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A simple and efficient method for solvent-free iodination of hydroxylated aromatic aldehydes and ketones using iodine and iodic acid by grinding method

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Abstract

Green, mild and efficient iodination of hydroxylated aromatic aldehydes and ketones using iodine and iodic acid in the solid-state by grinding under solvent-free conditions at room temperature. This method provides several advantages such as environmentally friendly, short reaction times, high yields, non-hazardous and simple work-up procedure.

Keywords: Iodination; Aromatic aldehydes; Aromatic ketones; Grinding

The grinding method has increasingly been used in organic synthesis. Recently Ball-milling grinding technique has been widely used in synthetic organic chemistry [1]. Compared with traditional methods, many organic reactions occur more efficiently in the solid-state than in solution and in many cases even more selectively, because molecules in the crystals are arranged tightly and regularly [2]. Furthermore, the solid-state reaction has many advantages: little pollution, low cost, and simplicity in progress and handling. A large number of organic reactions can be carried out simply and in high yield under mild conditions by this method [3]. Therefore, we focus on developing the novel procedure for iodination of hydroxylated aromatic aldehydes and ketones involving a solid-state reaction performed by grinding using iodine and iodic acid.

The different iodoaromatic compounds have been the subject of numerous studies due to the potential of the subject to act as bacterial and fungicidal agents [4]. Aromatic iodo compounds can be easily functionalized through metal-catalyzed cross-coupling reactions [5] in the synthesis of many interesting natural products [6] and bioactive material [7]. Iodoaromatic compounds are used in medicine as drug or diagnostic aids, contractors [8] and radioactively labeled markers [4]. They also have important in medicinal and pharmaceutical research [9]. The chemistry dealing with selective introduction of an iodine atom into organic molecules thus attracted broad interest in the wider specific community.

Recently direct iodination methods have been intensively developed using iodonium donating system, such as iodine–nitrogen dioxide [10], iodine F-TEDA-[1-chloromethyl-4-fluoro-1, 4-diazoniabicyclo [2,2,2] octane-bis-(tetrafluor-

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oborate)] [11], bis-N-iodosuccinimide [12], trichloroisocyanuric acid/I_2/Wet SiO_2 [13], mercury(II)-oxide–iodine [14], iodine–monochloride [15], bis(pyridine)iodonium(I), tetrafluoroborate CF_3SO_3H [16], NIS-CF_3SO_3H [17], iodine silver sulfate [18], iodine–mercury salts [19], NaOCl–NaI [20], iodine/$Na_2S_2O_8$ [21] and iodine–$(NH_4)_2S_2O_8$–$CuCl_2$ Ag_2SO_4 [22]. However most of these methods involve long reaction times, toxic reagents and organic solvents.

In present work grindstone technique was used for the iodination of hydroxylated aromatic aldehydes and ketones. This method is superior since it is environmentally friendly, high yielding, shorter reaction times, no organic solvent required (except for product recrytallisation), simple and convenient.

1. Experimental

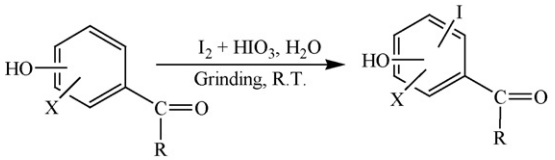
Melting points were determined in an open capillary tube and are uncorrected. IR spectra were recorded in KBr on a PerkinElmer spectrometer. ^{1}H NMR spectra were recorded on a Gemini 300-MHz instrument in $CDCl_3$ as solvent and TMS as an internal standard. Elemental analysis was carried out on a Carlo Erba 1108 analyzer. All the products were identified by comparison of their spectral and physical data with those of the known sample. The purity of products was checked by thin-layer chromatography (TLC) on silica-gel.

Hydroxylated aromatic aldehydes or ketones (10 mmol), iodine crystal (4 mmol) and iodic acid (2 mmol) and 2–4 drops of water were mixed in a morter. The reaction mixture was ground together in a mortar using pestle to generate violet coloured tacky solid within 20–30 min. The reaction proceeds exothermically (indicated by rise in temperature of 5–10 °C). After the reaction (TLC), saturated solution of sodium thiosulfate (5 mL) was added to remove unreacted iodine, solid separates out. The separated solid was filtered, washed with cold water and crystallized from ethyl alcohol. By using two equivalents of iodine and iodic acid and one equivalent of substrate, diiodinated products were obtained.

