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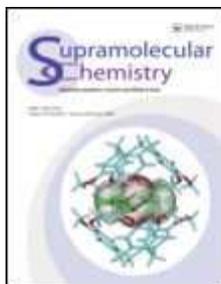
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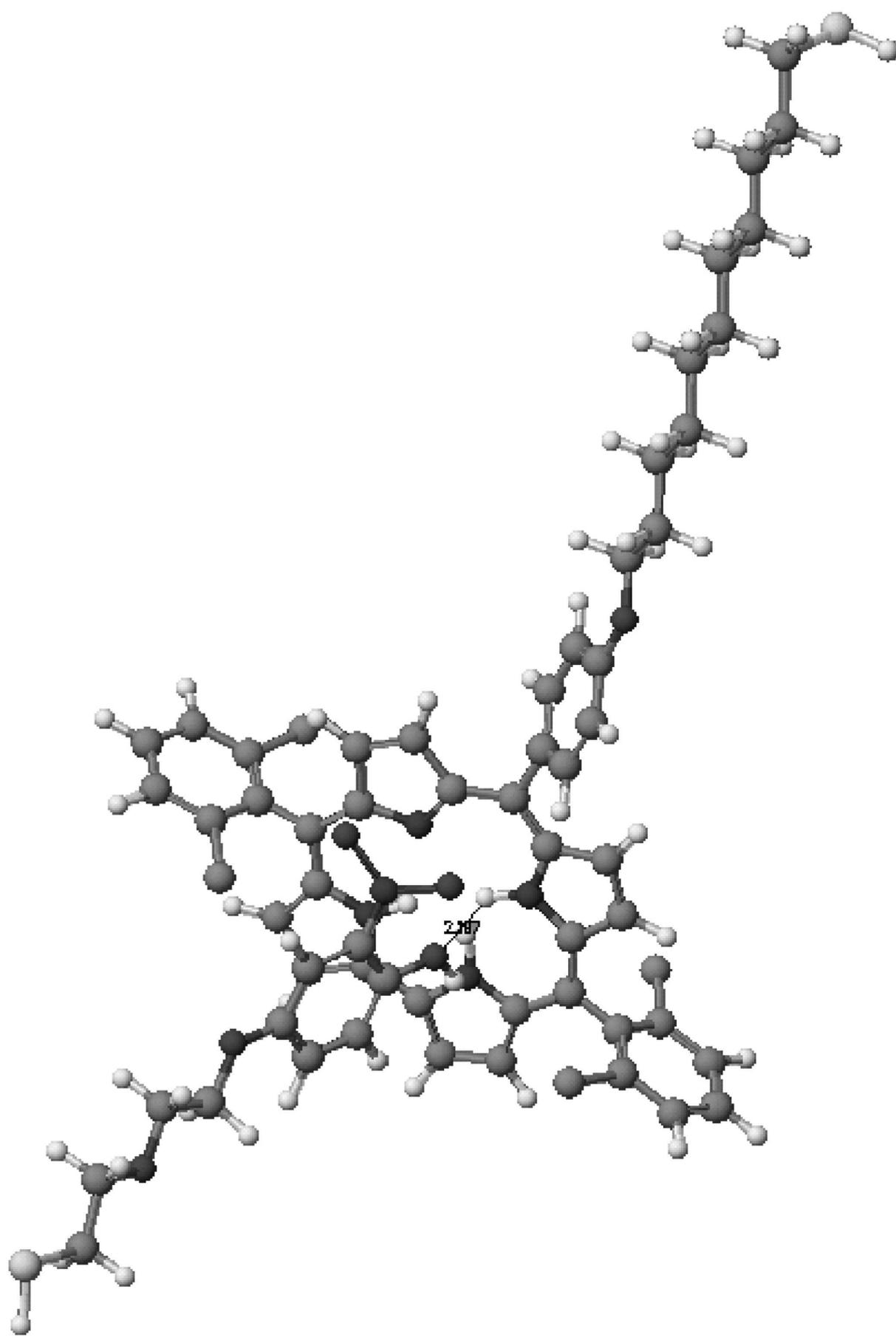
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Determination of Interaction Strength between Corrole and Phenol Derivatives in Aqueous Media Using Atomic Force Microscopy

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3 **Determination of Interaction Strength between Corrole and Phenol Derivatives in**
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5 **Aqueous Media Using Atomic Force Microscopy**
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Abstract

Atomic force microscopy (AFM) was used to measure single interaction forces between corrole (host) and phenol derivatives (guests) in aqueous media. A gold tip was modified with thiol derivatives of corrole via the Au-S covalent bond. Such a tip was used to measure adhesion forces with a planar gold substrate modified with thiol-derivatives of phenol and *ortho*-nitrophenol in aqueous solutions. The mean force between the corrole and *ortho*-nitrophenol was higher than that between corrole and phenol, probably reflecting stronger hydrogen bond interaction in the former complex. In the presence of supporting electrolyte (0.1 M K₂SO₄), the mean force increased, suggesting that electrostatic and π - π interactions play an essential role in the adhesion force. In addition, adhesion force measured at pH 6.0 was larger than that at pH 10, reflecting the electrostatic repulsion at the higher pH. These behaviors are consistent with the potentiometric responses of a liquid membrane based on corrole to phenolic compounds. Also, the values of forces for interaction between corrole – phenol derivatives showed the same tendency as energy calculated for these complexes. The Poisson method was used for the calculation of the single force of the chemical bond between the corrole host and the phenolic guests.

Keywords: atomic force microscopy, molecular recognition, corrole, phenol derivatives, aqueous media

INTRODUCTION

The exploring of the mechanism of the host – guest recognition at the molecular level is a valuable source of inspiration for researchers dealing with sensors which are working by mimicking physiological processes occurring with outstanding sensitivity and selectivity. The source of the intensive development of the above study is a new research field, nanoscience,

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3 which deals with the objects as small as 1 – 100 nm [1-2]. Images of surfaces at such an
4 extremely small scale, down to resolving individual atoms or molecules, can be obtained by
5 newly developed technologies, namely scanning tunneling microscopy (STM) and atomic
6 force microscopy (AFM) [3 - 9]. The introduction of chemically tailored STM tips by
7 Umezawa and co-workers dramatically improved the sensitivity of visualization of molecular
8 recognition processes at the membrane/solid interfaces [10-18]. The chemical modification of
9 STM tips [10-18] as well as AFM tips [19, 20] increases the chemical affinity between the
10 imaging tip and the substrates through formation of hydrogen bonds, metal – coordination –
11 bonds and charge – transfer interactions. This remarkable cutting-edge technique has opened
12 the possibility to explore the host –guest interactions at the molecular level between
13 nucleobases [18], drug – enzyme [21], antigen - antibody [22, 23], and other biomolecules
14 [24,25], just to name a few.

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The main objective of the research presented is showing the applicability of the AFM method together with chemically tailored tips for the exploring of the molecular recognition processes between corroles and phenol derivatives occurring at the solid /aqueous interface. It has been already discovered by the potentiometric method that liquid membrane electrodes incorporating macrocyclic polyamines [26-29], calix[4]pyrroles [30-33] or corroles [34-35] upon stimulation with undissociated phenol derivatives generated potentiometric responses. The mechanism of this unusual phenomenon, generation of potentiometric signals by neutral molecules, relies on the transport of protons from the interface to the aqueous layer adjacent to the organic phase.

The host molecule being the subject of this study is corrole. This molecule belongs to the tetrapyrrolic macrocyclic compounds with 18 π electrons. Corroles contain one direct linkage between two adjacent pyrrole rings. They display unusually high N-H acidity relative to other related macrocycles [36].

