SHORT PAPER

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Microwave assisted reduction of Schiff bases by triethylammonium formate/formic acid system[†]

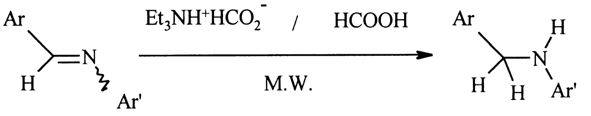
Firouz Matloubi Moghaddam*, Omid Khakshoor and Mohammad Ghaffarzadeh

Department of Chemistry , Sharif University of Technology , P.O.Box 11365-9516, Tehran, Iran

Aryl schiff bases were efficiently reduced to the corresponding secondry amines by triethylammonium formate/formic acid system under microwave irradiation in solvent–free condition.

Keyword: microwave irradiation, solvent-free condition, secondary amines, Schiff bases, reduction

The use of ammonium formates or formic acid as a reducing agent for functional groups in moderate reaction conditions is interesting and promising [1]. With these reagents carbonyl and amine-drivatives, in particular schiff bases are transformed into corresponding amines [2] . An azomethine reduction of this type is involved as the key step in the synthetically important reductive alkylation of ammonia and amines by aldehydes and ketones in the presence of formic acid [3]. The formic acid synthetic route to substituted amines shows some advantages even after the advent of complex hydride reagents. These types of reagents, formic acid or its drivatives, are cheap and the transformation process is rather straightforward. The disadvantages deal mainly with the poor yields due to the high sensitivity of the envisaged intermediate schiff bases or imines to hydrolysis. In the recent years, microwave dielectric heating technology with the combination of solvent-free condition have been used in many organic reactions, leading to shorter reaction times, higher yields, cleaner reaction products and environmentally benign condition comparing to the classical heating [4]. In the continuation of our increasing interest in microwave promoted organic reactions [5], we were interested in reductive amination of carbonyl compounds by formic acid and its derivatives in particular reduction of schiff bases (Scheme 1) which are the supposed intermediates.



Scheme 1

The literature survey shows, only one report on the reduction of schiff bases by concentrated formic acid [6]. Harsh reaction conditions (reflux at 90–120°C for 4–17 hr) have been used leading to products with low yields (27–60%). Our experiments showed that, benzalaniline as a model schiff base, produced resinous material under microwave irradiation with formic acid alone. However, when the acidity of the reaction mixture was decreased by adding triethylammonium formate, reduction occurred under microwave irradiation .

Triethylammoniumformate gave somewhat better yields than the ammonum formate, which has been recommended by Leuckart *et al.* [7] for the trasamination of carbonyl compounds. The reaction conditions were optimised by the examination of the different parameters such as time of irradiation, power of irradiation, the molar ratio of triethylammonium formate to formic acid and schiff base. After performing several experiments, the best molar ratio was found to be schiff base:triethylammonium formate:formic acid (1:6:3).In a typical procedure, schiff base (1 mmol) was mixed with reducing agent (1 ml) in a closed Teflon vessel (~20 ml) and subjected to microwave irradiation for about 6 minutes . After conventional work-up, good to excellent yield of secondary amines were obtained. Table 1 resume the results. While, the classical reaction, which to the best of our knowledge, has only been reported for benzalaniline at about 150°C in 2–4 hours refluxing time with triethylammonium formate only (97% yield)[8], our microwave methodology resulted in the same manner just in four minutes (Table 1, entry 1). The method has been used for the synthesis of several substituted N-benzylanilines and anilinomethylpyridines (see Table 1, entry 6,9).The physical and spectroscopic data of the products were compared to those of authentic samples [9]. Interestingly, the aromatic heterocyclic compounds such as quinoline could also be reduced to 1,2,3,4-tetrahydroquinoline in 81% yield in 10 min by this methodology (Table 1,entry 11). In conclusion, a simple, inexpensive and rapid method for the reduction of schiff bases to secondary amines via modified Leuckart reaction under microwave irradiation in solvent-free condition was developed.

Experimental

Schiff bases were prepared by modified known methods and purified by recrystallisation from 90% ethanol [10]. Their physical and melting points are identical with those reported in the literature [11]. 1H-NMR spectra were recorded on a Brucker FT-80 AC Spectrometer. IR Spectra were performed on a Mattson 1000 Spectrometer. Melting points were determined on a Buchi B-540 and are uncorrected.

General procedure for preparation of reducing reagent: To a stirred solution of triethylamine (13.8 ml) were added formic acid 98 %(5.8ml) dropwise for four hours. The reaction is exothermic. This mixture contains triethylammonium formate:formic acid (2:1).

