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GREEN SYNTHESIS OF 4-ACETYL-3-(4-SUBSTITUTED) PHENYL SYDNONES UNDER MICROWAVE IRRADIATION

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ABSTRACT

A rapid, efficient, clean and environmentally benign exclusive synthesis of a series of 4-acetyl-3-(4-substituted) phenyl sydnones has been developed using Friedel-Craft reaction with an excellent yields under microwaves irradiation. The results are compared with conventional method. Structural assignments are based on physical, analytical and spectroscopic data (IR, ^{1}H-NMR & ^{13}C-NMR).

Keywords: Green chemistry, Microwave irradiation, Sydnones, Friedel-Craft reaction.

INTRODUCTION

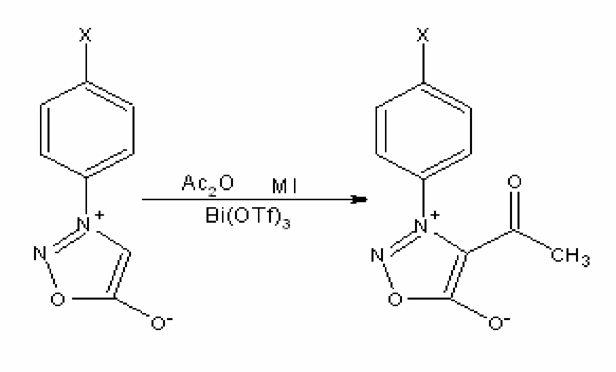
Green chemistry[1-4] is placed in the frontier areas of chemical research and has been focused for considerable recent research. Green chemistry revolves around the design, development and implementation of chemical processes and products that reduce or eliminate hazardous substances in a way that is feasible and economically viable. Microwave irradiation (MI)[5-6] has gained popularity in the past decade as a powerful tool for rapid and efficient synthesis of a variety of compounds because of selective absorption of microwave energy by polar molecules. The application of MI to provide enhanced reaction rate and improved product field in chemical synthesis has been extending to modern drug discovery in complex multi-step synthesis and it is proving quite successful in the formation of a variety of carbon-heteroatom bonds. Further, its unique capabilities allow its applications in transformations which are difficult or impossible to carry out by means of conventional methods.

Sydnones are a novel class of meso-ionic compounds with unique chemical and physical properties. A vast array of sydnone derivatives have been found to show varied biological properties[7], antioxidant activity [8], and liquid crystalline properties[9]. Furthermore, these have been used as precursors in 1, 3-dipolar additions[10], material chemistry[11], and in battery applications[12]. The extensive works on sydnone chemistry have been carried out by conventional methods with a few by green chemical methods[13,14]. However, the use of microwave technique in sydnone chemistry has not been explored commonly as expected. In continuation of our work[15] on sydnones the present paper deals with the use of green technique for the rapid, efficient, clean and environmentally benign exclusive synthesis of a series of **4-Acetyl-3-(4-substituted phenyl)sydnones** using Friedel-Craft reaction with excellent yields under microwaves irradiation.

EXPERIMENTAL

All starting reagents were purchased from commercial sources and used without further purification. Melting points were determined on the melting point apparatus and are uncorrected. Infrared spectra were recorded on Nicolet Impact-410 FTIR spectrophotometer. NMR spectra were recorded on a Brucker Varian-300 MHz NMR spectrometer in $CDCl_3$ with TMS as an internal standard. The chemical shifts are expressed in δ-scale downfield from TMS and proton signals are indicated as *s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet, *m* = multiplet. All compounds were analysed satisfactorily for C, H and N using Carl-Ebra 1106 elemental analyser in micro analytical laboratory.

General procedure for the synthesis of 4-substituted-3-phenylsydnones {Friedel-Crafts acylations}:
In a pressure tube 4-substituted phenyl sydnone ($6.167x10^{-4}$ mol), bismuth triflate ($1.542x10^{-4}$ mol, 25 mol %), and acetic anhydride ($2.467x10^{-4}$mol) were mixed and the reaction mixture was kept inside a microwave oven (BPL make-model, BMO: 700T) operating at 160 W for about fifteen minutes. After completion of the reaction the product was poured in water and then allowed to cool to room temperature. The reaction mixture was extracted with methylene chloride (3 x 10 mL), and the combined extracts were removed *in vacuo*. The resulting solid was recrystallized from hot ethanol. The progress of the reaction was monitored by TLC after every 3 minutes.



