

SYNTHESIS OF SCHIFF BASES DERIVED FROM 5-FORMYL ETHYLVANILLIN

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abstract: In the reaction between 5-formyl ethylvanillin and aromatic amines in equimolecular ratio, Schiff bases are formed with raised yields. By the Schiff bases formation, can be observed, that from the two carbonyl groups of the 5-formyl ethylvanillin molecule, the formyl group situated in the ortho position towards the hydroxyl group is more reactive. The synthesized Schiff bases were characterized by means of IR, ¹H-, and ¹³C-NMR spectra.

Introduction

Schiff bases are organic compounds with great utility in important fields as: medicine agriculture, cosmetic products [1÷11]. Some Schiff bases present anticancer [2], antitumor [3], antibacterial [4] activity; they play a prominent part in the enzymatic or unenzymatic transaminating reactions of the carbonyl compounds with amino acids [5]. In the coordinate chemistry field, a lot of Schiff bases operate as ligands [7,9]. Some of the Schiff bases complex combinations with metals are used as insecticides, fungicides, herbicides [10]. Can be remarked the large field of the biological action presented by the Schiff bases derived from aromatic 2-hydroxyaldehydes [11].

In order to obtain new compounds having practical importance, a series of Schiff bases derived from 5-formyl ethylvanillin were synthesized.

Experimental

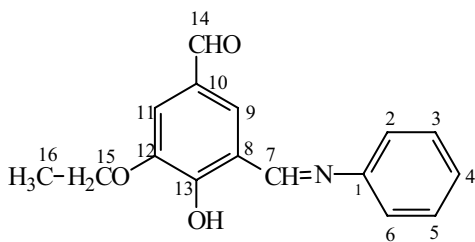
Melting points were determined in open capillary and are uncorrected. The IR spectra were recorded with a FTS 135-Biorad spectrophotometer, in KBr pellets. The NMR spectra were registered on Varian Gemini 300 and Varian EM360L NMR, 60 MHz. spectrometers, using CDCl₃ as solvent and TMS as internal standard. The purity of each compound was verified by TLC- silica gel plates (Merck). The elution was realized in the chloroform-methanol 9:1 (V/V). The spots visualization was done either with UV light ($\lambda = 254$ nm) or with iodine vapour.

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General procedure for the Schiff bases synthesis

0.01 moles of 5-formyl ethylvanillin were solved in 20 ml anhydrous ethanol, keeping warm conditions. To the room temperature cooled solution are added by dropping 0.01 moles aromatic amine solved in 20÷40 ml anhydrous ethanol, corresponding to the amine solubility. After 2 hours, the formed crystals are filtrated, washed with some methanol and dried. The reaction yields, the melting points and the recrystallization solvents for the obtained Schiff bases are presented in the Table 1.

N (3'-formyl-5'- ethoxy-6'-hydroxybenzyliden)aniline I



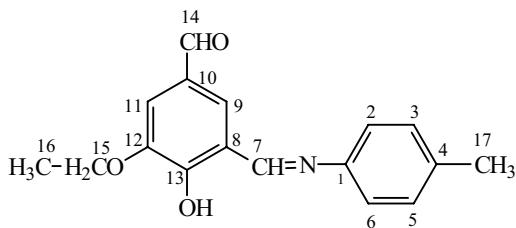
IR(CHCl₃):1663(ν C=O);1613(ν C=N),
1590,1482,1450 (benzene rings)
1293(ν C₂H₅-O-C aromatic);
1146(ν C-OH).

¹H-NMR(CDCl₃, 350 MHz, δ ppm, J, Hz): 1.54(t,6.9, 3H, H-16); 4.19(q, 6.9, 2H, H-15); 7.30-7.36(m,3H,H-2, H-4,H-6); 7.43(d, 1.8, 1H, H-11); 7.53(d, 1.8, 1H, H-9); 7.46(m, 2H, H-3, H-5); 8.70(s, 1H, H-7); 9.83(s, 1H, H-14).

