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A Rapid and Efficient Synthesis of Some Azide Molecules Under Microwave Irradiation

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ABSTRACT

A facile and greener synthesis of a series of azide derivatives was accomplished via one-pot reaction among different compounds and sodium azide in aqueous media by environmentally benign microwave induced technique**.** Microwave heating technique is simpler, greener and requires lesser reaction period. The reaction proceeded smoothly without interacting with the different functional groups such as alcohols, ether, ester, carboxylic acids etc.

Keywords: greener synthesis, microwaves, one pot, environmentally benign.

1. INTRODUCTION

In recent years, microwaves heating methodology has emerged as indispensable tool[1] in organic synthesis and it has received widespread acceptance among chemists. The implementation of microwave technology in chemistry is the biggest advancement in the last decade as by employing this technique it is generally possible to prepare organic compounds very fast[2,3], with high purity and better yields compared to other more conventional methods[4-6]. The chemical applications of microwave heating have been extended to almost all areas of chemistry and have consequently been the variety of excellent reviews. The current work has been motivated by the various advantages of this emerging technology[7].

The chemistry of azides has attracted the attention of chemists since the discovery of phenyl azide by Griess[8] over 142 years ago. However, after other important contributions, especially by Curtius and Bertho, interest waned until about 1950, when reviewed by Smith (acil azide)[9] and Boyler (aryl and alkyl azides)[10] stimulated further work. In more recent

times, completely new perspectives have been developed for their use in heterocyclic synthesis, combinatorial chemistry and peptide chemistry. Organic azides have assumed an important position at the interface between chemistry, biology, medicine, and material sciences. Interestingly numerous syntheses of these energy-rich molecules have been developed. The terminal nitrogen is mildly nucleophilic. Azides easily extrude diatomic nitrogen, a tendency that is exploited in many reactions such as the Staudinger Ligation or the Curtius rearrangement or for example in the synthesis of γ-imino-β-enamino esters[11]. Of topical interest, azidonucleosides (viz., AZT (3'- azido-3'–deoxythymidine) and CS- 85), have received international attention for the treatment of AIDS (acquired immune deficiency syndrome) and Arc (AIDS-related complex) [12-14]. HIV protease is responsible for the final stages of virus mutation and thus its inhibitors[15] are useful drugs for the treatment of AIDS. Azides react smoothly with triaryl phosphanes to form iminophosphoranes[16]. This imination reaction proceeds under mild conditions, almost quantitatively and without noticeable formation of any side products and these could be hydrolyzed to get primary amine, proceeds efficiently in aqueous environment and exhibit relatively low reactivity with chemical functionality in bio molecules (nucleic acids, proteins and metabolites) and have consequently been termed bioorthogonal[17]. ides are of a certain interest for soil disinfestating purposes[18]. Azides can be used as leading reagents to avoid different disadvantages, Diphenyl Phosphorazidate[19,20] has been used for diazo transfer[21] and a peptide coupling agent for the synthesis of cytotoxic cyclic peptides[22,23] and a straight chain peptide precursor to an indole alkaloid[24] where as *P-Tosyl* Azide is a shock-sensitive reagent[25].

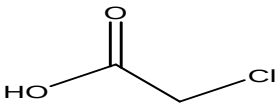
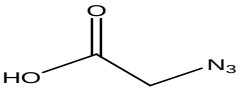
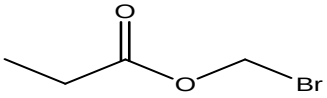
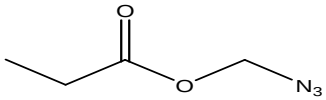
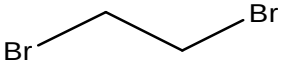
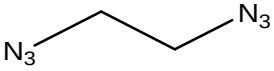
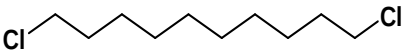
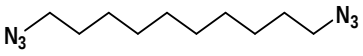
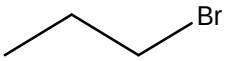
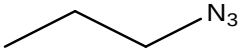
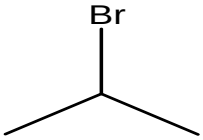
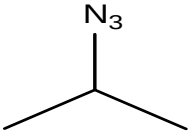
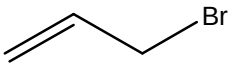
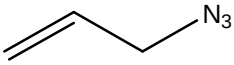
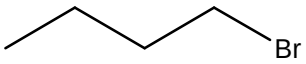
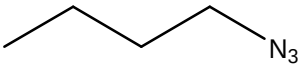
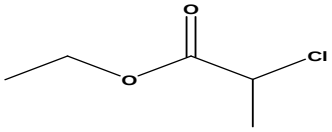
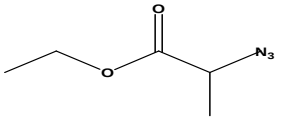
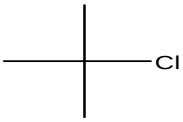
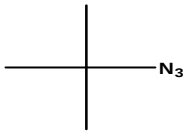
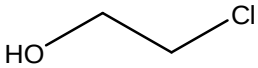
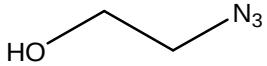
Quite evidently, syntheses of novel azide molecules require more attention for the easier performance of preparation of variety of compounds due to versatility of modern azide chemistry. In this publication the primary aim of our research was concerned on achieving reasonable yields of the synthesized heterocyclic products which might have biological and pharmaceutical prospective, using greener synthetic methodology. This work is inspired by Yuhang Ju et al.[26] and this publication is an good extension to their work. The aim of this text is to explore the numerous works which has been carried out in microwave induced chemistry.

