

Communication

Novel Schiff Bases of C-Methylresorcinarene Derivatives

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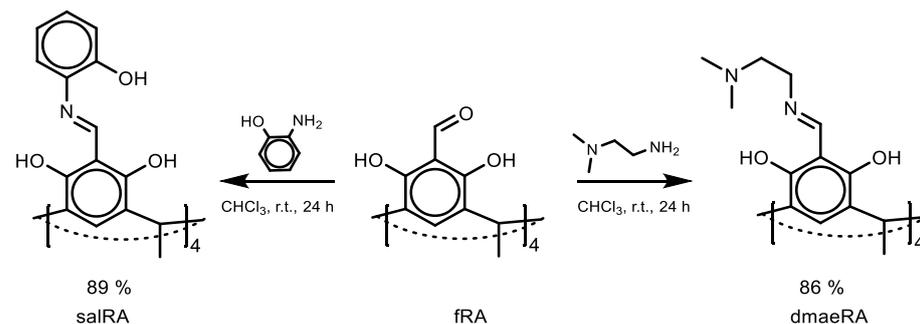
Abstract: The article presents the synthesis and properties of two new Schiff bases of resorcinarene derivatives. The Schiff bases were obtained by the reaction of formylresorcinarene with aromatic (*o*-aminophenol) and aliphatic (*N,N*-dimethyldiaminoethane) amines in chloroform. The synthesized Schiff bases exist in equilibrium of several tautomers, as evident from the IR, UV, NMR spectra and cyclic voltammetry data analysis. In DMF, methanol, and acetonitrile, the tautomeric equilibrium is shifted toward the enol-imine tautomers.

Keywords: schiff base; salicylimine; salen; aminoethylimine; resorcinarene; imine; tautomerism; cyclic voltamperometry

1. Introduction

Schiff bases are a well-known class of organic compounds. They are often used as intermediate and basic components to produce chemicals and new products in industry [1]. Schiff bases exhibit pharmacological properties (antimicrobial, antiviral, antituberculosis, and anticancer activities) and, therefore, they are common in drug development for medicine [2–4]. The Schiff bases conjugated to resorcinarene platforms are of greater interest because they combine the properties of both the azomethine groups and the macrocyclic cavity [5–8]. By organizing four azomethine groups, the resorcinarene platform enhances their ability to form complexes through a synergistic effect [9]. The Schiff bases of resorcinarene derivatives can function as sensors and containers by binding metal ions [10–13]. Furthermore, a wide spectrum of optical, electromagnetic, catalytic, and pharmacological properties is displayed by the complexes that are created during binding [14–16].

In this article we report on two new Schiff bases that are produced by reacting primary aromatic (*o*-aminophenol) and aliphatic (*N,N*-dimethyldiaminoethane) amines with the formyl derivative of resorcinarene (fRA, Scheme 1). The structure of the obtained compounds was investigated, and their tautomerism was evaluated by IR, NMR, and UV spectroscopy as well as cyclic voltammetry (CV).



Scheme 1. Synthesis of salRA and dmaeRA.



