Pergamon

Tetrahedron Letters 39 (1998) 8437–8440

TETRAHEDRON
LETTERS

Microwave-Accelerated Crossed Cannizzaro Reaction Using Barium Hydroxide Under Solvent-free Conditions

Rajender S. Varma*, Kannan P. Naicker and Per. J . Liesen

Department of Chemistry and Texas Research Institute for Environmental Studies (TRIES),
Sam Houston State University, Huntsville, Texas 77341-2117, U. S. A.
Fax: (409)-294-1585; E-mail: CHM_RSV@SHSU.EDU

Received 5 August 1998; accepted 8 September 1998

Abstract: A solventless and expeditious method for the preparation of alcohols is described from aldehydes using barium hydroxide, $Ba(OH)_2.8H_2O$, and paraformaldehyde. A comparison of this microwave-accelerated Cannizzaro reaction to the one under conventional heating mode is also reported.

The Cannizzaro reaction is the disproportionation of an aldehyde to an equimolar mixture of primary alcohol and carboxylic salt[1] and is restricted to aldehydes that lack the α-hydrogens and therefore can not undergo aldol condensation. Several mechanistic studies[2] have been made on this oxidation-reduction reaction which is usually carried out in a homogeneous and strongly basic solution. The relative importance of the Cannizzaro reaction in synthetic organic chemistry was lost after the discovery of lithium aluminum hydride, $LiAlH_4$, in 1946. Another limitation has been the lower yields of the desired product since it provides only 50 % of alcohol or 50% of the corresponding acid salt. The crossed Cannizzaro reaction,[2a] using a scavenger and inexpensive formaldehyde to produce alcohol in higher yields, however, had been a method of choice prior to the introduction of hydride reducing agents. This reaction is normally conducted in solution phase although we have observed the reaction on a variety of mineral oxide surfaces.[3] In continuation of our ongoing research program on solvent-free organic transformations,[4] we decided to explore Cannizzaro reaction in the solid state using microwaves[4] and compare the results with classical conditions. The exploration of this reaction with calcium hydroxide failed completely. Under the influence of a strong base such as sodium hydroxide, the reaction remained incomplete with concomitant formation of several unidentified products reminiscent of our earlier observations on basic alumina surface.[3] Interestingly, the reaction occurred readily on barium hydroxide, $Ba(OH)_2.8H_2O$, in a relatively short period of time. A recently described microwave-mediated intramolecular carbanilide cyclization to hydantoins with barium hydroxide,[5] prompts us to report our results on the utility of this reagent in a solventless crossed Cannizzaro reaction.

PII: S0040-4039(98)01922-4

Barium hydroxide has been used as a catalyst in a number of organic syntheses[6] including Wittig-Horner reaction,[7] in the synthesis of isooxazolines and pyrazolines[8] and the reaction of chalcones with hydroxylamine.[9] The Michael addition[10] and Claisen-Schmidt condensation[11] are some additional examples of reactions promoted by barium hydroxide. Herein, we report a facile reduction of aldehydes to alcohols using a formaldehyde equivalent, paraformaldehyde, under neat conditions in the absence of solvent. In a typical example, a mixture of benzaldehyde (1 mmol) and paraformaldehyde (2 mmol) is admixed with barium hydroxide octahydrate (2 mmol) and then irradiated in a microwave (100-110 °C) or alternatively heated in an oil bath (100-110 °C) (Eqn.).

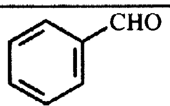
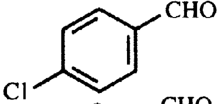
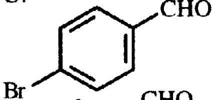
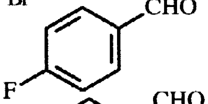
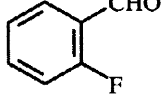
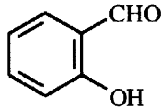
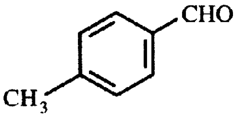
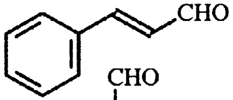
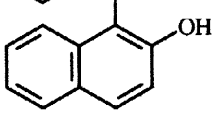
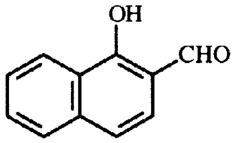
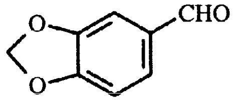
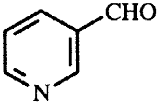
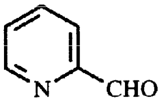
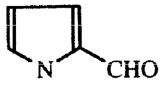
$$\mathrm{RCHO} + (\mathrm{CH_2O})_n \xrightarrow[\text{MW or in an oil bath}]{\mathrm{Ba(OH)_2 \cdot 8H_2O}} \underset{(80\text{-}99\%)}{\mathrm{RCH_2OH}} + \underset{(1\text{-}20\%)}{\mathrm{RCOOH}} \qquad \textbf{(Eqn.)}$$