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3 In this paper we present a study on the interaction forces between corrole and phenol
4 derivatives immobilized through Au-S bonds on a gold AFM tip and a gold substrate surface,
5 respectively. The influence of the pH and the composition of aqueous solution on the strength
6 of these interactions was also explored. These experiments have addressed to determination of
7 type of forces between corrole host and phenolic guests, measured in aqueous media.
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17 **EXPERIMENTAL**

18 *Materials and Reagents*

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20 The gold tip and substrates modification together with the chemical structures of the
21 corrole and phenol derivatives used in the present study are illustrated in Scheme 1. Phenol,
22 and *ortho* – nitrophenol possessing SH group were received from ProChimia Surfaces (Sopot,
23 Poland). Planar gold substrates (Au.1000.ALSI) were purchased from Platypus Technologies
24 (Madison, USA). AFM cantilevers, commercially available (contact mode, resonant
25 frequency 13 kHz, force constant 0.2 N/m) were obtained from Budgetsensors (Sofia
26 Bulgaria). All aqueous solutions were prepared with deionized water purified with a Milli-Q
27 water system. All the chemicals were analytical grade, used as received.
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41 *Synthesis of corrole*

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43 Corrole was synthesized at the Department of Chemistry (University of Leuven) using
44 method [37-39] as described below:
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48 **4-(10-Undecenoxy)benzaldehyde**

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50 A mixture of 7.030 g (28.64 mmol) of 11-bromo-1-undecene, 4.892 g (39.66 mmol) of
51 *p*-hydroxybenzaldehyde and 8.328 g (60.26 mmol) of potassium carbonate was heated at
52 reflux in 105 ml of acetone (p.a.) for 15 h. Upon cooling, the reaction mixture was filtered,
53 evaporated to dryness and the residue was taken into dichloromethane. The solution was
54 washed three times with aqueous NaOH, then three times with water and dried over MgSO₄.
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3 Upon filtration and removal of CH₂Cl₂ by distillation under reduced pressure, product **152**
4 was purified by column chromatography on silica. Eluting with 1:1 dichloromethane / light
5 petroleum ether afforded 7.450 g (95%) of the title product. δ_{H} (300 MHz) 9.88 (s, 1H,
6 aldehyde H), 7.82 (d, *J* 8.1, 2H, aryl H), 6.99 (d, *J* 8.1, 2H, aryl H), 5.81 (m, 1H, undecenyl
7 10-H), 4.97 (m, 2H, undecenyl 11-H) 4.04 (t, *J* 6.6, 2H, undecenyl 1-H), 2.04 (q, *J* 7.0, 2H,
8 undecenyl H), 1.81 (quintet, *J* 7.0, 2H, undecenyl 2-H), 1.46 – 1.31 (m, 12H, undecenyl H).

4-(11-Thioacetoxyundecyl)benzaldehyde

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22 4-(10-Undecenoxy)benzaldehyde (7.450 g; 27.15 mmol), thioacetic acid (4 ml; 56.23
23 mmol) and azo-*bis*-isobutyronitrile (229 mg; 1.37 mmol) were dissolved in 90 ml of toluene
24 (p.a.). The mixture was degassed with a stream of argon and then refluxed for 6.5 h. The
25 reaction was quenched with 5% aqueous NaHCO₃ (400 ml) and extracted three times with
26 ethyl acetate. The combined organic layers were washed with 5% aqueous NaHCO₃, then
27 brine and dried over MgSO₄. Upon filtration and removal of the solvent under reduced
28 pressure, the yellow solid residue was chromatographed on silica eluting with a gradient of
29 5:1 to 1:1 light petroleum ether / ethyl acetate. The crude product obtained was recrystallized
30 from methanol to afford 4.086 g (43%) of a white powder. δ_{H} (300 MHz) 9.88 (s, 1H,
31 aldehyde H), 7.83 (d, *J* 8.6, 2H, aryl H), 6.99 (d, *J* 8.6, 2H, aryl H), 4.04 (t, *J* 6.6, 2H,
32 undecenyl 1-H), 2.86 (t, *J* 7.3, 2H, undecenyl 11-H), 2.32 (s, 3H, CH₃), 1.81 (quintet, *J* 7.3,
33 2H, undecenyl 2-H), 1.46 – 1.28 (m, 16H, 8CH₂).

Meso-5,15-bis(2,6-dichlorophenyl)-10-(4-(11-thioacetoxy-1-dodecyloxy) phenyl)corrole

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55 2,6-Dichlorophenyldipyrromethane (1.522 g; 5.23 mmol) and 4-(11-
56 thioacetoxyundecyl)benzaldehyde (606 mg; 1.73 mmol) were dissolved in 146 ml of
57 dichloromethane. The reaction flask was wrapped in aluminium foil and placed in an ice bath.
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The solution was bubbled with Ar for 15 min. Ten μ l of TFA (0.13 mmol) was added and the mixture was stirred under an argon atmosphere for ~48 h. The ice bath was removed and 935 mg (3.77 mmol) of *p*-chloranil was added. After additional 1 h at room temperature, the mixture was evaporated with silica and chromatographed twice in a 1.5:1 mixture of dichloromethane and *n*-heptane to afford 452 mg (29%) of corrole. δ_{H} 9.00 (d, *J* 4.1, 2H, 2-H and 18-H of corrole), 8.62 (d, *J* 4.7, 2H, 8-H and 12-H of corrole), 8.53 (d, *J* 4.7, 2H, 7-H and 13-H of corrole), 8.42 (d, *J* 4.1, 2H, 3-H and 17-H of corrole), 8.08 (d, *J* 8.5, 2H, aryl *o*-H), 7.78 (d, *J* 7.7, 4H, dichlorophenyl *m*-H), 7.66 (dd, *J*₁ 7.7, *J*₂ 8.7, 2H, dichlorophenyl *p*-H), 7.27 (d partially overlapped with CHCl₃, *J* 8.5, 2H, aryl *m*-H), 4.24 (t, *J* 6.5, 2H, OCH₂), 2.89 (t, *J* 7.3, 2H, SCH₂), 2.32 (s, 3H, CH₃), 1.98 (quintet, *J* 7.4, 2H, \square -CH₂), 1.62 – 1.36 (m, 16H, 8CH₂), -2.30 (br. s, 3H, NH); δ_{C} 196.0, 158.9, 138.6 (quaternary C), 137.4 (quaternary C), 135.5 (CH), 134.0 (quaternary C), 130.3 (dichlorophenyl *p*-C), 128.0 (dichlorophenyl *m*-C), 127.2 (pyrrole CH), 125.7 (pyrrole CH), 120.8 (C-3 and C-17 of corrole), 116.2 (C-2 and C-18 of corrole), 113.2 (CH), 111.7 (quaternary C), 108.8 (quaternary C), 68.3, 30.6, 29.6, 29.5, 29.1, 28.8, 26.2; UV-Vis 410.1 (1.35 \cdot 10⁵), 566.1 (0.22 \cdot 10⁵); ESI-MS 907 (MH⁺).

