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Microwave-enhanced solvent-free synthetic approach is described that features simplicity, manipulative ease of the operation and conservation of solvents as the main advantages. This eco-friendly approach, which has found application in facile organic functional group transformations, is applied to rapid assembly of heterocyclic compounds. A variety of solid state reactions are described that occur rapidly at ambient pressure under solventless conditions and provide ready access to intermediates such as enamines and α-tosyloxyketones which can be transformed *in situ* to biologically significant heterocyclic compounds such as isoflav-3-enes, flavones, quinolones, 2-aroylbenzo[*b*]furans and thiazoles in one-pot operation. Multicomponent reactions under these solvent-free conditions can be adapted for high speed parallel synthesis and are exemplified by assembly of dihydropyrimidine-2(1*H*)-ones (Biginelli reaction) and imidazo[1,2-*a*]annulated pyridines, pyrazines and pyrimidines (Ugi reaction) which may have potential in building a library of such compounds.

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Microwave (MW) heating has been employed for the rapid synthesis of a wide variety of organic molecules [1-5] wherein chemical reactions are accelerated because of selective absorption of MW energy by polar molecules, non-polar molecules being inert to the MW dielectric loss. Heterogeneous reactions facilitated by supported reagents on various mineral oxide surfaces have received attention in recent years [6]. The application of microwave irradiation with the use of catalysts or mineral supported reagents, under solvent-free conditions, provide unique chemical processes with special attributes such as enhanced reaction rates, higher yields, greater selectivity and the ease of manipulation. Further, the limitations of the MW-assisted reactions in organic solvents namely the development of high pressures and the need for specialized sealed vessels, are circumvented *via* this solid state strategy which enables organic reactions to occur expeditiously at ambient pressure [1,2,5]. These solvent-free MW-assisted reactions [1,2,4,5] have gained popularity as they provide avenues to work with open vessels with an enhanced possibility of upscaling the reactions on preparative scale.

This eco-friendly microwave approach enables organic functional group transformations [5] such as deprotection (cleavage), condensation, cyclization, oxidation and reduction reactions to occur very rapidly and the strategy finds useful applications in the synthesis of heterocyclic compounds utilizing relatively benign and recyclable mineral supports. This solventless microwave methodology is exemplified by a concise synthesis of flavones, tetrahydroquinolones, 2-aroylbenzofurans, and thiazole derivatives and exploits the *in situ* generation of reactive intermediates as demonstrated in the one-pot synthesis of benzopyrans. Further, the adaptability of the process to rapid and parallel synthesis in solvent-free multicomponent reactions is demonstrated in the assembly of dihydroprimidine-2(1*H*)-ones (Biginelli reaction) and imidazo[1,2-*a*]-annulated pyridines, pyrazines and pyrimidines (Ugi reaction).

Synthesis of Flavonoids.

Flavonoids are a group of naturally occurring phenolic compounds widely distributed in the plant kingdom, the most abundant being the flavones. Members of this class display a wide variety of biological activities [7]. A manipulatively simple and rapid method for the synthesis of flavones (Scheme 1) proceeds *via* a solid state dehydrative cyclization of *o*-hydroxydibenzoylmethanes in clay microenvironment using microwaves [8]. The results for the synthesis of several substituted flavonoid derivatives are summarized in Table 1.

Scheme 1

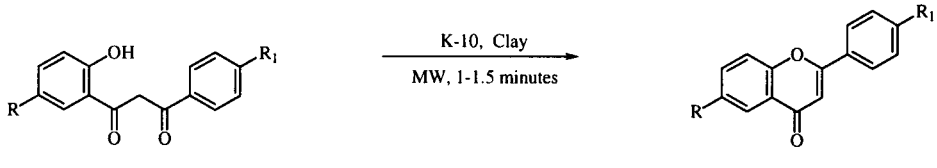


Table 1

Synthesis of Flavones *via* the Cyclization of *o*-Hydroxydibenzoylmethanes on Clay

Compound No.	R	R_1	Time	Yield (%) [a]
1	H	H	1.0 minute	75
2	H	Me	1.0 minute	77
3	H	OMe	1.5 minutes	76
4	H	NO_2	1.0 minute	78
5	OMe	H	1.0 minute	73
6	OMe	Me	1.5 minutes	80
7	OMe	OMe	1.0 minute	72

[a] Unoptimized and isolated yields of pure products that exhibited appropriate physical and spectral properties [8].

