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IDENTIFICATION, ISOLATION AND CHARACTERIZATION OF PROCESS-RELATED IMPURITIES IN IRBESARTAN

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ABSTRACT

Irbesartan is an angiotensin II receptor type 1 antagonist used in the treatment of hypertension, heart failure, myocardial infarction and diabetic nephropathy. During process development, two impurities at levels ranging from 0.01% to 3.0% were detected by high performance liquid chromatography (HPLC) using UV detector. Two impurities molecular weights were determined by LC–MS analysis and isolated by preparative HPLC. Based on the spectral data (NMR, MS and IR) the structures of these impurities were characterized as, Impurity-1 (4'-(2-{1-[(2'-cyanobiphenyl-4-yl)methyl]-4-oxo-1,3-diazaspiro[4.4]non-2-en-2-yl} pentyl)biphen yl-2-carbonitrile) and impurity-2 (1-{[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl}-2-{1-[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]pentan-2-yl}-1,3-diazaspiro[4.4] non-2-en-4-one). The chromatographic retention times of two impurities (Impurity-1 and 2) were determined by spiked with Irbesartan and the mechanism for the formation of these impurities also discussed in detail.

KEY WORDS: ***Irbesartan Impurities, Isolation, Characterization.***

1.0 INTRODUCTION

Irbesartan, an angiotensin II receptor antagonist, is used mainly for the treatment of hypertension. It is an orally active non peptide tetrazole derivative and selectively inhibits angiotensin II receptor type1. It is widely used in treatment of diseases like hypertension, heart failure, myocardial infarction and diabetic nephropathy [1 to 11]. It is chemically designated as 2-butyl-3-{[2'-(1H-tetrazol-5-yl) biphenyl-4-yl]methyl}-1,3-diazaspiro[4,4]non-1-en-4-one. Its molecular formula is $C_{25}H_{28}N_6O$ and molecular weight is 428.53 amu. Impurities are an extremely critical issue in the pharmaceutical industry especially due to the stringent regulations and manufacturing process. Impurity profile of an active pharmaceutical ingredients (APIs) and evaluation of their toxicity effect is necessary step in developing a safe and effective drug and is essential for medical safety reasons. Typically process-related impurities are unwanted chemicals that remain with the APIs and could be generated at any of the synthetic steps or contamination of any un-reacted molecule involved in the process development. As per regulatory requirement, new impurity present at a level of 0.05 to 0.1% in the drug substance need to be identified and characterized [12]. The HPLC studies were reported for the determination of impurities, degradation products [13-14]. During process development studies of Irbesartan, two impurities (Impurity 1 and 2) in the bulk drug samples were detected by

current available analytical method and these two unknown impurities are coming above ICH limit. Hence we isolated these impurities by preparative HPLC method and the subsequent spectral characterization to confirm the structures. The HPLC method developed for well separation of these two impurities, spectral characterization was discussed to confirm the structures and mechanism for the formation of these two impurities also discussed in detail.

2.0 MATERIALS AND METHODS

2.1 Sample, Chemicals and Reagents

Irbesartan and intermediate stage samples were received from Process Development Lab of Mylan laboratories limited, Plot No.35,36,38 to 40& 49 to 51, phase-IV, IDA Jeedimetla, Qutbullapur (Mandal) Rangareddy District, Hyderabad – 500055, Andhra Pradesh, India. Orthophosphoric acid (AR grade), Formic acid (AR grade), Ammonia solution (AR grade), Triethylamine (HPLC grade), methanol (HPLC grade) and acetonitrile (HPLC grade) and distilled water was purified by using Milli-Q water purification system. The synthetic scheme of Irbesartan [14 to 23] and impurities (Impurity-1 and Impurity-2) is shown in Fig. 1.

2.2 Synthetic Scheme of Irbesartan:

Stage-I: N-Alkylation of 2-N-butyl-1,3-diaza-spiro [4.4] non-1-en-4-one hydrochloride (BSI HCl) with 4'-bromomethyl biphenyl-2-carbonitrile in presence of tetra butyl ammonium bromide (TBAB). The product was isolated in ethanol to give 4'-(2-butyl-4-oxo-1,3-diaza-spiro[4.4]non-1-en-3-yl)methyl)-biphenyl-2-carbonitrile (stage-I).

Stage-II (Irbesartan): 4'-(2-Butyl-4-oxo-1,3-diaza-spiro[4.4]non-1-en-3-yl) methyl)-biphenyl-2-carbonitrile (stage-I) is reacted with sodium azide in presence of triethylamine (TEA) hydrochloride in o-xylene to give 2-Butyl-3-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1,3-diazaspiro[4.4]non-1-en-4-one (Stage-II).

