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ORGANIC SYNTHESIS AND INDUSTRIAL ORGANIC CHEMISTRY

Synthesis and Biological Activity of Schiff Bases Derived from Dehydroabietylamine and Benzaldehyde Derivatives

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Abstract—Previously unknown Schiff bases were prepared from dehydroabietylamine and substituted benzaldehydes. Their physicochemical properties were determined, and the bactericidal activity toward some microorganisms was evaluated.

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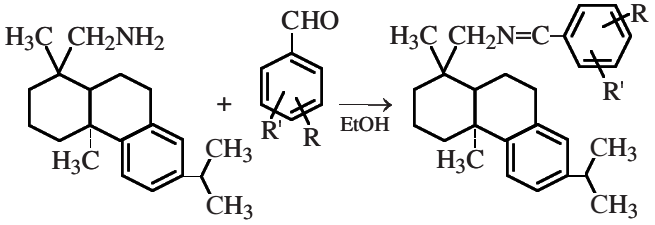
Schiff bases derived from primary amines and substituted benzaldehydes exhibit antibacterial, anticancer, and antitumor activity. Numerous studies have shown that such an activity of Schiff bases is caused by the presence of the >C=N– functional group. It is also known [1] that many amines derived from resin (diterpene) acids exhibit a wide spectrum of biological activity. In particular, Borglin has shown that dehydroabietylamine is an effective bactericidal and fungicidal agent [2]. It would be expected that Schiff bases derived from dehydroabietylamine will exhibit enhanced biological activity. However, data on the synthesis and properties of Schiff bases derived from dehydroabietylamine are lacking.

Here we report on the synthesis and biological activity of Schiff bases derived from dehydroabietylamine and substituted benzaldehydes. These Schiff bases were prepared in high yields (85–95%) by direct condensation in ethanol:



where R = R'= H (**a**); R = H, R' = *p*-OMe (**b**); R = H, R' = *p*-Cl (**c**); R = H, R' = *p*-F (**d**); R = H, R'= *o*-OH (**e**); R = *o*-OH, R' = *p*-NO_2 (**f**); R = *o*-OH, R' = *p*-Cl (**g**); R = *o*-OH, R' = *p*-OMe (**h**).

The rate of this reaction is fairly high. All the Schiff bases precipitate from the reaction mixture virtually immediately after the reactants solutions are mixed. They are insoluble in water and in ethanol at room temperature and soluble in dimethylformamide, chloroform, dimethyl sulfoxide, and some other solvents.

Table 1. Physicochemical properties of the Schiff bases

Compound	Empirical formula	Color	T_m, °C	Found, %			Calculated, %		
				C	H	N	C	H	N
a	$C_{27}H_{35}N$	White	104.5	86.22	9.49	3.61	86.86	9.39	3.75
b	$C_{28}H_{37}NO$	"	103.5	84.94	9.86	3.11	83.79	9.23	3.49
c	$C_{27}H_{34}NCl$	"	118.6	79.54	8.28	3.25	79.50	8.34	3.44
d	$C_{27}H_{34}NF$	"	106.5	82.78	9.40	3.19	82.86	8.69	3.58
e	$C_{27}H_{35}NO$	Yellow	153.2	82.84	9.51	3.75	82.86	8.95	3.58
f	$C_{27}H_{34}N_2O_3$	"	187.5	74.39	8.36	6.44	75.34	7.91	6.51
g	$C_{27}H_{34}NOCl$	"	177.8	76.11	8.50	3.17	75.96	7.97	3.28
h	$C_{28}H_{37}NO_2$	Red	105.2	79.84	9.23	3.36	79.43	8.75	3.31

The physicochemical parameters of the azomethines prepared are listed in Table 1.

The structures of the compounds were confirmed by IR and ^{1}H NMR spectroscopy (Table 2). The IR spectra of all the compounds contain a strong absorption band of the >C=N– group at 1660–1610 cm^{-1}. Its position only slightly depends on the structure of the compound and on substituents in the phenyl ring of the benzaldehyde moiety. The spectra of **e**–**h** also contrain a well-defined band of OH stretching vibrations at 3460–3410 cm^{-1}. In the spectra of the other compounds, this band is absent.

