Ain Shams University
University College of Women
For Arts, Science and Education
Chemistry Department

Factors Affecting the Condensation of ~, - Unsaturated Carbonyl Compounds with Different Amines

A Thesis Submitted for the Degree of Master
In
Organic Chemistry

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QUALIFICATION

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ABSTRACT

Microwave irradiation of a mixture from ٣-carboxy-٤-[phenyl- or (٤-methoxyphenyl)]-٣-butenoic acid (٢a or b), ٢-[phenyl- or (٤-methoxyphenyl)]methylenebutanedioic anhydride (٣a or b) or methyl ٣-carboxy-٤-[phenyl- or (٤-methoxyphenyl)-]-٣-butenoate (٤a or b) with different hydrazines, aliphatic or aromatic amines in ١٠٠٠ watt-microwave oven at ٣٠-٨٠٪ of its power for ٢-٢٠ minutes gives ١،٢-bis(٣-carboxy-٤-phenyl-٣-butenoyl)hydrazine (٨), ٢-(٤-methoxyphenyl)methylenebutanedioic hydarzide (٩), N-substituted-٣-carboxy-٤-aryl-٣-butenamides (٥, ١٢-١٦, ١٨, ٢٠, ٢٢, ٢٤, ٢٦, ٢٨, ٣٠, ٣٢ and ٣٤), N-substituted-٢-arylmethylenebutanimides (٦, ٧, ١٠, ١١, ١٣, ١٧, ١٩, ٢١, ٢٣, ٢٥, ٢٧, ٢٩, ٣١, ٣٣ and ٣٥) in excellent yields and high purity.

The structures were assigned in accordance to their elemental analysis and spectral data; IR, ^{١}HNMR and MS.

INTRODUCTION

Gedye R. N. et al., (*١٩٨٦*) published the first pioneering reports on the use of microwave heating to carry out synthetic organic transformations. It was realized that performing organic synthesis under microwave irradiation has some significant advantages as compared to classical heating techniques, to generate rapid intense heating of polar substances with consequent significant reduction in reaction times, cleaner reactions that are easier in working up, and in many cases offers higher yields. In fact, many reactions that do not occur by classical heating or that occur in very low yields can be performed in high yields under microwave irradiation.

The main advantage of microwave heating is the almost instantaneous "in core" heating of materials in homogeneous and selective manner (in contrast to conventional heating). Not surprisingly, interest in microwave-assisted organic synthesis (MAOS) from academic, governmental, and industrial laboratories, has increased in the recent years due to its characterestic accelerations for a wide range of organic reactions especially when carried out under solvent-free conditions. The combination of solvent-free reactions and microwave irradiation leads to a large reduction in reaction time, enhancement in conversions, and sometimes, in selectivity with several advantages of the echo-friendly approach, termed green chemistry ; ***Loupy A. et al., (١٩٩٨)*** and ***Varma R. S., (١٩٩٩)***.

١. Microwave Effects

The microwave region of the electromagnetic spectrum lies between infrared radiation and radio frequencies and corresponds to wavelengths between ١cm to ١m (frequencies of ٣٠ GHz to ٣٠٠ MHz respectively). In order to avoid interference with RADAR and telecommunication applications, domestic and ind- ustrial microwave reactors for chemical use operate at ٢,٤٥ GHz. In case of microwaves, the energy transfer does not occur by conduction or convection as in conventional heating but by dielectric loss. Materials dissipate microwave energy by two main mechanisms; dipole rotation and ionic conduction. When molecules with permanent (or inducible) dipoles are exposed to an electric field, they become aligned. If this field oscillates, the orientation changes with each alternation. The strong agitation provided by the reorientation of molecules which are in phase with the electrical field excitation, causes an intense internal heating.

The acceleration of reactions by microwave exposure results from material-wave interactions leading to thermal effects (which may be easily estimated by temperature measurements) and specific (non-purely thermal) effects. Clearly, a combination of these two contributions can be responsible for the observed effects.

