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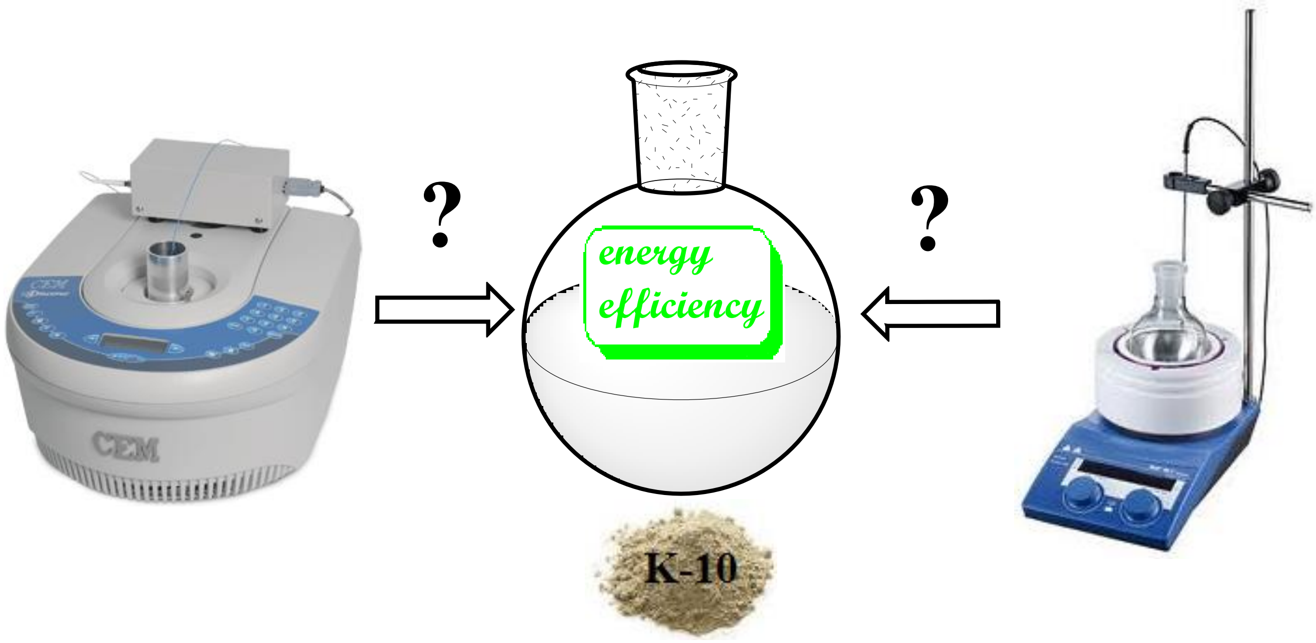
The energy efficiency of microwave-assisted and conventionally heated solvent-free heterogeneous catalytic reactions was studied.



Energy Efficiency of Heterogeneous Catalytic Microwave-assisted Organic Reactions

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The energy efficiency of microwave-assisted reactions was studied under heterogeneous catalytic conditions. Based on earlier publications the choice of catalyst was a semi-synthetic montmorillonite K-10. This material absorbs microwave energy effectively and is an excellent catalyst for microwave-assisted organic synthesis. The energy consumption of six different types of K-10 catalyzed reactions with multiple substrates and varied experimental parameters were determined under microwave irradiation and conventional heating. The parallel reactions were carried out under the same conditions to ensure the comparability of the data. While in the majority of the studied reactions, the microwave-assisted method appeared to be more energy efficient by various extents, in one case the conventional heating was found to be more efficient. The data, in agreement with a previous report, indicate that reactions should be studied on a case-by-case basis and that an automatic green label for microwave-assisted reactions is not warranted.

Introduction

Over the past three decades, microwave-assisted synthesis has become a mainstream method in organic chemistry. Due to the development of reliable commercially available microwave reactors, the field of microwave-assisted chemical synthesis has undergone an explosive growth, with over 5000 papers published during the past 25 years.[1] This technology played a significant role in the development of environmentally benign processes, although mostly at the laboratory scale. It is widely used in organic[2] inorganic, organometallic, polymer[3] and peptide[4] synthesis, and other applications in biology[5], geology, and chemical analysis can also be mentioned. While there is no doubt regarding the broad synthetic utility of this activation method, the history of microwave chemistry is not free of controversy (e.g the explanation of the thermal[6] vs. non-thermal activation[7]).

Among the many advantages of microwave activation, one that is particularly appealing to synthetic chemists is the dramatically reduced reaction times compared to the conventionally heated alternatives. Since the reduction of energy consumption is a key aspect in the design of green processes the shorter reaction times were consequently believed to be more energy efficient. As a result, microwave processes were automatically labeled as green. The contemporary explanation for the microwave effect,[8] however, may raise doubts concerning the above label. It is known that microwave-assisted reactions often occur at much higher temperatures than the set temperature of the instrument due to the relatively inaccurate temperature measurements of built-in infrared detectors. Thus, more precise fiberoptic probes have been applied for liquid phase reactions, however, the IR measurement remained the control of choice for solid phase reactions.[8, 9] These questions turned the attention toward the energy efficiency of microwave-assisted synthesis.[10]

While, according to the Arrhenius equation, the energy consumption of a short high temperature reaction may be less than a long but lower temperature alternative, a recent paper by Moseley and Kappe clarified this question. The authors critically assessed the energy efficiency of microwave-assisted trasformations in the context of scaling-up this technology to production quantities.[11] It was also argued that the extremely short reaction times experienced in microwave chemistry are typically restricted to small scale syntheses.[11] We agree with the major conclusion of the work, namely that a detailed analysis is clearly requried on a case-by-case basis.

It is worth noting, however, that the sample reactions in the above paper are limited to homogeneous experimental conditions. In general, an overwhelming majority of the reports studying the energy efficiency of microwave-assisted reactions were focused on homogeneous reactions under pressurized conditions.[11] Yet, there is a large number of publications in the microwave-related literature that apply a broad variety of solid catalysts ranging from natural/synthetic aluminosilicates to graphite.[12] As homogeneous catalysis has significantly different characteristics compared to heterogeneous systems it appears to be desirable to extend energy efficiency investigations to heterogeneous microwave-assisted systems as well. It is particularly important as many of these catalysts or catalyst supports act as microwave radiation absorbers and serve as the ultimate heating medium for heterogeneous catalytic reactions. Since several solids

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heat up faster and to a higher temperature than any solvent these characteristics might change the energy profile including the efficiency of these reactions.

Taking the above into consideration, we broadened our studies on solid catalysts by investigating the energy consumption of such reactions under conventional and microwave-assisted conditions. In the current work several heterogeneous catalytic processes were selected as model reactions and carried out under both conventional and microwave-assisted conditions and the energy efficiency of the reactions was assessed.

