Michael Reaction in the Solid State under Microwave Irradiations

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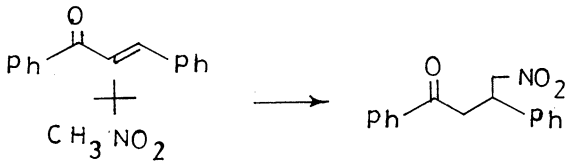
The Michael reaction of α,β-ethylenic ketones with nitroalkane, diethylmalonate, acetonitrile and acetylacetone in presence of alumina and without any solvent, under microwave irradiations proceeded very efficiently and furnished excellent yields of adducts.

The use of microwave energy to activate organic reactions has been taking a new dimension very recently.[1,2] It has been used for a great variety of organic reactions as esterification, etherification, oxidation, hydrolysis, Diels-Alder (4+2), Reformatsky, Knoevenagel and Bischler Napieralski reactions. However, to our knowledge there are no literature reports on the application of microwave energy to Michael reactions. Synthesis of derivatives which normally require long reflux periods can be achieved conveniently and very rapidly in microwave oven.[3] Herein, in this letter we report the first example of Michael addition of nitroalkane, diethylmalonate, acetonitrile and acetylacetone to ethylenic ketones in presence of alumina under microwave irradiations. The reaction proceeds efficiently in excellent yields at ambient pressure within minutes time and in the absence of solvent.

In a typical procedure, nitromethane (1.2 mmol), alumina (1 g, basic activated at 200 °C) and benzalacetophenone (1.2 mmol) were mixed together without solvent in an Erlenmeyer flask and placed in a commercial microwave oven (operating at 2450 MHz frequency) and irradiated for 18 mins. The reaction mixture was allowed to reach room temperature and extracted with chloroform. Removal of solvent and the residue on purification by thin layer chromatography using chloroform:petroleum ether (60-80), 3:2 as eluent gave the corresponding Michael adduct (entry 1) in 90% yields, mp



98-99 °C (Lit. mp 98-99 °C) without the formation of any side products. As reported by Kloetzel[4] this reaction takes about 15 days in 43% yields only. Similarly other substrates were reacted and the corresponding adducts were isolated in 72-90% yields.

As shown in Table 1, several structurally varried donors including diethylmalonate, nitroethane, acetonitrile and acetylacetone underwent clean and remarkably fast Michael additions with a variety of acceptors like benzalacetophenone, benzalacetone and methyl vinyl ketone under this procedure. The dramatic improvement observed is with regard to reaction time and yields. Many reactions are complete within a period of 15 to 20 minutes time. Interestingly, it was found that presence of solvent slowered the reaction, the reasons for the efficiency of the process on the solid phase are not clear. The yields, in general, are very high except in the additions of acetonitrile to benzalacetone where the isolated yields are relatively low presumably due to the formation of a hard resin and decomposition of adduct during isolation process. All the additions were carried out with 1:1 donor-acceptor proportions, methyl vinyl ketone with nitroalkane produced a small amount of bis-adducts (to the extent of 10%) when one equivalent of acceptors were used although the mono adducts were easily separated by chromatography.

Table. Michael addition of various substrates to α,β-ethylenic ketones

Entry	Donor	Acceptor	Microwave conditions		Conventional conditions[a]	
			Time min	Yield[b] %	Time h	Yield %
1	nitromethane	benzalaceto-phenone	18	90	15 days	43[c]
2	nitromethane	benzalacetone	20	75	12 days	58[c]
3	diethyl malonate	benzalaceto-phenone	15	80	1	78[d]
4	diethyl malonate	benzalacetone	18	82	1	77[d]
5	acetonitrile	benzalacetone	25	60	1	35[d]
6	nitromethane	methyl vinyl ketone	18	75	18	60[e]
7	nitroethane	methyl vinyl ketone	15	72	48	60[e]
8	acetylacetone	methyl vinyl ketone	15	75	30	91[f]

[a]The reactions are carried out at 30 or 40 °C. [b]All the yields refer to isolated, chromatographically pure compounds. All the assigned structures have been confirmed by spectroscopic data. [c]Ref. 4. [d]Ref. 5. [e]Ref. 6. [f]Ref. 7.

In conclusion, this new method of carbon-carbon bond formation without any solvent under microwave irradiation offers significant improvements over the existing procedures and thus help facile entry into a host of Michael adducts of potentially high synthetic utility. Also this simple and easily reproducible technique affords various adducts in shorter reaction time, with excellent yields without involvement of toxic and expensive material and without the formation of any undesirable side products, than the classical homogeneous reaction in solvents.

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