Thermal effects (dielectric heating) can result from dipolar polarization as a consequence of dipole-dipole interactions between polar molecules and the electromagnetic field. They originate in dissipation of energy into heat as an outcome of agitation and intermolecular friction of molecules when dipoles change their mutual orientation at each alternation of electric field at a very high frequency (υ= ٢٤٥٠ MHz); ***Perreux L. and Loupy A.,(***٢٠٠١***)***.

Microwave effects result from material-wave interaction and the dipolar polarization phenomenon, where the greater the polarity of a molecule (such as the solvent), the more pronounced the microwave effect when the rise in temperature is considered; ***Gedye R. N. et al., (***١٩٩٨***)***. In terms of reactivity and kinetics, the specific effect has therefore to be considered according to the reaction mechanism and particularly with regard to how the polarity of the system is altered during the progress of the reaction.

Specific microwave effects can be expected for the polar mechanisms, when the polarity is increased during the reaction from the ground state towards the transition state. The outcome is essentially dependent on the medium and the reaction mechanism. If stabilization of the transition state (TS) is more effective than that of the ground state (GS), this results in an enhancement of reactivity by a decrease in the activation energy.

Irradiation reactions in dry media is currently developed successfully, and have received a tremendous interest in organic chemistry. Remarkable decreases in reactions time and better yields have been reported with microwave irradiation. Synthesis without solvents under microwave irradiation offers several advantages, where absence of solvent reduces risk of hazardous explosions. Moreover, solvents with high boiling points are expensive and difficult to be removed from the reaction mixture.

During microwave induction of reactions under dry conditions, the reactants adsorbed on the supporting reagent such as surface of alumina, silica gel, clay, and others which absorb the microwaves. Such supporting reagents efficiently induce reactions under safe and simple conditions with domestic microwave ovens instead of specialized commercial microwave systems that require sealed Teflon bombs.

٢. Solvent Effect

Microwave effects should additionally be considered according to the reaction medium. Solvent effects are of particular importance as described by ***Langa F. et al., (٢٠٠٠):***

(i) If polar solvents are concerned, either protic (e.g. alcohols) or aprotic (e.g. DMF, $CH_{٣}CN$, DMSO etc.), the main interaction may occur between MW and polar molecules of the solvent and energy transfer take place from the solvent molecules to the reaction mixtures and the reactants. It would then be expected that any specific MW effects on the reactants would be masked by solvent absorption of the field. The reaction rates should therefore be nearly the same as those under conventional heating (Δ).

(ii) More interesting is the use of non-polar solvents (e.g. xylene, toluene, carbon tetrachloride) as they are transparent to microwave and only weakly absorb microwaves. They can therefore allow specific absorption by the reactants. If these reactants are polar, energy transfer occurs from the reactants to the solvent and the results may be different under MW and Δ.

(iii) ***Loupy A. et al., (١٩٩٨)*** described that microwave effects are most likely to be observed in solvent-free reactions. In addition to the preparative interest of these methods in terms of use, separation, economical, safe and clean procedures, absorption of microwave radiation should now be limited only to the reactive species. The possible specific effects will therefore be optimal since they are not moderated or impeded by solvents. They can be accomplished according to the following three methods:
(a) Reactions between the neat reagents in quasi-equivalent amounts, requiring preferably at least one liquid phase in heterogeneous media and leading to interfacial reactions as described by ***Toda F.*** and ***Tanaka K., (٢٠٠٠)***.

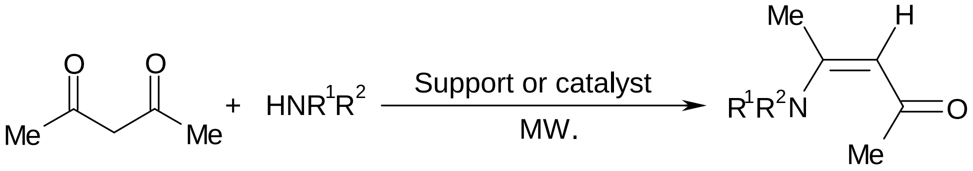
(b) ***Deshoyes S. et al.,(١٩٩٩)*** described the anionic reactions using the solid-liquid phase transfer catalysis (PTC) conditions, where the liquid electrophile is used as both reactant and organic phase in presence of a catalytic amount of tetraalkylammonium salts as the transfer agent.

