# Microwave activation of alumina and its use as a catalyst in synthetic reactions

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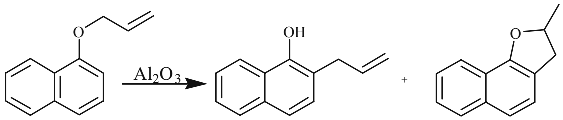
Microwave irradiation is a simple and efficient method of activating gamma alumina. Alumina activated in this manner is an excellent medium in which to carry out the Diels–Alder reaction and, in conjunction with additional microwave irradiation, the Claisen rearrangement. Several 2-allylphenols formed in the Claisen rearrangement rapidly undergo ring closure on alumina to form dihydrobenzofurans demonstrating the Brønsted acidity of the solid.

**Keywords:** alumina, microwave activation, Diel–Alder reactions, Claisen rearrangement, ring closure

Chemists continue to examine new phases in which to carry out reactions. Among these phases are the surfaces of solid metal oxides such as silica, clays, zeolites, and γ-alumina which is particularly interesting because of its unique surface characteristics that change when activated by heating under vacuum.[1-4] As a result, γ-alumina has been extensively used to carry out myriad organic transformations.[5] The major obstacle in using γ-alumina in organic chemistry is the activation procedure which requires using a home-built apparatus. We thus have examined microwave heating as a simpler, more readily available methodology for activating the solid.[6-8] We have tested this idea on the extensively studied Diels–Alder reaction[9-16] and Claisen rearrangement.[17-23] We have previously examined in detail the Diels–Alder reaction on thermally activated alumina,[24-30] but the Claisen rearrangement is new to us. The Claisen rearrangement of allyl phenyl ethers has been carried out on silica gel[31] and alumina.[32,33] The reaction of most relevance to the current study is the isomerisation of allyl 1-naphthyl ether to 2-allyl-1-naphthol and its subsequent cyclisation to 2,3-dihydro-2-methylnaphtho[1,2-*b*]furan on alumina (Scheme 1).[33]



**Scheme 1**

## Results and discussion

One of the best ways to probe the effectiveness of the alumina is to run selective reactions on the surface of the alumina. We chose the Diels–Alder and the Claisen rearrangement because of the vast research performed on these types of reactions. NMR and Raman spectroscopy clearly show that the surface hydroxyl group change during the course of the MW activation of the alumina.

### *Diels–Alder reactions*

When cyclopentadiene (CP) was treated with methyl acrylate (MA) on alumina from a freshly opened bottle at room temperature for 15 minutes, the *endo* and *exo* adducts (N and X) were formed in 30% yield, with N : X = 9; a neat mixture of CP and MA gave N : X = 2:1 (Scheme 2). When an older bottle of alumina was used, the yield (25%) and stereoselectivity (7 : 3) were reduced considerably which appears to be a consequence of the fact that the older alumina had adsorbed water from the atmosphere which decreased the number of catalytic sites on the surface. When the fresh and older alumina were separately heated by microwave irradiation at 130 °C and each then treated with CP and MA at 60 °C under microwave irradiation, the results were similar: fresh provided a 55% yield and N : X = 90 : 10; the older sample yielded a 55% yield and N : X = 87 : 13. Activation of fresh alumina had no effect on the stereoselectivity of the reaction but increased the reaction rate by roughly a factor of two; whereas activation of the older alumina enhanced both the yield of the reaction and its selectivity. When fresh alumina was first heated in a microwave reactor at 130 °C, cooled, and then treated with CP and MA at room temperature in the absence of microwaves, the selectivity of the Diels–Alder reaction was 91 : 9 and the yield was 45%. Thus, running the Diels–Alder reaction in the presence or absence of microwaves had little effect on the course of the reaction. Microwave activation of fresh alumina, which is more active than that used in our previous work, at 130 °C clearly exposes new catalytic sites on the surface (yield increases) but the sites are similar in character to those present before activation (selectivity remains the same). Microwave irradiation of the older alumina essentially restores the material to the initial, more active level. These observations are born out by the results described below.

That something significant is occurring on the surface during microwave irradiation is evident from Raman and NMR spectroscopy experiments. Raman spectroscopy of unactivated alumina reveals a broad OH stretch with a maximum absorption at approximately 3230 cm$^{-1}$. When alumina is microwave-activated at 130 °C for 20 min, the area under the peak due to the OH stretch decreases by approximately 15% (Fig. 1). The solid-state proton NMR spectrum of unactivated alumina reveals a sharp singlet due to the surface layer of hydroxyl groups. Activation at 130 °C under microwave irradiation reveals the presence of at least five broad singlets in the proton NMR spectrum. Knözinger and Ratnasamy note in their review that several OH stretches have been detected by vibrational spectroscopy when alumina was activated thermally at various temperatures.[4] Our studies clearly demonstrate that adjacent hydroxyl groups react via proton transfer to form water which is then driven from the surface. This ultimately isolates surface hydroxyl groups in different environments which yields different peaks in the NMR spectrum. This dehydration reaction also exposes aluminum ions at the surface which then catalyse the Diels–Alder reaction of CP and MA.