2. Result and discussion

In continuation of our earlier research works on iodination of some aromatics [23–29], herein, first time we would like to report a simple, efficient and solvent-free iodination of hydroxylated aromatic aldehydes and ketones using iodine and iodic acid by grinding method (Scheme 1).

A combination of iodine and iodic acid has been found to be an excellent reagent for the efficient iodination of hydroxylated aromatic aldehydes and ketones. These reactions are carried out by grinding method using mortar and



Scheme 1.

Table 1
Iodination of hydroxylated aromatic aldehydes and ketones using iodine and iodic acid by grinding.

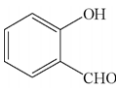
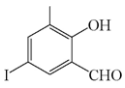
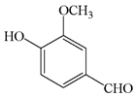
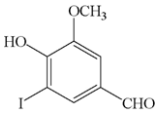
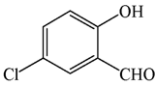
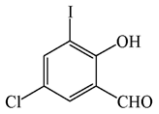
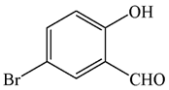
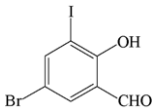
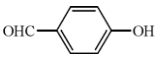
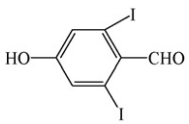
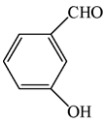
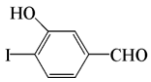
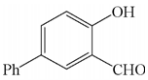
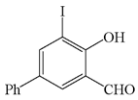
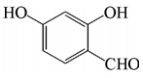
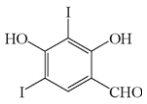
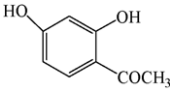
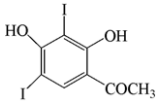
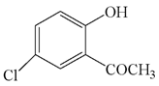
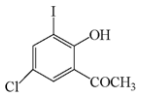
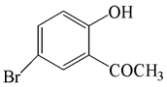
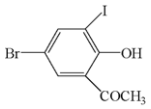
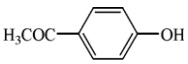
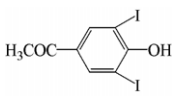
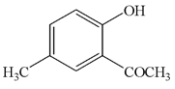
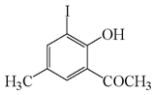
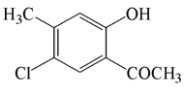
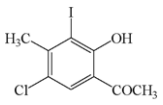
Entry	Substrate	Product	Time (min)	Yield	MP (°C) Found (Reported)
1			20	82	109 (110) [30]
2			20	94	183 (185) [29]

Table 1 (*Continued*)

Entry	Substrate	Product	Time (min)	Yield	MP (°C) Found (Reported)
3			23	86	78 (78) [29]
4			25	89	80 (81) [29]
5			20	83	194 (195) [30]
6			24	87	182 (182) [29]
7			20	90	85 (85) [29]
8			25	87	172 (173) [29]
9			27	92	177 (178) [23]
10			30	86	88 (89) [24]
11			30	88	105 (105) [24]
12			25	80	163 (162) [28]
13			20	85	81 (81) [24]
14			30	91	75 (76) [24]

pestle within shorter reaction times (20–30 min) with excellent yields (82–94%, Table 1). Few drops of water are required for easy grinding as well as iodic acid react properly in the presence of water with hydroiodic acid. A variety of *ortho*/*para* hydroxy substituted aromatic aldehydes and ketones were selected for the iodination reaction using iodine and iodic acid. The iodination occurs regioselectively and the C-iodination took place at *ortho* or/and *para* positions. When the *o*-position was blocked with a substituent, then iodination took place at *p*-position and vice versa. The diiodination occurs if ortho and para positions are unsubstituted. Iodination does not occur in the side chain, *i.e.* –$COCH_2$–R or –CH_3; only nuclear iodination takes place.

3. Conclusion

In conclusion, we have reported a simple and efficient method for solvent-free iodination of hydroxylated aromatic aldehydes and ketones using iodine and iodic acid by grinding method. The notable merits of the present method are shorter reaction times (20–30 min), simple work-up procedure; high yield (82–94%), environmentally friendly as it does not use any auxiliary or organic solvent. To the best of our knowledge this is first repot on iodination of hydroxylated aromatic aldehydes and ketones using iodine and iodic acid by grinding method.