***Meso*-5,15-bis(2,6-dichlorophenyl)-10-(4-(11-mercapto-1-dodecyloxy) phenyl)corrole**

Acetyl protected corrole (130 mg; 0.14 mmol) was dissolved in 7.5 ml of THF and 3 ml of methanol. The flask was placed in an ice bath and 1 ml of a 1.65 M solution of CH₃ONa in methanol (1.65 mmol of CH₃ONa) was added. The reaction mixture was stirred at 0°C for 30 min and then poured into diluted aqueous HCl (~0.02 M). This solution was extracted with ethyl acetate (some brine had to be added for a better separation) and then washed with brine, distilled water and dried over MgSO₄. Upon filtration and removal of the solvent under reduced pressure, 26 mg (21%) of corrole thiol was isolated by chromatography in mixtures of CH₂Cl₂ and hexane (1.5:1, column and 1:1, preparative plate). δ_{H} 8.97 (d, *J* 3.9, 2H, 2-H

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3 and 18-H of corrole), 8.61 (d, J 4.5, 2H, 8-H and 12-H of corrole), 8.51 (d, J 4.5, 2H, 7-H and
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5 13-H of corrole), 8.39 (d, J 3.9, 2H, 3-H and 17-H of corrole), 8.07 (d, J 8.2, 2H, aryl *o*-H),
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7 7.72 (m, 4H, dichlorophenyl *m*-H), 7.59 (dd, J_1 8.3, J_2 8.3, 2H, dichlorophenyl *p*-H), 7.24 (d
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9 partially overlapped with CHCl_3 , J 8.2, 2H, aryl *m*-H), 4.20 (t, J 6.4, 2H, OCH_2), 2.50 (t, J
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11 6.8, 2H, SCH_2), 1.93 (quintet, 2H, \square - CH_2), 1.60 (m, 4 H, 2 CH_2), 1.39 – 1.26 (m, 13H, 6 CH_2
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13 and SH), \sim -1.9 (br. s, 3H, NH); δ_{C} 158.8 (CO), 142.1 (9-C and 11-C of corrole), 139.8 (6-C
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15 and 14-C of corrole), 138.5, 137.4, 135.5, 134.6, 134.0, 130.7, 130.3, 128.0 (3-C and 5-C of
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17 5,15-dichlorophenyl), 127.1, 125.7 (8-C and 12-C of corrole), 120.8 (A and D ring \square -pyrrole
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19 C), 116.2 (A and D ring \square -pyrrole C), 113.2 (A and D ring \square -pyrrole C), 111.7 (5-C and 15-
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21 C of corrole), 108.9 (10-C of corrole); ESI-MS 865 (MH^+).
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29 *Formation of SAMs on gold substrates and gold tips*

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32 Before the modification the substrates were sonicated for 10 minutes in ethanol, dried
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34 with argon and annealed in a hydrogen flame. Next, the gold substrates were immersed in 10
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36 mM ethanolic solutions of derivatives of phenol (**Ph**) and nitrophenol (**PhNO₂**), for 20 hours.
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38 Next, the substrates were rinsed with ethanol and water and dried in air. At least, 3 repetitions
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40 of the substrate modification samples were done.
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44 The gold tips were washed with ethanol, pretreated in an UV/ozone chamber (Novascan
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46 Technologies, Ames, USA) for 30 min., and then immersed in 0.5 mM corrole (**COR**)
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48 chloroform solution for 24 hour. Thus, 5 tips were modified and used for the experiments.
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51 *AFM measurements*

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55 AFM measurements were carried out with a Molecular Imaging PicoSPM (Agilent
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57 Technologies, Tempe, USA). Substrates: Ph or PhNO₂ and cantilever COR/tip were loaded in
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59 a liquid cell, which was allowed to reach thermal equilibrium before starting the AFM
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3 operation. Adhesion forces were determined from force-displacement curves at room
4 temperature (ca. 20 °C) with the substrate and tip immersed in, milliQ water, an aqueous
5 solution containing 0.1 M K₂SO₄ at pH 6.0 or pH 10.0, with using the scanning rate of 1.17
6 lines/s. For each combination of tip and substrates, and appropriate pH of solution, at least
7 300 force-displacement curves were measured at different positions of each substrate – tip
8 combination.
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20 RESULTS AND DISCUSSION

21 22 23 24 *Strength of adhesion forces between the corrole host and the phenolic guests measured in* 25 26 27 *water by AFM*

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32 The experiments to study the interactions between the corrole host and the phenolic
33 guests were carried out by using modified gold substrates and tips. The modification
34 procedures are illustrated in Scheme 1.
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39 First, interactions between a COR/tip and Ph- or PhNO₂-substrates were assessed in
40 water at room temperature. The tip and substrate were mounted in liquid cell and the force –
41 displacement curves were monitored. Figure 1 shows a typical force-displacement curve
42 observed between a PhNO₂-substrate and a COR/tip. In many measurements, an adhesion
43 force as shown in the Figure 1 was observed in the retracting part of the curve. In this paper,
44 the host-guest interactions in water will be verified based on adhesion force, since it has often
45 been used to discuss various intermolecular interactions [40]. Adhesion forces obtained from
46 multiple measurements using a single tip on different locations of a sample were summarized
47 in a histogram, which show the probability of a given value of adhesion forces. Figure 2A and
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60 Figure 3A show histograms observed with a COR/tip on a PhNO₂-substrate and a Ph-