Results and discussion

Montmorillonite K-10, the catalyst used in this work, is a semi-synthetic clay, produced from natural montmorillonites by treatment with diluted mineral acid. It is a commercially available, stable, noncorrosive, inexpensive, and easily reusable solid.[13] Montmorillonite K-10 has a substantial surface area (~ 250 m^2g^{-1}) and a Hammett acidity constant of $H_0 \approx -8$, which corresponds approximately to the acidity of concentrated nitric acid. K-10 is also used to prepare other, usually bifunctional catalytic materials.[14] Many of these derivatives are already available from the major suppliers under different trade names.

The structure of montmorillonite K-10 shows strong similarities to the parent lamellar basic montmorillonite structure. It was determined; however, that it contains a mixture of different clays (such as kaolinite or a quartz-like material).[15] The clay structure also contains a significant amount of interlamellar water. Due to their physical nature, clays or clay-based catalysts absorb microwave energy efficiently and are therefore excellent catalysts for microwave-assisted organic synthesis, as indicated by the numerous earlier publications.[12, 13, 16] It is known that heterogeneous reactions, in general, suffer from mass transport limitations due to the necessary transport of the reactants from one phase to another. The heat transfer is also problematic since the diffusion and phase transfer coefficients are extremely low in the solid phase. These problems are typical in the generic solvent/solid catalyst based systems. Using a solid catalyst under solvent-free conditions, however, carries a number of benefits. These systems commonly use the solid not just as catalyst but also as a reaction medium. The reactants, preadsorbed on the surface of the catalyst, are mobile[17] and react without serious mass transport limitations usually observed in liquid/solid systems. If the catalyst is microwave absorber then the heat transfer problems are also largely eliminated, since the solid reaction system is heated uniformly from the inside of the reaction vessel. As K-10 montmorillonite is a strong microwave absorber, this material represents an efficient catalyst and heating medium for these reactions.

Based on our earlier studies, six groups of reactions were selected as model systems for this study, including a Paal-Knorr cyclization, a variety of electrophilic annelations and several multicomponent/multistep one-pot reactions involving both acid as well as metal catalysts. Each application was carried out as dry medium reaction without the use of any solvent during the reaction step. For two reactions, a commercial Pd/C catalyst was used in addition to K-10. For each category two reactions with different substrates were selected and the energy consumption of the microwave-assisted as well as conventionally heated (oil bath) systems was determined. Great care was taken to ensure identical reaction conditions in the microwave experiments and the oil-bath runs. The exact same reactant amounts and reaction volumes were employed for both sets of experiments. In practice, the reaction mixture was prepared together for both reactions and then the obtained material was divided into two equal portions for each parallel reaction. The reactions were carried out under solvent-free conditions in a CEM Discover microwave reactor and, for comparison, under conventional heating using an oil bath. The same microwave reaction vial was used for both heating methods. The measurement of the energy used was carried out by a power-meter with an accuracy of ±0.01 kWh. The heating instruments (the microwave reactor as well as the hot-plate stirrer) were directly receiving electricity via the power meter only with no other energy source used thus the overall energy input to the complete systems could be accurately determined. While the hot-plate was handled as one unit, in the case of the microwave reactor the reactor itself and a Gast oil-free diaphragm-type air pump (used for cooling) represented the complete unit. It was observed that the pump has used a considerable amount of energy around 30-35% of the total energy consumption of the microwave reactions. During the reactions the microwave power was set to 200 W. The temperature of the conventionally heated reaction was monitored both in the oil bath (external) as well as inside the vessel. The oil-bath experiments, commonly using 100 mL silicon oil, were started with ambient temperature system, thus the hotplate and the oil were not preheated. Experiments regarding the heating-up phase indicated that the system used only ~8% of the total energy consumption of a 5h, 90 ˚C reaction (Scheme 2 R=H) while for a 16h, 160 ˚C reaction (Scheme 3, R=H) this number was only 2%. Both the conventional and microwave reactions were continuously stirred (1000 rpm and 800 rpm, respectively). The temperature of the reactions was routinely controlled by a built-in infrared detector-controller (IR) in the microwave reactor and a thermocouple was used in the conventional reaction. While it is commonly known that the infrared temperature measurements in microwave reactions are not as accurate as the fiberoptic probes[18] in our experience these probes do not work sufficiently under solvent-free conditions. When stirred, an empty space developes between the solid reaction mixture and the fiberoptic probe, and a lack of an effective heat conducting medium (e.g. solvent) results in an ineffective heat-exchange with the probe, compromising temperature measurements. However, the fiberoptic probe was found to be effective in measuring the temperature of the solid catalyst/reaction mixtures when they reached the set-point and the IR measured temperature stabilized. Prior to engaging in reactions it was decided to investigate the effect and accuracy of the two heating methods on the temperature of the catalyst used in this study. Comparative heating profiles of K-10 by convective heating and microwave irradiation, using both infrared as well as fiberoptic temperature measurements, are illustrated in Fig. 1.