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2. Results

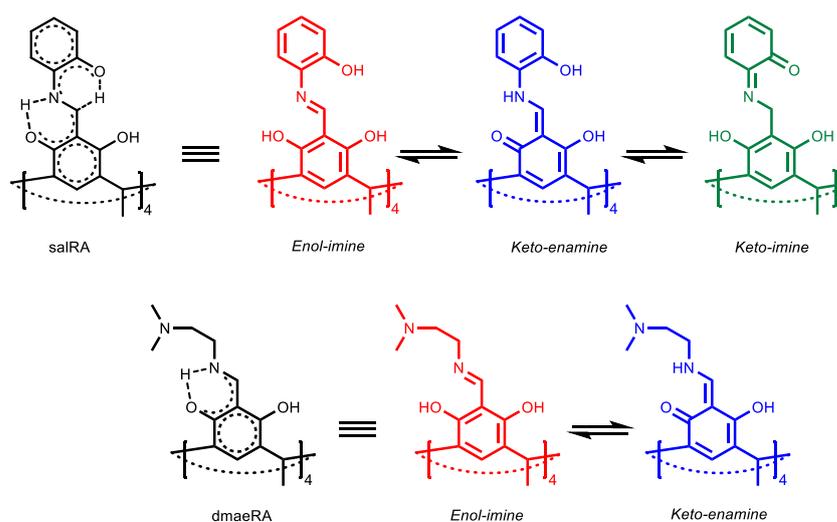
Formylresorcinarene (fRA) was obtained by the Duff reaction of resorcinarene with urotropine as described in [17]. The reaction was carried out in trifluoroacetic acid (TFA) at 120 °C for 1 h under microwave radiation, then diluted with 1 M hydrochloric acid and stirred vigorously at room temperature for 24 h. The resulting product was purified by repeated washing with water and dried. The yield was 53%.

The condensation of fRA with *o*-aminophenol and *N,N*-dimethyldiaminoethane gave two new Schiff bases (salRA and dmaeRA, respectively: Scheme 1). The reaction was carried out in chloroform at room temperature for 24 h. After completion, the products were filtered and washed several times with chloroform. The yield was 89% and 86% for salRA and dmaeRA, respectively.

In the ^{13}C NMR spectrum of salRA, the carbon signal of azomethine appears at 153.98 ppm. In the range of 160–105 ppm, the signals of resorcinarene and phenol rings are fixed (Figure S1 in Supplementary Materials (SM)). In the ^1H NMR spectrum of salRA, a peak of the azomethine group occurs at 8.30 ppm, while a signal of a proton intramolecularly bonded between the nitrogen and oxygen atoms NHO appears at 10.50 ppm. A signal of an intramolecularly bound proton between the hydroxyl groups of resorcinarene OHO is observed at 10.17 ppm, while a proton signal of the hydroxyl group of the phenol ring is at 9.05 ppm (Figure S1 in SM). All proton signals are strongly broadened, which is associated with tautomerism. However, the spectra only show one set of signals, which suggests a fast tautomeric exchange [18,19].

A similar picture is observed for dmaeRA (Figure S2 in SM). The azomethine proton is detected in the ^1H NMR spectrum at 8.5 ppm, whereas the intramolecularly bound hydrogens of the OH and NH groups are detected at 12.5 and 13.6 ppm. The carbon signal of imine groups appears at 162 ppm in the ^{13}C NMR spectrum, together with the signals of resorcinarene and dimethyldiaminoethane moieties.

SalRA and dmaeRA exist in equilibrium in several tautomeric forms [20–22], the structures of which are presented in Scheme 2. The presence of vibration stretching bands of both C=N bonds (1628 cm^{-1} and 1635 cm^{-1} for salRA and dmaeRA, respectively) and C=O bonds (1672 cm^{-1} and 1674 cm^{-1} for salRA and dmaeRA, respectively) in IR spectra in potassium bromide pellets indicates the formation of both imine- and keto-isomers (Figure 1a,b and Figures S3 and S4 in SM) [23].



Scheme 2. Tautomers of salRA and dmaeRA.