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3 substrate, respectively. The average of adhesion force, measured using multiple COR/tips,
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5 was slightly larger for the PhNO₂-substrates (2.1 ± 0.5 nN) in comparison with the Ph-
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7 substrate (1.7 ± 0.3 nN) (Table 1).
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11 In order to assess the contribution of nonspecific interactions to the aforementioned
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13 adhesion force data, force-distance curves on Ph- or PhNO₂- substrates were measured using
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15 unmodified gold tip. Figure 4A and 4B shows histograms obtained from adhesion force data
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17 for a single tip. The adhesion forces were 1.0 ± 0.2 nN and 0.7 ± 0.2 nN, for Ph- and PhNO₂-
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19 substrates, respectively. These values were smaller than those obtained with COR-tip. In
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21 addition, bare gold tips gave slightly larger adhesion force on Ph/substrates whereas COR-tips
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23 gave larger force on PhNO₂/substrate. These results suggest that the difference in adhesion
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25 force measured using COR-tips reflects from the host-guest interactions.
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30 The adhesion force reported above reflects not only the host-guest interactions but also
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32 the contact area originating from the variation in tip size [41]. The pull – off features in the
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34 retracting part of the force – distance curve can be used to calculate also the strength of a
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36 single chemical bond [42-46], which is not affected by the variation of the contact area. It has
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38 already been reported that AFM contact forces obeyed a Poisson distribution. Thus, the ratio
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40 of their variance to the mean gives the force of a single chemical bond between the tip and the
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42 substrate. The Poisson method requires relatively few measurements. By plotting a linear
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44 regression curve of the variance *vs.* the mean force taken from several sets of AFM
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46 measurements done at different locations on the surface and different tips, the magnitude of
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48 the individual bond force can be estimated. The lack of assumptions about the tip radius is
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50 another important advantage of this method. Indeed, the Poisson statistical analysis method
51
52 has been widely used for the calculation of individual bond forces between the AFM tip and
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54 the substrate, both functionalized [42-46]. Thus, the Poisson method was used in the present
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56 study for the evaluation of the strength of single molecule bond forces between corrole and
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3 phenol or *ortho* – phenol derivatives. Corroles due to the steric hindrance create less packed
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5 monolayers on the surface. Moreover, because of presence of short ethylene chains, the
6
7 phenol derivatives SAMs are less ordered. These factors cause that the density of the host and
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9 guest on the surface is rather low. Thus, the Poisson method is suitable for the systems
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11 studied.
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15 From the slope of the linear relationship between the mean force and its variance, the
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17 single molecule bond force can be calculated (Figure 2B, Figure 3B). The calculated single
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19 molecule bond forces were 16 ± 3 pN for the Ph- and 75 ± 11 pN for the PhNO₂-substrate,
20
21 respectively (Table 2). Thus, the strength of the individual bond force between corrole and
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23 *ortho*-nitrophenol was almost five times higher in comparison with the force between corrole
24
25 and phenol. These values are in a similar range as reported by Beebe Jr. et al. [42] and
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27 Hadziioannou et al. [47]. Their reports deal with a study of the hydrogen bonding, van der
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29 Waals and Coulombic interactions between ω - functional n – alkanethiol compounds with a
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31 variety of functional groups (CH₃, OH, NH₂, COOH and CONH₂) which were used for
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33 modification of scanning force microscopy probes and substrates.
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41 ***pH dependence on the strength of the adhesion forces between the corrole host and the***
42 ***phenolic guests measured in 0.1 M K₂SO₄ by the AFM method***
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49 In order to explore the influence of the pH and the electrolyte on the strength of
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51 interactions between the host and guests studied, subsequent experiments were done in the
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53 presence of 0.1 M K₂SO₄ at two pH values: 6.0 and 10.0.
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55 At pH 6.0, the shape of force-distance curves was similar to that observed in water
56
57 (Figure 1). At that pH, corrole exists as a mixture of electrically neutral and deprotonated
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3 molecules on the surface of the gold tip [34]. On the other hand, the phenol and *ortho*-
4
5 nitrophenol derivatives exist as the undissociated compound [31, 32].
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8 The histograms for the adhesion forces obtained for COR/tip and Ph- or PhNO₂-
9 substrate measured at pH 6.0 and their corresponding plots of mean force vs variance are
10 given in Figures 5 and 6. The average of adhesion force of COR-tips with PhNO₂/substrates
11 (5.0 ± 0.8 nN; Figure 5A and Table 1) is twice larger than that with Ph/substrates (2.2 ± 0.6
12 nN; Figure 5A and Table 1). The single bond force between corrole and PhNO₂ was also
13 larger (140.5 ± 33.0 pN; Figure 5B and Table 2) than that between corrole and Ph (59.3 ± 10
14 pN; Figure 6B and Table 2). This result is again consistent with the stronger interactions
15 between the corrole molecules and *ortho*-nitrophenol in comparison with phenol.
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26 Adhesion force between the tip modified with corrole and substrates was not observed at
27 pH 10 (Figure 7). Recorded force – distance curves displayed the typical shape for the
28 repulsive forces between the functionalized tip and surface [40]. This lack of adhesion force is
29 mainly caused by electrostatic repulsion between the tip and substrate. At pH 10.0, both
30 corrole molecules and phenol and *ortho*-nitrophenol derivatives exist in the negatively
31 charged forms. The pK_as of *ortho*-nitrophenol and phenol are 7.21 and 10.0, respectively.
32 Thus, at pH 10.0, both the host and guests molecules obtain a negative charge.
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43 Similar phenomena, namely the switching in binding forces in relation to a change of
44 the pH, were observed in several studies. The deprotonation effect of the ammonium group on
45 the surface of the substrate under basic condition caused a decrease in the interaction between
46 ammonium ion complexes with crown ethers moiety as presented by Kimura et al. [48]. A
47 decrease in adhesion force with increased H⁺ concentration for amino – or 2 – imidazolin – 1
48 –yl terminated SAMs is a result of the repulsion between the positively charged tip and the
49 substrate surfaces as reported by Umezawa et al. [49]. In the present study, we have
50 demonstrated that the individual interaction forces between corrole and phenol as well as
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3 *ortho*-nitrophenol derivatives attached to the surface of a gold tip and gold substrates depend
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5 on the protonation/deprotonation conditions of both the host and guests. By changing the pH
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7 of the electrolyte solutions, switching in the binding force is possible. As summarized in
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9 Table 2, the strongest single bond force was observed between the corrole and the *ortho* –
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11 nitrophenol derivatives measured at pH 6.0. The presence of electrolyte, 0.1 M K₂SO₄,
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13 increased the strength of the interactions, *ca* four times for corrole – phenol, and two times for
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15 corrole – *ortho* nitrophenol, in comparison to the values obtained in pure water. The larger
16
17 adhesion force in the presence of 0.1 M K₂SO₄ suggests the involvement of hydrophobic
18
19 interactions (e.g., π - π interactions) in the supramolecular complex formed between the corrole
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21 and phenols.
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29 *Computer simulation on the complexation between corrole and phenols*

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34 In addition, the difference in adhesion force observed for PhNO₂- and Ph- substrate
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36 would originate from hydrogen bond interactions with corrole. The creation of
37
38 supramolecular assemblies is controlled by N-H...X and O-H...X (X = O, N) hydrogen bonds.
39
40 The majority of recent publications are connected with molecular complexes of phenolic
41
42 substrates with a variety of receptors [50, 51]. These reports show that the supramolecular
43
44 assembly is controlled by strong and directional O-H...N hydrogen bonds. The phenolic
45
46 compounds can create a supramolecular complex with corrole [33, 34]. The interaction
47
48 involves the creation of a hydrogen bond between the NH group of the macrocyclic cavity of
49
50 the corrole and the OH group of the phenol derivative. The oxygen from the phenolic host is
51
52 an acceptor of hydrogen, while the NH group is a donor of hydrogen.
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58 The significance of the hydrogen bond interactions in the host-guest supramolecular
59
60 complex was verified using AM1 geometry procedure (MOPAC 2002 Version 2.5.3, J. J. P.

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3 Stewart, Fujitsu Limited, Tokyo, Japan). The calculation of a number of different
4 conformations of the corrole and guest compounds was done using the CaChe Workspace
5 programme in vacuum (CaChe Worksystem Pro Version 7.5.0.85). In Scheme 2, a model of
6 the complex formation between corrole and ortho – nitrophenol derivatives is presented, as
7 optimized by the AM1 geometry procedure. However, the calculation showed that the binding
8 energy of ortho – nitrophenol is in a range of -5.8 kcal/mol. On the other hand, the phenol
9 binding strength is a little less energetically favorable (-3.5 kcal/mol). In order to correlate the
10 energy binding and force of the complex formation of corrole with phenol and *ortho* –
11 nitrophenol, the procedure described by Reinhoudt was applied [52]. In this procedure, the
12 dependence of pull-off forces vs. energy was achieved for the spherical and cylindrical
13 integration approaches, according the following equations: $F = 32.60x \sqrt{-\Delta G + 2.39}$ or $F =$
14 $31.76x \sqrt{-\Delta G + 1.03}$, respectively (with $-\Delta G$ in kcal/mol and F in pN). Taking into account
15 cylindrical integration approaches, the calculated values of forces were 83.0 pN and 67.6 pN,
16 for PhNO₂ and Ph, respectively. The difference between predicted and experimental values is
17 therefore as follows: 83.0/140.5 and 67.6/59.3 pN, respectively, as compared for the values
18 obtained in 0.1 K₂SO₄, pH 6.0. The differences between calculated and experimental data
19 could be caused by possible contribution of other kind of forces (e.g. π - π interactions or
20 hydration of water molecules to the complex). However, the results of calculation show the
21 similar tendency as experimental data described in this paper.