General procedure for the reduction of schiff bases with reducing reagent under microwave irradiation: Schiff base (1 mmol) and reducing reagent (1ml) were mixed in a Teflon flask (~20 ml) and subjected to microwave irradiation [12] for given times (Table 1). After cooling, the reaction mixture was suspended in concentrated HCl solution (~120ml) and heated in such a way that the volume reduced to one third. Then carefully on cooling with ice the reaction mixture was neutralized with concentrated NaOH solution or potassium bicarbonate and extracted with diethylether (3×50 ml). The organic phase was dried on anhydrous Na_2SO_4. Evaporation of the solvent gave almost pure products. Further purification was carried out on column chromatography over silicagel and by eluting with a mixture of diethylether–petroleum ether.

Spectroscopic data: Amine **1**: IR(KBr)ν_{max}3415(N-H), 3023, 2923, 2850, 1607, 1515, 1445, 1330, 1275, 1184, 1115, 745, 692 cm^{-1}; ^{1}H-NMR (80 MHz, CDCl3) δ 4.1(1H,br s), 4.4(2H,s), 6.5–7.65(10H,m). Amine **2**: IR(KBr)ν_{max} 3423(N-H), 3025, 2961, 2853, 1600, 1500, 1445, 1330,1270, 1184, 1092, 1030, 815, 745, 700 cm^{-1}; ^{1}H-NMR (80 MHz, CDCl3) δ 3.9–4.1(1H,br s), 4.2(2H,s), 6.3–7.5(9H,m). Amine **3**: IR(KBr)ν_{max} 3415(N-H), 3023, 2915, 2850,

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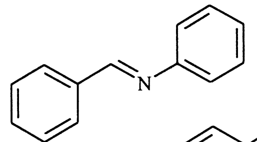
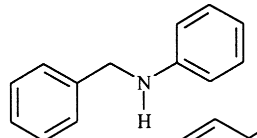
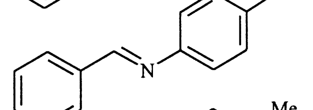
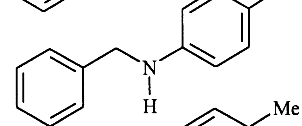
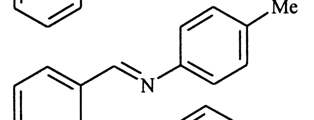
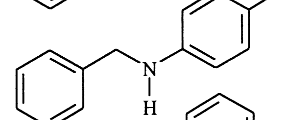
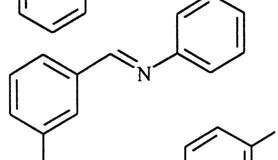
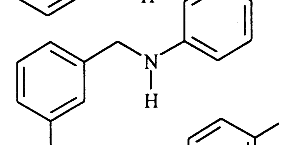
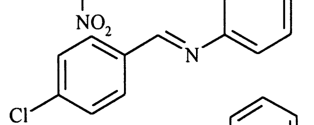
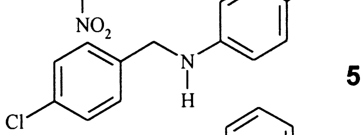
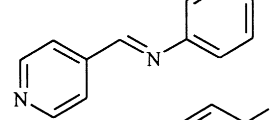
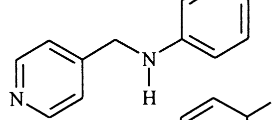
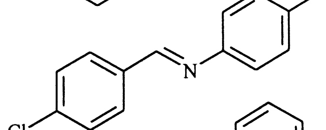
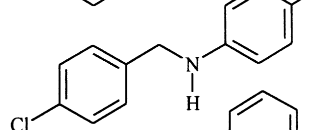
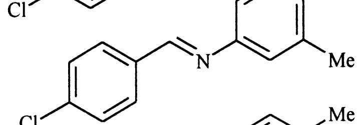
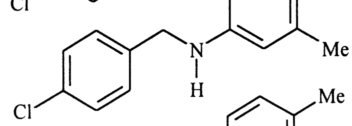
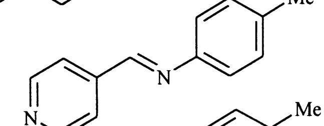
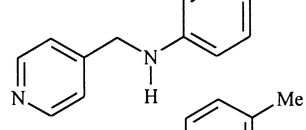
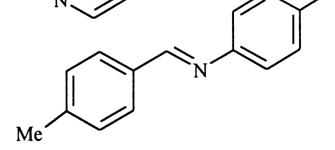
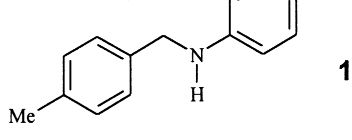
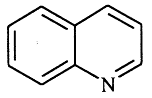
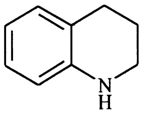
* To receive any correspondence. E-mail: Matloubi@sina.sharif.ac.ir