In the ^{1}H NMR spectra, the –N=C–H signal is observed at 8.2–8.4 ppm, and the OH signal, at 13.6–15.0 ppm.

The bactericidal activity of the compounds was studied with test cultures of *E. Coli*, *B. Subtilis*, and *S. Aureus*. The activity was evaluated by the diameter of the inhibition zone (cm) arising 48 h after introducing into the cultural medium 2×10^{-6} g ml^{-1}

Table 2. Spectroscopic characteristics of the Schiff bases

Compound	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm
a	2931, 1644, 1040, 832	8.265 (1H, N=C*H*–); 7.765, 7.423, 7.2204, 7.024, 6.906 (8H, C=C*H*–); 3.536 (1H, N–CH_2–); 2.879 [1H, –C*H*(CH_3)$_2$]; 2.858, 2.303, 1.967, 1.794, 1.579 (10H, –CH_2–); 1.485 (1H, >C*H*–); 1.271, 1.258, 1.084 (9H, –CH_3)
b	2938, 1645, 1086, 823	8.224 (1H, N=C*H*–); 7.692, 7.391, 7.223, 7.032, 6.910 (7H, C=C*H*–); 3.527 (1H, N–CH_2–); 2.898 [1H, –C*H*(CH_3)$_2$]; 2.851, 2.319, 1.939, 1.790, 1.528 (10H, –CH_2–); 1.439 (1H, >C*H*–); 1.272, 1.265, 1.008 (9H, –CH_3)
c	2944, 1645, 1036, 825	8.207 (1H, N–CH_2–); 7.725, 7.246, 7.225, 7.026, 6.938 (7H, C=C*H*–); 3.884 (1H, N–CH_2–); 3.868 (3H, –OCH_3); 3.541 [1H, –C*H*(CH_3)$_2$]; 3.389, 2.902, 2.367, 1.743, 1.715 (10H, –CH_2–); 1.498 (1H, >C*H*–); 1.475, 1.298, 1.086 (9H, –CH_3)
d	2941, 1650, 1229, 831	8.249 (1H, N–CH_2–); 7.763, 7.282, 7.227, 7.091, 6.934 (7H, C=C*H*–); 3.547 (1H, N–CH_2–); 2.919 [1H, –C*H*(CH_3)$_2$]; 2.879, 2.315, 1.847, 1.724, 1.456 (10H, –CH_2–); 1.456 (1H, >C*H*–); 1.309, 1.281, 1.092 (9H, –CH_3)
e	3442, 2937, 1628, 1153, 759	13.619 (1H, –OH); 8.336 (1H, N–CH_2–); 7.349, 7.300, 7.209, 7.023, 6.879 (6H, C=C*H*–); 3.530 (1H, N–CH_2–); 2.864 [1H, –C*H*(CH_3)$_2$]; 2.313, 1.837, 1.806, 1.585, 1.503 (10H, –CH_2–); 1.412 (1H, >C*H*–); 1.281, 1.243, 1.079 (9H, –CH_3)
f	3423, 2935, 1618, 1330, 1098	14.982 (1H, –OH); 8.342 (1H, N–CH_2–); 7.282, 7.204, 7.031, 6.979, 6.914 (6H, C=C*H*–); 3.523 (1H, N–CH_2–); 2.843 [1H, –C*H*(CH_3)$_2$]; 2.325, 1.877, 1.854, 1.565, 1.421 (10H, –CH_2–); 1.410 (1H, >C*H*–); 1.279, 1.234, 1.099 (9H, –CH_3)
g	3459, 2935, 1639, 1991, 826	13.572 (1H, –OH); 8.268 (1H, N–CH_2–); 7.283, 7.234, 7.024, 7.004, 6.904 (6H, C=C*H*–); 3.538 (1H, N–CH_2–); 2.861 [1H, –C*H*(CH_3)$_2$]; 2.333, 1.835, 1.807, 1.579, 1.435 (10H, –CH_2–); 1.402 (1H, >C*H*–); 1.274, 1.257, 1.073 (9H, –CH_3)
h	3452, 2934, 1629, 1076, 832	14.167 (1H, –OH); 8.369 (1H, N–CH_2–); 7.282, 7.172, 7.011, 6.943, 6.799 (6H, C=C*H*–); 3.913 (3H, –OCH_3); 3.549 (1H, N–CH_2–); 2.842 [1H, –C*H*(CH_3)$_2$]; 2.308, 1.802, 1.630, 1.500, 1.448 (10H, –CH_2–); 1.414 (1H, >C*H*–); 1.273, 1.243, 1.073 (9H, –CH_3)