The results are summarized in the Table. Benzaldehydes bearing an electron withdrawing substituent undergo reaction at a much faster rate as compared to benzaldehydes with electron releasing groups appended. Among the naphthaldehydes, the reaction is slower for 2-naphthaldehyde when compared to 1-naphthaldehyde. Similarly, the reaction rate is slower for 3-pyridinecarboxaldehyde in comparison to 2-pyridinecarboxaldehyde and the overall reaction is much slower in an oil bath when compared to microwave irradiation conditions.

General procedure for the conversion of aldehydes to alcohols:-- In a typical experiment, benzaldehyde (106 mg, 1 mmol) was added to the finely powdered paraformaldehyde (60 mg, 2 mmol). To this mixture, powdered barium hydroxide octahydrate (631 mg, 2 mmol) was added in a glass test tube and the reaction mixture was placed in an alumina bath (neutral alumina: 125g, mesh ~ 150, Aldrich; bath: 5.7 cm diameter) inside a household microwave oven and irradiated for the specified time at its full power of 900 Watts intermittently or heated in an oil bath at 100-110 °C (see Table). On completion of the reaction, as indicated by TLC (hexane:EtOAc, 4:1, v/v), the reaction mixture was neutralized with dilute HCl and the product extracted into ethyl acetate. The combined organic extracts were dried over anhydrous sodium sulfate and the solvent removed under reduced pressure. In all the cases (Table) the formation of the corresponding acids were determined by GC-MS analysis (Hewlett-Packard model 5890 gas chromatograph with a mass spectrometer). The pure benzyl alcohol (99 mg, 91%), however, is obtained by extracting the reaction mixture with ethyl acetate prior to neutralization and subsequent removal of the solvent under reduced pressure.

In conclusion, this solventless barium hydroxide promoted Cannizzaro reaction is a simple and facile method to produce alcohols in high yields. The operation simplicity, rapid reaction rates and high yield of pure alcohol formation makes this is a useful and attractive procedure.

Table: Product distribution in solvent-free crossed Cannizzaro reaction using barium hydroxide *via* microwave as well as classical conditions

Entry	Starting material	Reaction conditions		% Yield		Others
		MW (min.)	Oil bath (min.)	Alcohol	Acid	
1		0.5	10	99(98)	01(02)	00(00)
2		0.5	10	94(95)	05(04)	01(01)
3		0.5	15	83(85)	16(14)	01(01)
4		0.5	12	85(88)	14(11)	01(01)
5		0.25	10	80(90)	20(01)	00(00)
6		2.0	60	83(83)	13(11)	04(06)
7		2.0	37	80(85)	10(10)	10(05)
8		1.5	15	80(85)	19(10)	01(05)
9		1.0	180	85(86)	10(10)	05(04)
10		2.0	240	83(85)	09(09)	08(06)
11		1.5	40	82(80)	15(15)	03(05)
12		2.0	35	97(97)	03(03)	00(00)
13		1.0	20	97(98)	03(02)	00(00)
14		0.5	06	97(99)	03(01)	00(00)

[a] The relative amounts of product formation are determined by GC-MS analysis and the results in the parentheses refer to the corresponding yields obtained using oil bath; the products exhibited physical and spectral properties (NMR and IR spectra) in accord with the assigned structures.

ACKNOWLEDGMENT

We are grateful for financial support to the Texas Advanced Research Program (ARP) in chemistry (Grant # 003606-023) and Texas Research Institute for Environmental Studies (TRIES).