[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Microwave promoted reduction of schiff bases by triethylammonuim formate/formic acid system

Entry	Substrate	Producta		Yield/%a, (Time/min.)	m.p./°C (lit.–°C)
1			**1**	90 (4)	36.5–37.5 (37–38)^{9a}
2			**2**	74 (6)	45–46 (46–48)^{9a}
3			**3**	71 (5)	Liquid (19–20)^{9b}
4			**4**	65 (2.5)	83–84 (84–85)^{9c}
5			**5**	63 (5)	67–68.5 (69–70)^{9d}
6			**6**	69 (5)	100–101 (101–103)^{9e}
7			**7**	67 (6)	68.5–70 (70–71)^{9a}
8			**8**	72 (6)	34–36 (38)^{9f}
9			**9**	64 (6)	72–73 (74)^{9g}
10			**10**	68 (6)	55–56 (60–61)^{9f}
11^c			**11**	81 (10)	Liquid

^{a} All yields refer to isolated products. ^{b} All products were characterised by m.p., IR, ^{1}HNMR, and the physical data were similar to those reported in the literature. ^{c} 1.5 ml of reagent per 1 mmol of quinoline was required for reduction.

1623, 1523, 1453, 1307, 1261, 1130, 1030, 815, 745, 700 cm^{-1}; ^{1}H-NMR (80 MHz, CDCl3) δ 2.64(3H,s), 4.13(1H,s), 4.63(2H,s), 6.8–7.9(9H,m). Amine **4**: IR(KBr)ν_{max} 3407(N-H), 3025, 2923, 2850, 1607, 1530, 1455, 1353, 1340, 1275, 1076, 807, 750, 730, 692 cm^{-1}; ^{1}H-NMR (80 MHz, CDCl3) δ 4.35(1H,br s), 4.64(2H,s), 6.6–8.5(9H,m).Amine **5**: IR(KBr)ν_{max} 3400(N-H), 3025, 2938, 2855, 1515, 1481, 1415, 1253, 1240, 1154, 1092, 1038, 823, 745 cm^{-1}; ^{1}H-NMR (80 MHz, CDCl3) δ 2.1(1H,s), 3.7(3H,s), 4.2(2H,s), 6.5–6.9(4H,m), 7.2(4H,m). Amine **6**:IR(KBr)ν_{max} 3261(N-H), 3030, 2923, 2853, 1607, 1530, 1500, 1423, 1330, 1270, 1115, 1000, 815, 753, 700 cm^{-1}; ^{1}H-NMR (80 MHz, CDCl3) δ 3.6–4.6(1H,br s), 4.3(2H,s), 6.25–7.35(7H,m), 8.25-8.75(2H,m). Amine **7**: IR(KBr)ν_{max} 3400(N-H), 3030, 2925, 2850, 1600, 1500, 1315, 1084, 823 cm^{-1}; ^{1}H-NMR (80 MHz, CDCl3) δ 3.7–4.3(1H,br s), 4.2(2H,s), 6.25–7.5(8H,m). Amine **8**: IR(KBr)ν_{max} 3423(N-H), 3040, 2923, 2851, 1607, 1490, 1425, 1330, 1292, 1175, 1110, 1023, 815, 776, 700 cm^{-1}; ^{1}H-NMR (80 MHz,CDCl3) δ 2.3(3H,s), 3.85(1H,s), 4.25(2H,s), 6.3–7.4(8H,m). Amine **9**: IR(KBr)ν_{max} 3292(N-H), 3250, 3015, 2923, 2850, 1607, 1523,1415, 1310,1290, 1130, 1000, 815 cm^{-1}; ^{1}H-NMR (80 MHz, CDCl3) δ 2.35(3H,s), 3.6–4.4(1H,br s), 4.44(2H,s), 6.5–7.6(6H,m), 8.4-8.9(2H,m). Amine **10**: IR(KBr)ν_{max} 3380(N-H), 2915, 2853, 1615, 1523, 1461, 1307, 1250, 1130, 815 cm^{-1}; ^{1}H-NMR (80 MHz, CDCl3) δ 2.33(3H,s), 2.44(3H,s), 3–4(1H,br s), 4.36(2H,s), 6.5–7.6(8H,m). Amine **11**: IR(KBr)ν_{max} 3400(N-H), 3115, 2930, 2835, 1607, 1500, 1470, 1315, 1290, 1184, 1100, 753, 690 cm^{-1}; ^{1}H-NMR (80 MHz, CDCl3) δ 1.8-2.2(2H,m), 2.7–3.0(2H,t), 3.15–3.40(2H,t), 3.7(1H,s), 6.25–7.35(4H,m).

