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Microwave-enhanced bromination of a terminal alkyne in short time at ambient temperature: Synthesis of phenylacetylene bromide

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Abstract

The microwave-enhanced synthesis of phenylacetylene bromide (bromoethynylbenzene) from phenylacetylene and *N*-bromosuccinimide (NBS) in the presence of $AgNO_3$ was examined under non-thermal conditions in bulk solution with a microwave reactor coupled to a refrigeration unit. Generation of by-products from the thermal-induced synthesis of phenylacetylene bromide was suppressed under microwave (MW) irradiation when the temperature was maintained at near-ambient conditions. In the absence of MW radiation, formation of phenylacetylene bromide was an inefficient process under ambient conditions alone. Product yields were as low as 12% after 15 min under microwave irradiation at 157 °C (superheating of solvent DMF) and as high as 62% when temperature was maintained at ca. 18 °C under microwave radiation, compared to 14% under ambient conditions (no microwaves) for the same reaction time.

Keywords: Terminal alkyne; Phenylacetylene bromide; Microwave-assisted synthesis; Microwave reactor; Enhanced microwave synthesis

1. Introduction

The number of studies in microwave-assisted syntheses of organic compounds has increased rapidly since the first reports by Gedye et al. [1] and Giguere et al. [2], and as witnessed from several excellent recent reviews [3–9]. Many of the studies reported a decrease of the reaction times attributed to rapid heating induced by microwave (MW) irradiation, which was found to be more effective than conventional heating. In this regard, one of the objectives of recent studies has focused on the causes of this increased efficiency through an examination of microwave thermal and non-thermal effects [10–14]. The former are the result of dielectric heating as a consequence of dipole–dipole interactions between polar molecules and the electromagnetic field, whereas the latter have been attributed (i) to an increase in the pre-exponential factor A from an influence of the MW radiation field on the collision frequency between molecules, (ii) to a decrease in the free activation energy $\Delta G^{\#}$ ($=\Delta H^{\#} - T\Delta S^{\#}$) through an increase in the factor $-T\Delta S^{\#}$ of the MW-assisted reaction as a consequence of dipolar polarization, and (iii) to the intervention of localized microscopic high temperatures (so-called hot spots) generated by dielectric relaxation at the molecular scale [3]. Nonetheless, questions remain on the specific role(s) of MW-generated non-thermal effects, for which definitive evidence is often either lacking or are seldom dealt with.

In recent studies, we have addressed the question of the role of non-thermal effects in microwave-assisted photodegradations of organic pollutants using one of the advanced oxidation processes (AOPs) involving titanium dioxide [15,16]. The degradation reaction and the corresponding dynamics of the photo-assisted AOP system under MW irradiation were far more effective when the process was subjected to MW radiation as compared to conventional heating at otherwise identical temperatures. Most remarkable was the improvement in the photodegradation dynamics under MW irradiation but under conditions when the photodegradation was carried out at low temperatures [17]. External cooling of the reaction vessel while simultaneously administering microwave radiation to the reaction mixture has been referred to by some [8] as enhanced microwave synthesis (EMS), and some examples of the use of EMS have appeared

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[8,18]. The idea behind this EMS methodology is that simultaneous external cooling of the reactor, while simultaneously applying microwave radiation, enables a greater amount of the MW energy to be directly introduced into the reaction mixture. Without this external cooling of the reactor, conventional application of high-power microwave irradiation leads to a rapid rise in temperature at which the effective MW radiation decreases or is shut-off altogether [8]. Apparently, the EMS process is efficient only if absorption of the microwave radiation by the reactants can be sustained.

In this study, we examined the synthesis of phenylacetylene bromide by the bromination of the terminal alkyne phenylacetylene by *N*-bromosuccinimide (NBS) in the presence of $AgNO_3$ in DMF media using a microwave reactor coupled to a cooling system. The traditional thermal synthesis of phenylacetylene bromide with NBS was reported by Li and Wu [19] and typically required some 10–20 h at room temperature to obtain an 83% yield. Others have prepared this alkynyl bromide more efficiently but using traditional methodologies [20,21]. Herein we focus on promoting this bromination reaction with microwave radiation at ambient temperature and concomitantly we wished to test the efficacy of the fabricated microwave reactor.