1. X: Cl, 93%
2. X: Br, 89%
3. X: CH_3, 87%
4. X: OCH_3, 83%

Scheme-1: Synthesis of 4-acetyl-3-(4-substitutedphenyl) sydnones

Synthesis of 4-acetyl-3-(4-chlorophenyl) sydnone (1):
Using the standard procedure, 4-chlorophenyl sydnone (0.1219 g), bismuth triflate (0.1012g)) and acetic anhydride (232μL) were kept in microwave oven for about 9 minutes. The resulting solid was recrystallized with hot ethanol (0.1287 g, 93%) m.p. 127 - 8 °C.
%C = 50.3144, %H = 2.9350, %N = 11.7400, % O = 20.1275 & %Cl = 14.8644
I.R. (KBr): 3099.06, 1784.80 (sydnone C=O), 1660.42 (acetyl C=O), 1493.60 (stretch N=N), 1434.78 (stretch C-X), 1405.86 (stretch C-N), 1321.97 (stretch C-O), 1089.59 (in-plane bending of ring C-H) , 837.92 (out-of-plane-bending of ring C-H) cm^{-1}
^{1}H-NMR ($CDCl_3$): 7.75 (d, 2 H aromatic), 7.3 (d, 2 H aromatic), 2.5 (s, 3H acetyl methyl) ppm.
^{13}C-NMR ($CDCl_3$): 184.30, 166.01 (C=O), 138.85, 133.21, 129.75, 126.26, 106.01 (sydnone C-4), 28.11 (methyl C) ppm.

Synthesis of 4-acetyl-3-(4-bromophenyl) sydnone (2):
Using the standard procedure, 4-bromophenyl sydnone (0.1438 g), bismuth triflate (0.1012 g) and acetic anhydride (232 μL) were kept in microwave oven for about 10 minutes. The resulting solid was recrystallized from hot ethanol (0.1442 g, 89%), m.p. 168 – 70 °C.
%C = 42.4028, %H = 2.4734, %N = 9.8939, % O = 16.9611 & %Br = 28.2685
I.R. (KBr): 3095.58, 1788.66 (sydnone C=O), 1662.34 (acetyl C=O), 1432.85, 832.13 cm^{-1}
^{1}H-NMR ($CDCl_3$): 7.75 (d, 2 H aromatic protons), 7.3 (d, 2 H aromatic protons), 2.5 (s, 3H acetyl methyl) ppm.
^{13}C-NMR ($CDCl_3$): 184.28, 166.00 (C=O), 133.73, 132.74, 127.03, 126.41, 105.98 (sydnone C-4), 28.08 (acetyl methyl C) ppm.

Synthesis of 4-acetyl-3-(4-tolyl) sydnone (3):

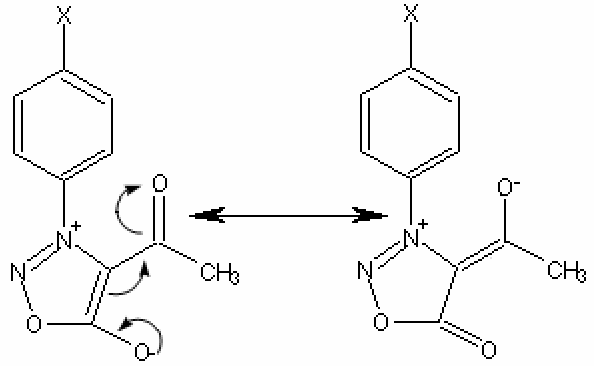
Using the standard procedure, 4-tolyl sydnone (0.1089 g), bismuth triflate (0.1012g) and acetic anhydride (232 μ L) were kept in microwave oven for about 12 minutes. The resulting solid was recrystallized from hot ethanol and afforded colorless crystals (0.1116 g, 87%), m.p. 113 – 4 ºC.
%C = 60.5505, %H = 4.5871, %N = 12.8440, & % O = 22.0183 %
I.R. (KBr): 2924.53, 1782.87 (sydnone C=O), 1667.17 (acetyl C=O), 1506.63, 1430.93, 1051.02, 824.42 cm^{-1}
^{1}H-NMR ($CDCl_3$): 7.37 (s, 4H aromatic), 2.53 (s, 3H acetyl methyl), 2.48 (s, 3H tolyl methyl) ppm.
^{13}C-NMR ($CDCl_3$): 184.33, 166.35 (C=O), 143.12, 132.45, 129.96, 124.58, 105.97 (sydnone C-4), 28.14 (methyl C), 21.49 (tolyl methyl C) ppm.