2.2 Analytical HPLC Conditions

Chromatographic separations were performed on Waters alliance 2695 high performance liquid chromatograph system equipped with 2487 UV detector and data processed with *Empower chromatography software*. Separations were achieved on Kromasil, C18 column with dimensions of 250 mm x 4.6 mm, 5µm maintained at 25°C. The mobile phase consisted of 1.0ml of triethylamine in 1000mL with water and the pH adjusted to 3.2 ± 0.05 with ortho phosphoric acid. Filter through 0.45µm nylon membrane and degassed the mobile phase (A), Acetonitrile (B) and detection was carried out at 220 nm. Flow rate was 1.0ml/min. Pump mode was gradient and was as follows, time (min)/A (v/v): B (v/v); T0/60:40, T18/60:40, T20/50:50, T30/30:70, T40/20:80, T45/55:45, T50/55:45.

2.3 LC–MS Conditions

ESI (electro spray ionization) mass spectra were recorded on Agilent 1100 Series LC-MSD-TRAP-SL system. Chemstation software was used for data acquisition and data processing. The turbo ion spray voltage was maintained at 4500V and temperature was set at 325°C. The auxiliary gas and sheath gas used was high pure Nitrogen. Zero air was used as Nebuliser gas. LC–MS spectra were acquired from *m/z 10*0–2000 in 0.1 amu steps

with 2.0 s dwell time. LC–MS analysis of the crude sample was carried out using Hypersil BDS, C18 column with dimensions of 250 mm x 4.6 mm, 5µm maintained at c25°C. The buffer consisted of water pH adjusted to 3.0 with formic acid. The mobile phase consisted of buffer and methanol in the ratio of 35:65 v/v. Flow rate was 1.0ml/min, Pump mode was isocratic.

2.4 Preparative LC Conditions

Agilent 1100 Series Auto purification preparative liquid chromatograph equipped with UV detector, pump and auto collector was used. Chemstation software was used for data acquisition and data processing. Separations were achieved on Reprosilpur basic C18-HD C18 column with dimensions of (250×20) mm X 10µm was utilized. The mobile phase consisted of 0.2% Formic Acid in water pH adjusted to 3.0 with ammonia solution (A). Filter through 0.45µm nylon membrane, degassed the Mobile phase (A) and acetonitrile (B). Flow rate was 15.0 ml/min and detection was carried out at 220 nm. Pump mode was gradient and was as follows, time (min)/A (v/v): B (v/v); T0/60:40, T32/60:40.

2.5 NMR Spectroscopy

The NMR experiments were performed on a Bruker AVANCE-300 instrument with a 5-mm BBO probe head equipped with shielded *Z*-gradient coil at 298 K using deuterated dimethyl sulfoxide (DMSO-d_6) as solvent and tetramethylsilane (TMS) as internal standard. The data were collected by XWIN-NMR software (Bruker) and processed with Topspin running on a PC with Microsoft Windows^{xp}. In the ^{1}HNMR analysis, 16 transients were acquired with a 1-s-relaxation delay using 32 K data points. The 90° pulse duration was of 11 µs and spectral width 6.000 kHz. The ^{13}C NMR and DEPT experiments were carried out with a spectral width of 16.500 kHz using 64 K data points. The two-dimensional experiments were performed using Bruker standard pulse sequences and parameters. The ^{1}H–^{1}H bond correlations confirmed by gCOSY experiment (cosygpqf). The protonated carbon positions were confirmed by a gHSQC experiment (hsqcetgpsi2). The non-protonated carbons were confirmed by a gHMBC experiment (hmbcgplpndqf). The ^{1}H chemical shifts are reported in ppm with reference to tetramethylsilane (δ0.0 ppm). The ^{13}C chemical shifts were referenced to the central peak of the solvent molecule DMSO-d_6 (δ 39.50ppm).

2.6 Mass Spectrometry

Mass spectra were recorded on Agilent 1100 Series LC-MSD-TRAP-SL system mass spectrometer equipped with a Turbo ion spray interface at 375°C. Detection of ions was performed in electro spray ionization, positive ion mode.

2.7 IR Spectroscopy

The FT-IR spectra were recorded on Perkin Elmer Spectrum One FT-IR Spectrometer by using potassium bromide pellet method.