Dramatic results were obtained when alumina, microwave-activated at 130 °C, was first treated with boron tribromide, a Lewis acid, at 0 °C, and then with CP and MA. The expected adducts were formed in 40% yield, with an *endo* to *exo* selectivity of 99 to 1. Previous results for the reaction of cyclopentadiene and methyl acrylate on $BBr_3$ treated alumina (unactivated) gave a much lower *endo* to *exo* ratio of 13 to 1, although the yield of products was higher (88% in 1 h).[29]

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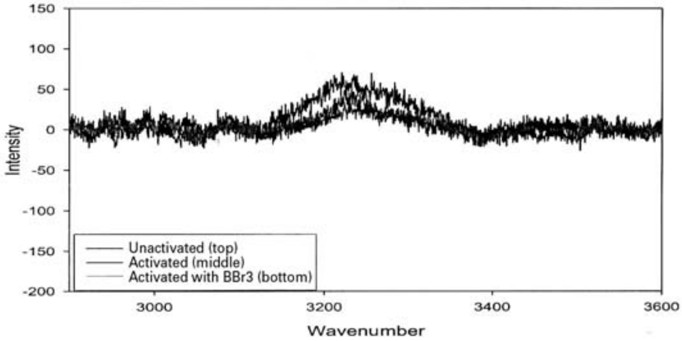


**Fig. 1** Raman spectrum of unactivated and activated alumina.

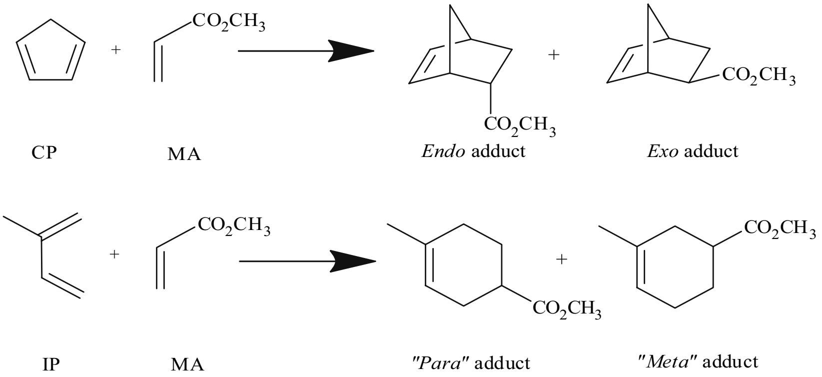
The reaction of isoprene (IP) with MA on $BBr_3$ treated alumina (microwave activated at 130 °C) at 0 °C for 5 min gave the *para* adduct exclusively (Scheme 2), although in very low yield (5%). Our previous result using $BBr_3$ treated alumina (unactivated) for the reaction of isoprene with methyl acrylate resulted in a 76% yield in 3 h, with a *para* to *meta* selectivity of 49 to 1.[30] Interestingly, both CP and IP polymerise when exposed to neat $BBr_3$.

Raman spectroscopy of the boron halide-treated alumina revealed that approximately 70% of the surface hydroxyl groups had been removed. Solid-state proton NMR spectroscopy of the boronated alumina revealed the presence of at least seven types of hydrogen on the surface. Solid-state $^{11}B$ NMR spectroscopy revealed the presence of boron atoms in four different environments. Boron tribromide reacts with the surface hydroxyl groups to yield both HBr and surface-bound boron esters. Bonding of the boron to varying numbers of bromine and oxygen atoms, accounts for the four boron resonances. The reaction also isolates unreacted hydroxyl groups in unique environments, which accounts for the large number of peaks in the proton NMR spectrum of the boronated alumina solid.

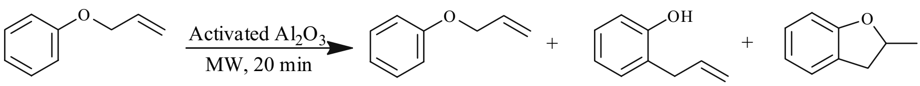
### *Claisen rearrangement*

This investigation represents the first attempt to carry out the Claisen rearrangement using both alumina and microwave activation. It was anticipated that, when the parent allyl phenyl ether was irradiated with microwaves on activated alumina, 2-allylphenol would be formed in high yield. Surprisingly, the major product (under a wide variety of conditions) was found to be 2,3-dihydro-2-methylbenzofuran (Scheme 3). For example, when the alumina was first activated by microwaves at 200 °C for 20 minutes, cooled, allyl phenyl ether added, and then the mixture heated by microwave irradiation to 150°C for 20 minutes, 2-allylphenol and 2,3-dihydro-2-methylbenzofuran were formed in a ratio of 1 : 32 in total yield of 88%. A large number of experiments demonstrated that the acid-catalysed cyclisation of the initially formed product was eight times faster than the Claisen rearrangement itself at all operating temperatures.