¹³C-NMR(CDCl₃, 350 MHz, d, ppm): 14.66(CH₃, C-16); 64.60(C-15); 111.90(C-11); 117.51(Cq,C-8);120.84(C-2;C-6);127.66(Cq,C-10);127.79(C-4);129.72(C-3,C-5); 129.90(C-9); 145.48(C-11); 149.37(Cq, C-1); 160.56(C-7); 161.40(Cq, C-13); 189.96(C-14).

Anal. Calcd. for C₁₆H₁₅O₃N: N, 5.20; Found: N, 5.28

4-Methyl-N(3'- formyl-5'- ethoxy-6'-hydroxybenzyliden)aniline II



IR(CHCl₃,cm⁻¹):1663(ν C=O);
1610(ν C=N);1580,1474,1447
(benzene rings); 1293(ν C₂H₅-O-C
aromatic) 1154(ν C-OH)

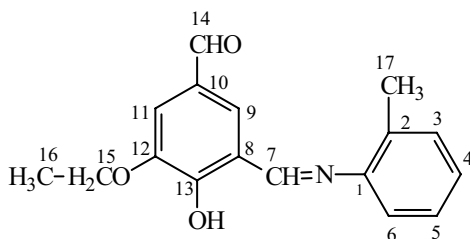
¹H-NMR(CDCl₃, 350 MHz, δ ppm, J, Hz): 1.53(t, 7.0, 3H, H-16); 2.40(s, 3H,H-17); 4.18(q, 7.0,2H, H-15); 7.23(d, 8.8, 2H, H-2, H-6); 7.26(d, 8.8, 2H, H-3, H-5); 7.41(d, 1.8, 1H, H-11); 7.51(d, 1.8, 1H, H-9); 8.69(s, 1H, H-7); 9.8(s, 1H, H-14).

¹³C-NMR(CDCl₃, 350 MHz, δ ppm): 14.61(CH₃, C-16); 21.06(C-17); 64.48(C-15); 111.49(C-11); 117.28(Cq, C-8); 120.54(C-2, C-6); 127.32(Cq, C-10); 130.01(C-9);

130.27(C-3, C-5); 137.99(Cq, C-4); 142.38(Cq, C-12); 149.45(Cq, C-1); 159.35(C-7); 161.19(Cq, C-13); 189.94(C-14).

Anal. Calcd. for $C_{17}H_{17}O_3N$: N, 4.94; Found: N, 5.07.

2-Methyl-N(3'-formyl-5'-ethoxy-6'-hydroxybenzyliden)aniline III

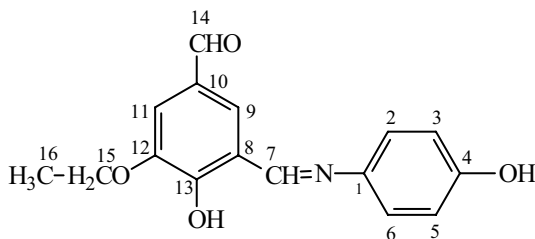


IR($CHCl_3$, cm^{-1}): 1663($\nu C=O$); 1610($\nu C=N$); 1590, 1478, 1443 (benzene rings); 1289(νC_2H_5-O-C aromatic); 1154($\nu C-OH$).

1H -NMR($CDCl_3$, 60 MHz, δ ppm, J, Hz): 1.53(t, 7.0, 3H, H-16); 3.5(s, 1H, H-17); 4.16(q, 7.0, 2H, H-15); 7.07-7.35(m, 6H, H-3-H-6, H-9, H-11); 8.61(s, 1H, H-7); 9.77(s, 1H, H-14).

Anal. Calcd. for $C_{17}H_{17}O_3N$: N, 4.94; Found: N, 5.11.

