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Synthesis of Schiff Bases by Condensation of Hetarylcarboxaldehydes with *p*-Phenetidine [1]

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Summary. Treatment of quinolinecarboxaldehydes and their derivatives with *p*-ethoxyaniline yields in a one-step reaction a series of new Schiff bases in 47–73% yield. The products [quinoline-2-, 6-methylquinoline-2-, quinoline-4-, quinoline-8-, and acridine-9-N-(*p*-ethoxyphenyl)formimidoyl], have been fully characterized.

Keywords. *p*-Phenetidine; Quinolinecarboxaldehydes; Schiff bases.

Synthese von Schiffschen Basen durch Kondensation von Hetarylaldehyden mit *p*-Phenetidin

Zusammenfassung. Umsetzung von Chinolinaldehyden und deren Derivaten mit *p*-Ethoxyanilin liefert in einer Einstufenreaktion neue Schiffsche Basen in 47 – 73%iger Ausbeute. Alle Produkte [Chinolin-2-, 6-Methylchinolin-2-, Chinolin-4-, Chinolin-8- und Acridin-9-N-(*p*-ethoxyphenyl)formimidoyl] wurden voll charakterisiert.

Introduction

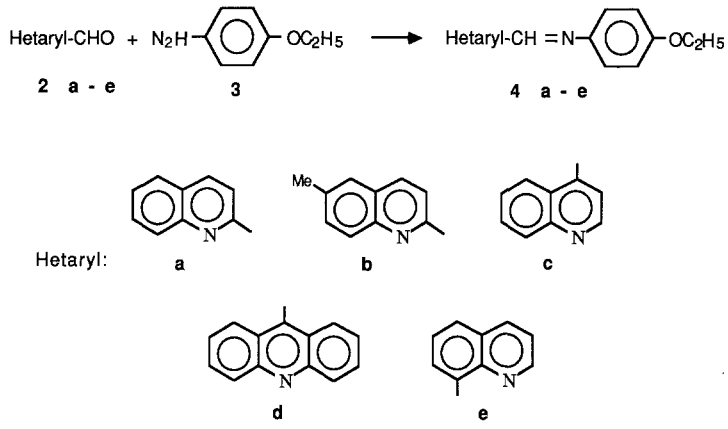
Schiff bases can occur as intermediates in many enzymatic reactions and are useful compounds in the preparation of plastics, pharmaceuticals and insecticides [2–7]. Furthermore, derivatives containing a hetaryl moiety have attracted much attention as potential anticancer agents and as active materials against the human immunodeficiency virus [8]. Most of the methods of preparation reported are based on the condensation of carbonyl compounds with primary amines with a large variety of solvents used. Besides, to our knowledges, not much has been mentioned in the literature using hetarylcarboxaldehydes for synthesis. We, however, as part of our program directed to the design of new compounds as medicinal and biological chemistry, had reported the preparation of some Schiff bases by condensation of hetarylcarboxaldehydes with *o*-aminophenol [9].

Results and Discussion

A simple one-step procedure was now developed using mild conditions for the formation of products **4a–e** from substrates **2a–e**.

A series of quinolinecarboxaldehyde as substrates were prepared using commercially available methylquinolines according to reported procedures by selenium dioxide oxidation [10–13]. All the starting materials prepared were sufficiently pure for further reactions and characterized by their IR-,

^{1}H-NMR-spectral data, and melting points (comparison with the reported literature values [10–15]).



In general, the rate-determining step of the formation of a Schiff base proceeds by the nucleophilic attack of an amine to the carbonyl carbon of the aldehyde function. For this reason, it would be expected that electronic and steric factors of the amine play a significant role in the reaction. Thus *p*-phenetidine (**3**) is the reagent of choice since it is bearing an electron-donating ethoxy substituent positioned *para* to the amino group and is therefore rendering the attack easier.

Absolute ethanol proved to be the most efficient solvent for the formation of products **4** in moderate yields (47–73%); the use of other solvents leads to mixtures with starting materials and lowers the yields of products. Besides, it was observed that the reactivities of substrates **2** are significantly heteroatom-dependent and increased by the presence of an electronegative nitrogen atom relatively near to the carbonyl group.