2. Experimental

2.1. Synthesis and characterization of product(s)

The enhanced microwave synthesis of phenylacetylene bromide was performed following closely the steps used in the traditional bromination of terminal alkynes [19]. *N*-bromosuccinimide (NBS, 1.8 g) and $AgNO_3$ (0.7 g) were added to magnetically stirred solvent DMF (20 mL) in a Pyrex cylindrical reactor under an inert nitrogen atmosphere, following which phenylacetylene (1 mL) was introduced into the solution also under inert conditions. The reactor was subsequently sealed with two Teflon rings and a stainless steel cap. The course of the phenylacetylene bromide synthesis was followed using four different protocols: (a) conventional microwave irradiation at a power of 141 W (MW/141 W); (b) application of 141 W of microwave radiation while the reaction was cooled by the silicone oil coolant (MW/Cool/141 W); (c) microwave irradiation at a power of 22 W under controlled ambient temperature using the cooling system (MW/Cool/22 W); and (d) under ambient temperature conditions in the absence of MW radiation (Ambient). In all cases the reaction time for the synthesis was 15 min. Products were separated and purified by flash column chromatography over Silica gel-300 (eluent was hexane). The resulting phenylacetylene bromide was analyzed by GC/MS techniques on a Shimadzu GC/MS Model QP5000 apparatus using an Ultra Alloy column (dimethylpolysiloxane 100%) from Frontier Laboratory Ltd.; helium was the carrier gas. Proton NMR spectra of the phenylacetylene bromide and by-products were recorded on a JEOL 500-MHz spectrometer (Model LA500) in $CDCl_3$ solutions against TMS as the reference.

2.2. The microwave reactor coupled to the cooling system (MCS)

In the environmental field, we recently reported the use of a microwave-/photo-assisted process under cooled conditions with a dry-ice/hexane bath to degrade the rhodamine B dye in aqueous media [22]. In the present study we used an industrial microwave reactor device composed of a Shikoku Keisoku (Model ZMW-001) system that included a Toshiba microwave generator (frequency, 2.45 GHz; maximal power, 1500 W), an isolator, a three-stub tuner, a power monitor and a multimode applicator (see Fig. 1). The temperature of the reactor solution was measured through a sealed optical fiber thermometer (Amoth FL-2000, Anritsu Meter Co. Ltd.). The cooling capacity of the refrigeration system corresponded to heating by the microwave radiation source at a power of ca.

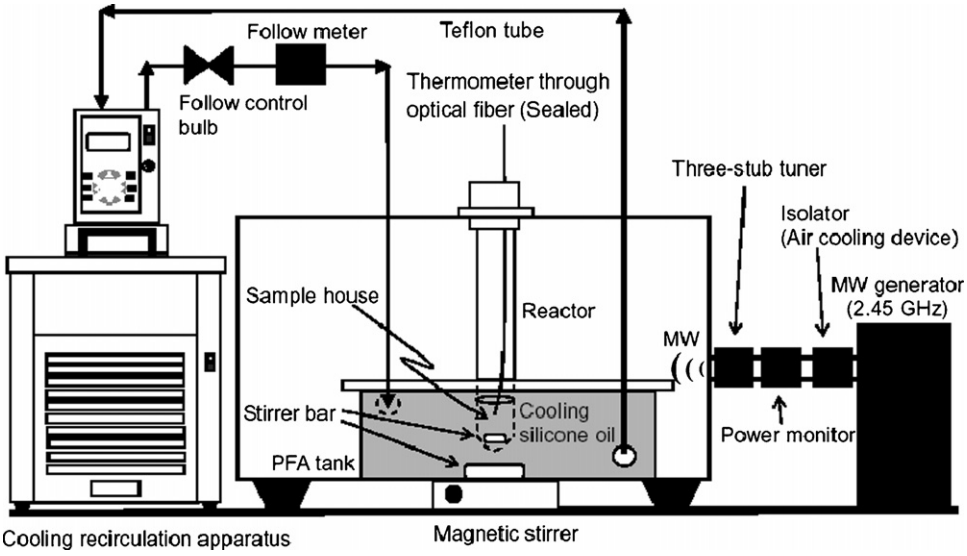


Fig. 1. Schematic illustration of the industrial microwave reactor system with the cooling apparatus and the microwave multimode applicator.