3.0 RESULTS AND DISCUSSION

3.1 Isolation of Impurities by Preparative

Impurities were present in the crude sample at percentage levels of 1.5% (Impurity-1) and 2.9% (Impurity-2) by area normalization. These impurities were isolated from crude sample that was subjected to preparative HPLC by using the conditions described in Section 2.4. Fractions of >95% were pooled together; concentrated on rotavapour to remove acetonitrile /methanol and then lyophilized on VIRTIS lyophilizer. Impurity-1 (RRT-2.28) was obtained as an off-white powder chromatographic purity of 84.3%, and Impurity-2(RRT-1.29) was obtained as an off-white powder with chromatographic purity of 88.7%.

3.2 Detection of Impurities

Sample solution equivalent to 0.5 mg/ml of Irbesartan prepared in diluent (methanol) was injected into the analytical LC using the solvent system as described in Section 2.2. Two impurities were detected at relative retention times (RRT) of 1.29 and 2.28 respectively with respect to Irbesartan whose retention time is about 20.12 min. The same samples were subjected to LC–MS analysis using conditions as described in Section 2.3 to identify the mass of the impurities. The masses of the impurities recorded in positive ion mode were 577(M+H) for Impurity-1 (RRT-2.28), and 663(M+H) for Impurity-2 (RRT-1.29) respectively. The isolated impurities were co-injected with Irbesartan to confirm the retention times. Two impurities were well resolved from Irbesartan. The resolution mixture chromatogram is shown in Fig. 2.

3.3 Structure Elucidation of Impurities

3.3.1 BMCP: This is one of the key raw material (in Fig.1) in the synthesis of Irbesartan. ESI mass displayed adduct ion at m/z 289 $[M+NH_4]^+$, protonated molecular ion at m/z 272$[M+H]^+$ indicating the molecular weight of the compound as 272. The fragmentation pathway of the protonated molecular ion at m/z 272 was obtained: m/z at 192,179, 118. The ^{1}H NMR spectrum of BMCP shows the eight protons (H-3,4,5,6,9,9',10 and 10') in aromatic region and two protons (H-14) as a singlet in aliphatic region and this raw material ^{1}H NMR and Mass data also matching with the literature [14] reported data. The ^{13}C NMR displayed one methylene group C12 at δ 33.78ppm; one C≡N group C1 at δ 118.44ppm, four aromatic quaternary carbons C2 at δ 110.09ppm, C7 at δ 143.84ppm, C8 at δ 138.52ppm, C11 at δ 137.63ppm and eight aromatic carbons C3 at δ 133.81ppm, C4 at δ 130.03ppm, C5 at δ 133.47ppm, C6 at δ 128.29ppm, C9,9' at δ 129.58ppm and C10,10' at δ 128.99ppm The above spectral data confirms the BMCP as 4'-(bromomethyl)biphenyl-2-carbonitrile with molecular formula $C_{14}H_{10}BrN$ and molecular weight 272.

3.3.2 BSI HCl: This is one of the key raw material (in Fig.1) in the synthesis of Irbesartan. The ESI mass displayed 195 $[M-HCl+H]^+$ indicating the molecular weight of the compound as 230. The fragmentation pathway of the protonated molecular ion at m/z 195 was obtained: m/z at 166. The ^{1}H NMR spectrum of BSI HCl shows the seventeen protons in aliphatic region (H-17 to 20; H-22 to 25) and two exchangeable protons (N^+-H_2) at δ 13.52 ppm as a broad singlet, which are confirmed by D_2O exchange experiment confirms the BSI as HCl salt and this raw material ^{1}H NMR and Mass data also matching with the literature [14] reported data. The ^{13}C NMR displayed one methyl group C25 at δ 13.35ppm, seven methylene groups C17,20 at δ 36.48ppm, C18,19 at δ

24.94ppm, C22 at δ 26.62ppm, C23 at δ 27.30ppm, C24 at δ 21.41ppm; one aliphatic quaternary carbon C16 at δ 72.14ppm, one quaternary carbon in aromatic region C21 at δ 173.01ppm and a quaternary carbonyl carbon C15 at δ 179.77ppm. The above spectral data confirms the BSI HCl as 2-N-butyl-1,3-diazaspiro[4.4]non-1-en-4-one hydrochloride with molecular formula $C_{11}H_{19}ClN_2O$ and molecular weight 230.