(c) Reactions using impregnated reagents on solid miniral supports (aluminas, silicas, clays) in dry media as discribed by ***Bram G. et al, (١٩٩٢)***. Some apparent specific effects could however arise from the supports. The mineral supports are generally poor heat conductors whereas they behave as efficient absorbants of microwave energy with consequently more homogeneity in temperature.

Some Microwave Synthetic Reactions

Reactions of aldehydes and ketones with amines

Benno R. et al., (١٩٩٣) described the reaction between β-diketones such as acetyl acetone with a variety of amines over K-١٠ clay or silica under microwave irradiation in open vessel to give within a few minutes the corresponding enaminoketones (Ia-f) in good yields.

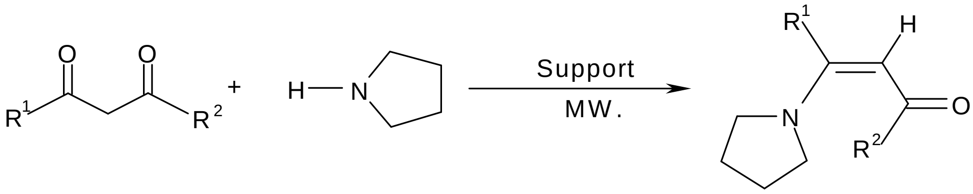


(Ia-f)

I	$R^{١}$	$R^{٢}$
a	H	Bu
b	H	Ph
c	$-(CH_{٢})_{٤}-$	

d	$-(CH_{٢})_{٥}-$	
e	Bu	Bu
f	Bu	Me

In the same way, they checked the reactivity of various dicarbonyl compounds (IIa-c) with pyrrolidine.

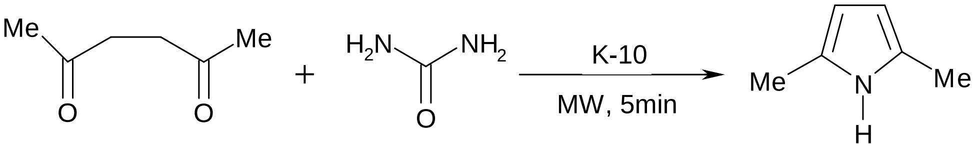


(IIa-c)

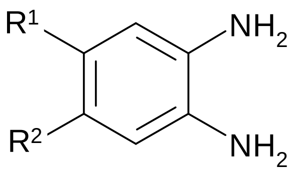
(IIIa-c)

III	R^{١}	R^{٢}
a	Me	Ph
b	Ph	Ph
c	Me	OMe

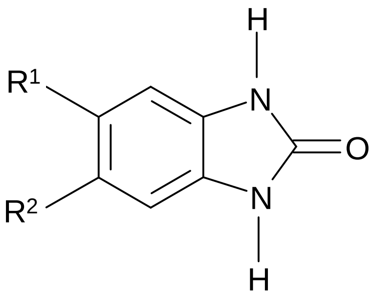
Ruault P. et al., (١٩٩٤) described the synthesis of ٢،٥-dimethylpyrrole by the reaction of urea and acetonylacetone adsorbed over montmorillonite K-١٠ in a domestic microwave oven.



Mohammad S. K. et al. (*١٩٩٦*) reported an efficient synthesis of benzimidazolin-٢-ones (Va-c), N-(α-methylvinyl)-benzimidazolin-٢-ones (VIa and VIb), ١،٥-benzodiazepin-٢-ones (VIIa and VIIb) and benzoxazolin-٢-one (VIII) from *o*-substit- uted anilines (IVa-c) and urea or a β-ketoester under microwave irradiation. This method of condensation under microwave irra- diation provides products of high purity with simple work up.



IVa; $R^1 = R^2 = H$
IVb; $R^1 = CH_3$, $R^2 = H$
IVc; $R^1 = R^2 = CH_3$



Va; $R^1 = R^2 = H$
Vb; $R^1 = CH_3$, $R^2 = H$
Vc; $R^1 = R^2 = CH_3$