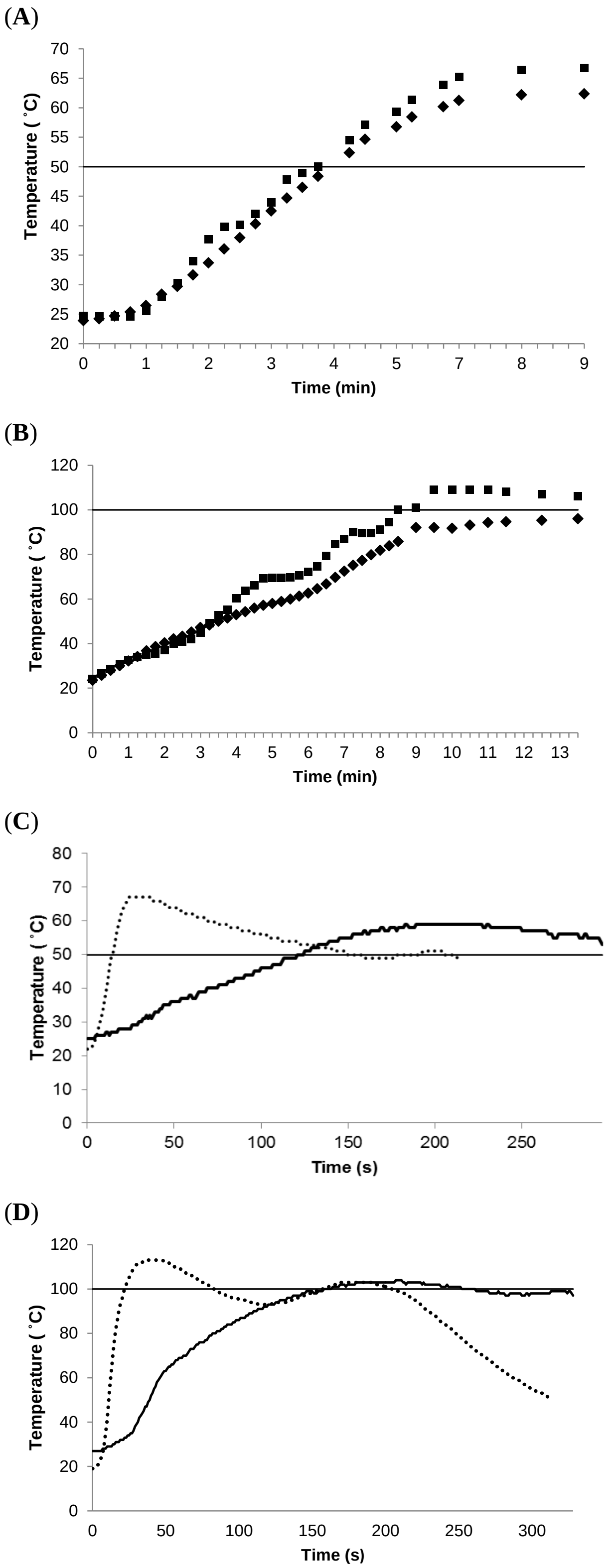


Figure 1 Heating profiles of K-10 using conventional heating at (A) 50 ˚C, (B) 100 ˚C (■-oil bath ♦-reaction mixture inside the vessel), and microwave heating with infrared (solid line) and fiberoptic (dotted line) temperature monitoring at (C) 50 ˚C, (D) 100 ˚C. The continuous horizontal lines represent the set-point of the heating.

The heating profiles obtained in the conventionally heated system clearly show that the temperature measured outside (in the external oil bath) and inside the reaction vessel only differ in a moderate extent (~ 4 ˚C for at 50 ˚C and ~10 ˚C at 100 ˚C; Fig. 1. A and B). It was also observed, that at lower temperature set-point, the system overheats moderately and it takes several minutes until the temperature decreases back to the set-point (data not shown). The last important observation is that in contrast to the general expectations it requires relatively short time to heat the entire system, including the hotplate, oil bath and reaction/catalyst, to the required set-point (~4 min to 50 ˚C and ~8-9 min to 100 ˚C). This may cause problems in the case of short reactions, however, reactions requiring several hours of heating are only affected by this lag-phase to a negligible extent. It was also determined that the energy needed to reach the set-point is not as significant as expected; to reach 50 ˚C required 4 min and consumed only 0.01 kWh energy, while the same features to heat the system to 100 ˚C were 8 min and 0.03 kWh.

The microwave experiments (Fig. 1. C and D) indicated that the fiberoptic probe controlled reactions required only 20-25 s to reach the set-points regardless of the temperature. The rapid heating and possibly partially inappropriate contact with the medium, however, resulted in significant overheating in both experiments. The IR detector controlled reactions appeared to reach the set-points remarkably slower, but still under 3 min. This observation is attributed to the slower heat transport to the wall of the vessel; practically it required minutes to heat up the microwave-transparent glass to the set point. However, once the set-point was reached the temperature remained stable. Since it is well-known in homogeneous systems that the two temperature probes result in different temperatures with the same set-point, the temperature of the catalyst was measured by the fiberoptic probe at the end of the IR controlled measurements. The results support the earlier observations[9]; at 50 ˚C (IR temperature) the fiberoptic probe measured 108 ˚C while the difference at 100 ˚C heating is even more striking; 99 ˚C (IR) *vs.* 208 ˚C as determined with the fiberoptic probe. While this may result in higher inside temperatures than the set temperature limit, it would not affect the measurement of the consumed energy as the complete energy input is measured. The conventionally heated reactions were carried out by using a temperature-controlled hot plate with an oil bath in which the reaction vessel was immersed. The oil-bath heated reactions were also carried out using baths of varying size as well as volume of silicon oil in order to observe the effect of these variables on the systems.

The goal of the reactions was to reach approximately similar yields (within 10-15%) for both types of reactions at close to complete conversion (75% < yield <100%) of the reactants. Low and full conversion values did not appear practical for comparison. Low yield reactions would have reflected just the initial energy consumption, while the lack of real-time monitoring made it difficult to determine the exact reaction time (and the energy used) needed to reach 100% transformation. While the temperatures of the model reactions were given in the sources, separate reactions were carried out to determine the optimum times for all studied reactions. Each run was stopped only after the desired time and additional runs rather than reheating of the same sample were used to check the effect of longer times. Based on the determined optimum times the energy use measurements were always carried out in full time uninterrupted reactions. Six model reactions, depicted in Schemes 1-6, have been selected to study the energy efficiency of the different heating methods. The above heating profiles (Fig. 1) describe only how the different heating methods affect the temperature of the K-10 catalyst. Since, however, the energetics of a reaction could significantly change the heating profile; it was decided to determine similar profiles in an actual reaction. Based on the specific temperatures and reaction times one of Scheme 2 (R=H) reactions was selected for these investigations. These annelation reactions required moderately high temperature (90 ˚C) and reaction times (1h vs 5h) that make the system well measurable. In addition, the reactants did not show any trace of a product formation on the catalyst without heating. The data are shown in Fig. 2.

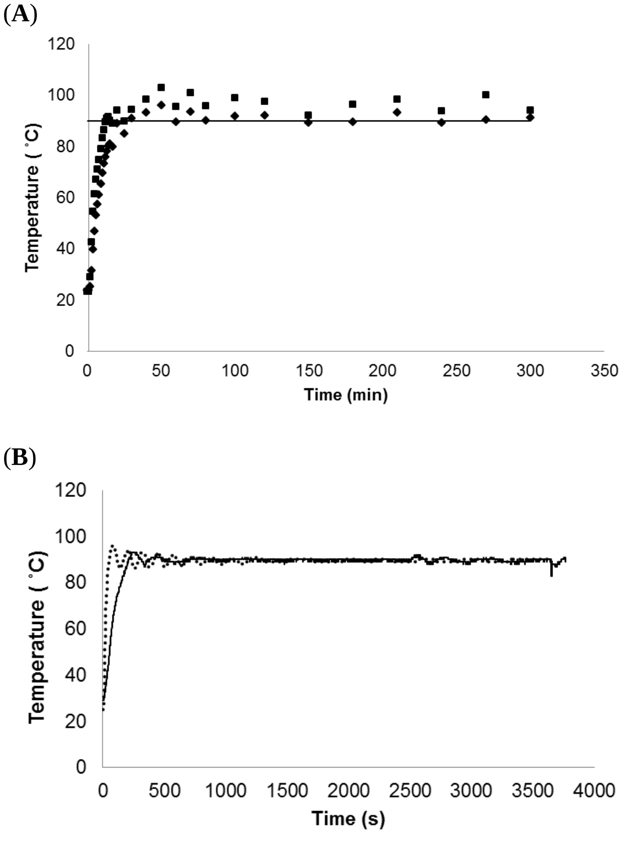
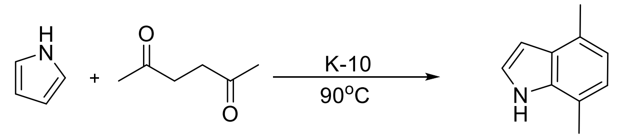