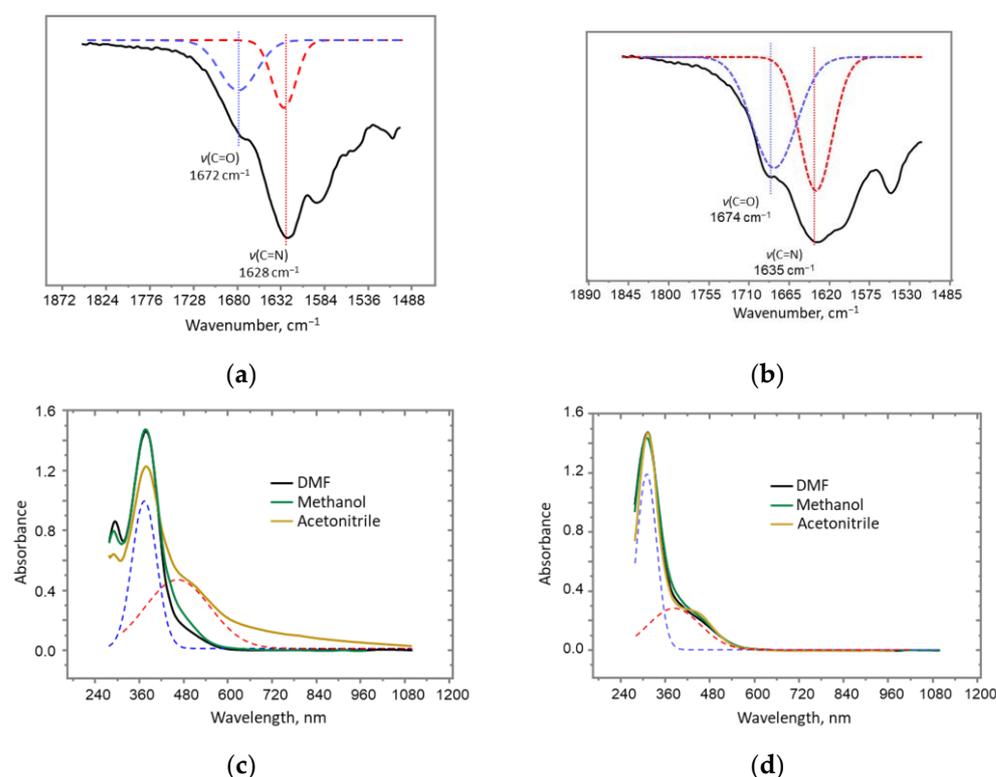


Figure 1. (a,b) Fragments IR spectra of (a) salRA and (b) dmaeRA; (c,d) UV spectra of (c) salRA and (d) dmaeRA in DMF, methane and acetonitrile (dotted line indicates bands for imine- (blue) and keto-groups (red)), $C = 0.04$ mM.

The UV spectra of salRA and dmaeRA were studied in the aprotic polar solvents DMF and acetonitrile, as well as in the protic solvent methanol (Figure 1c,d). The UV spectra of all Schiff base solutions show two absorption bands in the 300–500 nm range, which are related to π - π^* transitions of the imine- and keto-tautomers [24,25]. For dmaeRA, the absorption band related to the transition of conjugated imine occurs at 330 nm. The band of the keto-enamine tautomer is apparent as a small shoulder at 420 nm, and its optical density is solvent-independent. The conjugation of resorcinolic, phenolic, and azomethynic moieties causes a bathochromic shift of bands in the UV spectra of aromatic salRA (Figure 1c). The band of conjugated imines appears at 375 nm, while the shoulder of ketone moieties occurs at 460 nm. In acetonitrile, an increase in shoulder absorption is observed.

It can be concluded from UV studies that the tautomeric equilibrium in solutions of both Schiff bases is shifted towards the enol-imine tautomers. However, for salRA in acetonitrile, an increase in the proportion of keto tautomers is also detected.

The cyclic voltammetry (CV) of dmaeRA reveals two reduction peaks (C_1 and C_2) at -1.34 V and -1.83 V, respectively, attributed to the reduction of imine- and keto-groups of enol-imine and keto-enamine tautomers (Figure 2a, Scheme 2). Both peaks were irreversible due to proton transfer from hydroxyl groups to nitrogen and oxygen atoms during the reduction.

A more complex picture is observed for salRA (Figure 2a). In this case, four reduction peaks are recorded on the CV. At -2.45 V and -1.99 V (peaks C_4 and C_3 , respectively) irreversible reduction of the imine of the enol-imine tautomer and the quinone of the keto-enamine tautomer occurs (Scheme 2). At potentials of -1.43 V and -1.65 V (peaks C_2 and C_1), the imine and quinone groups of the keto-imine tautomer are reduced (Figure 2b, Scheme 2). These peaks are reversible, and the reverse scan shows two peaks at 0.30 and 0.62 V from the reoxidation of the reduced *o*-aminophenol fragments.

