Microwave Induced Synthesis of Hydrazones and Wolff-Kishner Reduction of Carbonyl Compounds

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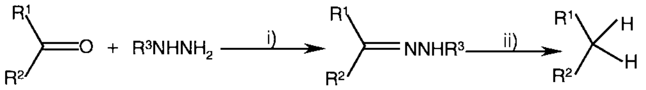
Abstract: Carbonyl compounds **1** are converted to hydrazones **3** and then to hydrocarbons **4** by Wolff-Kishner reductions under microwave irradiations within 25-30 mins in excellent yields.

Key words: Wolff-Kishner reductions, carbonyl compounds, microwave irradiation, hydrazones and solid state reactions

The deoxygenation of aldehydes and ketones to methyl or methylene derivatives, developed by Wolff and Kishner[1] is one of the key functional group interconversions in the synthesis of complex organic molecules.[2] The original protocols introduced involved the addition of preformed hydrazone directly to hot potassium hydroxide with or without[3] added crushed platinized porous plate or palladium/barium sulfate[4] at atmospheric pressure or boiling the hydrazone with sodium ethoxide in a sealed tube at 160-200°C. Following these pioneering investigations, other reduction systems, particularly catechol borane[5] (hazardous and expensive) have been introduced to effect reductions. Other methods including catalytic hydrogenation,[6] reductions using Raney nickel[7] and trichlorosilane-trialkylamine[8] and metal hydride reductions[9] have been applied more specifically to aryl aldehydes and ketones. But most of these methods have some disadvantages in relation to their general applicability, selectivity, operational inconvenience or toxicity. Currently the use of microwave energy to accelerate organic reactions has been taken to a new dimension and is a matter of increasing interest and offers several advantages.[10] We wish to report here the application of microwave energy[11] for the synthesis of hydrazone **3** and its subsequent conversion to hydrocarbons **4** via one of the major reaction of organic chemistry i.e Wolff-Kishner reaction under microwave irradiations. The reaction proceeds efficiently in excellent yields at ambient pressure within minutes and in the absence of solvent.



i) microwave, ii) KOH, microwave

Table Characteristics of Hydrazones **3** and Hydrocarbons **4**

Product	R^1	R^2	Reaction time (min.)	Reaction time(lit)	Yield (%)	Yield (%)(lit)
3a	Ph	Ph	16	24h	95	95[14a]
3b	4-$MeOC_6H_4$	4^1-$MeOC_6H_4$	10	24h	97	95[14a]
3c	4-$MeOC_6H_4$	Me	12	24h	92	88[14a]
3d	Ph	Me	10	24h	96	97[13]
4a	Ph	Ph	30	4h	95	85[14b]
4b	Ph	Me	25	5h	75	94[14b]
4c	Ph	H	25	4h	75	85[14b]
4d	4-$MeOC_6H_4$	Me	30	6h	85	92[14b]
4e	4-$MeOC_6H_4$	4^1-$MeOC_6H_4$	30	2h	90	92[14c]
4f	4-MeC_6H_4	4^1-MeC_6H_4	28	2h	90	89[14c]
4g	4-MeOOC-C_6H_4	Ph	30	25h	75	40[14b]
4h	2-ClC_6H_4	2'-ClC_6H_4	25	6h	80	91[14b]

[a] All the compounds obtained were characterised by infrared and ^1H NMR spectroscopy and finally by comparison with an authentic sample.

In a typical case, a mixture of benzophenone (1.82g, 10 mmol) and 80% hydrazine hydrate (1g, 20 mmol) in toluene (15ml) was taken in an Erlenmeyer flask and placed in a commercial microwave oven operating at 2450 MHz frequency. After irradiation of the mixture for 20 mins., (monitored by tlc) it was cooled to room temperature, extracted with chloroform and dried over anhydrous Na_2SO_4. Removal of solvent gave the benzophenone hydrazone in 95% yield. Similarly other hydrazones **3b-d** were prepared. These hydrazones were obtained much faster compared to literature methods in excellent yields. For the Wolff-Kishner reductions, a mixture of hydrazone **3a** (5 mmol) and KOH (2g) were taken in an Erlenmeyer flask and placed in a microwave oven. After irradiation for 30 mins. and usual work-up gave the corresponding diphenylmethane in 95% yield. Similarly other hydrazones were reduced to hydrocarbons and their characteristics are recorded in the table. The conditions do not affect methoxyl, methyl, chloro and carbomethoxy groups which have been reported[12] to be problemsome on occasion. Other conditions for the reaction were tried, but were less effective. Thus with dimethylsulfoxide as solvent under microwave irradiations diphenylmethane was formed in 30% yield after 50 mins of irradiations. When benzophenone hydrazone was prepared in situ from benzophenone and hydrazine, and re-

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acted under microwave a mixture of benzophenone azine and diphenylmethane was isolated. All the compounds obtained were characterised by infrared and ^{1}H NMR spectroscopy and finally by comparison with an authentic sample.