Figure 2 Heating profiles of Scheme 2, R=H reaction catalyzed by K-10 using (A) conventional heating at 90 ˚C, (■-oil bath ♦-reaction mixture inside the vessel, solid line is the set-point), and (B) microwave heating with infrared (solid line) and fiberoptic (dotted line) temperature monitoring at 90 ˚C

The data on Fig. 2 display similar tendencies that were observed with the neat catalyst. In the conventional heating experiment the set-point temperature was reached after ~9 min (same as without the reaction mixture) and the temperature difference between the oil bath and internal temperatures was rather moderate. The microwave-induced heating profiles of the reaction/catalyst are also similar to those in Fig. 1. The most significant observation is that the difference between the temperature of the IR detector-controlled reaction and the temperature measured by the fiberoptic probe at the end of the reaction is remarkably lower (observed 115 ˚C, ΔT=25 ˚C) than in the case of the neat catalyst (ΔT=106 ˚C). Most likely the highly endothermic reaction can be accounted for the rapid consumption of the extra heat generated by the interaction of the catalyst with the microwaves.

In order to observe the effect of the elevated temperature determined in the IR-controlled microwave experiment on the conventionally heated reaction, it was carried out at 115 ˚C. The comparative data are summarized in Fig. 3.



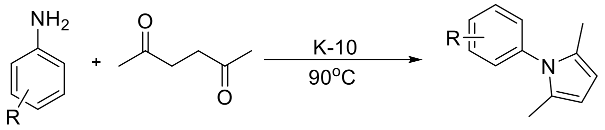
	T_{set} (°C)	T_{actual} (°C)	Yields (%)	Energy use (kWh)	Efficiency (kWh/%)
MW_{60min}	90	115	81	0.45	$5.74 \cdot 10^{-3}$
CH_{5h}	**90**	92	84	0.28	$\mathbf{3.34 \cdot 10^{-3}}$
CH_{5h}	**115**	116	90	0.30	$\mathbf{3.33 \cdot 10^{-3}}$

Figure 3 Comparative performance data for Scheme 2, R=H reaction catalyzed by K-10 using conventional heating at 90 and 115 ˚C and microwave heating with infrared temperature monitoring set at 90 ˚C (the data are averages of three separate experiments)

It was observed that the reaction when carried out at 115 ˚C produced higher yield than at 90 ˚C, as expected. The energy consumption of the reaction was also slightly higher due to the higher temperature applied. However, the efficiency, the energy required to obtain 1% yield, compared in the case of the conventional reactions at different temperatures was observed to be the same. This observation suggests that, under the same heating conditions, independently of the exact reaction temperatures, the reactions will possess reasonably similar (in the present case the same) energy efficiency. Thus, measuring the consumed energy and calculating the kWh/% ratio adequately describes the energy efficiency of a heating method. Based on the above observations it was decided to extend the study to several reactions all catalyzed by K-10 montmorillonite.

In heterocyclic chemistry reactions often occur, fully or partially, just by mixing the reactants together with (or without) the catalyst. Since the sample preparation of the reactions involved the mixing of the reactants with K-10 in a solvent, which was removed in vacuum, each sample has been tested for the actual amount of potential product formation before it was subjected to heating. The result of the analysis will be mentioned at the individual reactions.

In the first model reaction hexan-2,5-dione was used as a cyclialkylating agent with anilines in a solvent-free K-10-catalyzed reaction for the synthesis of 2,5-dimethyl-1-arylpyrroles (Scheme 1).[19] This reaction is an environmentally benign alternative to the classical Paal–Knorr cyclization[20] for the preparation of pyrroles. It was observed that during the sample preparation 37% product formation occured. This amount was taken into account during the energy consumption/efficiency calculations.

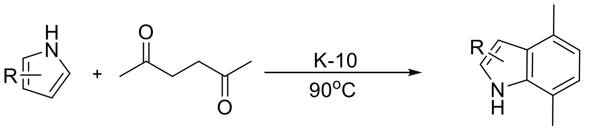


		Yields	Energy use
R = H	MW_{1min}	99%	0.01 kWh
	$CH_{50\ min}$	97%	0.06 kWh
R = 4-Et	MW_{1min}	99%	0.01 kWh
	CH_{30min}	79 %	0.04 kWh

Scheme 1 Paal-Knorr cyclization of aniline and 4-ethylaniline with 2,5-hexan-dione to a trisubstituted pyrrole. MW – microwave irradiation; CH – conventional heating (the data are averages of three separate experiments)

Both of the two Paal-Knorr cyclizations rapidly provided the expected product in high yields. The microwave-assisted reaction proceeded to 99% conversion in 1 min. No byproduct formation was observed in either case. Due to the relatively short reaction time, a minimal amount of energy was required in order for the reaction to proceed. It appeared that the conventional heating used more energy than the microwave-assisted version. The same was observed for the similar reaction of 4-ethylaniline although the difference between the energy consumed by the two heating methods was less significant.

The second model reaction was the electrophilic annelation of pyrroles with hexan-2,5-dione to prepare the corresponding indole derivatives (Scheme 2).[17] Mechanistically, this process was proposed to occur via a step-wise mechanism; first hydroxyalkylation occurs, predominantly in the 2-position of pyrrole, to form an unstable intermediate. This intermediate immediately undergoes dehydration and a water molecule is eliminated. It is followed by a second hydroxyalkylation-dehydration sequence at the 3-position of the pyrrole to provide the cyclized and aromatic product. In the reference work, the yields are practically quantitative, thus, during the current investigations the reaction time was shortened in order to obtain somewhat lower yields for more accurate comparison. The sample preparation resulted in no product formation, thus only the starting materials were present when the heating was commenced.

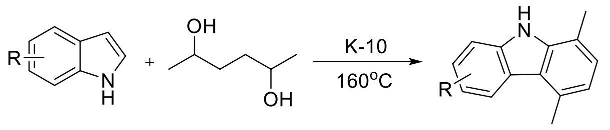


		Yields	Energy use
R = H	MW_{60min}	81%	0.45kWh
	CH_{5h}	84%	0.28kWh
R = 2-Et	MW_{90min}	80%	0.71kWh
	CH_{8h}	80%	0.48kWh

Scheme 2 Electrophilic annelation of pyrrole with 2,5-hexandione to 4,7-dimethylindole. MW – microwave irradiation; CH – conventional heating (the data are averages of three separate experiments)

As shown in Scheme 2 pyrrole and 2-ethylpyrrole were used as substrates in these reactions. Both reactions proceeded with approximately 80% yield under the experimental conditions used. At that point in the reaction of pyrrole, the microwave-assisted process appeared to be using more energy. The reaction of 2-ethylpyrrole provided similar results; the conventional heating was found to be more energy efficient producing the same amount of product using less energy.