4-Hydroxy-N(3'-formyl-5'-ethoxy-6'-hydroxybenzyliden)aniline IV

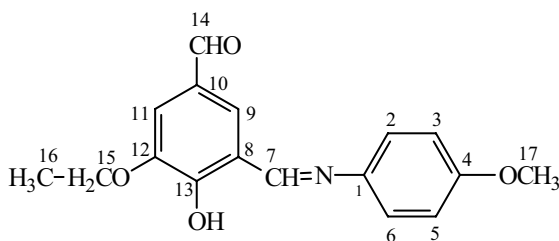


IR($CHCl_3$, cm^{-1}): 1671($\nu C=O$); 1612($\nu C=N$); 1590, 1480, 1443 (benzene rings); 1289(νC_2H_5-O-C aromatic); 1154($\nu C-OH$).

1H -NMR($DMSO-d_6$, 60 MHz, δ ppm, J, Hz): 1.52(t, 7.0, 3H, H-16); 4.17(q, 7.0, 2H, H-15); 7.08(dd, 9.0, 4H, H-2, H-3, H-5, H-6); 7.36(d, 1.8, 2H, H-9, H-11); 8.7(s, 1H, H-7); 9.81(s, 1H, H-14).

Anal. Calcd. for $C_{16}H_{15}O_4N$: N, 4.91; Found: N, 5.10

4-Methoxy-N(3'-formyl-5'-ethoxy-6'-hydroxybenzyliden)aniline V

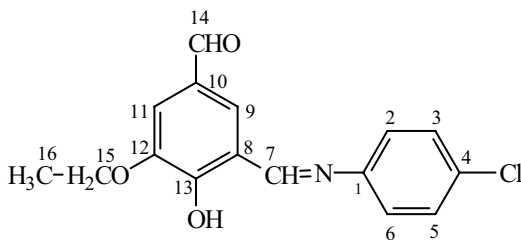


IR($CHCl_3$, cm^{-1}): 1675($\nu C=O$); 1617($\nu C=N$); 1587, 1480, 1447 (benzene rings); 1293(νC_2H_5-O-C aromatic); 1146($\nu C-OH$).

1H -NMR($CDCl_3$, 60 MHz, δ ppm, J, Hz): 1.53(t, 7.03, 3H, H-16); 3.5(s, 3H, H-17); 4.16(q, 7.03, 2H, H-15); 7.07(dd, 8.8, 4H, H-2, H-3, H-5, H-6); 7.35(d, 1.8, 2H, H-9, H-11); 8.61(s, H-7); 9.77(s, 1H, H-14).

Anal. Calcd. for $C_{17}H_{17}O_4N$: N, 4.68; Found: N, 4.81.

4-Chloro-N(3'-formyl-5'-ethoxy-6'-hydroxybenzyliden)aniline VI



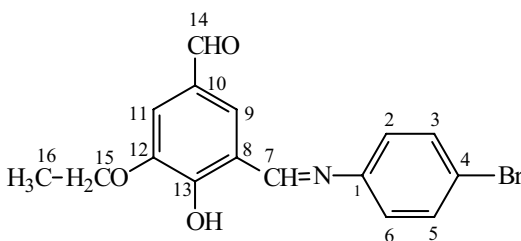
IR($CHCl_3$, cm^{-1}): 1667($\nu C=O$);
1617($\nu C=N$); 1580, 1482, 1443
(benzene rings); 1289(νC_2H_5-O-C
aromatic); 1146($\nu C-OH$).

1H -NMR($CDCl_3$, 350 MHz, δ
ppm, J, Hz): 1.53(t, 7.0, 3H, H-
16); 4.2(q, 7.01, 2H, H-15);
7.25(d, 8.8, 2H, H-3, H-5);
7.42(d, 8.8, 2H, H-2, H-6);
7.47(d, 1.8, H-11); 7.54(d, 1.8, H-
9); 8.69(s, 1H, H-7); 9.84(s, 1H,
H-14).

^{13}C -NMR($CDCl_3$, 350 MHz, δ ppm, J, Hz): 14.61(C-16); 64.76(C-15); 112.47(C-11);
117.80(Cq, C-8); 122.26(C-2, C-6); 128.05(Cq, C-10); 129.31(C-9); 129.77(C-3, C-5);
133.36(Cq, C-4); 144.83(Cq, C-1); 148.99(Cq, C-12); 158.75(Cq, C-13); 161.24(C-7);
189.90(C-14).