In conclusion, this new method of Wolff-Kishner reduction under microwave irradiation offers significant improvements over the existing procedures[13] and thus help facile entry into a variety of hydrocarbons of potentially high synthetic utility. Also this simple and easily reproducible technique affords various hydrocarbons in shorter reaction time with excellent yields without involvement of toxic and expensive material and without the formation of any undesirable side products.

References and Notes

(1) Todd, D.; *Org. Reactions*, **1948,** *4*, 378.

(2) Huang-Minlon, *J. Am. Chem. Soc.*, **1946**, *68*, 2487.

(3) a) Cook, A. H.; Linstead, R. P.; *J. Chem. Soc.*, **1934,** 946; (b) Barrett, J. W.; Linstead, R. P.; *J. Chem. Soc.*, **1935**, 436;

(4) Linstead, R. P.; Meade, E. M.; *J. Chem. Soc.*, **1934,** 935.

(5) Kabalka, G.W.; Baker, J.D. Jr.; *J Org Chem.*, **1975**, *40*, 1834.

(6) Zelinski, N.D.; Packendorff, K.; Leder-Packendorff, L.; *Ber.*, **1937**, *67B*, 300; Letsinger, R.L.; Jamison, J.D.; *J. Am. Chem. Soc.*, **1961,** *83*, 193; Mulholland, T.P.C.; Ward, G.; *J. Chem. Soc.*, **1954**, 4676.

(7) Cook, P.L.; *J. Org. Chem.*, **1962,** *27*, 3873; Papa, D.; Schwenk, E.; Whitman, B.; *J. Org. Chem.*, **1942,** *7*, 587.

(8) Benkeser, R.A.; *Acc. Chem. Res.*, **1971**, *4*, 94; Benkeser, R.A.; Smith, W.E.; *J. Am. Chem. Soc.*, **1969,** *91*, 1556.

(9) Conover, L.M.; Tarbell, D.S.; *J. Am. Chem. Soc.*, **1950,** *92*, 3586; Brown, B.R.; White, A.M.S.; *J. Chem. Soc.*, **1957**,3755; Nystrom, R.F.; Berger, C.R.A.; *J. Am. Chem. Soc.*, **1958,** *80*, 2896.

(10) Majdoub, M.; Loupy, A.; Peter, A.; Roudesli, M.S.; *Tetrahedron*, **1996**, *52*, 617; Caddick, S.; *Tetrahedron*, **1995,** *51*, 10453.

(11) For a recent report on microwave induced Cannizzaro reaction see: Sharifi, A.; Mojtahedi, M.M.; Saidi, M.R.; *Tetrahedron Lett.*, **1999**, *40*, 1179.

(12) Combic, R.C.; Hayward, R.C.; Missen, A.W.; *Aust. J. Chem.*, **1974**, *27*, 2413; Santesson, J.; *Act. Chem. Scand.*, **1970,** *24*, 3373.

(13) For methods using Ni-Al alloy require long reflux time and often give mixture of products see: Papa, D.; Schwenk, E.; Whitman, B.; *J. Org. Chem.*, **1942,** *7*, 587; Kleiderer, E.C.; Kornfield, E.C.; *J. Org. Chem.*, **1948**, *13*, 455; Cook, D.L.; *J. Org. Chem.*, **1962,** *27*, 3873**;** Tyman, J.H.P.; *J. Appl. Chem.*, **1970**, *20A*, 179.

(14) (a) Szmant, H. H.; Mc Ginnis, C.; *J. Am. Chem. Soc.*, **1950**, *72*, 2890.; *Org. Synthesis.*, **1970,** *Vol. 50*, p-102.
(b) Grundon, M. F.; Henbest, H. B.; Scott, M. D.; *J. Chem. Soc.*, **1963**, 1855.(c) Nystrom, P. F.; Rainer, C.; Berger, A.; *J. Am. Chem. Soc.*, **1958**, *80*, 2896.

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