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The results obtained using AFM together with a chemically modified tip also correlate well with those obtained potentiometrically, which concern the studies of corroles as the selective receptors for phenol derivatives existing as the electrically neutral analytes [33-35]. The presence of a nitro group on the benzene ring increases the acidity of the phenolic OH group, and as a consequence, a stronger potentiometric signal was observed. The significant part of the recognition process is the formation of weak hydrogen bonds between the electron

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3 pairs of the phenolic OH group and the NH units belonging to the corrole. This phenomenon
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5 was proved here, on the molecular level, by AFM method together with a chemically
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7 modified tip and substrates.
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10 11 12 CONCLUSIONS

13
14 We presented a study on the strength of the interactions between a corrole host and
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16 phenolic guests using the AFM method together with gold substrates and tips modified with
17
18 SAMs thorough Au-S covalent bonds. The specific intermolecular forces between corrole
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20 covalently immobilized on the gold AFM tip and derivatives of phenol, also attached via a
21
22 sulfur – gold bond to the surface of substrates was observed by means of atomic force
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24 microscopy. The dominant nature in the selectivity of interactions between corrole host and
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26 phenolic guest are hydrogen bonds. Also, hydrophobic and π - π interactions between phenol
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28 and pyrrole rings are involved. The strength of the single adhesion forces between corrole
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30 host and phenolic guest were determined by the Poisson method analysis. The sequence of
31
32 the strength of the single bond force obtained with the AFM method correlate well with the
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34 calculated values of energy and the selectivity of potentiometric signals obtained by liquid
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36 membrane electrodes incorporating corrole after stimulation with neutral phenolic guests [33-
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38 35]. The results obtained confirm the possibility to apply the atomic force microscopy for the
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40 observation at the molecular level of the creation of supramolecular complexes between
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42 nitrogen containing macrocycles and uncharged phenol derivatives. Notably, the nitrophenol
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44 isomers were recently identified as vasodilators which can mimic hormones, and can be
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46 considered as endocrine disrupting chemicals possessing estrogenic activity [53]. Thus,
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48 looking for the compounds which could specifically bind these molecules is very important
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50 from the theoretical and practical point of view. On the other hand, taking into account the
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52 interesting features of corrole which might be protonated and associate with a low pH cancer
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3 cell, these molecules can be used as sensors in biological systems and therefore there is still
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5 need for basic research connected with analogous systems.
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8 9 *Acknowledgements*

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13 and the Ministerie voor Wetenschapsbeleid (to E. D., W. D., W. M.) and Kansas State
14 University (to T.I.).
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List of Figures and Tables:

Scheme 1.

Schematic representation of corrole - SH molecules (**COR**) immobilized on the surface of a gold AFM tip (**A**) and **Ph** (**B**), **PhNO₂** (**C**) compounds immobilized on gold substrates.

Scheme 2.

Structure of the complex between corrole with an ortho – nitrophenol derivative optimized by AM1 geometry (CaChe Worksyssem Pro Version 7.5.0.85).

Figure 1.

Typical force curves (line “B” –approaching, b line “A” – retracting) observed for PhNO₂-substrates using COR/tip made in water.

Figure 2.

(A) Histogram of adhesion forces obtained from the repetitive force measurements between single **COR**/tip and **Ph**/substrate in water. (B) A plot of mean vs. variance of adhesion force measured for **Ph**/substrates using five separate COR/tips in water.

Figure 3.

(A) Histogram of adhesion forces obtained from the repetitive force measurements between single COR/tip and a PhNO₂/substrate in water. (B) A plot of mean vs. variance of adhesion force measured for PhNO₂/substrates using three separate COR/tips in water.

Figure 4.

Histograms of adhesion forces (n = 300) obtained from the repetitive force measurements between a bare gold AFM tip and a Ph/substrate (A) and a PhNO₂/substrate (B) in water.

Figure 5.

(A) Histogram of adhesion forces obtained from the repetitive force measurements between single COR/tip and a Ph/substrate in 0.1 M K₂SO₄ (pH 6.0). (B) A plot of mean vs. variance of adhesion force measured for Ph/substrates using three separate COR/tips in 0.1 M K₂SO₄ (pH 6.0).

Figure 6.

(A) Histogram of adhesion forces obtained from the repetitive force measurements between single COR/tip and the PhNO₂/substrate in 0.1 M K₂SO₄ (pH 6.0). (B) A plot of mean vs. variance of adhesion force measured for PhNO₂/substrates using four separate COR/tips in 0.1 M K₂SO₄ (pH 6.0).

Figure 7.

Typical force curves (line “B” –approaching, b line “A” – retracting) observed for PhNO₂-substrates using COR/tip made in 0.1 M K₂SO₄ at pH 10.0.

Table 1.

Adhesion forces measured with unmodified and corrole-modified tips and gold substrates modified with Ph or PhNO₂ in different aqueous solutions.

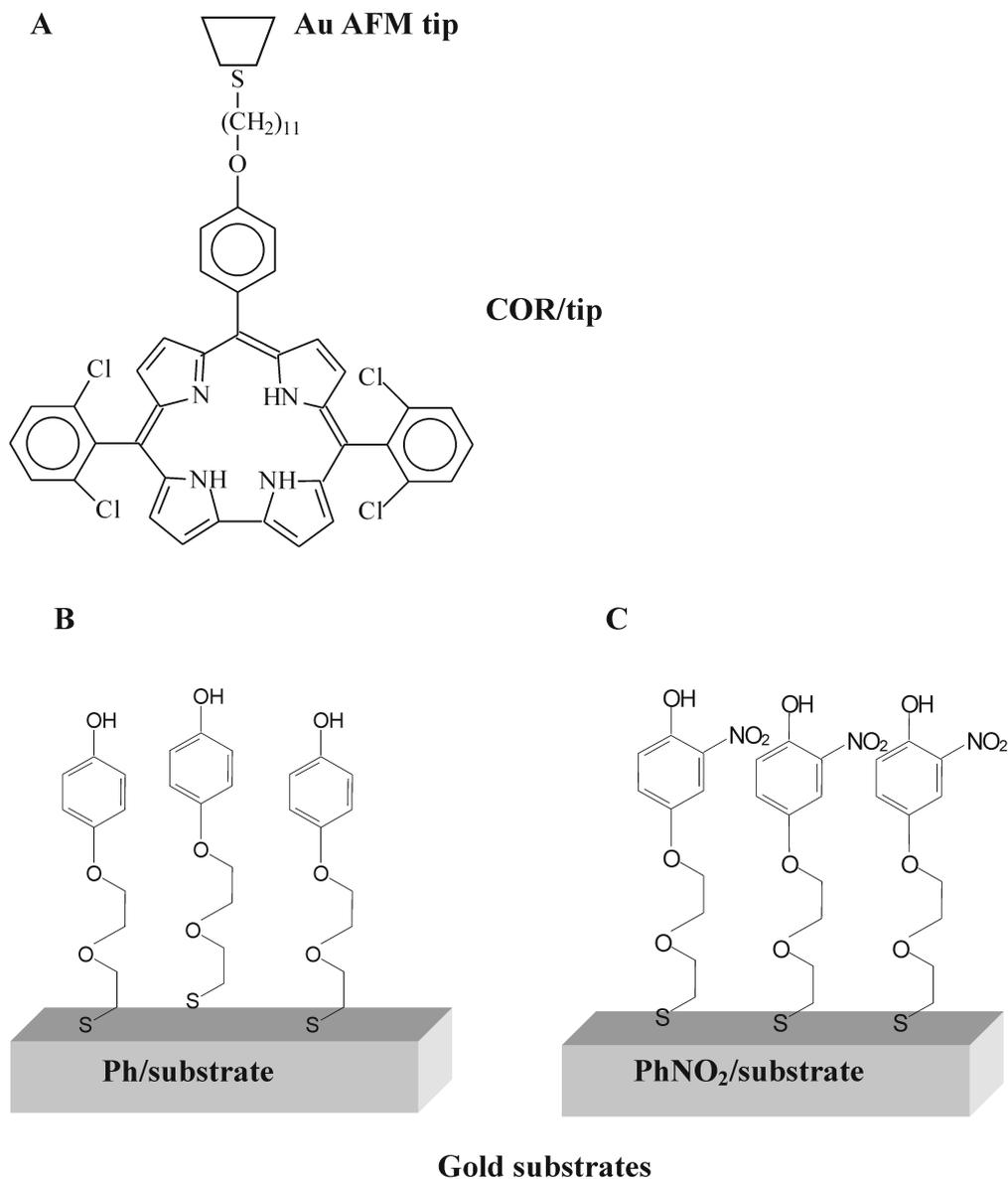
Table 2.