Anal. Calcd. for $C_{16}H_{14}O_3NCl$: N, 4.61; Found: N, 4.76.

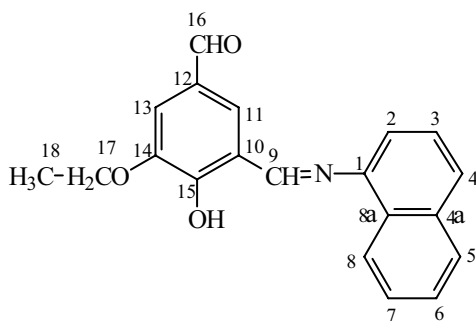
4-Bromo-N(3'-formyl-5'-ethoxy-6'-hydroxybenzyliden)aniline VII



IR($CHCl_3$, cm^{-1}): 1667($\nu C=O$);
1611($\nu C=N$); 1585, 1485, 1443
(benzene rings); 1293(νC_2H_5-O-C
aromatic); 1154($\nu C-OH$).

1H -NMR($CDCl_3$, 60 MHz, δ ppm,
J, Hz): 1.5(t, 6.8, 3H, H-16);
4.17(q, 6.8, 2H, H-15); 7.14(d,
8.0, 4H, H-2, H-3, H-5, H-
6); 7.47(m, 2H, H-9, H-11);
8.67(s, 1H, H-7); 9.8(s, 1H, H-14)

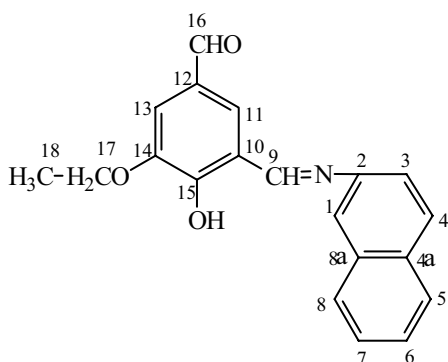
Anal. Calcd. for $C_{16}H_{14}O_3NBr$: N, 4.02; Found: N, 4.20

N-(3'-formyl-5'-ethoxy-6'-hydroxybenzyliden) α -naphthylamine VIII

IR(CHCl₃, cm⁻¹): 1678(ν C=O);
1610(ν C=N); 1600, 1570, 1470, 1430
(benzene and naphthalene rings);
1289(ν C₂H₅-O-Caromatic);
1157(ν C-OH).

¹H-NMR(CDCl₃, 60 MHz, δ ppm, J, Hz): 1.53(t, 6.0, 3H, H-18); 4.18(q, 6.0, 2H, H-17); 7.16-7.60(m, 4H, H-2, H-3, H-6, H-7); 7.68-7.92(m, 2H, H-11, H-13); 8.16-8.28(m, 3H, H-4, H-5, H-8); 8.61(s, 1H, H-9); 9.76(s, 1H, H-16).

Anal. Calcd. for C₂₀H₁₇O₃N: N, 4.38; Found: N, 4.51.

N-(3'-formyl-5'-ethoxy-6'-hydroxybenzyliden) β -naphthylamine IX

IR(CHCl₃, cm⁻¹): 1668(ν C=O);
1609(ν C=N); 1600, 1572, 1460, 1430
(benzene and naphthalene rings);
1293(ν C₂H₅-O-C aromatic);
1154(ν C-OH).