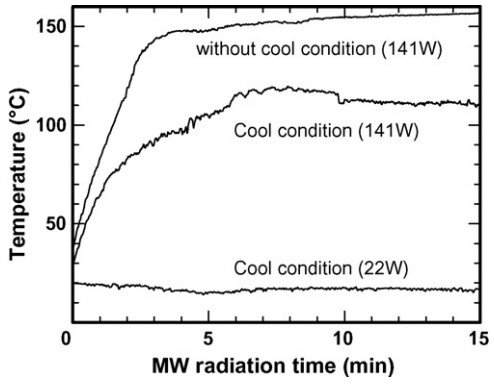


Fig. 2. Temporal changes of dispersion temperature with irradiation time.

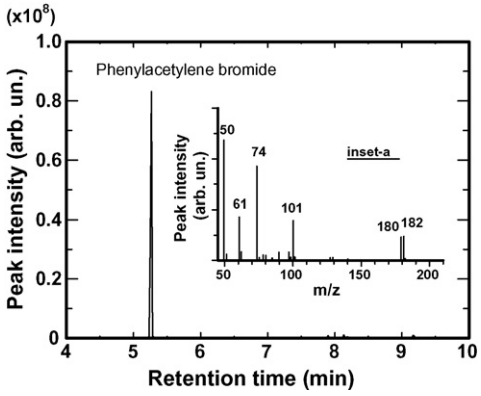


Fig. 3. Gas chromatogram of the product obtained using the Ambient protocol (see text for details); Inset shows the mass spectrum of the phenylacetylene bromide product obtained from the Ambient procedure after a 15-min reaction time.

22 W. However, the boiling point of DMF (153 °C) was not attained at this microwave power, but it was if the microwave power were set at 141 W. Accordingly, the irradiation power of the microwave source in further experiments was set at either 22 W or 141 W depending on the desired reaction conditions.

The entire microwave reactor device coupled to the cooling system is illustrated in Fig. 1. The Pyrex cylindrical reactor (maximal pressure, 1 MPa; volume, 250 mL) was immersed in a Teflon container incorporating the silicone oil coolant, which was maintained at −10 °C by the refrigeration unit and circulated through the reactor using the cooling apparatus. Note that the silicone oil (ignition point, 443 °C) absorbed negligible quantities of the microwave radiation below 25 °C as determined by a network analyzer (dielectric loss factor: $\varepsilon'' = 0.009$).

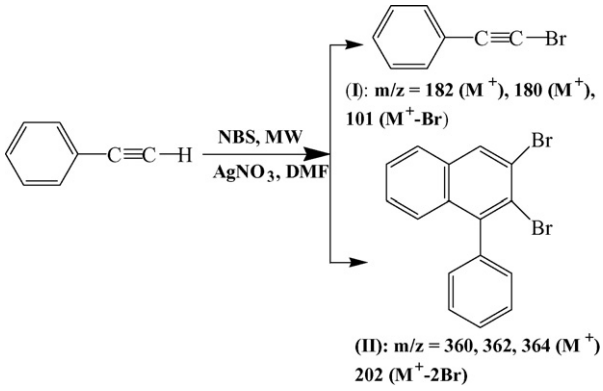
2.3. Temperature time profiles

The temperature time profiles in the sample housing are reported in Fig. 2. The initial temperature was ca. 28 °C in the case of the MW/Cool/141 W protocol. On absorption of MW radiation for ca. 7 min increased the temperature to ∼118 °C. No further increase in temperature occurred by continued MW irradiation. For the MW/141 W protocol the initial temperature was 29 °C increasing rapidly under MW irradiation to reach ca. 143 °C, and after a few minutes reached a steady-state temperature of 157 °C. When using the MW/Cool/22 W protocol to synthesize the brominated alkyne the temperature was maintained constant at 18 ± 1 °C. In the absence of the silicone oil coolant the temperature of the sample reached ca. 72 °C after 15 min of microwave irradiation (22 W). The cooling capacity of the silicone oil was estimated to be ca. 50 °C from the temperature gap between the MW/Cool/22 W and MW/22 W methods.