Synthesis of 4-acetyl-3-(4-methoxyphenyl) sydnone (4):

Using the standard procedure, 4-methoxyphenyl sydnone (0.1185 g), bismuth triflate (0.1012 g) and acetic anhydride (232 μL) were kept in microwave oven for about 12 minutes. The resulting solid was recrystallized from hot ethanol to afford colourless crystals (0.1134 g, 83 %), m.p. 96 – 98 °C.
%C = 56.4102, %H = 4.7735, %N = 11.9658, & % O = 27.3504 %
I.R. (KBr): 3079.78, 1788.66, 1776.12 (sydnone C=O), 1665.24 (acetyl C=O), 1606.42, 1511.92, 1438.64, 1408.75, 1259.29, 1175.40, 1051.02, 1024.02, 833.10, 593.00 cm^{-1}
^{1}H-NMR ($CDCl_3$): 7.65 (d, 2 H), 7.1 (d, 2 H), 3.9, (s, 3H), 2.6 (s, 3H) ppm.
^{13}C-NMR ($CDCl_3$): 184.260, 166.42 (C=O), 162.44, 127.45, 126.31 114.44, 105.90 (sydnone C-4), 55.78 (methoxy C), 28.16 ppm (acetyl methyl C).

RESULTS AND DISCUSSION

Friedel-Crafts acylation at the 4-position of the sydnone ring, it was of interest to find a method with milder conditions, preferably using a catalytic amount of reagent. With Green Chemistry becoming more important, an environmentally-friendly catalyst was desirable and metal triflate (particularly Bi), was previously reported as effective catalysts in the Friedel-Crafts reaction[14], appeared to fit the bill. Bi triflate is also considered "Green" reagents because it can be used in small amounts and can be reused due to their stability to aqueous work-up. The use of ^{13}C-NMR gave evidence of complexation of the bismuth to the carbonyl as evidenced by a downfield shift of the ^{13}C=O signal. It appears that a bridged structure is involved rather than the aroyl or alkanoyl triflate. The mechanistic rationale for this result is shown as:



Scheme-2: Mechanistic rationale of reaction

With successful acylation of 3-phenyl sydnone[15] with other alkyl anhydrides, it was of interest to explore the utility of acetic anhydride with sydnones having different para position. Using the general electron withdrawing and donating substituents in the procedure, their electron withdrawing and donating effects had an effect on the reaction time (**Figure-1**). It was exciting to see that the yields achieved were relatively high. Further, the relative effect of the electron withdrawing substituents, chlorine and bromine was observed when the two reactions were run simultaneously. The reaction with para-chlorophenyl sydnone was complete within 8 minutes (one and half hour in traditional methods) and parabromophenyl sydnone was completely reacted to acetyl-3-(4-bromophenyl) sydnone (**2**) after 10 minutes (which requires two hours in traditional methods). The tables-**1** and **-2** present the characterisation data of the compounds under investigation.

Table-1: Comparision of MW and Traditional methods

Compound	X	MW Method		Traditional Methods	
		Time (min.)	*yield (%)*	*Time (min.)*	*yield (%)*
1	Cl	08	93	90	84
2	Br	10	89	120	81
3	CH_3	12	87	120	81
4	OCH_3	12	83	120	78

Table-2: Melting points, Chemical for purification and % yield of products:

Compound	X	Observed M.P. (^{0}C)	Literature M.P. (^{0}C)	Chemical	Yield (%)
1	Cl	127-128	128-131	hot ethanol	93
2	Br	168-170	169-170	hot ethanol	89
3	CH_3	113-118	119-120	hot ethanol	89
4	OCH_3	96-98	97-98	hot ethanol	83

CONCLUSIONS

In the present protocol, we observed better yields in a shorter period compared to the reactions carried out in the aqueous medium. The compounds have been characterized by comparing their melting points and by the spectral and analytical data (provided in the experimental part).

In conclusion, we have described here an efficient and environmentally benign synthesis of 4-acyl-3-(4-substituted phenyl) sydnones under microwave irradiation using water and ethanol as solvents and Bi-triflate as green catalyst. Further, this method is simple, mild and ecofriendly from green chemistry point of view.

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