Synthesis of 2-Aryl-1,2,3,4,-tetrahydro-4-quinolones.

In an analogous manner, a microwave-expedited preparation of 2-aryl-1,2,3,4-tetrahydro-4-quinolones is facilitated under mild and solvent-free conditions on montmorillonite K-10 clay surface [5g] from readily accessible 2'-aminochalcones (Table 2). These tetrahydro-4-quinolones are valuable precursors to medicinally important quinolone derivatives [9] especially those bearing substituents in either of the aromatic rings (Scheme 2).

Synthesis of 2-Aroylbenzo[*b*]furans.

Benzo[*b*]furans encompass a large group of naturally occurring compounds which display a wide variety of pharmacological activity [10]. Although there are few methods available for their synthesis [11], a simple preparation of 2-aroylbenzo[*b*]furans proceeds readily *via* the condensation of *in situ* generated α-tosyloxyketones with a variety of salicylaldehydes on potassium fluoride 'doped' alumina [5h] and the process (Scheme 3) avoids the use of lachrymatory starting materials.

The procedure in its entirety involves a simple mixing of salicylaldehydes with solid potassium fluoride 'doped' alumina ($KF\text{-}Al_2O_3$) followed by the addition of α-tosyloxyketones which, in turn, are obtained by the reaction of hydroxy(tosyloxy)iodobenzene with the corresponding arylmethyl ketones. The reaction mixture is subjected to irradiation in a household microwave oven for 3-5 minutes and the product extracted from the support to afford benzo[*b*]furans in 89-95% yields (Table 3).

Synthesis of Substituted Thiazole Derivatives.

Thiazoles are conventionally prepared from α-haloketones and thioureas (or thioamides) *via* a method pioneered by Hantzsch [12]. In a lengthy preparation (25 hours), King and coworkers have synthesized 2-aminothiazoles

Scheme 2

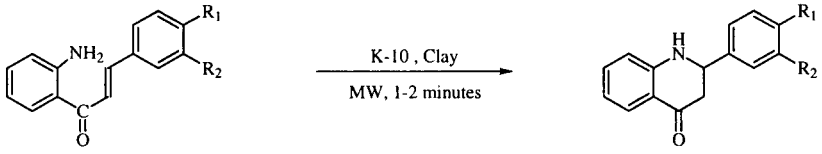


Table 2

Preparation of 2-Aryl-1,2,3,4-tetrahydro-4-quinolones on K-10 Clay Surface

Compound No.	R_1	R_2	Time	Yield (%) [a]
1	H	H	1.0 minute	80
2	Me	H	1.0 minute	77
3	OMe	H	2.0 minutes	78
4	Cl	H	1.5 minutes	80
5	Br	H	1.5 minutes	72
6	NO_2	H	2.0 minutes	70
7	OMe	OMe	1.5 minutes	72

[a] Unoptimized and isolated yields of pure products that exhibited appropriate physical and spectral properties [5g].