Table 3. Bactericidal activity of Schiff bases

Bacteria	Diameter of the inhibition zone, cm, for indicated compound							
	a	**b**	**c**	**d**	**e**	**f**	**g**	**h**
S. Aureus	1.05	0.95	1.20	1.65	0.90	1.25	1.10	1.10
B. Subtilis	0.95	1.20	1.72	1.32	0.85	0.90	1.20	0.90
E. Coli	1.15	1.01	1.12	0.90	0.90	0.80	0.85	0.92

solutions of the Schiff bases in dimethylformamide (Table 3).

All the compounds prepared exhibit bactericidal activity. Compound **c** derived from Cl-substituted benzaldehyde is the most active toward *B. Subtilis* (diameter of inhibition zone 1.72 cm), and compound **d** derived from fluorinated benzaldehyde, toward *S. Aureus* (diameter of inhibition zone 1.65 cm). It should be noted that the most active agent toward *E. Coli* is compound **a** derived from unsubstituted benzaldehyde (diameter of inhibition zone 1.15 cm); introduction of substituents into the benzaldehyde moiety does not enhance the bactericidal activity of the Schiff base.

Thus, introduction of substituents into the phenyl ring of the benzaldehyde moiety appreciably affects the bactericidal activity of Schiff bases. However, this effect is ambiguous and depends on numerous factors, primarily on the structure of the molecule, presence and nature of substituents in the dehydroabietylamine and benzaldehyde moieties, and particular microorganism.

EXPERIMENTAL

All the chemicals used for preparing Schiff bases (dehydroabietylamine; benzaldehyde and its derivatives) were of chemically pure or analytically pure grade and were used without additional purification.

Elemental analysis was performed with an RE-2400CHN device. The IR spectra were recorded on a Bio-Rad FTS-185 IR spectrophotometer using KBr cells. The ^{1}H NMR spectra were measured on a DPX-300 Bruker Avance 300 spectrometer (solvent $CDCl_3$, reference TMS). The melting points were determined with an XT-5 device.

Syntheses were performed in a vessel equipped with a stirrer, reflux condenser, and dosing unit. The vessel was charged with a solution of 10 mmol of dehydroabietylamine in 200 ml of ethanol, after which a solution of 10 mmol of benzaldehyde or its derivative in 100 ml of ethanol was slowly added from the dosing unit. The mixture was stirred for 3 h at 20°C. The crystals of the Schiff bases were filtered off, recrystallized three times from ethanol, and dried in a vacuum.

The bactericidal activity of each of the Schiff bases synthesized was evaluated by measuring the diameter of the inhibition zone [3, 4]. For this purpose, 0.5 ml of a suspension of spores of each test culture was added to a sterile agarized cultural medium just before its solidification, after which the mixture was poured into sterile Petri dishes (9 cm in diameter) and allowed to solidify. Solutions of the Schiff bases in dimethylformamide (2×10^{-6} g ml^{-1}) were prepared. Then sterile disks made of filter paper (7 mm in diameter) were wetted in a solution of appropriate Schiff base and placed into the Petri dishes. The Petri dishes were kept at 35°C for 48 h, after which the inhibition zones of bacterial growth were revealed and the diameter of each zone was measured. Three replicate experiments were performed with each Schiff base.

CONCLUSION

The Schiff bases synthesized from abietylamine and substituted benzaldehydes exhibit noticeable bactericidal activity toward certain microorganisms. The correlation between the molecular structure and biological activity is ambiguous.

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