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Iodination of acetamides using iodine and iodic acid under conventional method as well as microwave irradiation technique

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Abstract
Iodoacetamides were synthesized by iodination using iodine and iodic acid as an iodinating reagent in ethanol under conventional method as well as microwave irradiation. Microwave technique has several advantages over conventional technique in terms of simple reaction procedure, easy work up and yields of product.

Keywords: Iodination, Iodoacetamide, iodine, iodic acid, microwave irradiation.

INTRODUCTION

The aromatic iodination reaction is important electrophilic substitution reaction and the resultant iodo products are useful intermediate in organic synthesis [1]. They are useful for the preparation of organometallic reagents, and some are potential intermediates for the synthesis of pharmaceutical and bioactive materials [2].

Iodination of organic aromatic substrates simply by molecular iodine is not possible due to involved HI oxidizes the iodo product formed, hence an oxidizing agent is used along with molecular iodine to oxidize HI formed. Various oxidants such as chromium oxide [3 and 4], silver sulphate [5], sodium iodate [6], iodic acid [7], iodine–nitrogen dioxide [8], iodine-f-TEDA [9], N-iodoscuccinamide [10], iodine-diiodine pentoxide [11], iodine monochloride [12], iodine- mercury (II) oxide [13] and NaOCl-NaI [14] have been used along with elemental iodine for effective iodination process.

In view of medicinal importance of iodoaromatics and in continuation of earlier research work on iodination of aromatic compounds [15,16 and 17], we report here iodination of acetamide derivatives using iodine and iodic acid under conventional method as well as microwave irradiation.

MATERIALS AND METHODS

Melting points were determined in an open capillary tube and are uncorrected. IR spectra were recorded in KBr on a Perkin-Elmer spectrometer. ^{1}H NMR spectra were recorded on a Gemini 300-MHz instrument in $CDCl_3$ as solvent and TMS as an internal standard. The purity of products was checked by thin layer chromatography (TLC) on silica gel.

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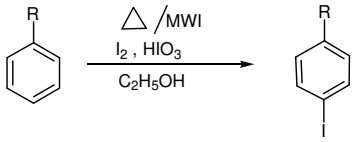
Conventional procedures for iodination of acetamides

Acetamide (50 mmol), iodine (20 mmol) dissolved in ethanol (20 ml) by warming and then iodic acid (10 mmol) dissolved in water (1 ml) was added with shaking and refluxed 6-10 min. On cooling solid separated out. Obtained solid product was filtered and crystallized from ethanol. Melting point, percentage yield data is given in (Table 1).

Microwave assisted procedure for iodination of acetamides

Acetamide (50 mmol), iodine (20 mmol) dissolved in ethanol (20 ml) by warming, iodic acid (10 mmol) dissolved in water (1 ml) was added with shaking and resultant reaction solution was irradiated in microwave oven for 2-3 min (12-18 times, 10 seconds at a time and cooling with given short interval of time to avoid excess evaporation of solvent). The progress of reaction was monitored on TLC. On cooling reaction mixture, solid product obtained crystallized from ethanol. Melting point and mixed melting point with product obtained by conventional method was not depressed.



2a: R= $NHCOCH_3$
2b: R= $NHCOC_6H_5$
2c: R= $NHCOC_2H_5$
2d: R= $NHCOCH_2CH_2CH_3$
2e: R= $NHCOCH_2Cl$
2f: R= $CH_2NHCOCH_3$

Scheme1. Iodination of Acetamides using iodine and iodic acid

N-(4-iodophenyl)acetamides (2a)

IR (KBr) : 3250 (NH), 1652 (C= O) cm^{-1}. ^{1}H NMR (300 MHz, DMSO): δ 2.37 (s, 3H, CH_3), 7.12-7.68 (m, 4H, Ar-H), 10.12(s, 1H, NH). MS m/z 261(M^+). Anal.Calcd for C_8H_8ONI: I, 48.65. Found: I, 48.72.

N-(4-iodophenyl)benzamide (2b)

IR (KBr): 3252 (NH), 1655 (C= O) cm^{-1}. ^{1}H NMR (300 MHz, DMSO): δ 7.16-7.88 (m, 9H, Ar-H), 10.14 (s, 1H, NH). MS m/z: 327

(M+). Anal. Calcd for $C_{13}H_{10}ONI$: I, 38.83. Found: I, 38.80.

N-(4-iodophenyl)propionamide (2c)

IR (KBr): 3254 (NH), 1658 (C= O) cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 1.7 (t, 3H, CH_3), 2.3 (9, 2H, CH_2). 7.14-7.71 (m, 4H, Ar-H), 10.08 (s, 1H, NH). MS m/z : 275 (M+). Anal. Calcd for $C_9H_{10}ONI$: I, 46.18. Found: I, 46.23.

N-(4-iodophenyl)butyramide (2d)

IR (KBr): 3250 (NH), 1652(C= O) cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 0.92 (t, 3H, CH_3), 1.22 (m, 2H, CH_2). 2.23(t, 2H, CH_2), 7.12-7.69 (m, 4H, Ar-H), 10.12 (s, 1H, NH). MS m/z : 289 (M+). Anal.Calcd for $C_{10}H_{12}ONI$: I, 43.94. Found: I, 43.99.

2-chloro- N-(4-iodophenyl)acetamides (2e)

IR (KBr): 3252 (NH), 1650 (C= O) cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 3.21 (s, 2H, CH_2), 7.14-7.68 (m, 4H, Ar-H), 10.12(s, 1H, NH). MS m/z 295(M+). Anal.Calcd for C_8H_7ONClI: (I+Cl), 54.91. Found: (I+Cl), 54.87

4-iodo-N-benzyl acetamides (2f)

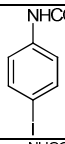
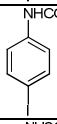
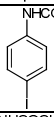
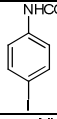
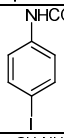
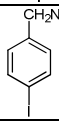
IR (KBr): 3250 (NH), 1655 (C= O) cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 2.32 (s, 3H, CH_3), 3.12 (s, 2H, CH_2), 7.14-7.72 (m, 4H, Ar-H), 10.14(s, 1H, NH). MS m/z 275(M+). Anal.Calcd for $C_9H_{10}ONI$: I, 46.18. Found: I, 46.26.

RESULTS AND DISCUSSION

A variety of aromatic acetamide derivatives were investigated for the iodination using iodine and iodic acid in ethanol; afforded the corresponding iodinated compounds with excellent yields and high regioselectivity at para position (Scheme 1).

The iodination of acetamide derivatives were also carried out using iodine and iodic acid in solvent ethanol under microwave irradiation (MWI). High yields and purity of compounds with short reaction time are notable merits of this method. Structure of the synthesized iodo compounds were confirmed by IR, ^1H NMR, Mass and halogen analysis.

Table 1. Physical data of iodoacetamides 2a-f.

Sl. No.	Product	M.P. °C	Conventional method		MWI method	
			Time (min)	Yield (%)	Time (sec)	Yield (%)
2a		185 [21*]	6	77	120	83
2b		140	9	75	180	81
2c		160	10	72	120	80
2d		120	6	80	180	87
2e		150	8	81	180	90
2f		72	7	76	120	81

* Reported m.p. 184 °C.

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