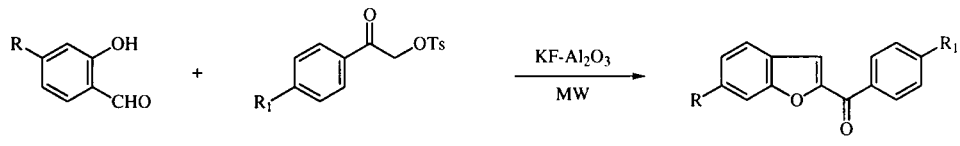
Table 3

Synthesis of 2-Aroylbenzo[*b*]furans from α-Tosyloxyketones and Salicyladehydes on KF/Al_2O_3

Compound No.	R	R_1	Time	Yield (%) [a]
1	H	H	3.0 minutes	94
2	H	Cl	3.0 minutes	94
3	H	Me	2.5 minutes	91
4	H	OMe	3.5 minutes	89
5	Cl	H	2.5 minutes	95
6	Cl	Me	2.5 minutes	96
7	Cl	OMe	3.5 minutes	89

[a] Isolated yields of pure products that exhibited appropriate physical and spectral properties [5h].

Scheme 3



by replacing α-haloketones [13] which is followed by other methods in view of the pharmacological importance of the thiazole derivatives [14]. The obvious limitations have been the use of strong mineral acids under drastic reaction conditions. The present solvent-free strategy for the synthesis of thiazoles involves a simple mixing of thioamides with α-tosyloxyketones in a clay-catalyzed reaction [5h] (Scheme 4).

The typical procedure entails mixing of thioamides and *in situ* produced α-tosyloxyketones with montmorillonite K-10 clay in an open glass container. The reaction mixture is irradiated in a microwave oven for 3-6 minutes with intermittent irradiation and the product extracted into ethyl acetate to afford substituted thiazoles in 88-96% yields (Table 4).

Scheme 4

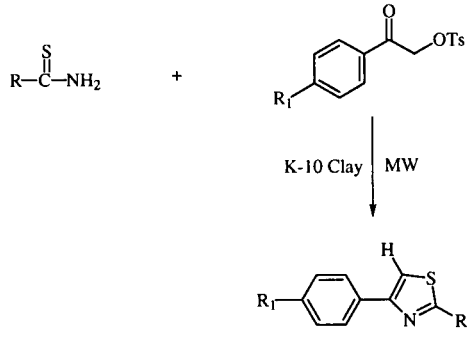


Table 4

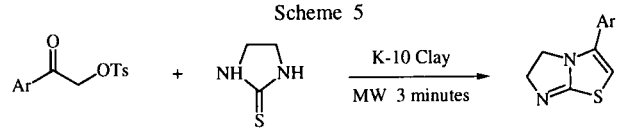
Microwave-assisted Synthesis of Thiazoles from α-Tosyloxyketones and Thiourea

Compound No.	R_1	R	Time	Yield (%) [a]
1	H	Cl	3.0 minutes	90
2	Cl	*p*-ClC_6H_4	2.0 minutes	94
3	Me	*p*-ClC_6H_4	5.0 minutes	92
4	MeO	*p*-ClC_6H_4	3.0 minutes	90
5	H	*p*-$MeOC_6H_4$	4.0 minutes	91
6	MeO	*p*-$MeOC_6H_4$	3.5 minutes	88
7	Cl	*p*-$MeOC_6H_4$	4.0 minutes	96
8	Me	*p*-$MeOC_6H_4$	3.0 minutes	92

[a] Isolated yields of pure products that exhibited appropriate physical and spectral properties [5g].

The synthesis of corresponding bridgehead heterocycles is also accessible *via* this general strategy using cyclic ethylene thiourea [5h] (Scheme 5). It appears that there is not a significant difference between the reaction rates using MW irradiation and alternate heating mode for thioamides (require 10-40 minutes for completion at 135° in an oil bath). However, the corresponding reactions with cyclic thioureas remain incomplete after heating at 150° for 24 hours in an oil bath.

Scheme 5



Ar = C_6H_5, *p*-ClC_6H_4, *p*-MeC_6H_4, *p*-$MeOC_6H_4$: 83-92% yields

Synthesis of 2-Substituted (2*H*)-1-Benzopyrans.