3.3.3 Irbesartan Stage-I: This is one of the intermediate (in Fig.1) in the synthesis of Irbesartan. ESI mass spectrum of Stage-I in positive ion mode showed a molecular ion peak at m/z 386 $[M+H]^+$ indicating the molecular weight of the compound as 385. The fragmentation pathway of the protonated molecular ion at m/z 385 was obtained: m/z at 192. The ^1H NMR spectrum of Stage-I shows the eight protons in aromatic region and nineteen protons in aliphatic region. The ^{13}C NMR displayed one methyl group C25 at δ 13.51ppm, eight methylene groups C17,20 at δ 36.77ppm, C18,19 at δ 25.40ppm, C22 at δ 27.47ppm, C23 at δ 26.60ppm, C24 at δ 21.48ppm; one aliphatic quaternary carbon C16 at δ 75.81ppm; three quaternary carbons in aromatic region C1 at δ 118.38ppm, C2 at δ 110.14ppm, C7 at δ 143.97ppm, C8 at δ 137.71ppm, C11 at δ 136.88ppm, C21 at δ 160.94ppm and a quaternary carbonyl carbon C15 at δ 185.667ppm and this intermediate NMR and Mass data also matching with the literature [15,16] reported data. The above spectral data confirms the Irbesartan Stage-I as 4'-(2-Butyl-4-oxo-1,3-diaza-spiro[4.4]non-1-en-3-ylmethyl)-biphenyl-2-carbonitrile with molecular formula $C_{25}H_{27}N_3O$ and molecular weight 385.

3.3.4 Irbesartan: ESI mass spectrum of Irbesartan in positive ion mode showed a protonated molecular ion peak at m/z 429 $[M+H]^+$ indicating the molecular weight of the compound as 428. The fragmentation path way of the protonated molecular ion at m/z 429 was obtained: at m/z 207. The structure of the Irbesartan was confirmed by ^1H NMR, ^{13}C NMR and DEPT and this data also matching with the literature [14,16 to 21] reported data.

3.3.5 Impurity-1: ESI mass spectrum of Impurity-1 in positive ion mode showed a molecular ion peak at m/z 577 $[M+H]^+$ indicating the molecular weight of the compound as 576. The fragmentation pathway of the protonated molecular ion at m/z 577 was obtained: m/z at 303,192. In the ^1H NMR spectrum of Impurity-1, biphenyl carbonitrile moiety corresponding to Irbesartan stage-1 protons signals with double integration were observed, a triplet signal with integration of two protons H-22, at δ 2.37ppm corresponding to methylene group in butyl moiety disappeared and a multiplet signal with integration of three protons H-14',H-22 at δ 2.85-3.00ppm were observed. When compared to Irbesartan stage-1 ^{13}C NMR spectrum, in this impurity C-22 signal of Irbesartan stage-1 at δ 27.47 ppm disappeared, one extra methine group signal at δ 40.63ppm was seen to appear In this impurity C-15 (δ 185.66 ppm to δ 194.73ppm), C-21 (δ 160.94ppm to δ 185.56ppm) signals were deshielded to higher ppm, in gHMBC spectrum, H-14 shows the correlation with C-21 which confirms that one of the methylene biphenyl carbonitrile moiety was attached on nitrogen adjacent to C-21. In gHCOSY spectrum of this impurity H-22 at δ 2.85-3.00ppm shows the correlation with H-23 at δ 1.50-1.77ppm. The above spectral data confirms the impurity as 4'-(2-{1-[(2'-cyanobiphenyl-4-yl)methyl]-4-oxo-1,3-diazaspiro[4.4]non-2-en-2-yl}pentyl)biphenyl-2-carbonitrile(Impurity-1) with molecular formula $C_{39}H_{36}N_4O$ and molecular weight 576.73.

3.3.6 Impurity-2: ESI mass spectrum of Impurity-2 in positive ion mode showed a molecular ion peak at *m/z* 663 $[M+H]^+$ indicating the molecular weight of the compound as 662. The fragmentation pathway of the protonated molecular ion at m/z 663 was obtained: m/z at 607,413,207. In the ^{1}H NMR spectrum of this impurity, biphenyl tetrazole moiety corresponding to Irbesartan stage-2 protons signals with double integration were observed, a triplet signal with integration of two protons H-22, at δ 2.28ppm corresponding to methylene group in butyl moiety in Irbesartan disappeared, appeared as multiplet with integration of one proton at H-22 at δ 2.89ppm and a multiplet signal with integration of two protons H-14'at δ 2.68-2.73 ppm was observed. When compared to Irbesartan ^{13}C NMR spectrum, in this impurity, C-22 signal of Irbesartan at δ 27.45 ppm disappeared, one extra methine group signal at δ 40.64ppm appeared. In this impurity, C15 (δ 185.62 ppm to δ 194.88ppm), C-21 (δ 161.12ppm to δ 185.43ppm) signals were deshielded to higher ppm, in gHMBC spectrum, H-14 shows the correlation with C-21 which confirms that one of the methylene biphenyl carbonitrile moiety was attached on nitrogen adjacent to C-21. In gHCOSY spectrum of this impurity, H-22 at δ 2.89ppm shows the correlation with H-23 at δ 1.38-1.84ppm. From the observations in the above spectral data Impurity-2 is confirmed as 1-{[2'-(1*H*-tetrazol-5-yl)biphenyl-4-yl]methyl}-2-{1-[2'-(1*H*-tetrazol-5-yl)biphenyl-4-yl]pentan-2-yl}-1,3-diazaspiro[4.4]non-2-en-4-one with molecular formula $C_{39}H_{38}N_{10}O$ and molecular weight 662.79.