In a follow up study, the electrophilic annelation has been carried out by an even greener reagent 2,5-butanediol and using indoles as target substrates to synthesize carbazole derivatives (Scheme 3).[21] The reaction was initiated by the solid acid and a water molecule was eliminated to form a tetrahydrofuran derivative. This intermediate underwent protonation and ring opening followed by the immediate Friedel-Crafts alkylation in the 3-position of indole. A second intramolecular Friedel–Crafts alkylation resulted in a tetrahydrocarbazole. Under the experimental conditions, the tetrahydrocarbazole underwent a K-10-catalyzed oxidative aromatization forming 1,4-dimethylcarbazole. No product formation was observed during the sample preparation thus only starting materials were present before the heating.

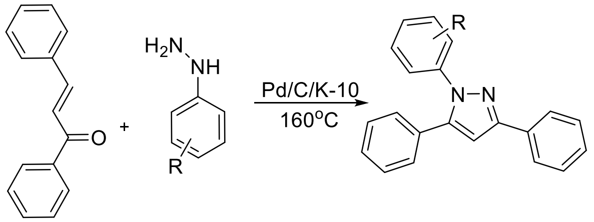


		Yields	Energy use
R = H	MW_{45min}	73%	0.50kWh
	CH_{16h}	89%	1.87kWh
R = 5-Cl	MW_{45min}	88%	0.42kWh
	CH_{16h}	94%	1.72kWh

Scheme 3 Friedel-Crafts cyclialkylation and subsequent dehydrogenation of indoles with 2,5-hexandiol to carbazoles. MW – microwave irradiation; CH – conventional heating (the data are averages of three separate experiments)

The reaction was carried out using two different substrates indole and 5-chloroindole. As shown, both the conventional and the microwave-assisted reactions ran properly reaching 73-94 % yields, respectively. It is worth mentioning that, in contrast to the above discussed reactions (Scheme 1), reaching the desired yield required significantly more time (45 min for the microwave and 16 h for the conventional reaction). While this maybe unfortunate for synthetic purposes, using more energy in the process by both variations increased the accuracy of the energy measurements. It was observed that the microwave-assisted synthesis consumed reasonably less energy than the conventional system.

The fourth model system was the synthesis of 1,3,5-triphenyl-pyrazoles *via* a domino condensation-cyclization-aromatization reaction from chalcones and hydrazines. Although, montmorillonite K-10 performed the aromatization partially, in a similar manner as shown in Scheme 3, a mixture of Pd/C and K-10 had to be employed to achieve complete aromatization effectively. Adding an effective hydrogenation/dehydrogenation catalyst to K-10 resulted in pyrazoles in good yields (Scheme 4).[22] The bifunctional catalyst was a simple mechanical mixture of commercially available Pd/C and K-10 montmorillonite. The reaction involved a condensation of chalcones with hydrazines and cyclization. These two steps were catalyzed by K-10. Pd/C ensured high rates and yields in the last aromatization step to form the corresponding 1,3,5-triphenyl pyrazoles. Samples prepared for the reaction showed no sign or any product formation before the heating.

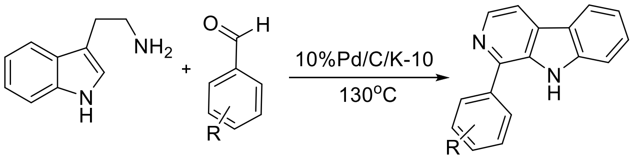


		Yields	Energy use
R = H	MW_{1h}	86%	0.47kWh
	CH_{24h}	79%	2.50kWh
R = 3-CF_3	MW_{45min}	78%	0.34kWh
	CH_{24h}	77%	2.65kWh

Scheme 4 Domino condensation-cyclization-aromatization reactions of chalcone with hydrazines to yield triphenyl-pyrazoles. MW – microwave irradiation; CH – conventional heating (the data are averages of three separate experiments)

Similarly to Scheme 3 the process was evaluated by using a set of two hydrazine derivatives. The reactions proceeded with the expected rate and gave appropriate yields in relatively long reactions. The microwave reaction was significantly shorter (45 min-1h) while the conventional heating required 24 h to reach proper yields. This is clearly reflected in the energy use; the microwave reactions consumed only about 25-30% of the energy which required for the conventional counterpart.

As an extension to the above one-pot synthesis of pyrazoles, the bifunctional Pd/C/K-10 catalyst was also applied in a similar synthesis of β-carbolines starting with tryptamine and benzaldehyhdes, respectively (Scheme 5).[23] The final products were formed *via* a three-step domino sequence. In the first step, the aldehyde reacted with the primary amino group of tryptamine *via* condensation to form an imine, which then underwent a K-10-catalyzed Pictet–Spengler cyclization reaction. In the third and final step, the tetrahydro-β-carboline intermediate underwent a Pd/C-catalyzed dehydrogenation to form β-carbolines in good to excellent yields. No product formation was observed during the sample preparation.

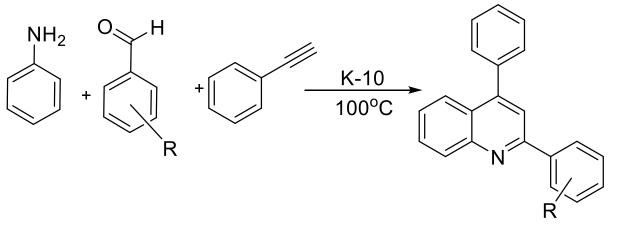


		Yields	Energy use
R = H	MW_{45min}	95%	0.44kWh
	CH_{20h}	97%	2.04kWh
R = 4-F	MW_{45min}	78%	0.46kWh
	CH_{17h}	88%	1.69kWh

Scheme 5 Domino Pictet-Spengler cyclization-dehydrogenation reactions of tryptamine with benzaldehydes to form carbazoles. MW – microwave irradiation; CH – conventional heating (the data are averages of three separate experiments)

The reaction times shown in Scheme 5 are similar to those in Schemes 2-4. In the case of both activation methods the required time to reach a sufficiently high yield is relatively long (45 min and 17-20 h, respectively). During the required time period the conventional method appeared to consume approximately 3-4 times more energy than the microwave-assisted process in the case of both benzaldehyde derivatives.

The last model reaction evaluated in this study was the synthesis of 2,4-diarylquinolines by a three component reaction of anilines, benzaldehydes and terminal phenylacetylenes in the presence of K-10 montmorillonite under solvent-free conditions (Scheme 6). Practically any combination of the three components could be used to synthesize the corresponding 2,4-diarylquinolines in good yields.[24] The analysis of the samples prepared for the reactions indicated that the aniline reacted with the benzaldehyde to form a Schiff-base (88%) while the rest of the starting materials (12%) remained intact. Neither the cyclized intermediate nor the aromatic final product formed during the sample preparation.