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3 Single bond forces measured with corrole-modified tips and Ph and PhNO₂ compounds
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5 immobilized on gold substrates in different aqueous solutions.
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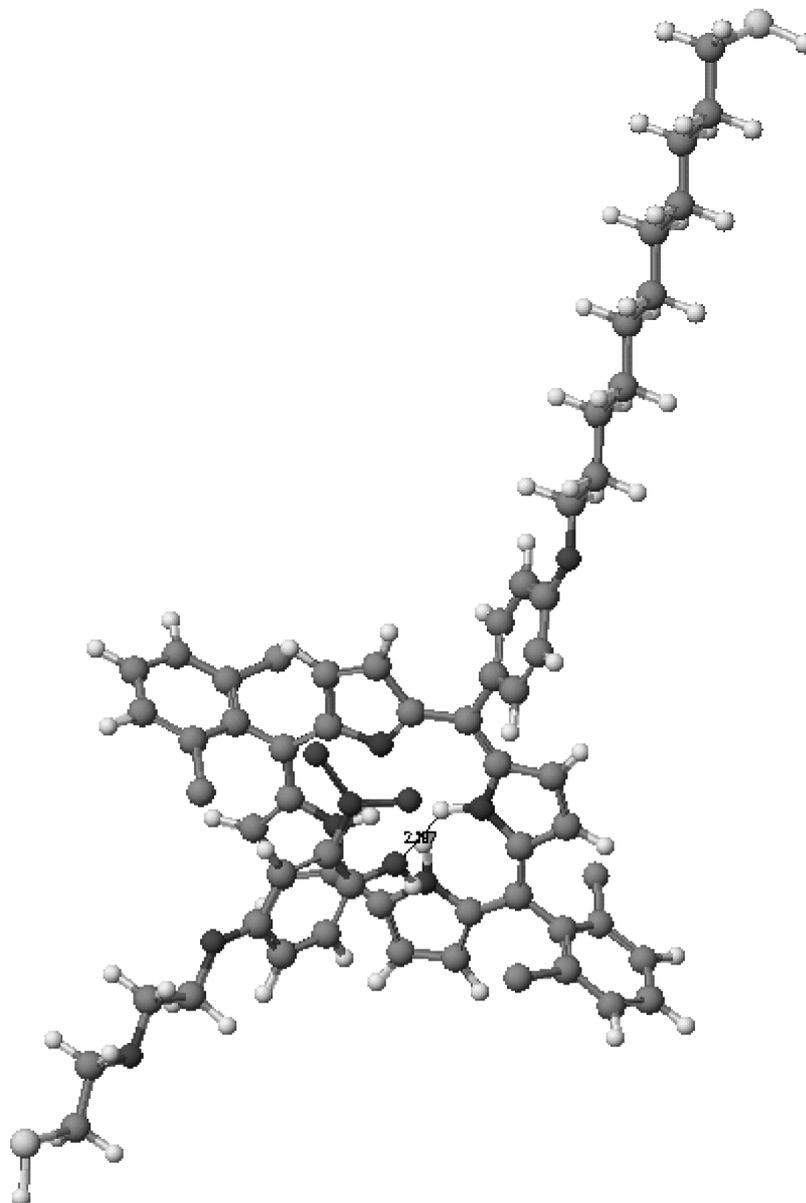
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Schematic representation of corrole - SH molecules (**COR**) immobilized on the surface of a gold AFM tip (**A**) and **Ph** (**B**), **PhNO₂** (**C**) compounds immobilized on gold substrates.



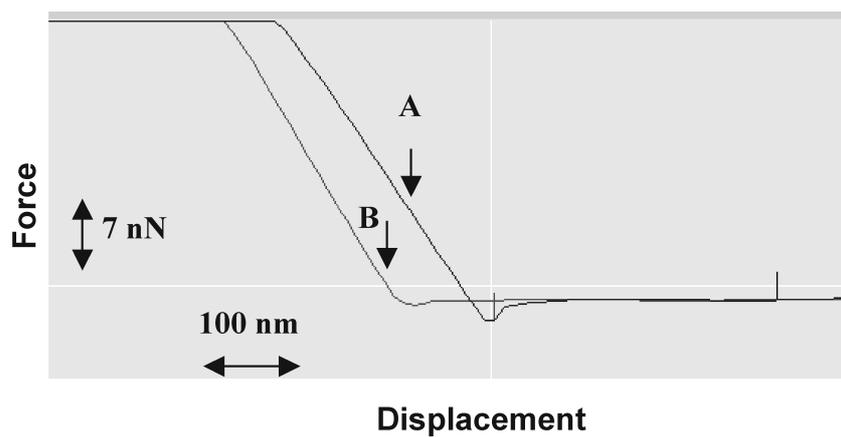
Scheme 2.

Structure of the complex between corrole with an ortho – nitrophenol derivative optimized by AM1 geometry (CaChe Worksyssem Pro Version 7.5.0.85).



1
2 **Figure 1.**
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5 Typical force curve (line “B” –approaching, b line “A” – retracting) observed for PhNO₂-substrates
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7 using COR/tip made in water.
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60**Figure 2.**

(A) Histogram of adhesion forces obtained from the repetitive force measurements between single **COR**/tip and **Ph**/substrate in water. (B) A plot of mean vs. variance of adhesion force measured for **Ph**/substrates using five separate **COR**/tips in water.