2. RESULTS AND DISCUSSIONS

Following the microwave heating technique, different azide derivatives were synthesized. This rapid and efficient microwave promoted synthesis of various azides involved halides and sodium azides and it is very interesting that during the course of reactions a variety of active functional groups such as alcohols, ether, ester, carboxylic acids etc. have been tolerated.

All the reactions were carried out using 1 mmol of halides and 1.3 mmol of sodium azide in an aqueous medium for 27-30 minutes in a microwave oven in bursts of 30-45 seconds. The reaction mixture was cooled and suspended in water and filtered. The solid was washed with water to afford

the azide derivatives. These compounds were recrystallized from water. The reaction details of precursor halide and the target compound is given as under.

Compound No.	Starting Halide	Final Product
1.		
2.		
3.		
4.		
5.		
6.		
7.		
8.		
9.		
10.		
11.		

3. EXPERIMENTAL

Melting points were taken in an electrically heated instrument and are uncorrected. Compounds were routinely checked for their purity on silica gel TLC

plates and the spots were visualized by iodine vapors. PMR spectra were recorded on Buker DRX 300 MHz FT NMR spectrometer using TMS as internal standard and chemical shift values are expressed in δ units. Mass spectra were run on Jeol SX-102 spectrometer. The reactions were performed for 27-30 minutes in a microwave oven.

3.1 Synthesis of 2-azidoacetic acid (1)

For the synthesis of 2-azidoacetic acid the mixture of 2-chloroacetic acid (0.094 g) and sodium azide (0.072 g) was irradiated for 30 minutes by the general method as described above. Yield: 86%, m.p. 158 ^{0}C, PMR (DMSOd_6): 2.3 (s, 2H, C$\underline{H}_2$), MS (m/e): 101 (M^+), 60 ($C_2H_4O_2$), 57 (CH_3N_3), 46 (CH_2O_2), Anal Cal. C, 23.77; H, 2.99; N, 41.58 Found C, 23.75; H, 2.93; N, 41.60.

3.2. Synthesis of azidomethyl propionate (2)

For the synthesis of azidomethyl propionate the mixture of bromomethyl propionate (0.166 g) and sodium azide (0.072 g) was irradiated for 30 minutes by the general method as described above. Yield: 61%, m.p.191 ^{0}C, PMR (DMSOd_6): 4.0 (s, 2H, C$\underline{H}_2$), 2.2 (q, 2H, C$\underline{H}_2$), 1.4 (t, 3H, C$\underline{H}_3$), MS (m/e): 129 (M^+), 101 ($C_2H_3N_3O_2$), 88 ($C_4H_8O_2$) 60 ($C_2H_4O_2$), 29 (C_2H_5),. Anal Cal. C, 37.21; H, 5.46; N, 32.54 Found C, 37.22 H, 5.45 N, 32.55.

3.3. Synthesis of 1, 2-diazidoethane (3)

For the synthesis of 1, 2-diazidoethane the mixture of 1,2-dibromoethane (0.187 g) and sodium azide (0.072 g) was irradiated for 30 minutes. Yield: 83% m.p. 198 ^{0}C, PMR (DMSOd_6): 1.4 (s, 4H, C$\underline{H}_2$), MS (m/e): 112 (M^+), 71 ($C_2H_5N_3$), 30 (C_2H_6), Anal Cal. C, 21.43; H, 3.60; N, 74.97 Found C, 21.42 H, 3.58 N, 74.96.

3.4. Synthesis of 1,10-diazidodecane (4)

For the synthesis 1,10-diazidodecane the mixture of 1,10-dichlorodecane (0.210 g) and sodium azide (0.072 g) was irradiated for 30 minutes by the general method as described above. Yield: 87% m.p. 208 ^{0}C, PMR (DMSOd_6): 1.2 (s, 12H, C$\underline{H}_2$), MS (m/e): 224 (M^+), 169 ($C_9H_{19}N_3$), 128 (C_9H_{20}), 86 (C_6H_{14}), 44 (C_3H_8), Anal Cal C, 53.55; H, 8.99; N, 37.47 Found C, 53.56; H, 8.97; N, 37.45.

3.5. Synthesis of 1-azidopropane (5)

For the synthesis of 1-azidopropane the mixture of 1-bromopropane (0.122 g) and sodium azide (0.072 g) was irradiated for 29 minutes by the general method as described above. Yield: 77% m.p. 206 ^{0}C, PMR (DMSOd_6): 0.9 (t, 3H, C$\underline{H}_3$), 1.3-1.4 (m, 4H, CH_2), MS (m/e): 85 (M^+), 71 ($C_2H_5N_3$), 44 (C_3H_8), Anal Cal C, 42.34; H, 8.29; N, 49.37 Found C, 42.32, H, 8.27 N, 49.33.