Isoflav-3-enes possessing a 2*H*-1-benzopyran nucleus are important chromene derivatives which display interesting estrogenic and antiestrogenic properties [15] and are useful in the synthesis of medicinally important molecules [16]. Our earlier uncovered enamine-mediated general route to isoflav-3-enes bearing basic moieties at the 2 position [17] is now possible in one-pot *via* the microwave-expedited process [5j] (Table 5).

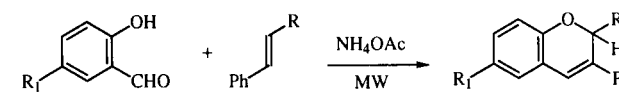
Table 5

One-pot Microwave-assisted Synthesis of Isoflav-3-enes *via in situ* Generated Enamines

Compound No.	R_1	Morpholinyl Time (minutes)	Morpholinyl Yield (%)	Piperidinyl Time (minutes)	Piperidinyl Yield (%)	Pyrrolidinyl Time (minutes)	Pyrrolidinyl Yield (%)
1	H	5	80	5	72	4	79
2	NO_2	6	82	2	85	2.5	83
3	Cl	4	81	4	88	2	79

This one-pot synthesis of biologically active benzopyrans involves the reaction of *in situ* generated enamines [5e] with salicylaldehyde derivatives in the presence of a catalytic amount of ammonium acetate [5j] (Scheme 6). Isoflav-3-enes are thus readily obtained by irradiating the reaction mixture for 4-6 minutes in MW oven and the products are further purified easily by passing through a bed of basic alumina to afford pure isoflavenes in high yields (70-90%). The environmentally benign feature of these simple and rapid protocols is that they require neither the use of excess hydrocarbon solvents nor the Dean-Stark apparatus for azeotropic removal of water.

Scheme 6



R = morpholinyl or piperidinyl or pyrrolidinyl

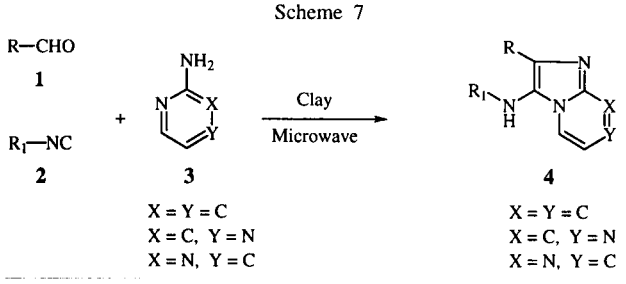
Microwave-accelerated Multicomponent Reactions.

Combinatorial chemistry has gained great importance as a tool for the synthesis of a wide variety of useful compounds including pharmaceuticals [18]. In this context, the multiple component condensation (MCC) approach is specially appealing due to the fact that products are formed in a single step and the diversity can be achieved simply by varying the reacting components. The recent surge of activity focuses on the generation of small-molecule libraries targeted for bioactive compounds, an endeavor that requires development of efficient methodologies with special emphasis on ease of reaction manipulation. We now report a facile and rapid protocol that is amenable to the generation of a library of imidazo[1,2-*a*]pyridines, imidazo[1,2-*a*]pyrazines and imidazo[1,2-*a*]pyrimidines under solvent-free conditions using microwave irradiation. The conventional two-component synthesis of imidazo[1,2-*a*]annulated pyridines, pyrazines and pyrimidines requires lachrymatory α-haloketones and the corresponding 2-amino-pyridines, pyrazines or pyrimidines respectively which restricts the generation of a diverse library of these molecules [19].