Thus, the results of the CV study showed that the obtained Schiff bases exist in equilibrium in several tautomeric forms, caused by the intramolecular movement of protons from hydroxyl groups to azomethines and by the conjugation of resorcinols with azomethine and with aminophenols in the case of salRA. As a result, each tautomer is reduced at a distinct potential, as is evident from the multistage reduction in the CV curves. Such features make compounds promising for the creation of “smart materials”.

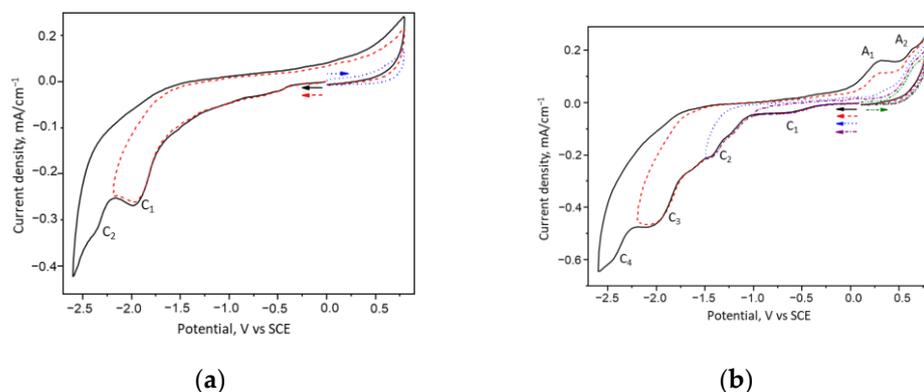


Figure 2. CV curves of (a) dmaeRA and (b) salRA in DMF/0.1 M Bu₄NCl, C = 1 mM, ν = 0.1 V/s.

3. Materials and Methods

General. NMR spectra were recorded on a Bruker Avance 600 MHz spectrometer. IR spectra were recorded using a Vector-27 FTIR spectrometer (Bruker, Ettlingen, Germany) in the 400–4000 cm⁻¹ range. The samples were prepared as KBr pellets. UV/Vis spectra were recorded with a PerkinElmer Lambda 25 UV/Vis spectrometer. A cuvette with an optical path length of 1 cm was used in all experiments. The elemental analysis was carried out on a CHNS analyzer Vario Macro cube (Elementar Analysensysteme GmbH, Langensfeld, Germany). The samples were weighed on Sartorius Cubis II (Sartorius AG, Göttingen, Germany) microbalance in tin capsules. VarioMacro Software V4.0.11 was used to perform quantitative measurements and evaluate the data received.

Cyclic voltammograms were recorded using a P-305 potentiostat (without IR compensation) at a potential scan rate of 100 mV/s in an argon (99.9999%) atmosphere. The stationary potential or the preliminary keeping potential was set as the initial one. A GC disk electrode (dia. 2.0 mm) sealed into a glass tube was used as the working electrode. Prior to each measurement, the electrode was mechanically polished. A platinum wire was used as the auxiliary electrode. Potentials were measured versus SCE connected to the solution being studied through a bridge containing the supporting electrolyte and having a potential of -0.41 V relative to formal potential E_0' Fc^{+/0} (internal standard). The temperature was 295 K. Commercial Bu₄NCl salt (Sigma-Aldrich, St. Louis, MO, USA) and DMF solvent (Acros Organics, Waltham, MA, USA) were used without additional purification.

Formylresorcinarene (fRA) was synthesized as described in [17].