The probable mechanisms for the formation of the Impurities 1 and 2 are given in Fig. 3.The ^{1}Hand ^{13}CNMR chemical shift values of Irbesartan, Irbesartan stage-1 and impurities (Impurity-1 and Impurity-2) are given in Tables 1 and 2 respectively. The FT-IR spectral data is given in Table 3.

3.5. Formation of Impurities

3.5.1 Formation of Impurity-1

In Spiro Hydrochloride on reacts with two molecules of 4'-(bromomethyl)biphenyl-2-carbonitrile in presence of potassium hydroxide and yields the Impurity-1.

3.5.2 Formation of Impurity-2

In the synthesis of Irbesartan, reaction involves the conversion of cyano groups in stage-I into tetrazole ring. Two cyano groups present in the impurity-1 also expected to undergo similar kind of chemical reaction and yield the Impurity-2.

Fig. 1: The synthetic scheme of Irbesartan

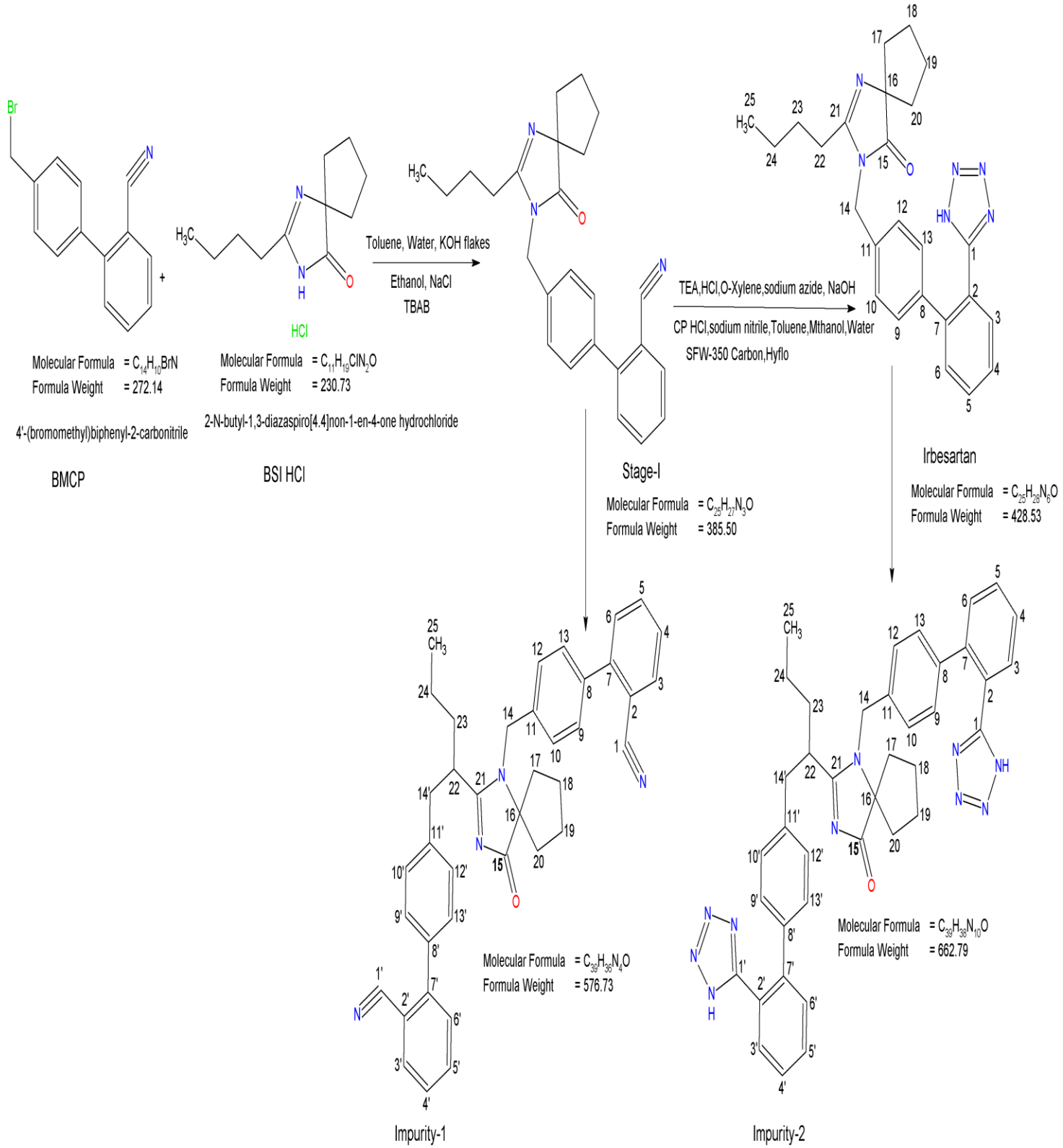

Fig. 2: Typical LC-chromatogram of Irbesartan, Stage-I samples spiked with Impurity-1 and Impurity-2.

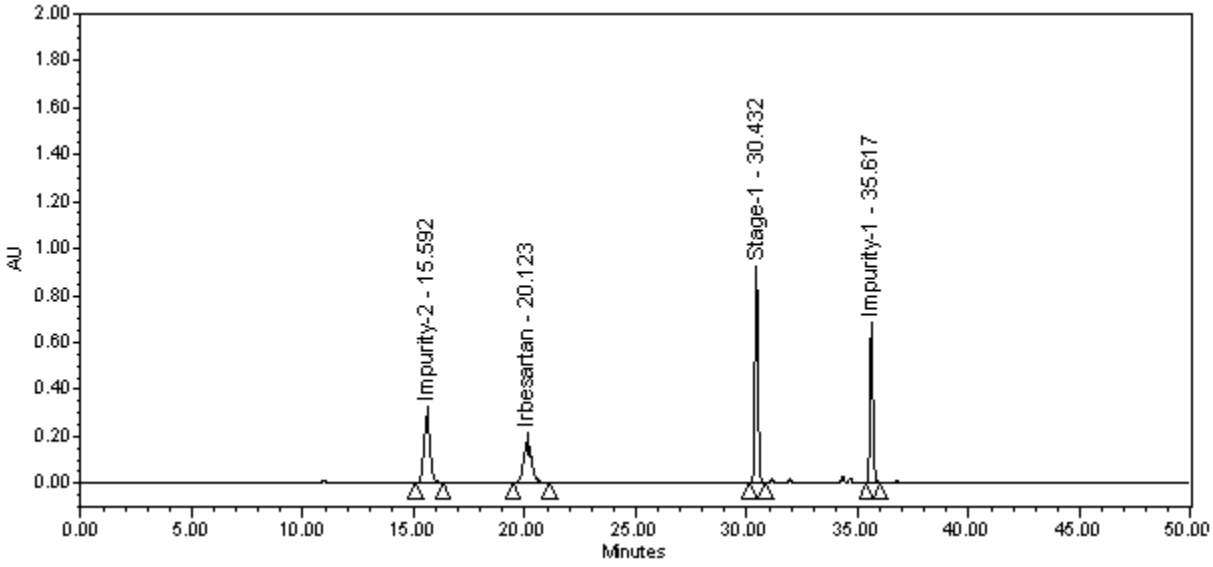

Fig. 3: Probable mechanism for the formation of the impurities 1 and 2.