This solventless one-pot method involves irradiating a mixture of aldehydes and corresponding 2-aminopyridine, pyrazine or pyrimidine in the presence of a small amount of clay (50 mg) with microwaves to generate iminium ion. Subsequently, isocyanide is added to the same container and the reactants are further exposed to microwaves at a reduced power level (50%) for an appropriate time (Table 6) to afford the corresponding imidazo[1,2-*a*]pyridines, imidazo[1,2-*a*]pyrazines and imidazo[1,2-*a*]pyrimidines **4** (Scheme 7). The protocol is general for all the three components, *e.g.* aldehydes (aliphatic, aromatic and vinylic), isocyanides (aliphatic, aromatic and cyclic) and amines (2-aminopyridine, 2-aminopyrazine and 2-aminopyrimidine). Thus, a library of imidazo[1,2-*a*]pyridines, imidazo[1,2-*a*]-pyrazines and imidazo[1,2-*a*]pyrimidines can be readily obtained by simply varying the three components. Additionally, the use of inexpensive clay and its recyclability renders this an economical and eco-friendly procedure [24].

The strategy has now been applied to the parallel synthesis of 4-aryl-3,4-dihydropyrimid-2(1*H*)-ones (DHPM) employing a solventless Biginelli multicomponent condensation reaction. The novel method uses neat mixtures of aryl aldehydes, β-ketoesters and urea derivatives in the presence of polyphosphate ester (PPE) as a reaction mediator (Scheme 8). The irradiation of these components for 90 seconds in a microwave oven provides dihydropyrimidones, **8** in 61-95% yield after aqueous workup [21]. In collaboration with Dr. Oliver Kappe, we have extended the scope of this microwave/PPE-mediated Biginelli procedure and conducted the efficient and parallel synthesis of a number of DHPM analogs in a single microwave irradiation experiment. As an example, 10 reaction vessels containing the appropriate mixtures of β-ketoesters **5**, aldehydes **6**, urea **7**, and PPE were placed inside an alumina bath and simultaneously irradiated in the microwave oven. After the usual aqueous workup the individual DHPMs **8** were obtained in yields identical to the ones obtained in the conventional MW experiment thus enabling the parallel synthesis of single compound DHPM libraries. In view of the readily accessible aromatic aldehydes, β-ketoesters, and urea derivatives large collections of DHPMs can potentially be prepared, applying the recently developed automated, high throughput robotic technologies for performing microwave-assisted combinatorial synthesis [22].

Scheme 7

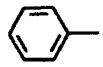
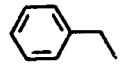
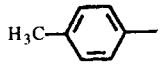
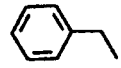
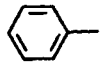
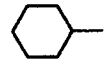
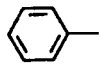
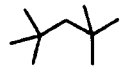
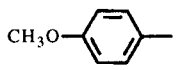
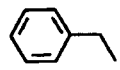
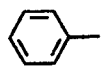
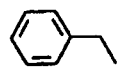
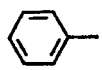
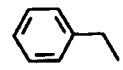
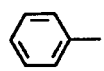
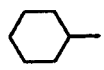
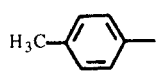
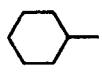
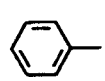
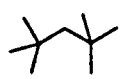
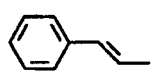
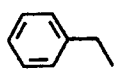
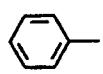
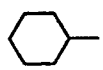
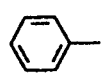
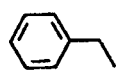


Miscellaneous Reactions.

Several other reagents can be used under these solventless conditions to expedite the chemical reactions. As an example, an expeditious conversion of flavones, isoflavones, coumarins and various ketones, amides and esters to the corresponding thio analogues is possible using the Lawesson's reagent in a solvent-free microwave protocol that avoids the usage of dry solvents and excess of the reagent [23]. Similarly, a general protocol, that is applicable to the oxidation of dihydropyridine derivatives to the corresponding pyridines, utilizes elemental sulfur under solvent-free conditions [5i].