REFERENCES

1. (a) Cannizzaro, S. *Ann.* **1853,** *88,* 129; (b) Geissman, T. A. *Organic Reactions* **1944,** *II,* 94; (c) Nemtsov, M. S.; Trenke, K. M. *Zh. Obshch. Khim.* **1952,** *22,* 415; *Chem. Abstr.* **1952,** *46,* 8485i.
2. (a) Swain, C. G.; Powell, A. L.; Sheppard, W. A.; Morgan, C. R. *J. Am. Chem. Soc.* **1979,** *101,* 3576; (b) Chung, S. K. *J. Chem. Soc., Chem. Commun.* **1982,** 480; (c) Ashby, E. C.; Coleman III, D. T.; Gamasa, M. P. *Tetrahedron Lett.* **1983,** *24,* 851.
3. Varma, R. S.; Kabalka, G. W.; Evans, L. T.; Pagni, R. M. *Synth. Commun.* **1985,** *15,* 279.
4. (a) Varma, R. S. *"Microwave-Assisted Reactions under Solvent-Free 'Dry' Conditions"* in *Microwaves: Theory and Application in Material Processing IV* Clark, D.; Sutton, W.; Lewis, D., Eds., American Ceramic Society, Ceramic Transactions **1997,** *80,* pp 357-365. For cleavage-deprotection reactions see: (b) Varma, R. S.; Chatterjee, A. K.; Varma, M. *Tetrahedron Lett.* **1993,** *34,* 3207; (c) Varma, R. S.; Chatterjee, A. K.; Varma, M. *Tetrahedron Lett.* **1993,** *34,* 4603; (d) Varma, R. S.; Varma, M.; Chatterjee, A. K. *J. Chem. Soc., Perkin Trans. 1* **1993,** 999; (e) Varma, R. S.; Lamture, J. B.; Varma, M. *Tetrahedron Lett.* **1993,** *34,* 3029; (f) Varma, R. S.; Saini, R. K. *Tetrahedron Lett.* **1997,** *38,* 2623; (g) Varma, R. S.; Meshram, H. M. *Tetrahedron Lett.* **1997,** *38,* 5427; (h) Varma, R. S.; Meshram, H. M. *Tetrahedron Lett.* **1997,** *38,* 7973; (i) Varma, R. S.; Dahiya, R.; Saini, R. K. *Tetrahedron Lett.* **1997,** *38,* 8819; For condensation-cyclization reactions see: (j) Varma, R. S.; Dahiya, R.; Kumar, S. *Tetrahedron Lett.* **1997,** *38,* 2039; (k) Varma, R. S.; Dahiya, R. *Synlett* **1997,** 1245; (l) Varma, R. S.; Dahiya, R.; Kumar, S. *Tetrahedron Lett.* **1997,** *38,* 5131; (m) Varma, R. S.; Saini, R. K. *Synlett* **1997,** 857; For oxidation reactions see: (n) Varma, R. S.; Dahiya, R. *Tetrahedron Lett.* **1997,** *38,* 2043; (o) Varma, R. S.; Saini, R. K.; Meshram, H. M. *Tetrahedron Lett.* **1997,** *38,* 6525; (p) Varma, R. S.; Dahiya, R.; Saini, R. K. *Tetrahedron Lett.* **1997,** *38,* 7029; (q) Varma, R. S.; Saini, R. K.; Dahiya, R. *Tetrahedron Lett.* **1997,** *38,* 7823; (r) Varma, R. S.; Saini, R. K.; Dahiya, R.*J. Chem. Res. (S)* **1998,** 120; (s) Varma, R. S.; Dahiya, R. *Tetrahedron Lett.* **1998,** *39,* 1307; (t) Varma, R. S.; Dahiya, R.; Kumar, D. *Molecules Online* **1998,** *2,* 82; (u) Varma, R. S.; Saini, R. K. *Tetrahedron Lett.* **1998,** *39,* 1481; (v) Varma, R. S.; Kumar, D.; Dahiya, R. *J. Chem. Res. (S)* **1998,** 324; (w) Varma, R. S.; Naicker, K. P. *Molecules Online* **1998,** *2,* 94; (x) For reduction reactions see: (y) Varma, R. S.; Saini, R. K. *Tetrahedron Lett.* **1997,** *38,* 4337; (z) Varma, R. S.; Dahiya, R. *Tetrahedron* **1998,** *54,* 6293.
5. Gong, Y. D.; Sohn, H. Y.; Kurth, M. J. *J. Org. Chem.* **1998,** *63,* 4854.
6. (a) Barrios, J.; Rojas, R.; Alcanrara, A. R.; Sinisterra, J. V. *J. Catal.* **1988,** *112,* 528; (b) Sinisterra, J. V.; Marinas, J. M.; Riquelme, F.; Arias, M. S. *Tetrahedron* **1988,** *44,* 1431.
7. Sinisterra, J. V.; Fuentes, A.; Marinas, J. M. *J. Org. Chem.* **1987,** *52,* 3875.
8. Sinisterra, J. V. *React. Kinet. Catal. Lett.* **1986,** *30,* 93.
9. Sinisterra, J. V.; Marinas, J. M. *Bull. Soc. Chim. Belg.* **1987,** *96,* 293.
10. Iglesias, M.; Marinas, J. M.; Sinisterra, J. V. *Tetrahedron* **1987,** *43,* 2335.
11. Aguilera, A.; Alcantara, A. R.; Marinas, J. M.; Sinisterra, J. V. *Can. J. Chem.* **1987,** *65,* 1165.