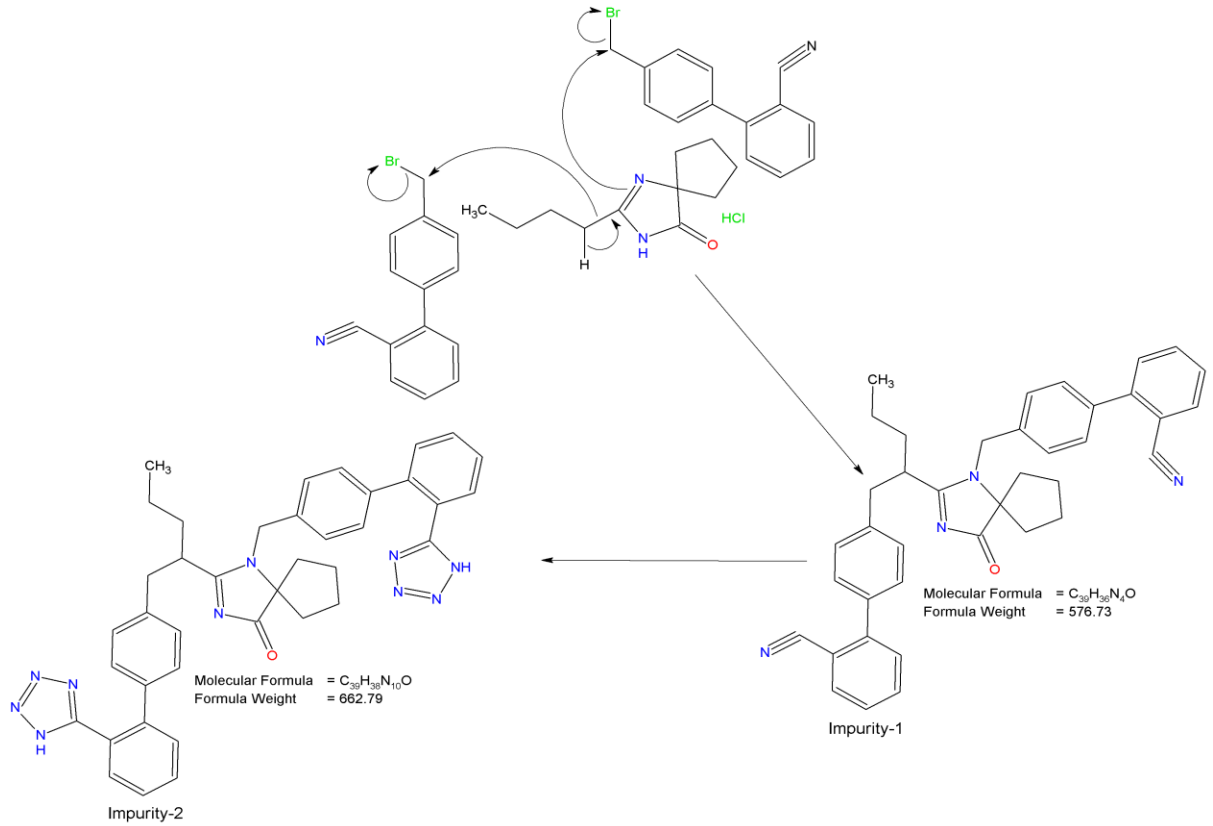

Table.1: [1]HNMRchemical shift values of Irbesartan, Irbesartan steg-1 and impurities (impurity-1 and impurity-2)

Position[a]	Stage-1	Irbesartan	Position[a]	Impurity-1	Impurity-2
3	7.95, 1H, d(7.5)[b]	7.65-7.71,1H,m	3,3'	7.92-7.96,2H,m	7.46-7.68,2H,m
4	7.56-7.63,1H,m	7.53-7.60,1H,m	4,4'	7.49-7.66,2H,m	7.46-7.68,2H,m
5	7.56-7.63,1H,m	7.65-7.71,1H,m	5,5'	7.74-7.79,2H,m	7.46-7.68,2H,m
6	7.56-7.63,1H,m	7.53-7.60,1H,m	6,6'	7.49-7.66,2H,m	7.46-7.68,2H,m
9,13	7.32,2H,d(8.1)[b]	7.08,2H,s	9,13,9',13'	7.49-7.66,4H,m	7.01-7.08,4H,m
10,12	7.56-7.63,1H,m	7.08,2H,s	10,12,10',13'	7.16-7.24,4H,m	7.01-7.08,2H,m
14	4.78,2H,s	4.68,2H,s	14	4.25-4.54,2H,m	3.86-4.25,2H,m
-	-	-	14'	2.85-3.00,2H,m	2.68-2.73,2H,m
17,20	1.64,4H,m	1.66-1.84,2H,m	17,20	1.50-1.77,4H,m	1.38-1.84,2H,m
18,19	1.64,4H,m	1.66-1.84,2H,m	18,19	1.50-1.77,4H,m	1.38-1.84,2H,m
22	2.37,2H,t(7.4)[b]	2.28,2H,t(7.5)[b]	22	2.85,1H,m	2.89,1H,m
23	1.45-1.55,2H,m	1.42-1.52,2H,m	23	1.50-1.77,2H,m	1.38-1.84,2H,m
24	1.21-1.33,2H,m	1.20-1.32,2H,m	24	1.18-1.23,2H,m	1.08-1.23,2H,m
25	0.80,3H,t(7.4)[b]	0.80,3H,t(7.2)[b]	25	0.77,3H,t(7.2)[b]	0.73,3H,t(7.1)[b]
NH	-	16.28,1H,br	NH	-	15.90-16.50,2H,br

[a] Refer structures (Fig. 1) for numbering. s, singlet; m, multiplet; br-broad

[b] ^{1}H-^{1}H Coupling constants.