¹H-NMR(CDCl₃, 350 MHz, δ , ppm, J, Hz): 1.55(t, 7.1, 3H, H-18);
4.21(q, 7.1, 2H, H-17); 7.40-7.60(m, 2H, H-6, H-7); 7.71(d, 1.8, 1H, H-1);
7.12(d, 8.7 1H, H-4); 7.45(d, 1.7, H-13); 7.56(d, 1.7, 1H, H-11);
7.41(dd, 8.7, 1.8, H-3); 7.87(m, 2H, H-8, H-5); 8.70(s, 1H, H-9); 9.84(s, 1H, H-16)

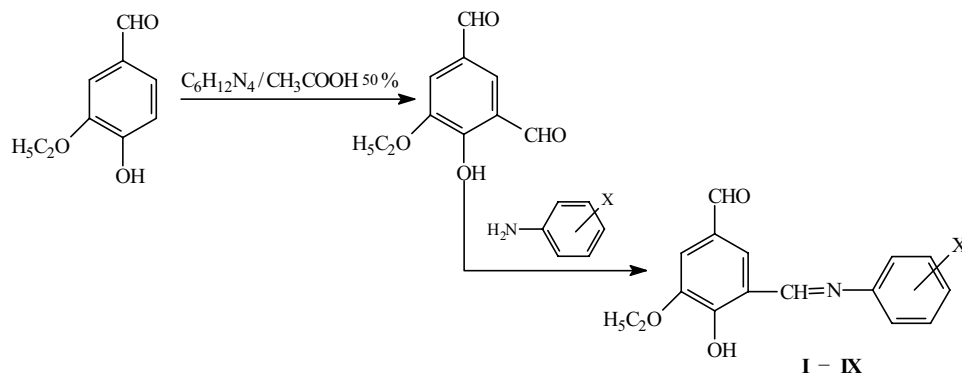
¹³C-NMR(CDCl₃, 350MHz, δ ppm.): 14.70(C-18); 64.71(C-17); 111.97(C-13); 117.69(Cq, C-10); 119.34(CH); 126.49(CH); 127.08(CH); 127.19(CH); 127.73(Cq, C-12); 127.86(CH); 127.9(Cq); 128.16(CH); 129.80(CH); 129.88(C-11); 132.64(Cq); 133.75(Cq); 142.91(Cq); 159.36(Cq); 160.48(C-9); 189.90(C-16).

Anal. Calcd. for C₂₀H₁₇O₃N: N, 4.38; Found: N, 4.56.

Results and Discussion

5-Formyl ethylvanillin (4-hydroxy-5-ethoxy-isophthalaldehyde) obtained by Duff reaction from ethylvanillin, hexamethylenetetramine in acid medium [12], was condensed with aromatic amines in order to obtain Schiff bases (Scheme 1).

The reaction of 5-formyl ethylvanillin with aromatic amines was realized in equimolecular ratio between the reagents.



where: **I**. X = H; **II**. X = p.CH₃; **III**. X = o.CH₃; **IV**. X = p.OH; **V**. X = p.OCH₃;
VI. X = p.Cl; **VII**. X = p.Br; **VIII**. X = α .C₁₀H₇; **IX**. X = β .C₁₀H₇

Scheme 1

When the Schiff bases are formed one can observe that from the two formyl groups of the 5-formyl ethylvanillin, more susceptible in the reaction is the CHO group, situated in the ortho position towards the hydroxyl group. The greater reactivity of the formyl group, explained by the possibility to form a chelate with the neighbouring OH group was also observed in the condensation reactions with bases containing nitrogen and with compounds containing "methylene active" groups [12].

In Table 1 the yields reaction and some of the characteristic constants regarding the synthesized Schiff bases are presented. The obtained compounds were characterized by IR and NMR spectra, and their purity was confirmed by thin layer chromatography (TLC) and elemental analysis.

By TLC can be observed that the Schiff bases **I-IX** spots are coloured. Nevertheless the spots visualization is carried out either with iodine, or in ultraviolet light and afterwards with 2,4-dinitrophenylhydrazine in order to verify the compounds purity. The synthesized Schiff bases R_f values are presented in Table 1.