		Yields	Energy use
R = H	MW_{30min}	83%	0.25kWh
	CH_{24h}	96%	1.47kWh
R = 4-F	MW_{30min}	91%	0.24kWh
	CH_{19h}	96%	1.22kWh

Scheme 6 Multicomponent domino cyclization-aromatization of anilines, benzaldehydes and phenylacetylene to diphenylquinolines. MW – microwave irradiation; CH – conventional heating (the data are averages of three separate experiments)

The characteristics of the domino cyclization-aromatization to quinolines are similar to that of the previous reactions. The microwave-assisted reactions occurred more rapidly than the conventional alternatives in the duration of only 30 min. As discussed previously, the longer microwave reaction times ensured the reproducibility of the energy use measurements. The conventional reactions consumed approximately five times more energy than the microwave-assisted counterparts.

A qualitative analysis of the above data indicates that the conventional heating activated reactions required significantly longer time to progress to a similar yield than those conducted in the microwave systems. It was also observed that the energy consumption of the systems was quite different; in five of the six model reactions the conventional method used about 3-5 times more energy than the microwave systems depending on the substrates.

As it was our intention to provide a systematic investigation of these solid acid-catalyzed reactions, the above presented data were evaluated and the two heating methods compared. Since the different yields did not allow a direct quantitative comparison of the two systems, the energy needed to produce 1% yield was calculated as an equalizing unit of measure for the easy comparison of the energy consumption, named energy consumption factor, of the two activation methods as already represented in Fig. 3. Such comparison may not be accurate when applied to significantly altering yields, due to the reasonable change that can be observed in the slope of the kinetic curves over time. In the present case, however, consequently similar yields were achieved in the reactions (all yields were approximately 75-90%), which ensured that both methods were evaluated at similar positions on their respective product accumulation vs. time curves.

Accordingly, the energy consumption factors (energy/yield given in kWh/%) have been calculated and used to determine the energy efficiency ratio of the two methods used. The data are summarized in Table 1.

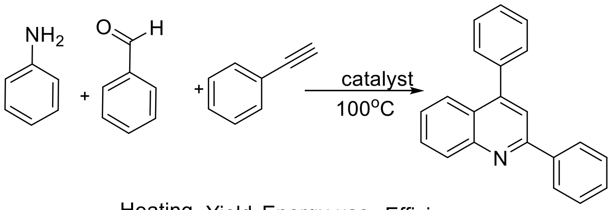
Table 1. The energy consumption and efficiency of conventional reaction and their microwave-assisted counterparts (all calculated data are averages of three separate experiments)

Entry	Reactant	Method	Energy/Yield (kWh/%)	E_{CH}/E_{MW} ratio
Scheme 1	Aniline	MW_{1min}	0.0002	5.0
		CH_{1h}	0.0010	
	4-Et-aniline	MW_{1min}	0.0002	5.0
		CH_{40min}	0.0010	
Scheme 2	Pyrrole	MW_{60min}	0.0055	0.6
		CH_{5h}	0.0033	
	2-Et-pyrrole	MW_{90min}	0.0089	0.7
		CH_{5h}	0.0060	
Scheme 3	Indole	MW_{45min}	0.0068	3.1
		CH_{16h}	0.0210	
	5-Cl-indole	MW_{45min}	0.0048	3.8
		CH_{16h}	0.0183	
Scheme 4	phenylhydrazine	MW_{1h}	0.0055	5.7
		CH_{24h}	0.0316	
	3-CF_3-phenylhydrazine	MW_{45min}	0.0044	7.8
		CH_{24h}	0.0344	
Scheme 5	Benzaldehyde	MW_{45min}	0.0046	9.1
		CH_{20h}	0.0210	
	4-F-benzaldehyde	MW_{45min}	0.0059	3.3
		CH_{17h}	0.0192	
Scheme 6	benzaldehyde	MW_{30min}	0.0030	5.1
		CH_{24h}	0.0153	
	4-F-benzaldehyde	MW_{30min}	0.0026	4.9
		CH_{19h}	0.0127	

[a] MW – microwave irradiation; CH – conventional heating

Table 1 depicts the energy consumption factor i.e. the energy usage of each reaction as kWh/% yield, while the energy efficiency ratio (E_{CH}/E_{MW}) compares the energy consumption of the two activation methods (last column). The reactions depicted in Schemes 4 and 5 showed the most significant difference between the microwave-assisted and conventional heating methods, the efficiency ratio average is as high as 9.1. For the other reactions the efficiency ratio ranges from 3 to 6, with the exception of one reaction in which conventional heating appeared to be slightly more efficient (Scheme 2 entries in Table 1). The obtained ratios (0.6 and 0.7) are close to 0.5, indicating that the conventional heating is more efficient by about a factor of two. The two methods, however, are still reasonably comparable in terms of energy efficiency in this reaction. While the obtained results generally favor the microwave activation as more energy efficient they also indicate that the energy efficiency could significantly be different for various reactions and must be investigated on a case by case basis.

There could be several reasons behind the generally higher energy efficiency of the heterogeneous reactions as compared to their homogeneous counterparts. One such factor is the rapid and effective heating of solids as discussed above. Another factor is the acidity of the catalysts, particularly in acid-catalyzed reactions. As acidity is a thermodynamic phenomenon,[25] the increasing temperature would result in significantly higher acidity for the catalyst. In many acid-catalyzed reactions the presence of a stronger acid is beneficial for the reaction. While the formation of local hot-spots coupled with the relative accuracy of the infrared temperature detection in heterogeneous medium is discussed above their effect may have more extensive consequences than a simple temperature or activation energy-related effect. In many of the above reactions, the elimination of water, occasionally multiple times, is involved, thus, these reactions are strongly affected by the acidity of the medium. Our own investigations showed that the stronger the acidity, the more effectively elimination will occur.[26] Based on this; in such heterogeneous acid catalyzed reactions, the potentially elevated acidity may play a role in making the reactions more effective and faster, thus more energy efficient. It must be emphasized, however, that this statement is true for the majority of the reactions only, and not an exclusive phenomenon in these systems. To test this hypothesis the Scheme 6, R=H reaction was carried out with a significantly weaker solid acid, SiO_2 under the same reaction conditions used in the K-10 catalyzed reactions. SiO_2 serves a dual purpose in this comparison: it is a well-known weak solid acid with an estimated Hammett acidity constant of $H_0 \approx -3$. In comparison SiO_2 is about 5 order of magnitude weaker acid than K-10.[27] In addition, it is a weak microwave absorber, thus the intrinsic acidity increase is largely absent using this catalyst. Using SiO_2 as a catalyst under identical conditions, the reactions were performed with both heating methods. The data are summarized in Fig. 4.