Synthesis of salRA. A 65.6 mg (0.1 mmol) quantity of formylresorcinarene, and 43.6 mg (0.4 mmol) of *o*-aminophenol, were placed in a 10 mL vial, and 5 mL of chloroform was added. The mixture was stirred for 24 h at room temperature. The precipitate was separated by centrifugation, washed with chloroform and dried under reduced pressure. Yield: 91 mg (89%). Decomp.p. is 240 °C. The IR spectrum (KBr, ν , cm⁻¹) was: 2966 (C–H), 1672 (C=O), 1628 (C=N), 1459 (C–C). The ¹H NMR spectrum (DMSO-*d*₆, ppm) was: 1.76 (*d*, *J* = 7.5 Hz, 12H, CH₃), 4.64 (*qtr*, *J* = 7.4 Hz, 4H, CH), 6.86, 6.97, 7.11 (*m*, 12H, H_{ar}), 7.59 (*d*, *J* = 8.2 Hz, 4H, H_{ar}), 7.78 (*s*, 4H, H_{ar}), 8.32 (*s*, 4H, CH–N), 9.06 (*s*, 4H, O–H), 10.16 (*s*, 4H, O–H), 10.50 (*s*, 4H, N–H–O). The ¹³C NMR spectrum (DMSO-*d*₆, ppm) was: 18.6, 27.8, 107.8, 116.5, 118.6, 120.6, 124.9, 127.7, 128.6, 133.0, 149.3, 154.0. The anal. calcd. which was for C₆₀H₅₂N₄O₁₂ (%) yielded: C, 70.58; H, 5.13; N, 5.49. The amounts that were found (%) were: C, 70.20; H, 5.61; N, 5.32.

Synthesis of dmaeRA. It was synthesized similarly to salRA with the use of 0.5 g (0.76 mmol) of fRA, 0.333 mL (3 mmol) of *N,N*-dimethylethane-1,2-diamine and 15 mL of chloroform. Yield: 0.61 g (86%). Decomp.p. 220 °C. The IR spectrum (KBr, ν , cm^{-1}) was: 2964 (C–H), 1674 (C=O), 1634 (C=N), 1672 (C=O), 1457 (C–C). The ^1H NMR spectrum (DMSO- d_6 , ppm) was: 1.66 (*d*, $J = 7.5$ Hz, 12H, CH_3), 2.19 (*s*, 24H, CH_3), 2.50 (*m*, 8H, CH_2), 3.68 (*m*, 8H, CH_2), 4.48 (*qtr*, $J = 7.6$ Hz, 4H, CH), 7.57 (*s*, 4H, H_{ar}), 8.57 (*s*, 4H, CH–N), 12.31 (*s*, 4H, O–H), 13.68 (*s*, 4H, NHO). The ^{13}C NMR spectrum (DMSO- d_6 , ppm) was: 18.4, 27.8, 45.6, 48.2, 58.9, 106.4, 119.0, 132.0, 161.7, 163.0. The anal. calcd. which was for $\text{C}_{52}\text{H}_{72}\text{N}_8\text{O}_8$ (%) yielded: C, 66.54; H, 7.74; N, 11.96. The amounts that were found (%) were: C, 66.35; H, 7.27; N, 11.87.

4. Conclusions

The two Schiff base derivatives of resorcinarene (salRA and dmaeRA) were produced via condensation of formylresorcinarene with *o*-aminophenol and *N,N*-dimethyldiaminoethane, respectively. The resulting Schiff bases have two (in the case of dmaeRA) or three (in the case of salRA) tautomers in equilibrium. The cyclic voltammetry data show that each tautomer is reduced at a defined potential, which is encouraging for the development of materials with particular functionality.

Supplementary Materials: The following supporting information can be downloaded online. Figure S1. ^1H and ^{13}C NMR spectra of salRA in DMSO- d_6 ; Figure S2. ^1H and ^{13}C NMR spectra of dmaeRA in DMSO- d_6 ; Figure S3. IR spectrum of salRA; Figure S4. IR spectrum of dmaeRA.

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Conflicts of Interest: There are no conflicts to declare.

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