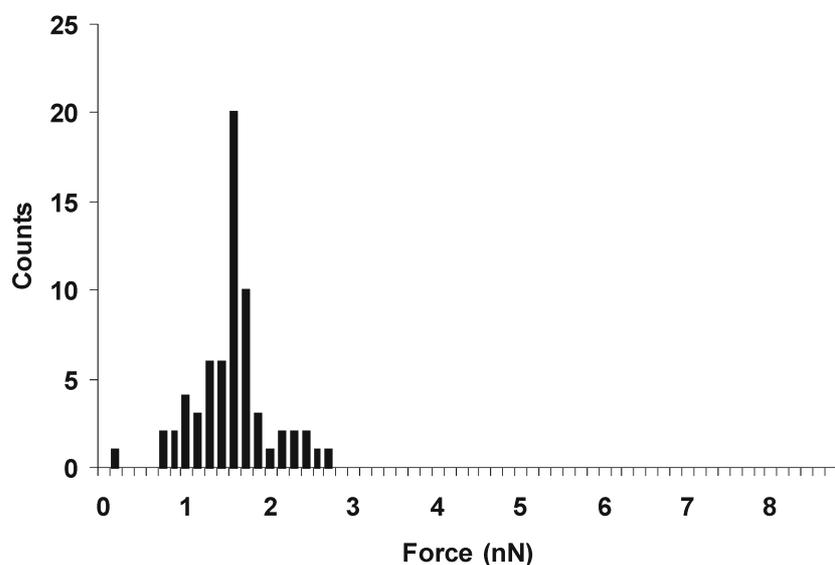
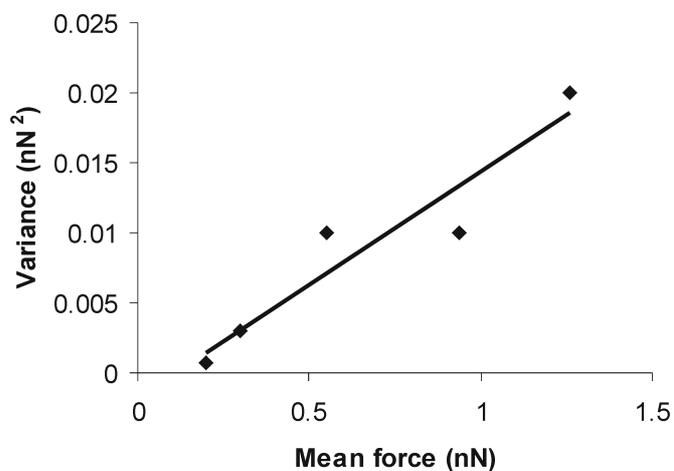
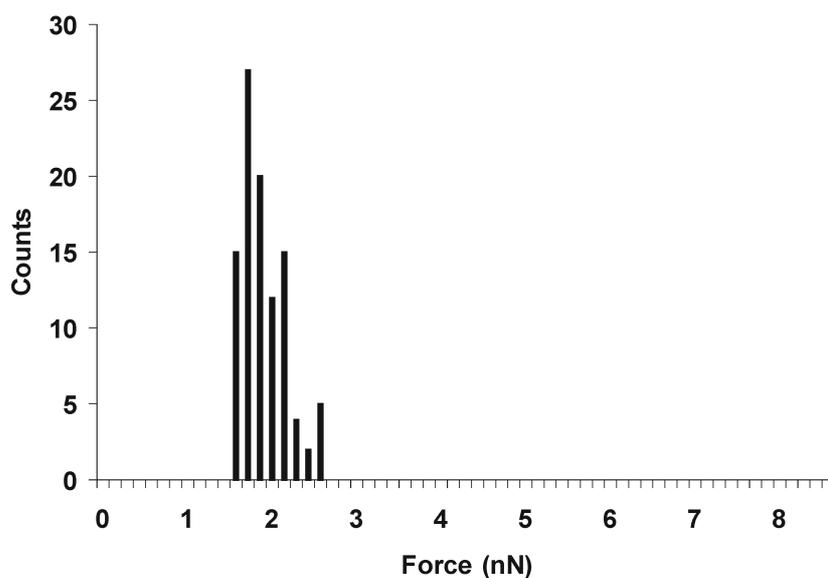
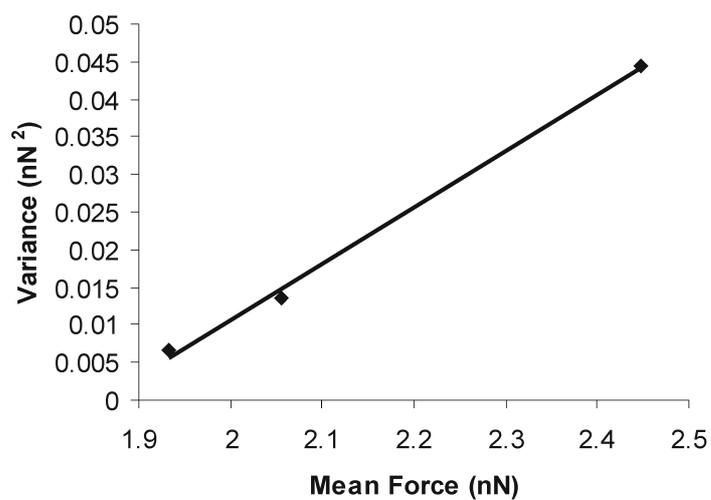
A**B**

Figure 3.

(A) Histogram of adhesion forces obtained from the repetitive force measurements between single COR/tip and a PhNO_2 /substrate in water. (B) A plot of mean vs. variance of adhesion force measured for PhNO_2 /substrates using three separate COR/tips in water.

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60**Figure 4.**

Histograms of adhesion forces ($n = 300$) obtained from the repetitive force measurements between a bare gold AFM tip and a **Ph**/substrate (**A**) and a **PhNO₂**/substrate (**B**) in water.

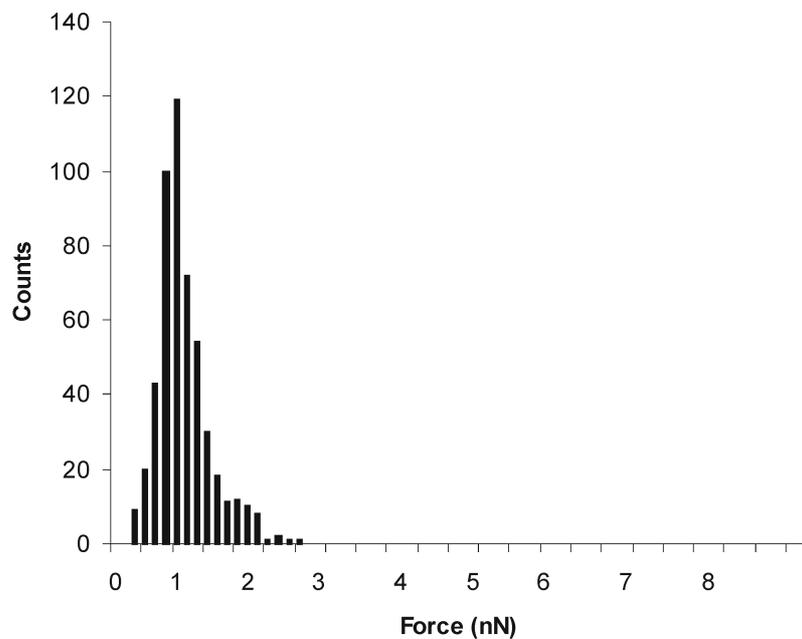
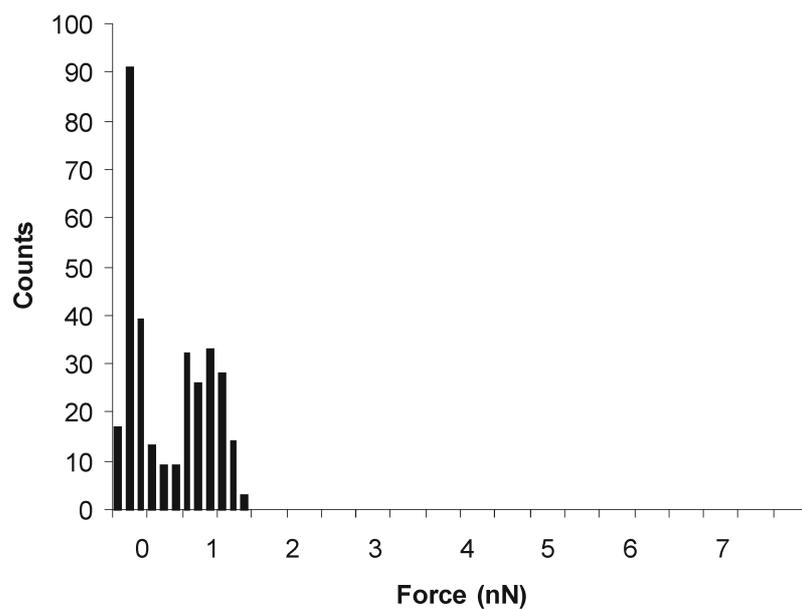
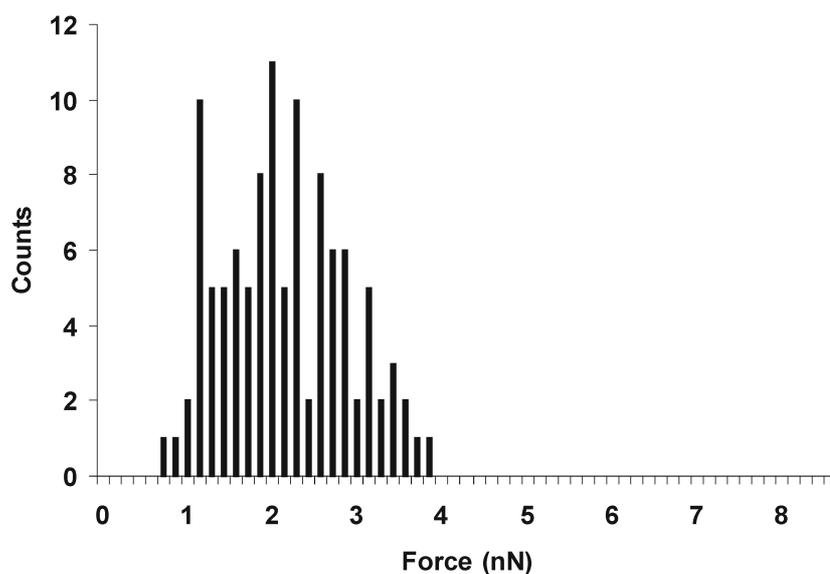
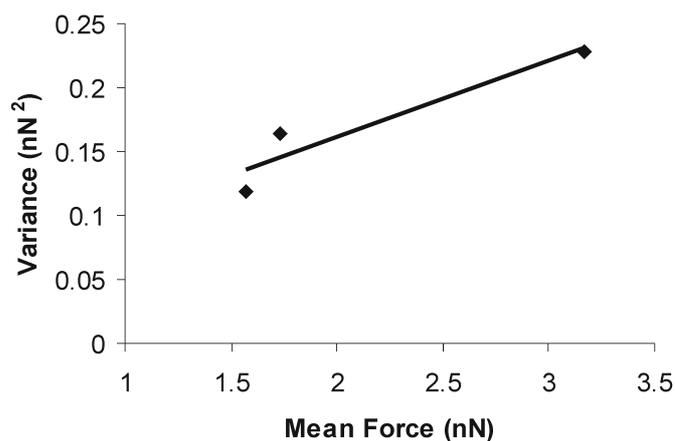
A**B**