Table.2: ^{13}C NMR chemical shift values of Irbesartan, Irbesartan steg-1 and impurities (Impurity-1 and Impurity-2)

Position[a]	Stage-1	Irbesartan	Position[a]	Impurity-1	Impurity-2
	^{13}C (δ, ppm)/	^{13}C (δ, ppm)/		^{13}C (δ, ppm)/	^{13}C (δ, ppm)/
1	118.38,-	154.99,-	1,1'	118.35,118.57, -	155.12,155.30, -
2	110.14,-	123.45,-	2,2'	110.09,110.19, -	123.59, -
3	133.77, CH	130.57, CH	3,3'	133.79,133.84, 2xCH	130.64,130.30, 2xCH
4	129.98, CH	127.80, CH	4,4'	128.10,129.25,	127.69,127.83,
5	133.41, CH	131.05, CH	5,5'	133.46,133.50,	130.54,130.49,
6	128.15, CH	130.57, CH	6,6'	129.38, 2xCH	130.96,131.01,
7	143.97, -	140.99, -	7,7'	143.84,144.34, -	140.95,141.44, -
8	137.71, -	138.34, -	8,8'	137.85,139.67, -	138.00,138.56, -
9,13	129.10, 2XCH	129.23, 2XCH	9,13,9',13'	129.03,128.73, 4XCH	128.85, 4XCH
10,12	126.67, 2xCH	126.25, 2xCH	10,12,10',12'	126.59,129.94, 4xCH	126.14,128.85, 4xCH
11	136.88,-	136.28,-	11,11'	139.19,136.93,-	136.33,138.00,-
14	42.26, CH_2	42.20, CH_2	14	44.39, 1xCH_2	44.36, 2xCH_2
-	-	-	14'	38.67, 1xCH_2	38.67, 2xCH_2
15	185.66, -	185.62, -	15	194.73, -	194.88, -
16	75.81, -	75.78, -	16	73.42, -	73.40, -
17,20	36.77, 2x CH_2	36.77, 2x CH_2	17,20	34.24, 2x CH_2	34.28, 2x CH_2
18,19	25.40, 2xCH_2	25.42, 2xCH_2	18,19	25.05,25.15, 2xCH	25.25,25.42, 2xCH
21	160.94, -	161.12, -	21	185.56, -	185.43, -
22	27.47, CH_2	27.45, CH_2	22	40.63, CH	40.64, CH
23	26.60, CH_2	26.55, CH_2	23	35.39, CH_2	35.33, CH_2
24	21.48, CH_2	21.49, CH_2	24	19.83, CH_2	19.91, CH_2
25	13.51, CH_3	13.59, CH_3	25	13.90, CH_3	13.94, CH_3

[a] Refer structures (Fig. 2) for numbering.

Table. 3:.IR spectral data of Irbesartan, Irbesartan stage-1 and impurities (Impurity-1 and Impurity-2).

S.NO	Name of the compound	FT-IR (KBr) **Wave number (cm^{-1})**
1	Stage-1	3054, 3030 Aromatic C-H Stretching; 2951, 2871 Aliphatic C-H Stretching; 2221 C≡N Stretching; 1720 C=O Stretching; 1629C=C/C=N Stretching; 1480, 1468, 1446, 1402 Aliphatic C-H Bending; 1339,1310,1205,1171 C-N Stretching; 777,760 Aromatic C-H Bending.
2	Impurity-1	3062,3030 Aromatic C-H Stretching; 2956,2930,2865 Aliphatic C-H Stretching; 2224 C≡N Stretching; 1697 C=O Stretching; 1596,1508 C=C/C=N Stretching; 1476,1444,1411 Aliphatic C-H Bending; 1319,1307,1292,1270,1145,1117 C-N Stretching; 838,765 Aromatic C-H Bending.
3	Irbesartan	3446, N-H Stretching; 3058,3033 Aromatic C-H Stretching; 2960,2933,2874 Aliphatic C-H Stretching; 1733 C=O Stretching; 1617 C=C/C=N Stretching; 1485,1435,1409 Aliphatic C-H Bending; 1337,1314,1238 C-N Stretching; 781,758 Aromatic C-H Bending.
4	Impurity-2	3424, N-H Stretching; 3060 Aromatic C-H Stretching; 2959,2928,2872 Aliphatic C-H Stretching; 1784 C=O Stretching; 1667,1605,1560 C=C/C=N Stretching; 1462,1411 Aliphatic C-H Bending; 1322,1298,1276,1234,1151,1109,1066,1050 C-N Stretching; 840,824,778,761 Aromatic C-H Bending.

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