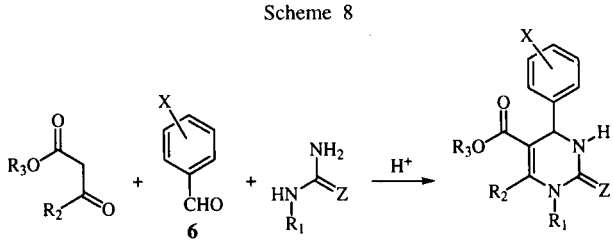
In conclusion, this eco-friendly solventless approach using microwave irradiation opens up numerous possibilities for conducting rapid synthesis and organic functional group transformations more efficiently and expeditiously using a variety of supported reagents on mineral oxides. The use of an unmodified household microwave oven (multimode applicator) and conventional glass apparatus, demonstrates the numerous practical applications in laboratory scale experiments. Additionally, there are distinct advantages of these solvent-free protocols since they provide reduction or elimination of solvents thereby preventing pollution in organic synthesis 'at source'. Although not well understood at the present time, the reaction rate enhancements obtained in these solvent-free methods may be ascribable to non-thermal effects. The chemo-, regio- or stereoselective synthesis of high value chemical entities and parallel synthesis to generate a library of small molecules may see the growth of microwave-enhanced reactions in the near future.

Table 6
Synthesis of Imidazo[1,2-*a*]annulated Pyridines, Pyrazines and Pyrimidines Using Microwave Irradiation

Product [a]	X, Y	R	R_1	Time (minutes)	Yield (%) [b]
4a	X = Y = C			3.0	86
4b	X = Y = C			3.0	88
4c	X = Y = C			3.0	86
4d	X = Y = C			3.5	85
4e	X = Y = C			3.5	82
4f	X = Y = C		*t*-Bu	3.0	84
4g	X = Y = C	$(CH_3)_2CH$		3.0	85
4h	X = C, Y = N			3.0	81
4i	X = C, Y = N			3.0	82
4j	X = C, Y = N			3.0	81
4k	X = C, Y = N			3.0	83
4l	X = C, Y = N			3.5	64
4m	X= N, Y = C			3.5	58
4n	X= N, Y = C			3.5	56

[a] All the compounds were analyzed for the C, H, and N and the results are in agreement with the theoretical values; [b] yields refer to pure isolated products.

Scheme 8



5 6 7 8

EXPERIMENTAL

Melting points were determined on a Mel-Temp II hot stage apparatus using Fluke 51 K/J digital thermometer and are uncorrected. The ^1H and ^{13}C nmr spectra were recorded in deuteriochloroform on Jeol Eclipse 300 (300 MHz for ^1H nmr and 75 MHz for ^{13}C nmr) spectrometer using tetramethylsilane as an internal standard. Mass spectra were recorded on a Hewlett Packard® 5890 mass spectrometer (70 eV) using a GC/MS coupling or direct inlet system. The chemicals and reagents were obtained from Aldrich Chemical Co. A Sears Kenmore household microwave oven equipped with a turntable and operating at

2450 MHz was used at its full power, 900 W, for all the experiments. An alumina bath (neutral alumina: 125 g, mesh ~150, Aldrich; bath: 5.7 cm diameter) was used as a heat sink inside the MW oven to irradiate the reaction mixtures. The average bulk temperature at the end of the reaction was measured by inserting a thermometer in the alumina bath housing the reaction vessel. Thin layer chromatography was performed on silica gel plates supplied by Analtech, Inc. Products are identified by comparison of their mp, ir and nmr spectra with those of authentic samples. The elemental analysis of new chemical entities was performed by the Galbraith Laboratories, Knoxville, TN.

The following are representative procedures for the preparation of various heterocycles.

Typical Procedure for Flavonoids. (4'-Methyl-6-methoxyflavone, Entry 6, Table 1).