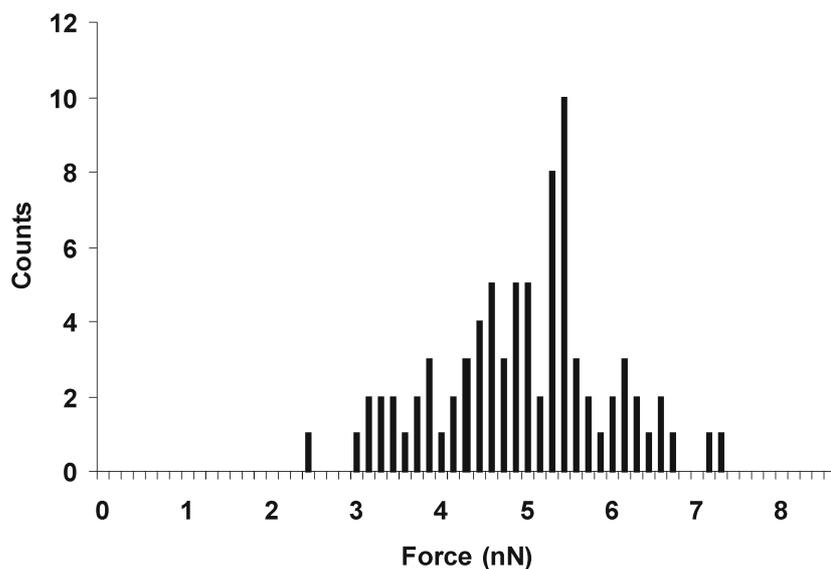
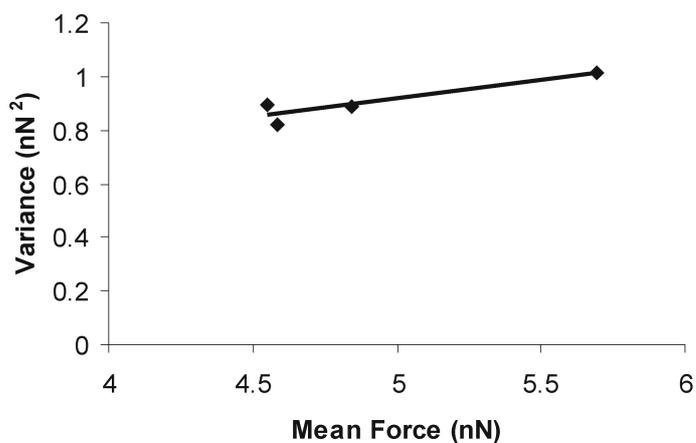
Figure 5.

(A) Histogram of adhesion forces obtained from the repetitive force measurements between single **COR**/tip and a **Ph**/substrate in 0.1 M K_2SO_4 (pH 6.0). (B) A plot of mean vs. variance of adhesion force measured for **Ph**/substrates using three separate **COR**/tips in 0.1 M K_2SO_4 (pH 6.0).

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60**Figure 6.**

(A) Histogram of adhesion forces obtained from the repetitive force measurements between single COR/tip and the PhNO₂/substrate in 0.1 M K₂SO₄ (pH 6.0). (B) A plot of mean vs. variance of adhesion force measured for PhNO₂/substrates using four separate COR/tips in 0.1 M K₂SO₄ (pH 6.0).

A**B**

1
2 **Figure 7.**

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5 Typical force curve (line “B” –approaching, b line “A” – retracting) observed for PhNO₂-substrates
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8 using COR/tip made in 0.1 M K₂SO₄ at pH 10.0.
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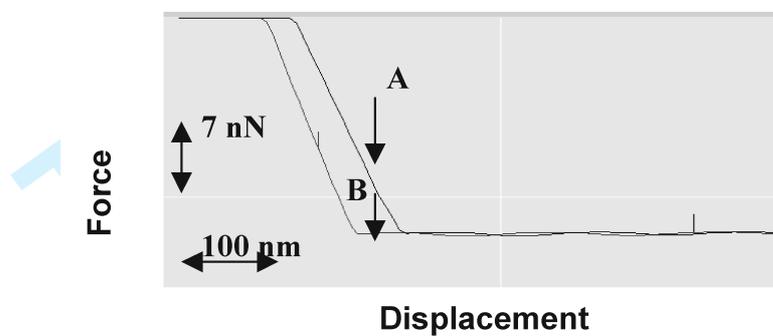


Table 1.

Adhesion forces measured with unmodified and corrole-modified tips and gold substrates modified with Ph or PhNO₂ in different aqueous solutions.

	Ph/substrate	PhNO ₂ /substrate
unmodified tip, water	1.0 ± 0.2 nN	0.7 ± 0.2 nN
COR/tip, water	1.7 ± 0.3 nN	2.1 ± 0.5 nN
COR/tip, 0.1 M K ₂ SO ₄ , pH 6.0	2.2 ± 0.6 nN	5.0 ± 0.8 nN
COR/tip, 0.1 M K ₂ SO ₄ , pH 10.0	0 nN	0 nN

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Table 2.

Single bond forces measured with corrole-modified tips and Ph and PhNO₂ compounds immobilized on gold substrates in different aqueous solutions.

	Ph/substrate	PhNO ₂ /substrate
COR/tip, water	16.1 ± 3.0 pN	75.1 ± 11 pN
COR/tip, 0.1 M K ₂ SO ₄ , pH 6.0	59.3 ± 10.0 pN	140.5 ± 33.0 pN
COR/tip, 0.1 M K ₂ SO ₄ , pH 10.0	0 pN	0 pN

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