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References

1 S. Ram and R.E.Ehrenkaufer, *Synthesis* 1988, 91.

2 J. March, *Advanced Organic Chemistry* 4 ed, J.Wiley & Sons, New York, 1992, p 899-900; D. Barton; W.D. Ollis, *Comprehensive Organic Chemistry*, Pergamon Press, Oxford, 1979, Vol. 2, pp. 440-441.

3 O. Wallach, *Liebig's Ann.*1905, 343, 54.

4 R.S. Varma, In: *Microwaves:Theory and Application in Material Processing IV*; D.E. Clark; W.H. Sutton; D.A. Lewis Eds. Microwave-assisted reactions under solvent-free 'dry' conditions.American Ceramic Society, Ceramic Transactions, 1997; vol. 80, pp 357.

5 F. Matloubi M. Moghadda; M. Ghaffarzadeh and S.H. Abdi-Oskoui, *J. Chem. Res. (S)* 1999, (9), 575; F. Matloubi Moghaddam and R. Emami, *Synth. Commun.* 1997, **27**, 4073. F. Matloubi Moghaddam and M. Ghaffarzadeh, *Tetrahedron Lett.* 1996, **37**, 1855; F. Mattloubi Moghaddam, A. Sharifi and M.R. Saidi, *J. Chem. Res. (S)* 1996, 388; F. Matloubi Moghaddam and M.G. Dakamin, *Tetrahedron Lett.* 2000, **41**, 3479; F. Mattloubi Moghaddam, M. Ghaffarzadeh and M.G. Dakamin, *J. Chem. Res. (S)* 2000, 228.

6 R. Baltzly and O. Kauder, *J. Org. Chem.* 1951, **16**, 173.

7 R. Leuckart, *Ber.*,1885, 18, 2341; M.L. Moore, *Org. React.* 1949, **5**, 301-330. N.C. Deno, M.J. Peterson and G.S. Saines, *Chem.Rev.* 1960, **60**, 7-14; R. Carlson, T. Lejon, T. Lundstedt and E. Le Clouerec, *Acta. Chem. Scand.* 1993, **47**, 1046-1049.

8 E.R. Alexander and R.B. Wildman, *J. Am. Chem. Soc.* 1948, **70**, 1187.

9 (a) J.H. Billman and A.C. Diesing, *J. Org. Chem.* 1957, **22**, 1069. (b) A.V. Kirsunov and Ya.N. Ivashchenko, *Chem. Abstr.* 1953, **30**:1775; (c) Vogel's. *Textbook of Practical Organic Chemistry*, 4th edn., Longman Inc., New York, 1978, pp 672; (d) K. K. Kitzi, R. Goeschke and R. Pfister, *Chem. Abstr.* 1968, **69**: 106548z; (e) M. Hamana; K. Funakoshi, *Chem. Abstr.* 1962, **58**: 3385; (f) H.D. Law, *J. Chem. Soc.* 1912, **101**, 154; (g) S. Miyano; A.Uno; N. Abe, *Chem. Pharm. Bull.* 1967, **15**, 515.

10 R. Bianchini, C. Forte, G. Musumarra, C. Pinzino and C. Sergi, *Tetrahedron* 1997, **53** 6907.

11 (a) R.W. Layer, *Chem.Rev.* 1963, **63**, 489; (b) A. Roe and J.A. Montgomery, *J. Am. Chem. Soc.* 1953, **75**, 910; (c) Vogel's. *Textbook of Practical Organic Chemistry*, 4th edn., Longman Inc., New York, 1978, pp. 672; (d) R.F. Shuman and E.D. Amstutz, *Chem. Abstr.* 1965, **63**: 5596g also J.S. Dave and M.J.S. Dewar, *J. Chem. Soc.* 1955, 4305; (e) P.K. Kadaba, *J. Heterocycle. chemistry* 1975, 143; (f) H.D. Law, *J. Chem. Soc.* 1912, **101**, 154. (h) D. Vorlunder, R. Wilke, U. Haberlund, K. Thinius, H. Hempel and J. Fischer, *Chem. Abstr.* 1938, **32**: 4847.

12 The microwave oven used for this work was a Westinghouse (1300 W) at 2450 MHz which was modified to a focused monomode system in our laboratory.