1-(2-Hydroxy-5-methoxyphenyl)-3-(4-methylphenyl)propane-1,3-dione (0.2 g, 0.70 mmole) is taken in a glass tube, dissolved in small amount of dichloromethane (1 ml) and adsorbed on montmorillonite K-10 clay (1.0 g). The test tube is placed in an alumina bath inside the microwave oven and irradiated for 1.5 minutes. The crude product is extracted into dichloromethane (2 x 15 ml) which is then crystallized from methanol to afford product, mp 161-62° [8], yield 80%; ^{1}H nmr (deuteriochloroform): δ 2.26 (s, 3H, C4'-CH_3), 3.36 (s, 3H, C6-OCH_3), 6.26 (s, 1H, C3-H), 6.53-7.33 (7H, m, aromatic-H); m/z 266 (100%).

2-Phenyl-1,2,3,4,-tetrahydro-4-quinolones.

The irradiation of *o*-aminochalcone (Entry 1, Table 2) is representative of the general procedure employed. *o*-Aminochalcone (0.1 g, 0.45 mmoles) was mixed with montmorillonite K-10 clay (1.0 g) in solid state using a pestle and mortar. The adsorbed material was transferred to a glass tube and was placed in an alumina bath (alumina: 100 g, mesh 65-325, Fisher Scientific; bath: 5.7 cm diameter) inside the microwave oven. The mixture was irradiated for 1.5 minutes (the temperature of alumina bath reached 110° at the end of this period) and the completion of the reaction is monitored by tlc examination. The product is extracted into dichloromethane (2 x 15 ml) and clay is filtered off. Removal of the solvent under reduced pressure affords 2-phenyl-1,2,3,4-tetrahydro-4-quinolone as crystalline solid, mp 148-150°, (lit 149-150°) [20], yield 80% .

General Procedure for the Synthesis of α-Tosyloxyketones.

A mixture of arylmethylketone (1 mmole) and hydroxy(tosyloxy)iodo benzene (1.2 mmoles) was mixed in a glass tube and was placed in an alumina bath inside the MW oven and irradiated for 30 seconds at 50% power level. After completion of the reaction, as determined by tlc examination, the crude products were washed with hexane to afford pure α-tosyloxyarylmethylketones which were used further in subsequent reactions.

Synthesis of 2-Aroylbenzo[*b*]furans (Scheme 3, Table 3).

Salicylaldehyde (0.122 mg, 1 mmole), potassium fluoride (KF)-alumina (0.620 g, 0.2 mmole of KF) and α-tosyloxyketone (1 mmole) were placed in a glass tube and were mixed thoroughly on a vortex mixer. The glass tube was then placed in an alumina bath inside the MW oven and irradiated (intermittently with a 1.5 minute interval; 130°) for a specified time in the Table 3. On completion of the reaction, followed by tlc examination (hexane: ethyl acetate, 9:1), the product was extracted into methylene chloride (3 x 10 ml). The solvent was then removed under reduced pressure and the residue was crystallized from ethanol to afford nearly quantitative yield of 2-aroylbenzo[*b*]furans [5h].

General Procedure for the Synthesis of 2,4-Disubstituted Thiazoles (Scheme 4, Table 4).

α-Tosyloxyketone (1 mmole), appropriate thioamide (1 mmole) and montmorillonite K-10 clay (125 mg) were mixed thoroughly using a pestle and mortar. The reaction mixture was placed into a glass tube and exposed to microwave irradiation in an alumina bath for 2-5 minutes (intermittently with a 1.5 minute interval; 130°). The product was extracted into methylene chloride (2 x 10 ml) and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the residue was crystallized from ethanol-hexane to afford corresponding thiazoles (Table 4) [5h].

General Procedure for the Synthesis of 3-Aryl-5,6-dihydroimidazo-[2,1-*b*]thiazole (Scheme 5).