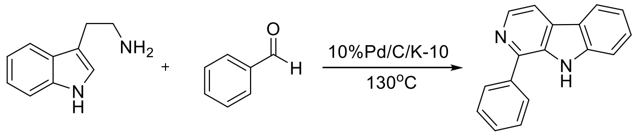
Catalyst	Heating Method	Yield (%)	Energy use (kWh)	Efficiency (kWh/%)	E_{CH}/E_{MW}
K-10	MW	83	0.25	$3.0 \cdot 10^{-3}$	5.1
	CH	96	1.47	$1.5 \cdot 10^{-2}$	
SiO_2	MW	5	0.24	$4.8 \cdot 10^{-2}$	1.7
	CH	20	1.64	$8.2 \cdot 10^{-2}$	

Figure 4 Comparative performance data for Scheme 6, R=H reaction catalyzed by K-10 and SiO_2 solid acids using microwave (MW) and conventional heating (CH) at 100 °C

It was observed that weaker acidity as well as the weak microwave absorbing capability of the silica catalyst resulted in poor yield (5%). Similar strong drop in the yield was observed with conventional heating as well, although this method resulted in more product formation. Accordingly, the efficiency ratio (E_{CH}/E_{MW}) observed with K-10 (5.1) dropped to 1.7, indicating that using the silica catalyst the two heating methods display reasonably similar energy efficiency. This observation supports the above discussion; the increased intrinsic acidity generated by the strong microwave absorber properties provides a much better performance as well as energy efficiency to the K-10 catalyzed microwave-assisted reactions.

Both the microwave-assisted and the conventionally heated reactions were conducted in a vessel with the reaction mixture always the same by mass to the comparable reactions. While the size of the oil bath and the volume of the heating oil were also kept the same throughout the measurements the effect of the size of the bath/amount of oil on the energy consumption of the reactions and the yields should also be considered. Accordingly a reaction (originally Scheme 5) was selected and carried out in different sized oil baths using varying volumes of the silicone oil. The results are tabulated in Table 2.

Table 2. The energy consumption and efficiency of the domino Pictet-Spengler cyclization-dehydrogenation reactions of tryptamine with benzaldehyde to form carbazoles activated by conventional heating.



Size of oil bath (mL)	Energy consumption (kWh)	Yield (%)	kWh/%Yield
15	1.94	93	0.0208
30	2.06	98	0.0210
50	1.95	96	0.0203
100	2.08	98	0.0212

[a] applied method: conventional heating, 20 h

The data show that the increasing the amount of the silicone oil, applied as a heat transfer medium affects the energy consumption of the systems only moderately. It is clear that the impact of the oil bath volume on the reaction and the consumed energy, within the assessed range, is not significant under the applied experimental conditions. The slight effect may partially be due to the relatively low specific heat of the silicon oil (1480 J/kg K; as a comparison the specific heat capacity of water is 4.183 J/kg K).[28] In the light of this data, increasing the volume from 15 to 100 mL will have a negligible effect on the energy consumption of the overall system. While discussing the specific engineering details is beyond the scope of this work, the heat loss *via* the upper wall of the reaction tube or the plate of the hot plate etc. may also play roles in minimizing the effect of oil volume on the energy consumed, while such energy losses are minimal in the microwave oven, even in the open vessel setup.

Finally, efforts were made to observe whether the energy efficiency of a reaction would change when the reactions are carried out in a larger scale. As one of the most conveniently measurable reactions in this study, the Scheme 6, R=H reaction was selected for these experiments. The amount of each reagent as well as the catalyst was quadrupled and the reactions were performed. It was observed that the microwave-assisted reaction provided similar data (89% *vs.* 83% yield, 0.22kWh *vs.* 0.24 kWh energy use) while in the conventionally heated reaction the yield decreased to 50% from 96%. The 4 times increase in the mass of the sample resulted in negligible increase in the consumed energy (1.48kWh vs. 1.47 kWh). It is worth noting that since the same reaction tube was used the stirring was not as effective as with the original amount. These data clearly show that despite the less effective stirring, the strong microwave absorbing medium is still able to heat up properly and produce high yield, while for the conventionally heated reaction the lack of efficient heat transfer caused a significant problem. It appears that using a larger amount of reaction mixture does not affect the efficiency. In this catalytic system, most likely due to the narrow diameter of the reaction vessel, the expected loss of efficiency as a result of the limited penetration depth of the microwaves was not obsereved.

Since the above experiments were inconclusive, it was decided to further increase the scale of the reaction by a factor of 40. The 40 times higher amounts (the reaction mixture was ~ 17g as compared to 0.45g in the original experiments), however, required the use of a larger glass vessel; a 50 mL pyrex round bottomed flask. Both the microwave and the conventional reactions were carried out in the same vessel. The microwave-assisted reaction provided 90% yield requiring 0.24 kWh energy (efficiency: 0.0027 kWh/%). The conventional reaction produced 71% yield using 1.47 kWh energy (efficiency: 0.0207 kWh/%). First of all, the energy data clearly indicate, that the increase in size of the vessel and the mass of the reaction mixture did not affect the energy used in either case. It suggests that a significant amount of energy was dissipated to the environment in small scale reactions. In other words, the small scale reactions appear to waste reasonable amount of energy. This wasted energy is, most likely, used for the activation of the significantly more reactants. Accordingly, the higher scale reactions appear more energy efficient, as they used the same amount of energy, but produced 40 times more product.

The other important observation is that despite the significantly higher diameter of the larger vessel, that could have resulted in less effective heating and lower yields due to the limited penetration depth of the microwaves, the yield remained the same. It is proposed that the highly effective microwave-absorber K-10 coupled with the stirring overcame the potentially problematic limited microwave penetration. Thus even at the ~17 g scale the efficiency is excellent, reasonably greater than in the small scale reaction.

CONCLUSIONS

With the advent of the microwave heating approach, and significant developments in the manufacturing of commercially available instruments, microwave-assisted synthesis has become a mainstream method in organic chemistry. The application of microwave irradiation became a general activation method of primary importance and such instruments can be found in most synthetic laboratories. Additionally, recent advances in material science resulted in a boom of new practical solid catalysts. The combination of these two approaches has made possible the development of effective, rapid, and most importantly, environmentally benign synthetic methods.

While the general green character of the heterogeneous catalytic methods is well-established, the question of energy efficiency was still an open question. Recent findings brought this problem to the forefront, illustrating that homogeneous microwave-activated reactions cannot automatically be labeled green. These findings incited us to investigate the energy consumption of microwave-assisted heterogeneous catalytic, solvent-free reactions and compare it to that of same reactions under conventional heating. Six different types of reactions were investigated under similar conditions. K-10 montmorillonite was used as the solid acid catalyst in these reactions. It was found that the energy consumption factor was generally higher for the conventional reactions (Schemes 1, 3-6) with one exemption (Scheme 2) for the opposite characteristic. For the reactions in Scheme 2 conventional heating required slightly less but reasonably comparable amount of energy. Commonly, however, the conventional heating consumed 3-9 times more energy than the microwave-assisted counterparts.