3. Results and discussion

3.1. Synthesis of phenylacetylene bromide

The relevant process for the synthesis of phenylacetylene bromide, Ph–C≡C–Br (**I**), is reported in reaction (1) (NBS is *N*-bromosuccinimide). To determine the nature of the product(s) resulting from the microwave-irradiated process, we first



(1)

examined the product obtained by the Ambient method. The product was identified by gas chromatographic and mass spectral techniques (GC/MS). Fig. 3 illustrates the resulting chromatogram after separation and purification of the products. It displays only one peak at a retention time of 5.3 min, whereas the inset depicts the corresponding mass spectrum that we identify as corresponding to phenylacetylene bromide in line with the reported mass spectrum no. ID_WID-DLO-018004-1 (Chemical Abstract Service Registry No. 932-87-2). The ^{1}H NMR analysis (solvent $CDCl_3$, 500-MHz spectrometer) confirmed the nature of this product; $\delta = 7.35$–7.43 ppm (m, 2H) and 7.45–7.62 ppm (m, 3H) corresponding to the phenyl protons in C_6H_5–C≡C–Br.

The yields of phenylacetylene bromide after silica-gel treatment of the products are listed in Table 1 for the various experimental protocols. The yield of phenylacetylene bromide

Table 1
Chemical yields of products from the bromination of phenylacetylene under various experimental conditions (reaction time was 15 min)

Protocols	Temperature (°C)	Yields (%)
MW/141 W	157	12
MW/Cool/141 W	118	38
MW/Cool/22 W	18	62
Ambient[a]	25	14

[a] No microwaves.

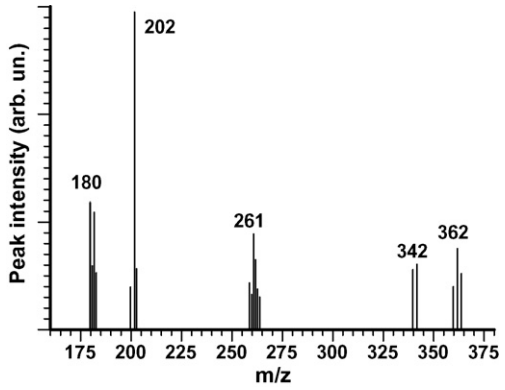


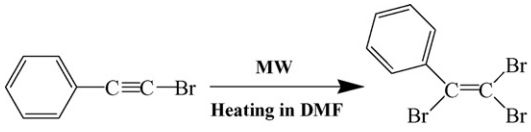
Fig. 4. Mass spectra of the phenylacetylene bromide and by-products of the synthesis.

under super-heating conditions [23] of the reaction mixture induced by microwave irradiation but without the cooling system was 12% at 157 °C (b.p. of DMF = 153 °C). The yield increased to 38% when the reactor was cooled down to 118 °C. With the MW/Cool/22 W protocol, the yield improved to 62% by microwave irradiating the reaction mixture maintained at 18 °C. In the case of the Ambient method (ca. 25 °C), the yield of phenylacetylene bromide was only ca. 14% after the 15-min period. Clearly, the yield of phenylacetylene bromide increases on cooling the reaction mixture, but decreases at the higher temperatures induced by the applied microwave radiation. No doubt, optimizing the experimental conditions and increasing the reaction time might significantly improve the yield of the brominated alkyne product. At this stage, however, the objective was to show the practicality of the industrial microwave reactor system. Accordingly, this aspect was attempted no further.