α-Tosyloxyketone (1 mmole), ethylenethiourea (1 mmole) and montmorillonite K-10 clay (100 mg) were mixed thoroughly in a pestle and mortar. The contents were transferred into a glass tube followed by intermittent microwave irradiation in an alumina bath for 3 minutes. The ensuing thiazole salt was neutralized by the addition of a dilute aqueous sodium hydroxide. The product was extracted into methylene chloride (2 x 10 ml), dried over anhydrous sodium sulfate and the solvent removed under reduced pressure to afford residues that were crystallized from benzene-hexane to afford corresponding 3-aryl-5,6-dihydroimidazo-[2,1-*b*]thiazole (Scheme 5) [5h].

One-pot Synthesis of Substituted Isoflav-3-enes.

Synthesis of 2-morpholinoisoflav-3-ene, (Entry 1, Table 5), is representative of the general procedure employed. A mixture of phenyl acetaldehyde (0.6 g, 5 mmoles) and morpholine (0.48 g, 5.5 mmoles) was placed in a small beaker and irradiated in a microwave oven at its full power (900 Watts) for 2 minutes. Salicylaldehyde (0.61 g, 5 mmoles) and ammonium acetate (0.02 g, 0.25 mmole) were then added to the same reaction vessel and the contents were further irradiated in the MW oven at its 50% power for 5 minutes (successive intervals of 2 minutes with a cooling period of 1 minute after each irradiation to avoid overheating of the reactants). Upon completion of the reaction, followed by tlc, the reaction mixture was passed through a bed of basic alumina using hexane:ether (9:1, v/v) as an eluent to afford pure 2-morpholinoisoflav-3-ene in 80% yield, mp 103-105° (lit mp 105°) [17a].

Synthesis of Imidazo[1,2-*a*]pyridines, Pyrazines and Pyrimidines **4**.

The synthesis of **4a** (Table 6) is representative of the general procedure employed. A mixture of benzaldehyde (106 mg, 1 mmole) and 2-aminopyridine (94 mg, 1 mmole) was irradiated in the microwave oven for 1 minute (at full power of 900 W) in the presence of montmorillonite K-10 clay (50 mg). After addition of benzyl isocyanide (117 mg, 1 mmole), the reaction mixture was further irradiated successively (2 minutes) at 50% power level for a duration of 1 minute followed by a cooling period of 1 minute. The ensuing product was dissolved in dichloromethane (2 x 5 ml) and the clay was filtered off. The solvent was removed under reduced pressure and the crude

product was purified either by crystallization or by passing it through a small bed of silica gel using ethyl acetate:hexane (4:1, v/v) as eluent to afford **4a** as crystalline solid, mp 112-113° (from methanol) [24]; ^{1}H nmr (deuteriochloroform): δ 4.14 (s, 2H, CH_2-NH), 6.72 (dd, 1H, J = 1.1, 6.9 Hz, H-6), 7.10 (dd, 1H, J = 1.1, 7.7 Hz, H-7), 7.21-7.49 (m, 9H, H-Ar), 7.53 (d, 1H, J = 8.8 Hz, H-8), 7.96-7.98 (m, 3H, H-Ar, H-5); ^{13}C nmr (deuteriochloroform): δ 52.47, 111.85, 117.40, 122.46, 124.26, 125.75, 127.11, 127.56, 127.72, 128.24, 128.75, 134.08, 139.04, 141.49.

Solventless Parallel Synthesis of 4-Aryl-3,4-dihydropyrimid-2(1*H*)-ones (**8**).

The appropriate β-ketoesters **5** (1.1 mmoles), aldehydes **6** (1.0 mmole), urea (**7**) (3.0 mmoles) and PPE (150 mg) were placed in individual glass beakers (10 ml) immersed in a crystallization dish (13.5 cm diameter) filled with alumina (400 g). This setup was subjected to microwave irradiation 3 times at the 50% power level for 40 seconds with a 1 minute and 2 minute cooling period after the first and second irradiation cycle, respectively. The usual aqueous workup provided DHPMs **8** in 61-95% yields [21]. A conventional (unmodified) houesehold microwave oven equipped with a turntable (Panasonic NN-3356/3306, 2450 MHz, 800 W) was used for this parallel synthesis.

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