3.6. Synthesis of 2-azidopropane (6)

For the synthesis of 2-azidopropane the mixture of 2-bromopropane (0.122 g) and sodium azide (0.072 g) was irradiated for 30 minutes by the general method as described above. Yield: 73% mp. 200 ^{0}C, PMR (DMSOd_6): 1.8 (m, 1H, C$\underline{H}$), 0.9 (d, 4H, C$\underline{H}_2$), MS (m/e): 85 (M^+), 71 ($C_2H_5N_3$), 44 (C_3H_8). Anal Cal C, 42.34; H, 8.29; N, 49.37 Found C, 42.33, H, 8.27, N, 49.35.

3.7. Synthesis of 3-azidoprop-1-ene (7)

For the synthesis of 3-azidoprop-1-ene the mixture of 3-bromoprop-1-ene (0.120 g) and sodium azide (0.072 g) was irradiated for 30 minutes by the general method as described above. Yield: 82% m.p. 205 ^{0}C, PMR ($DMSOd_6$): 5.7 (s, H, C<u>H</u>), 4.9-5.0 (d, 2H, C<u>H_2</u>), 2.0 (bs, 2H, C<u>H_2</u>), MS (m/e): 83 (M^+), 57 (CH_3N_3), 42 (C_3H_6), 28 (C_2H_4). Anal Cal C, 43.36; H, 6.07; N, 50.57 Found C, 41.34; H, 6.05; N, 50.54.

3.8. Synthesis of 1-azidobutane (8)

For the synthesis of 1-azidobutane the mixture of 1-bromobutane (0.135 g) and sodium azide (0.072 g) was irradiated for 30 minutes by the general method as described above. Yield: 80%, m.p. 204 ^{0}C, PMR ($DMSOd_6$): 1.3-1.3 (s, 6H, C<u>H_2</u>), 0.9 (t, 3H, C<u>H_3</u>), MS (m/e): 99 (M^+), 71 ($C_2H_5N_3$), 58 (C_4H_{10}), 57 (CH_3N_3), 44 (C_3H_8), 30 (C_2H_6). Anal Cal C, 48.46; H, 9.15; N, 42.39 Found C, 48.44; H, 9.13; N, 42.36.

3.9. Synthesis of ethyl-2-azidopropanoate (9)

For the synthesis ethyl-2-azidopropanoate the mixture of ethyl-2-chloropropionatethe (0.136 g) and sodium azide (0.072 g) was irradiated for 30 minutes by the general method as described above. Yield: 89%, m.p. 210 ^{0}C, PMR ($DMSOd_6$): 4.1 (q, 2H, CH_3C<u>H_2</u>), 2.5 (q, 1H, C<u>H</u>), 1.3 (t, 3H, C<u>H_3</u>), 1.1 (d, 3H, C<u>H_3</u>), MS (m/e): 143 (M^+), 129 ($C_4H_7N_3O_2$), 71 ($C_2H_5N_3$), 46 (CH_2O_2), 30 (C_2H_6), Anal Cal. C, 50.07; H, 9.68; N, 22.85 Found C, 49.02; H, 9.61; N, 22.76.

3.10. Synthesis of 2-azido-2-methylpropane (10)

For the synthesis of 2-azido-2-methylpropane the mixture of t-butylchloride (0.092 g) and sodium azide (0.072 g) was irradiated for 30 minutes by the general method as described above. Yield: 86%, m. p. 189 ^{0}C, PMR ($DMSOd_6$): 1.0 (s, 9H, CH_3), MS (m/e): 99 (M^+), 85 ($C_3H_7N_3$), 58 (C_4H_{10}), Anal Cal C, 48.46; H, 9.15; N, 42.39 Found C, 48.47; H, 9.13; N, 42.37.

3.11. Synthesis of 2-azidoethanol (11)

For the synthesis of 2-azidoethanol the mixture of 2-chloroethanol (0.080 g) and sodium azide (0.072 g) was irradiated for 28 minutes by the general method as described above. Yield: 84% m.p. 190 ^{0}C, PMR ($DMSOd_6$): 3.6 (t, 2H, CH_2), 1.5 (t, 2H, CH_2), MS (m/e): 87 (M^+), 71 ($C_2H_5N_3$), 46 (C_2H_6O), 30 (C_2H_6), Anal Cal C, 27.59; H, 5.79; N, 48.25 Found C, 27.56; H, 5.77; N, 48.24.

4. CONCLUSIONS

Microwave irradiation technique has been proved to be the environmentally benign and most efficient synthetic methodology. The synthesis of azide molecules could easily be carried out in a simpler and easier way by the microwave heating. The different functional groups were purely intact during the core synthesis. This greener technical method can be widely accepted, and it provides better result in shorter time than other conventional methods.

5. ACKNOWLEDGEMENTS

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