An efficient, microwave assisted solvent-free synthesis of polarized enamines

Kaushik Chanda, Milan Ch. Dutta, E. Karim and J. N. Vishwakarma*

Organic Research Laboratory, Department of Chemistry, St. Anthony’s College, Shillong-793 001, India

E-mail: jnvishwakarma@rediffmail.com

Reactions of acetophenones (1a-e), phenylacetonitriles (1f-h) and nitromethane (1i) with dimethylformamide-dimethylacetal were carried out in domestic microwave oven to give 3-dimethylamino-1-arylprop-2-en-1-ones (2a-c), 3-dimethylamino-1-arylacrylonitriles (2f-h) and 2-dimethylamino-1-nitroethene (2i), respectively, in very good to excellent yields. This methodology represents an eco-friendly green approach to these valuable synthons and has the advantage of involving shorter reaction times, solvent-less conditions and higher yields.

Microwave assisted organic reactions have blossomed into an important tool with a variety of applications, particularly after the development of Microwave-induced Organic Reaction Enhancement (MORE) chemistry techniques. These techniques require open vessels with little or no solvents and are free of the risk of explosion. MORE chemistry reactions are extremely faster, cleaner than conventional reactions and lead to higher atom economy (less chemical waste). Because of short time requirement, ease of workability and eco-friendliness, microwaves provide an alternative to environmentally unacceptable procedures using toxic and expensive reagents.

In connection with our ongoing programme on the development of newer synthetic strategies for heterocyclic compounds, we required some formylated active methylene compounds of type 2 (Scheme 1). Our literature survey at this stage revealed that few formylated active methylene compounds are known but their preparations involve thermal conditions, longer reaction time, toxic solvents and poor yields.

Prompted by the above, we took up the formylation of some active methylene compounds using dimethylformamide-dimethylacetal (DMF-DMA) under microwaves and the results of our studies are described herein.

Results and discussion

When a mixture of acetophenone (5 mmol) and DMF-DMA (10 mmol) was irradiated in a domestic microwave oven at 300 watt for 22 min, the reaction was found to be complete (monitored by TLC). Work-up of the reaction mixture gave the desired compound 2a in 70% yield. The structure of 2a was established with help of physical and spectral data (Table 1). The reaction followed similar trend with substituted acetophenones and the formylated ketones 2b-e were obtained in 73–92% overall yields. The 1H NMR spectra of 2a-e exhibited a doublet due to the vinylic proton at C-2 between $\delta$ 5.69-5.88 with $J$ 12.2-14.4 Hz while the proton at C-3 appears along-with the aromatic protons. The coupling constant values suggest that these molecules exist in E-form. The six protons of the two-methyl groups of NMe$_2$ group appear as a single singlet at $\delta$ 3.10 except in 2d and 2e in which they appear as two singlets at $\delta$ 3.08 and 3.28 and 2.96 and 3.09, respectively for three protons each. This exclusive observation in case of 2d could be attributed to the presence of nitro group in the para position of the benzene ring, which would decrease the electron density at the carbonyl carbon. This decreased electron density at the carbonyl carbon would facilitate delocalization of the lone pair of electrons of nitrogen atom of NMe$_2$ resulting in double bond character in C$_3$-N bond thus making the pro-
tons of the two methyl groups non-equivalent. The appearance of the two singlets due to the two methyl group protons of NMe₂ in 2e is probably due to the dominance of –I effect of the methoxy group over its +R effect.

The methodology could successfully be applied for the synthesis of formylated acetonitriles and compounds 2f-h could be obtained in 83–95% yields. In the ¹H NMR spectra of 2f-h, the vinylic proton appears between δ 6.86–7.09 ppm. This is due to the effect of the methoxy group over its +R effect.

The strategy proved to be equally useful for the construction of 2i (97% yield) derived from nitromethane. The ¹H NMR spectrum of 2i showed two doublets at 6.73 ppm (J 11.7 Hz) and 8.30 (J 11.7 Hz) ppm for the vinylic protons, which suggest that the alkene exists in E form. The six NMe₂ protons give two singlets at 2.90 and 3.23 ppm for three protons each.

In conclusion, we have demonstrated a practical application of microwave-assisted, solvent-free formylation of active methylene compounds in domestic microwave oven in very good to excellent yields.

### Experimental

M.ps. were recorded by open capillary method and are uncorrected. The IR spectra on KBr disc were recorded on a Perkin-Elmer 983 spectrometer. ¹H NMR (90 MHz) spectra were recorded on Varian EM-390 spectrometer. High resolution ¹H NMR (300 MHz) spectra were recorded on Bruker ACF-300 spectrometer. The chemical shifts (δ ppm) and the coupling constants (Hz) are reported and TMS is used as the internal standard. The FAB mass spectra were recorded on a Jeol SX 102/DA-6000 mass spectrometer/data system using Argon/Xenon (6 KV, 10 mA) as the FAB gas. Microwave irradiation was carried out in a Samsung domestic oven, CE2733G, operating at 2450 MHz.