The above notwithstanding, however, we sought to examine the causes for the low 12% yield obtained under our present conditions at the highest temperature (157 °C) obtained at the applied MW power of 141 W, as the yield was five-fold smaller than the 62% yield obtained when the MW-assisted synthesis was carried out at 18 °C. By-products formed from the synthesis of phenylacetylene bromide (**I**) by the MW/141 W protocol were confirmed by direct injection of the reaction sample into the mass spectrometer system bypassing the GC column; the relevant mass spectrum is displayed in Fig. 4. Main signals were observed in the range of m/z = 178–364. The fragmentation patterns at m/z 202 and 362 are associated with the 1-phenyl-2,3-dibromonaphthalene (**II**) [24] or with (though less likely) Ph–C=C(Br)=C(Br)=C–Ph [25] by-product formed alongside phenylacetylene bromide (**I**). On the other hand, the fragmentation patterns at m/z 180, 261 and 342 are associated with an olefinic structure containing three bromine groups ($C_8H_5Br_3$) (**III**) that we tentatively describe as ($PhBrC{=}CBr_2$) 1,1,2-tribromo-2-phenylethylene [26,27] formed by the thermal reaction through microwave generated heat. We further examined the thermal degradation of pure Ph–C≡C–Br (**I**) by microwave heating at 150 °C for 1 min in DMF solvent. In this way, we hoped to explore and identify whether there were any side-products formed during or subsequent to the formation of phenylacetylene bromide as a result of the prevailing high temperature. The gas chromatograms of the resulting products indicated that a by-product was formed having a GC retention time of 8.4 min under our conditions. A mass spectral analysis of this by-product is depicted in Fig. 5a (assignments noted in reaction (2)). We therefore deduce that the by-product formed along with, or subsequent to formation of phenylacetylene bromide in reaction (1) at the higher temperatures through microwave heating is also associated with $PhBrC{=}CBr_2$ (**III**) [26,27].

A by-product with a GC retention time of 8.2 min was confirmed from the thermal degradation of pure Ph–C≡C–Br (**I**) by conventional heating (oil bath) at 150 °C for 1 min in DMF solvent. The corresponding mass spectrum of the by-product is reported in Fig. 5b, which we associate with the epoxide species, phenyloxyrene (**IV**) [28,29]—reaction (3).

Reaction (1) is hence modified to reflect formation of these by-products (reaction (4)). Accordingly, for the MW/141 W method, the formation of the by-product containing three bromines ($C_8H_5Br_3$) by the dibromination of the Ph–C≡C–Br



(III): m/z = 338, 340, 342 (M^+)
239, 261, 263 (M^+-Br),
180, 182 (M^+-2Br) (2)