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References

[1] (a) G.W. Wang, J. Gao, Org. Lett. 11 (2009) 2385;
(b) G.W. Wang, Y.W. Dong, P. Wu, et al. J. Org. Chem. 73 (2008) 7088;
(c) X.L. Wu, J.J. Xia, G.W. Wang, Org. Biomol. Chem. 6 (2008) 548;
(d) Y.W. Dong, G.W. Wang, L. Wang, Tetrahedron 64 (2008) 10148;
(e) G.W. Wang, X.L. Wu, Adv. Synth. Catal. 349 (2007) 1977.
[2] K. Tanaka, F. Toda, Chem. Rev. 100 (2000) 1025.
[3] (a) M. Veit, U. Hoffmann, Chem. Ing. Tech. 68 (1996) 1279;
(b) K. Tanaka, S. Kishigami, F. Toda, J. Org. Chem. 56 (1991) 4333;
(c) F. Toda, K. Tanaka, K. Hamai, J. Chem. Soc. Perkin Trans. 1 (1990) 3207;
(d) F. Toda, T. Suzuki, S. Higa, J. Chem. Soc. Perkin Trans. 1 (1998) 3521.
[4] R.H. Seevers, R.E. Counsell, Chem. Rev. 82 (1982) 575.
[5] F. Diederich, P.J. Stang, Metal Catalysed Cross Coupling Reactions, Wiley-VCH, Weinheim, Germany, 1988.
[6] (a) R.C. Larock, N.H. Lee, J. Org. Chem. 56 (1991) 6253;
(b) R.C. Larock, E.K. Yum, J. Am. Chem. Soc. 113 (1991) 6689;
(c) C.A. Busacca, R.E. Johnson, Tetrahedron Lett. 33 (1992) 165;
(d) J.S. Swenton, A. Callinan, S. Wang, J. Org. Chem. 57 (1992) 78.
[7] (a) R.H. Seevers, R.E. Counsell, Chem. Rev. 82 (1982) 574;
(b) K.C. Nicolaou, Angew. Chem. Int. Ed. Engl. 32 (1993) 1377.
[8] M. Sovak, Radiocontrast Agents: Handbook of Experimental Pharmacology, Springer, Berlin, 1993.
[9] N.D. Heindel, H.D. Burnes, T. Honds, et al. (Eds.), Chemistry of Radiopharmaceuticals, Masson, New York, 1997.
[10] Y. Noda, M. Kashima, Tetrahedron Lett. 38 (1997) 6225.
[11] M. Zupan, J. Iskra, S. Stavber, Tetahedron Lett. 38 (1997) 6305.
[12] M.C. Carreno, J.G. Ruano, G. Sanz, et al. Tetrahedron Lett. 37 (1996) 4081.
[13] B. Akhlaghinia, M. Rahmani, J. Turk. Chem. 31 (2009) 1.
[14] K. Orito, T. Hatakeyama, M. Takeo, Synthesis (1995) 1273.
[15] S.M. Hubig, W. Jung, J.K. Kochi, J. Org. Chem. 59 (1994) 6233.
[16] J. Barluenga, J.M. Gonzalez, M.A. Garcia-Martin, et al. J. Org. Chem. 58 (1993) 2058.
[17] G.A. Olah, D. Wang, G. Sandford, et al. J. Org. Chem. 58 (1993) 3194.
[18] W.W. Sy, Tetrahedron Lett. 34 (1993) 6223.
[19] A. Bachki, F. Foubelo, M. Yus, Tetrahedron 50 (1994) 5139.
[20] H.J. Edgar, S.N. Falling, J. Org. Chem. 55 (1990) 5287.
[21] K. Elbs, A. Jaroslawzee, J. Proki. Chem. 88 (1913) 92.
[22] D.M. Marko, U.A. Belyoew, Khim. Referat. Zhur. 4 (1941) 49.

[23] Y.B. Vibhute, M.H. Jagdale, J. Indian Chem. Soc. 58 (1981) 1115.
[24] B.S. Dawane, Y.B. Vibhute, J. Indian Chem. Soc. 77 (2000) 999.
[25] B.R. Patil, S.R. Bhusare, R.P. Pawar, et al. Tetrahedron Lett. 46 (2005) 7179.
[26] B.R. Patil, S.R. Bhusare, R.P. Pawar, et al. Arkivoc I (2006) 104.
[27] S.V. Khansole, S.B. Junne, M.A. Sayyed, et al. Synth. Commun. 38 (2008) 792.
[28] S.V. Khansole, S.S. Mokle, M.A. Sayyed, et al. J. Chin. Chem. Soc. 55 (2008) 871.
[29] M.A. Sayyed, S.B. Junne, A.Y. Vibhute, et al. Int. J. Chem. Sci. 6 (2008) 192.
[30] W. Tong, A. Taurug, I.L. Chaikoff, J. Biol. Chem. 59 (1954) 207.