Table 1. Schiff bases **4a–e** Hetaryl-CH = N – C_6H_4-*p*-OC_2H_5

Compound no.	Yield [%]	Crystallized from [a]	M.p. [°C], crystals	Molecular formula
4a	73	Ethanol	104–105° Colorless plates	$C_{18}H_{16}N_2O$ (276.34)
4b	72	Ethanol	124–125° Pale brownish yellow	$C_{19}H_{18}N_2O$ (290.37)
4c	56	*n*-Hexane/*PE* (2/1)	106–107° Yellow rods	$C_{18}H_{16}N_2O$ (276.34)
4d	69	Benzene	180–181° Orange	$C_{22}H_{18}N_2O$ (326.40)
4e	47	*n*-Hexane/*PE* (2/1)	114–115° Yellow needles	$C_{18}H_{16}N_2O$ (276.34)

[a] *PE* = petroleum ether b.p. 40–60°C

Table 2. Spectral data and elemental analyses of compounds **4a–e**

Compound no.	IR (KBr) ν [cm^{-1}]	^{1}H-NMR ($CDCl_3/TMS_{int}$) δ [ppm]	MS *m/e* (M^+)	Analysis (%)		
				C found (calcd.)	H found (calcd.)	N found (calcd.)
4a	3100–3010, 3010–2840, 1620, 1582 and 1500, 1248, 1042	1.41–1.48 (t, $-CH_2CH_3$, 3H); 4.03–4.14 (q, $-CH_2CH_3$, 2H); 6.93–8.83 (m, *Ar*H and CH, 11H)	276	77.79 78.23	5.80 5.83	9.98 10.13
4b	3080–3000, 2990–2830, 1610, 1590 and 1500, 1225, 1050	1.40–1.47 (t, $-CH_2CH_3$, 3H); 2.58 (s, CH_3, 3H); 4.02–4.13 (q, $-CH_2CH_3$, 2H); 6.92–8.80 (m, *Ar*H and CH, 11H)	290	78.49 78.59	6.18 6.24	9.79 9.64
4c	3100–3020, 3000–2860, 1610, 1570 and 1505, 1248, 1050	1.42–1.49 (t, $-CH_2CH_3$, 3H); 4.04–4.15 (q, $-CH_2CH_3$, 2H); 6.96–9.17 (m, *Ar*H and CH, 11H)	276	78.15 78.23	5.70 5.83	10.08 10.13
4d	3080–3010, 3010–2850, 1620, 1500 and 1470, 1250, 1050	1.43–1.50 (t, $-CH_2CH_3$, 3H); 4.05–4.16 (q, CH_2CH_3, 2H); 7.00–9.63 (m, *Ar*H and CH, 13H)	326	80.84 80.95	5.45 5.55	8.67 8.58
4e	3080–3020, 3000–2840, 1620, 1605 and 1500, 1248, 1050	1.40–1.50 (t, $-CH_2CH_3$, 3H); 4.02–4.12 (q, $-CH_2CH_3$, 2H); 6.91–9.94 (m, *Ar*H and CH, 11H)	276	78.13 78.23	5.80 5.83	10.01 10.13

The structures assigned to the products **4a–e** are based upon microanalyses, IR, ^{1}H-NMR and MS. Results are summarized in Tables 1 and 2.

Experimental

Melting points are uncorrected and were determined in open capillaries with a Büchi 510 apparatus. ^{1}H-NMR spectra were determined with a Bruker AC-20 FT-NMR spectrometer. IR spectra were recorded on a Perkin-Elmer Model 983 infrared spectrophotometer and mass spectra on a Varian MAT 111 spectrometer at 70 eV. Elemental analyses were obtained from Karl-Franzens University Laboratories, Graz, Austria.

Preparation of Schiff Bases **4a–e**; *General Procedure*

The hetarylcarboxaldehyde (2.7 mmol) is dissolved in hot absolute ethanol (15 ml) and an equimolar amount of *p*-phenetidine, dissolved in a minimum volume of absolute ethanol, is added. By heating the resulting faintly yellow reaction mixture to reflux for a period of 5 hours, the color gradually turns deep yellow. After the reaction is over, the mixture is allowed to cool to room temperature. Most of the solvent is removed on a rotatory evaporator with gentle heating an the mixture is kept in a refrigerator. The deposited crystalline precipitate is suction collected, washed with a small amount of cold ethanol and air-dried. Examination of the reaction product against starting materials by thin-layer chromatography shows that it consisted of a single compound. Three further crystallizations of the crude product from appropriate solvent gives an analytical sample of Schiff base.

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