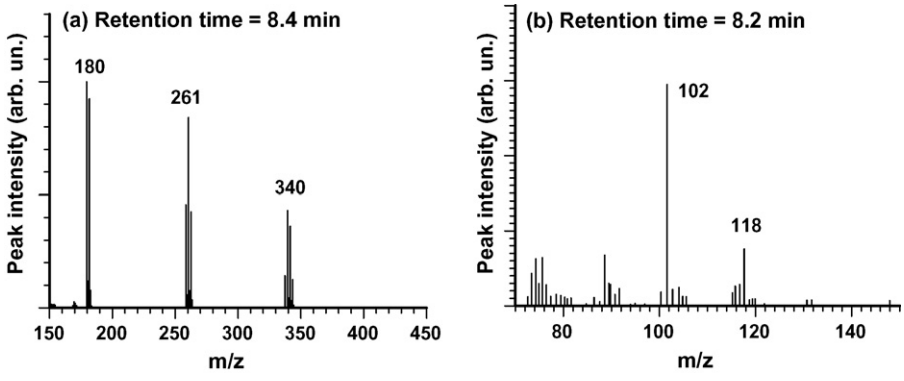
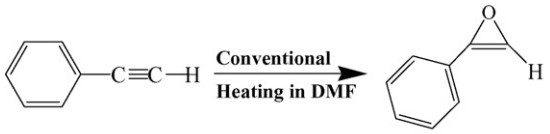
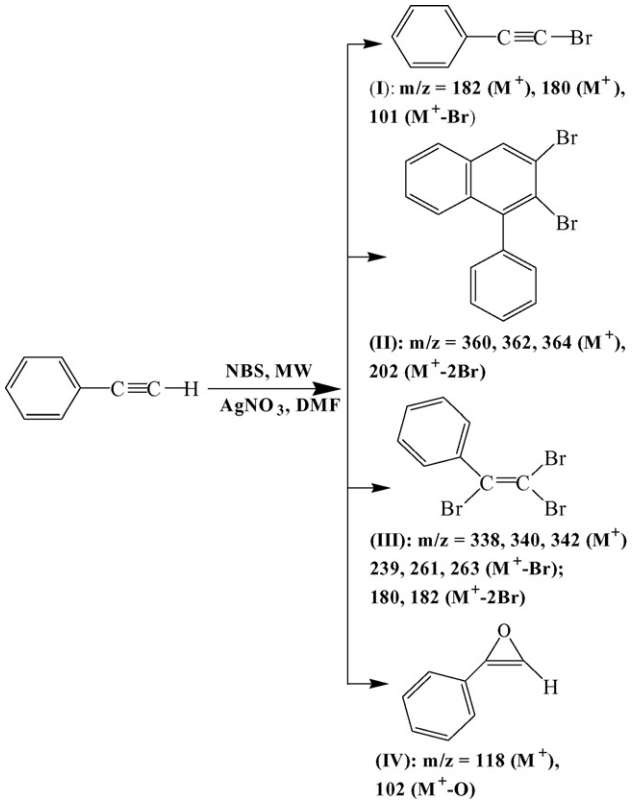


Fig. 5. Mass spectra of two possible by-products formed along with or subsequent to phenylacetylene bromide at the high temperatures through microwave heating (a), and conventional heating (b) at 150 °C in DMF solvent.



(IV): m/z = 118 (M^+), 102 (M^+-O) (3)

structure (**I**) during or subsequent to the formation of other by-products may be responsible for the low yields of phenylacetylene bromide obtained when its synthesis was carried out at the higher temperature, regardless of whether the temperature was reached by conventional means or by microwave irradiation. Evidently, formation of by-products appears to have been minimized or suppressed when the MW/Cool/22 W protocol was used for the synthesis of (**I**), as the temperature was maintained constant at 18 °C by the external cooling system.



(I): m/z = 182 (M^+), 180 (M^+), 101 (M^+-Br)

(II): m/z = 360, 362, 364 (M^+), 202 (M^+-2Br)

(III): m/z = 338, 340, 342 (M^+) 239, 261, 263 (M^+-Br); 180, 182 (M^+-2Br)

(IV): m/z = 118 (M^+), 102 (M^+-O) (4)

3.2. Summary

In summary, there are certain distinct advantages of the enhanced microwave-assisted synthesis of phenylacetylene bromide by the bromination of the corresponding terminal alkyne with *N*-bromosuccinimide (NBS) over the traditional procedure involving bromination of phenylacetylene with Br_2 in alkaline aqueous media at 25 °C, as the latter requires about 60 h to obtain suitable yields [30] or the 10–20 h needed for the bromination of the alkyne with *N*-bromosuccinimide at room temperature [19]. Such advantages are the relatively short reaction times (ca. 15 min) and the suppression of by-products that would normally accompany the synthesis of the brominated alkyne by the conventional microwave methodology. The latter would inherently cause the reaction mixture to be superheated. However, maintaining the reaction temperature of the microwaved reaction mixture at near ambient temperatures leads to substantive increase in product yield of the phenylacetylene bromide without the by-products. Evidently, the thermal factor is detrimental to reaction (1) and to product yields. Thus, excessive heating (i.e. superheating) with microwaves is to be avoided in organic reactions. The microwave reaction device coupled to the cooling system (MCS) reported herein and the associated EMS methodology can easily be adapted toward enhanced microwave syntheses of other interesting organic compounds [8].

Acknowledgments

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