In the IR spectra of the synthesized Schiff bases, characteristic is the ν CH=N stretching vibration, which appears as an intense band from 1605 to 1621 cm^{-1} . The infrared spectra of the Schiff bases, are observed bands corresponding to the structural elements characteristic for the 5-formyl ethylvanillin nucleus, namely; the stretching vibration band of the formyl group around 1663÷1678 cm^{-1} , the bands for the symmetrical and asymmetrical stretching vibration of the ethoxy group at about 2829÷2890 cm^{-1} and 2921÷2971 cm^{-1} , the ν C-OH stretching vibrations at 1146÷1157 cm^{-1} and at 3500÷3300 cm^{-1} . Besides these bands, appear also bands characteristic for the aromatic nucleus of the synthesized products (1600÷1580 cm^{-1} , 1480÷1470 cm^{-1} , 1453÷1440 cm^{-1}). In the range at 700÷1200 cm^{-1} are superposed a lot of vibrations characteristic both aromatic nucleus and ν Ar-N, δ CH from the azomethine group.

Table 1. Characteristic constants of Schiff bases I-IX

No.	Compound		Yield (%)	M.P. (°C) (solvent)	Cristal colour	T.L.C. R _f
	No.	M.W.				
1.	I	269.30	81.0	109-110 (toluene)	Red	0.74
2.	II	283.33	78.6	113-114 (ethanol)	Yellow	0.737
3.	III	283.33	67.90	107-108 (diethyl ether)	Yellow	0.77
4.	IV	285.30	94.04	213.5-214.5 (ethanol)	Red-orange	0.56
5.	V	299.33	92.35	99.5-100.5 (toluene)	Yellow	0.80
6.	VI	303.75	91.60	131-132.5 (ethanol)	Orange	0.70
7.	VII	348.20	89.67	134-135 (toluene)	Light red	0.71
8.	VIII	319.36	90.90	146-147 (ethanol)	Orange	0.75
9.	IX	319.36	87.77	148-149 (ethanol)	Orange	0.77

The IR absorptions values for each compound are presented in the experimental part. The IR spectra confirm the suggested structures.

The molecular structure confirmation of compounds **I-IX** was realized by the NMR spectra and the main signals are presented for the each compound in the experimental part.

The ¹H-NMR spectra of new compounds shows that the chemical shift for the CH=N group appear like a singlet at values between $\delta = 8.61\div 8.70$ ppm. There were emphasized signals as triplet for the methyl group protons ($\delta = 1.5\div 1.55$ ppm), as quartet for those from ethyl group ($\delta = 4.16\div 4.21$ ppm), as singlet for formyl group proton ($\delta = 9.77\div 9.84$ ppm). The aromatic protons from the two substituted benzene rings are found again in the region $\delta = 7.07\div 8.28$ ppm. Also, appear additional signals caused by the substituents from the aniline nucleus. For instance, for the Schiff bases **II** and **III** can be observed an additional singlet at $\delta = 2.40\div 2.43$ ppm, corresponding to the methyl group protons, and for the compound **V**, the singlet at $\delta = 3.5$ ppm corresponds to the methoxy group protons.

In ¹³C-NMR spectra, the chemical shifts for the carbon atoms of azomethine group are at $\delta = 159.35\div 161.24$ ppm, while the carbon atoms from the formyl groups absorbs at $\delta = 189.90\div 189.96$ ppm, and the carbon atoms involved in the bond with the hydroxyl group, adjacent to the azomethine group are found again at $\delta = 161.40\div 159.36$ ppm. The ¹³C-NMR spectra were only carried out for the Schiff bases **I**, **II**, **VI**, **IX** and the chemical shifts are presented in the experimental part.

The synthesized Schiff bases belong to a series of compounds, which follow to be tested as ligands in order to obtain coordination compounds with bivalent and trivalent metal ions.

Conclusions

5-Formyl ethylvanillin was condensed with aromatic amines in equimolecular ratio between the reagents, obtaining the corresponding Schiff bases with 68÷94% yields.

When the Schiff bases are formed, one can observe that from the two formyl groups from the 5-formyl ethylvanillin molecule, more susceptible in the reaction is the group situated in ortho position towards the hydroxyl group.

The structure of the new compounds was confirmed by analytical and spectroscopic methods (IR, ^1H and ^{13}C - NMR).

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