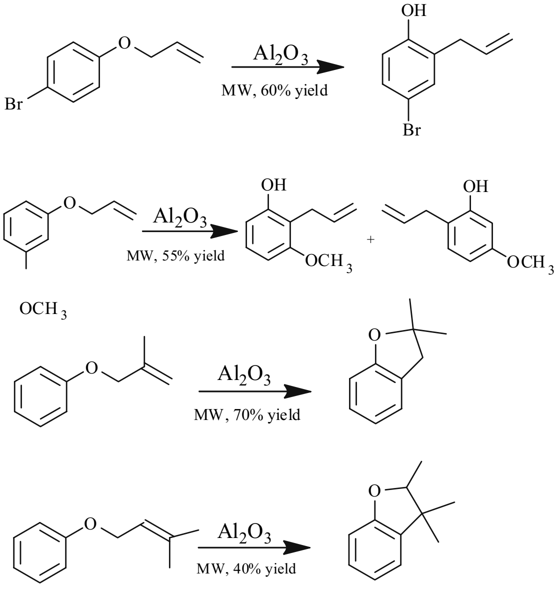
Several other Claisen rearrangements were carried out under similar conditions (Scheme 4). When the phenyl ring is unsubstituted, the major product is the benzofuran. In the two examples employing ethers with a substituent on the phenyl ring, the reactions stop after the Claisen rearrangement and no benzofurans form. A plausible explanation for this unusual behaviour is that allylphenols with lone pairs of electrons on the substituents are tightly adsorbed to sites on the alumina making them inaccessible to the Brønsted acidic sites (and further reaction). When these substituents are absent, the allylphenols are free to migrate to the Brønsted acidic sites on the alumina where they undergo the cyclisation reaction.



**Scheme 2**



**Scheme 3**



**Scheme 4**

In the case of allyl 3-methoxyphenyl ether, two allylphenols are formed in approximately equal yields. There is little *ortho/para* preference.

The results demonstrate that microwave irradiation of alumina for short periods of time provides an effective method for activating the solid surface, one that is more convenient to carry out than the previously employed thermal activation methodology using a vacuum. Alumina activated in this manner also generates Brønsted acid sites sufficiently acidic to cyclise the initially formed 2-allylphenols. The Diels–Alder reaction of cyclopentadiene with methyl acrylate shows excellent selectivity, superior to that previously observed using thermally activated alumina. The Claisen reaction affords unusual results in several cases in that the initial products undergo facile cyclisation to yield benzofurans. Since phenols are readily alkylated with allyl halides, the alumina/microwave methodology may represent a convenient synthesis of benzofurans from phenol precursors.

## Experimental

*General procedure*

All glassware was oven dried at 110 °C and flushed with argon prior to use. All reactions were conducted under argon in a 10 mL glass tube sealed with a plastic cap. Microwave heating was performed in a CEM Discover microwave apparatus at 2.45 GHz in the open vessel mode. The irradiation power, as well as the temperature, was monitored during the course of the reaction. For the activation of alumina**,** neutral alumina, Brockmann Activity I, moisture content 2.2% (Fisher Chemicals) (1 g) was introduced into the tube, which was then capped and flushed with argon. The tube was fitted with a needle connected to a commercial vacuum pump (to aid in the removal of water). Microwave irradiation was carried out at 300 W for 20 min at 130 °C with a ramp time of 5 min. The reaction was carried out under argon flow to prevent condensation of water at the top of the test tube (which was not under irradiation). The average weight lost after the irradiation was monitored. Gas chromatographic mass spectrometry was carried out using a HP GC-MS (6890 GC/5973 MSD (using a HP-5 msi column). All yields reported were calculated from peak areas generated by GC/MS using decane as an internal standard for mass calculations. Solid-state $^1$H, $^{11}$B, and $^{13}$C NMR spectra were carried using a 400/MHz solid-state instrument. The reference standard for solid state NMR was a mixture of sodium tetraphenylborate and D$_2$O. Raman spectroscopy was carried out using a Dilor XY Instrument (S.A., Inc., Edison, NJ). Liquid reagents that were moisture/oxygen sensitive (such as BBr$_3$) were transferred under positive argon pressure. Solids reagents that were sensitive to moisture/oxygen were transferred in a glove bag and were used under an argon or nitrogen environment.