### General procedure. Synthesis of 3-dimethylamino-1-arylprop-2-en-1-ones (2a-e):

A mixture of the ketone 1 (5 mmol) and DMF-DMA (10 mmol) was taken in a 100 ml conical flask and the content was irradiated in a domestic microwave oven for an appropriate length of time (Table 1). After the completion of the reaction (monitored by TLC), the excess of DMF-DMA and methanol formed were removed under reduced conditions.

### Table 1. Characterization data of 3-dimethylamino-1-arylprop-2-en-1-ones (2a-e), 3-dimethylamino-2-arylacrylonitriles (2f-h) and 2-dimethylamino-1-nitroethene (2i)

| Compd | Power (watt)/ Time (min) | M.p. (°C) | Yield % | Mol formula | IR (cm⁻¹) | MS, m/z (M⁺) | ¹H NMR, δ (ppm) |
|-------|-----------------|----------|---------|-------------|----------|-------------|----------------|
| 2a    | 300/22          | 88-90(88-90)⁵ | 70   | C₁₁H₁₃NO   | 1596, 1619 | – | 3.11 (6H, s, two CH₃), 5.87 (1H, d, J 12.2 Hz, -CH=CH-N), 7.42–8.42 (6H, m) |
| 2b    | 180/20          | 82–83     | 88    | C₁₁H₁₂ClNO | 1546, 1580 | – | 3.10 (6H, s, two CH₃), 5.83 (1H, d, J 12.2 Hz, -CH=CH-N), 7.20–7.80 (2H, m), 7.83–8.36 (3H, m) |
| 2c    | 300/13          | 80–81     | 92    | C₁₁H₁₄BrNO | 1541, 1574 | 254 | 3.06 (6H, s, two CH₃), 5.76 (1H, d, J 14.4 Hz, -CH=CH-N), 7.36–8.26 (5H, m) |
| 2d    | 100/8           | 144–146   | 90    | C₁₁H₁₂N₂O₃ | 1553, 1603 | – | 3.08 (3H, s, CH₃), 3.28 (3H, s, CH₃), 5.88 (1H, d, J 12.5 Hz, -CH=CH-N), 7.95–8.75 (5H, m) |
| 2e    | 300/15          | 95–97     | 73    | C₁₂H₁₃NO₂  | 1580, 1602 | 2638 | 2.96 (3H, s, CH₃), 3.09 (3H, s, CH₃), 3.85 (3H, s, OCH₃), 5.72, (1H, d, J 12.2 Hz, -CH=CH-N), 6.90 (2H, d), 7.79 (1H, d, J 12.2 Hz, -CH=CH-N), 7.90 (2H, d) |
| 2f    | 300/15          | 80–81     | 95    | C₁₁H₁₂N₂   | 1572, 1592 | – | 3.26 (6H, s, two CH₃), 7.09 (1H, s, C=CH), 7.20–7.73 (5H, m) |
| 2g    | 300/7           | 87–89     | 83    | C₁₁H₁₂Cl₂N₂ | 1561, 1590 | 206 | 3.29 (6H, s, two CH₃), 7.09 (1H, s, C=CH), 7.29–7.69 (4H, m) |
| 2h    | 300/22          | 85–86     | 83    | C₁₁H₁₄N₂O  | 1510, 1619 | 202 | 3.30 (6H, s, two CH₃), 3.86 (3H, s, OCH₃), 6.86 (1H, s, C=CH), 7.06 (2H, d), 7.43 (2H, d) |
| 2i    | 100/2           | 105–106(104)⁷ | 97    | C₁₂H₁₃NO₂  | 1538, 1634 | – | 2.90 (3H, s, CH₃), 3.23 (3H, s, CH₃), 6.73 (1H, d, J 11.7 Hz, N=CH=CH), 8.30 (1H, d, J 11.7 Hz, N=CH=CH) |

*¹H NMR spectrum was recorded on 300 MHz instrument.

**¹³C NMR (CDCl₃) of 2i: 38.1, 45.5, 112.3, 151.2.
pressure and the residue left was triturated with hexane to
give pure desired compounds 2a-e in 70-92% overall yields.
The products were crystallized from ethylacetate/hexane
mixture.

General procedure. Synthesis of 3-dimethylamino-2-
arylacrylonitriles (2f-h):

The reaction of phenylacetonitriles (1f-h) with DMF-
DMA was carried out as mentioned above producing pure
2f-h in 83–95% overall yields, which were crystallized from
methanol. An identical experimental procedure yielded 2-
dimethylamino-1-nitroethene (2i) in 97% yield, the crystal-
lization of which could be effected in methanol.

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