reactor to carry out the nitration, instead of a domestic microwave, thereby decreasing the time required for the reaction to proceed as well as the amount of materials required, decreasing the total potential waste. A starting phenol was chosen, also as a result of its relatively benign safety profile, and a green microwave method for the nitration of 4-hydroxyacetophenone ($C_8H_8O_2$, *Acros Organics*) was developed.

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[1] Bose, A.K.; Ganguly, S.N.; Manhas, M.S.; Rao, S.; Speck, J.; Pekelny, U.; Pombo-Villars, E. "Microwave promoted rapid nitration of phenolic compounds". *Tetrahedron Lett*. **2006**, *47*, 1885-1888.

METHOD: To a 10 mL microwave pressure tube is added 4-hydroxyacetophenone (0.5010 g; 3.68 mmol), calcium nitrate (1.2509 g; 6.91 mmol), and glacial acetic acid (2.5 mL). The tube is capped with a Teflon pressure cap and irradiated for 1 minute, at constant power, ranging from 1 to 32 W. Samples are filtered and recrystallized in ethyl acetate (*ca.* 2 mL). Students can verify they have made the intended product, 4-hydroxy-3-nitroacetophenone, through melting points, FTIR, and H-NMR spectra.

Table 1: *Optimized microwave conditions. Averages were taken of all results from similar power conditions. All samples were run for 1:00 minute. Literature melting point of 4-hydroxy-3-nitroacetophenone is 131-133 ºC.*

Power (W)	# of trials	mp (ºC)	Yield
<4	3	131-132	13.4%
8	5	131-132	16.7%
16	16	131-132	40.5%
24	3	131-132	38.2%
>24	13	Not in 120-150 range	-