*Representative procedure for the reaction of CP and MA*

A 10 mL test tube containing a magnetic stir bar and a cap was flushed with argon and weighed. Alumina (1 g) was added under argon and the test tube was capped, weighed and placed in a microwave chamber. A commercial vacuum pump was attached to the test tube using a needle placed through the septum cap. Microwave irradiation was then used to activate the reaction in the open vessel mode at 300 W for 5 min, ramp time (20 °C /minute) with a final 20 minute hold time at 130 °C. When activation was complete, the test tube was weighed and the percentage weight loss was calculated. Cyclopentadiene (0.12 mL, 1.5 mmol) was added dropwise to the test tube followed by the addition of methyl acrylate (0.13 mL, 1.5 mmol). Cyclopentadiene was prepared by cracking (distillation) dicyclopentadiene at 38 °C (Acros Organics). The reaction mixture was placed in the microwave chamber, activated in the open vessel mode at 100 W for 15 minutes, ramp time of 3 °C /min, and then maintained for 15 min at 60 °C. When activation was complete, the alumina mixture was washed using diethyl ether (10 mL), with decane (0.5 mmol) added as an internal standard for GC analysis, and the ether solution analysed by GCMS. The reactions of isoprene and methyl acrylate were run and analysed in a similar fashion.

*Procedure for the reaction of CP and MA on BBr$_3$/Al$_2$O$_3$*

A 10 mL test tube containing a magnetic stir bar and a cap was flushed with argon and weighed. Alumina (1 g) was added under argon and the test tube was capped, weighed, and placed in a microwave chamber. A commercial vacuum pump was attached to the test tube using a needle placed through the septum cap. Microwave irradiation was then used to activate the reaction in the open vessel mode at 300 W for 5 min with a ramp time of 20 °C/min, and then held for 20 min at 130 °C. When activation was complete, the test tube was weighed and the percentage weight loss was calculated. The test tube was placed in ice bath and flushed with argon via a needle inserted through the septum and an exit needle attached to an oil trap. Boron tribromide (0.15 mL, 1.5 mmol) was added dropwise and the mixture stirred for 5 min. Cyclopentadiene (0.12 mL, 1.5 mmol) was added dropwise to the test tube, followed by the addition of methyl acrylate (0.13 mL, 1.5 mmol). Cyclopentadiene was prepared by cracking dicyclopentadiene dimer at 38 °C. The reaction mixture was allowed to stir for 15 min. The Al$_2$O$_3$/BBr$_3$ and reaction mixture were then washed using diethyl ether (10 mL) and the ether solution analysed by GCMS.

*Representative procedure for 2-allyl-4-bromophenol*

In a round-bottomed flask, one equivalent of sodium iodide (20 mmol, 3.0 g) was dissolved in acetone (15 mL) along with one equivalent of allyl chloride (20 mmol, 1.6 mL). The precipitated NaCl was removed using vacuum filtration and the remaining liquid was placed in a rotary evaporator. GCMS was carried out to confirm the formation of the allyl iodide. In a round-bottomed flask, one equivalent of 4-bromophenol (1.5 mmol, 2.6 g) was dissolved in THF (1 mL). The flask was capped and flushed with argon and one equivalent of butyllithium (1.5 mmol, 1.4 mL) was added dropwise, followed by the addition of allyl iodide (2.0 mmol, 1.7 mL). The reaction mixture was placed in an oil bath at 70 °C for 48 h. Diethyl ether (10 mL) was added and the organic layer was washed sequentially with aqueous NaOH (10 mL, 0.5 *M*) and then H$_2$O (10 mL). Then alumina (60 g) was microwave activated (300 W, 130 °C, 40 min) and packed into a column. The ether solution collected previously was passed through the column using hexane/ethyl acetate (95/5) as eluant. Solvents were removed and GCMS was carried out to confirm the formation of the 1-(allyloxy)-4-bromobenzene. A 10 mL test tube was flushed with argon and weighed along with a magnetic stir bar and a cap. Alumina (1 g) was added and the test tube was capped and weighed. The test tube was flushed with argon and placed in a microwave chamber. A commercial vacuum pump was attached via a needle inserted through the cap. Microwave activation was carried out in an open vessel mode at 300 W, and heated to 130 °C with a ramp time of approximately 25 °C/min, then held at 130 °C for 20 min. After activation, the test tube was weighed again and the percentage weight loss was calculated. 1-(Allyloxy)-4-bromobenzene (0.08 mL, 0.5 mmol) was added dropwise to the test tube. The reaction mixture was placed in the microwave chamber and microwaved in the open vessel mode at 300 W and heated to 150 °C with a ramp time of approximately 30 °C/min, then held at 150 °C for 20 min. After activation, the reaction mixture was washed with diethyl ether (10 mL) and the ether solution injected on to a GCMS for analysis. For *m*-methoxyphenol, methanol was used to extract the product (replacing the diethyl ether).

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