Based on the results described above, we can conclude that microwave-assisted heterogeneous solid acid catalyzed reactions appear to be more energy efficient than the conventionally heated reactions for the majority of the models studied. However, we are in agreement with earlier observations[11] and conclusions that the “green” label for microwave-reactions is not automatically justified. It is very likely that the very effective microwave-absorbing property, hence the very rapid and efficient heating, gives the advantage in the K-10-catalyzed reactions. While the solvents used in Kappe’s homogeneous experiments[11] are also good microwave-absorbers, they are less efficient than K-10 and many other solids of mineral or oxide-based origin. Experiments with low acidity and weak microwave absorbing solids also support this claim.

It also must be added that the above studies were limited to solid acid and supported metal catalyzed systems. Further investigations on catalysts prepared from other materials, for example graphite-supported catalysts, would provide a more comprehensive assessment of the topic.

Experimental Section

Materials and Methods: All chemicals used in the reactions (anilines, pyrrole, indoles, chalcone, phenylhydrazines, tryptamine, benzaldehydes, phenylacetylene, 2,5-hexanediol, 2,5-hexanedione), and the catalyst montmorillonite K-10 were purchased from Aldrich and used without further purification. Pd/C was purchased from Acros Organics. $CDCl_3$ used as a solvent (99.8%) for NMR studies was an Aldrich product. Other solvents used in synthesis with minimum purity of 99.5% were Fisher products.

The microwave reactions were carried out in a CEM Discover Benchmate microwave reactor (nominal power 300±10% W), using the open vessel technique. Commercial CEM thick wall Pyrex reaction vessels were used in the experiments with continuous stirring (800 rpm). The temperature control was maintained by the built in infrared detector/controller. In several experiments a fiberoptic probe was also used to determine the internal temperature of the reaction. An IKA RCT thermocouple controlled hot plate stirrer (1000 rpm) was used to carry out the conventional heating experiments. Silicon oil (Aldrich 85409, from -50 C to 200 C, b.p. > 140 C/0.002mmHg) was applied as heating medium (100ml). The same glass vessel that was used in the microwave experiments was applied in these experiments as well. A P4460 Kill A Watt EZ (P3 Int. Corp.) was used to measure the energy consumption of the reactions. The accuracy of the meter was ± 0.01 kWh. Before the reactions, the power-meter unit was connected to an outlet and the heating equipment was connected to the unit. This meant the hotplate only or the microwave reactor and its auxiliary air pump. The unit was reset to zero kWh before stating the reactions. The number was read on the unit when the reaction was completed.

NMR Analysis: The ^{1}H and ^{13}C spectra were obtained on a 300 MHz Varian NMR spectrometer, in $CDCl_3$ with tetramethylsilane as internal standards or the residual solvent signals. The temperature was 25 °C (accuracy ±1 °C) and controlled by the Varian control unit. All spectral data were in agreement with the literature.

GC-MS Analysis: The mass spectrometric identification of the products have been carried out by an Agilent 6850 gas chromatograph-597 mass spectrometer system (70 eV electron impact ionization) using a 30m long DB-5 type column (J&W Scientific).

Paal–Knorr cyclization:
Synthesis of 1-phenyl-2,5-dimethylpyrrole

Sample preparation: Aniline (91 μL, 1 mmol) and 2,5-hexanedione (117 μL, 1 mmol) were dissolved in 10 mL CH_2Cl_2 in a round bottomed flask. Then, montmorillonite K-10 (500 mg) was added to the above solution. The mixture was stirred for 5 min at room temperature to ensure the homogeneous distribution of the reactants on the surface of the catalyst; then the solvent was evaporated under vacuum. The dry mixture was equally divided into two portions. The first half of the mixture was transferred into a microwave reaction vial and irradiated in the microwave reactor at the desired temperature for the specified time at atmospheric pressure in an open system. The other half was transferred to same microwave reaction vial and stirred for the given time at the same temperature with the correlated MW reaction. The energy consumption of both reactions was measured by a P4460 Kill A Watt EZ Power Meter. After the reaction was complete, CH_2Cl_2 was added to the reaction mixture and the used catalyst was removed by filtration. The filtrate was concentrated, and the product yield was determined by gas-chromatography.

Electrophilic annelation of pyrrole with 2,5-hexandione:

Synthesis of 4,6-dimethyl-1H-indole

Pyrrole (84 μL, 1.2 mmol) and 2,5-hexanediol (117 μL, 1 mmol) were dissolved in 10 mL CH_2Cl_2 in a round bottomed flask. Then, K-10 (500 mg) was added to the above reaction mixture. The reaction was carried out using the same procedure as above including the measurement of the energy used.

Friedel-Crafts cyclialkylation and subsequent dehydro-genation reaction:

Synthesis of substituted carbazoles

Indole (117 mg, 1 mmol) and 2,5-hexanediol (177 mg, 1.5 mmol) were dissolved in 10 mL CH_2Cl_2 in a round bottomed flask. Then, K-10 (500 mg) was added to the above reaction mixture. The further preparation of the samples followed the above described method. The reaction was carried out using the same procedure as above including the measurement of the energy used.

Domino condensation-cyclization-aromatization reaction:

Synthesis of substituted pyrazoles

Chalcone (208 mg, 1 mmol) and phenylhydrazine (147 μL, 1.5 mmol) were dissolved in 3 mL CH_2Cl_2 in a round bottomed flask. Then, the mechanically premixed combination of Pd/C (21 mg) and K-10 (500 mg) was added to the above reaction mixture. The further preparation of the samples followed the above described method. The reaction was carried out using the same procedure as above including the measurement of the energy used.

Domino Pictet-Spengler cyclization-dehydro-genation reactions:

Synthesis of substituted β-carbolines

Tryptamine (100 mg, 0.62 mmol) and benzaldehyde (63μL, 0.62 mmol) were dissolved in 3 mL CH_2Cl_2 in a round bottomed flask. Catalyst was prepared by mixing 21 mg 10%

Pd/C and 500 mg of K-10. The catalyst was mixed with the above reaction mixture as described above and a few drops of MeOH were added to dissolve the tryptamine. The reaction was carried out using the same procedure as above including the measurement of the energy used.

Multicomponent domino cyclization-aromatization reactions:

Synthesis of substituted quinolines

Aniline (109 μL, 1.2 mmol), benzaldehyde (122μL, 1.2 mmol) and phenylacetylene (110 μL, 1mmol) were dissolved in 3 mL CH_2Cl_2 in a round bottomed flask. 500 mg of K-10 was mixed with the above reaction mixture. The further preparation of the samples followed the above described method. The reaction was carried out using the same procedure as above including the measurement of the energy used.

The scale-up experiments of this reaction were carried out using the original amounts increased to four fold.

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