Tetrahedron 64 (2008) 6705–6710

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

A color version of the Hinsberg test: permethylated cyclodextrin and crown-appended azophenol for highly selective sensing of amines

Jong Hwa Jung [a,*], Hye Young Lee [a], Sung Ho Jung [a], Soo Jin Lee [a], Yoshiteru Sakata [b], Takahiro Kaneda [b,*]

[a] Department of Chemistry, Research Institute of Natural Science, Gyeongsang National University, Jinju 660-701, South Korea
[b] Institute of Scientific and Industrial Research, Osaka University, Osaka 569-0047, Japan

ARTICLE INFO

Article history:
Received 21 March 2008
Received in revised form 1 May 2008
Accepted 1 May 2008
Available online 7 May 2008

Keywords:
Alanines
Amphiphiles
Helical ribbons
Self-assembly

ABSTRACT

Azophenol dyes **1**–**5** having the permethylated cyclodextrin and/or crown moieties have been synthesized. Compounds **1** and **2** provide critical information for discrimination among 1°–3° amines by unique color changes. Addition of 1° and 2° amines to solutions of **1** or **2** in chloroform shifts the absorbance maximum of the initial solutions from 380 nm to ~580 nm and ~530 nm, respectively, but no change is observed with 3° amines. The high selectivity of **1** is mainly due to H-bonding between the ammonium H atoms of the amine and oxygen atoms of the crown-6. The selectivity of **1** possessing the β-cyclodextrin moiety toward amines was higher than that of **2** possessing the α-cyclodextrin moiety. On the other hand, chloroform solutions of **3** or **4**, which lack the crown ether moiety, changed from yellow (380 nm) to pink (500 nm) with the addition of 1° and 2° amines, but with no selectivity. These results indicate that the crown unit in **1** or **2** plays an important role in discriminating among the types of amines.

1. Introduction

Amines and ammonia are used for the preparation of colorants, medicines, surfactants, catalysts, pesticides, polymers, etc. These compounds are toxic both in the gas phase and when dissolved in liquids. A variety of sensors have been developed for their determination in environmental, industrial, food, biological, and clinical samples. The detection of amines based on optical-sensing methods can be based on pH indicator dyes, solvatochromic dyes,[1] metal complexes,[2] organic reactions,[3] chromophores,[4] etc. Among the methods for the detection of amines is the *Hinsberg* test,[5] based on an organic reaction, which forms characteristic base-soluble sulfonamides. Developed more than 100 years ago and well documented in textbooks, the *Hinsberg* test can be used to discriminate among 1°–3° amines. Recently, many functional host molecules such as cyclodextrins,[6] calix[4]arenes,[7] and crown ethers, based on coordinative or hydrogen-bonding interactions as the main driving force, have been reported as reagents for the detection of amines.

For amine recognition, macrocyclic polyethers have been shown to bind primary ammonium ions by anchoring the R–NH_3^+ group into their circular cavity via three H-bonds (N–H···O).[8–11] However, the selective recognition toward specific alkylamines has not been achieved due to the lack of selectivity. By overcoming the low selectivity and low sensitivity for the discrimination of types of amines with regard to the color changes, we report here unique chemosensors **1** and **2** (Scheme 1), which are capable of exhibiting selective color changes toward 1°–3° amines, and may be viewed as the *color version of the Hinsberg test*.

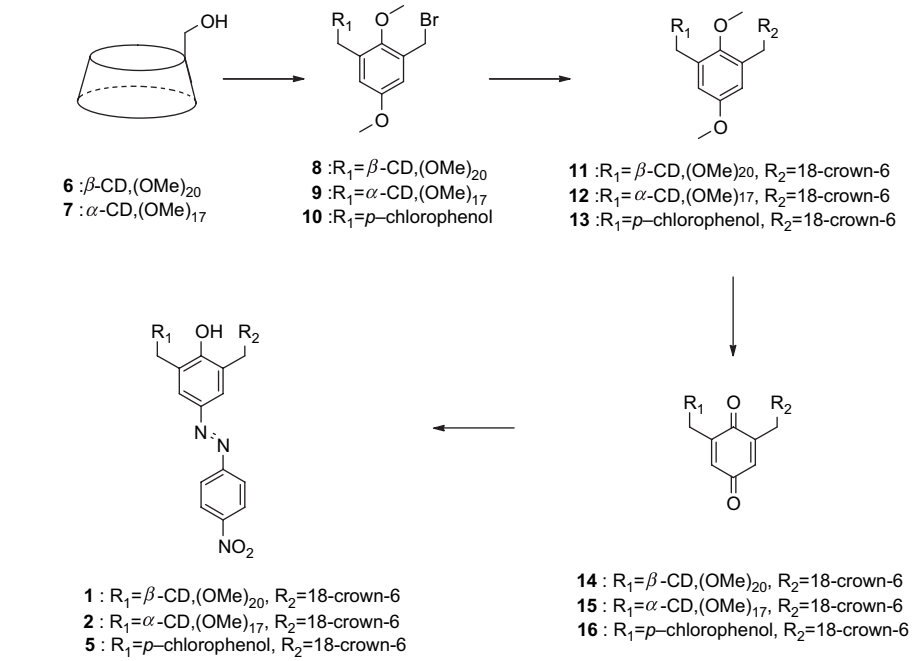
2. Results and discussion

Syntheses of compounds **1**, **2**, and **5** are summarized in Scheme 1. Permethylated α- or β-cyclodextrin-6-monoalcohol[12] was reacted with 2,6-bis(bromomethyl)-1,4-dimethoxybenzene to yield the corresponding permethylated α-cyclodextrin (α-CD) and β-cyclodextrin (β-CD) in 75% and 80% yields, respectively. 2-(Hydroxylmethyl)-18-crown-6 was reacted with permethylated α- or β-CD-appended-bromomethyl-1,4-dimethoxybenzene (**16** or **17**) to give the corresponding asymmetric permethylated α- or β-cyclodextrin in 50% and 65% yields, respectively. Then, after the oxidation of 18-crown-6-appended permethylated α-CD or β-CD with cerium(IV) ammonium nitrate (CAN), treatment with *p*-nitrophenylhydrazine gave the desired **1** and **2** in 45% and 30% yields, respectively. Compounds **4** and **5** were also synthesized in 20% and 25% yields by similar methods as used for **1**, respectively. Compounds **3** and **4** were prepared by adaptation of procedures reported earlier.[12,13] The structures of **1**–**5** were confirmed by ^{1}H NMR, MALDI-TOF mass spectroscopy, and elemental analysis (Fig. 1).

The binding behaviors of **1**–**5** toward various amines were investigated by UV–vis spectrophotometry. Association constants[14] were also determined from the UV–vis band changes upon the addition of 1°–3° amines to chloroform solutions of **1**–**5** and are

* Corresponding authors. Tel.: +82 55 751 6027; fax: +82 55 758 6027.
E-mail address: jonghwa@gnu.ac.kr (J.H. Jung).

0040-4020/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.05.013



Scheme 1. Synthetic method of compounds **1**, **2**, and **5**.

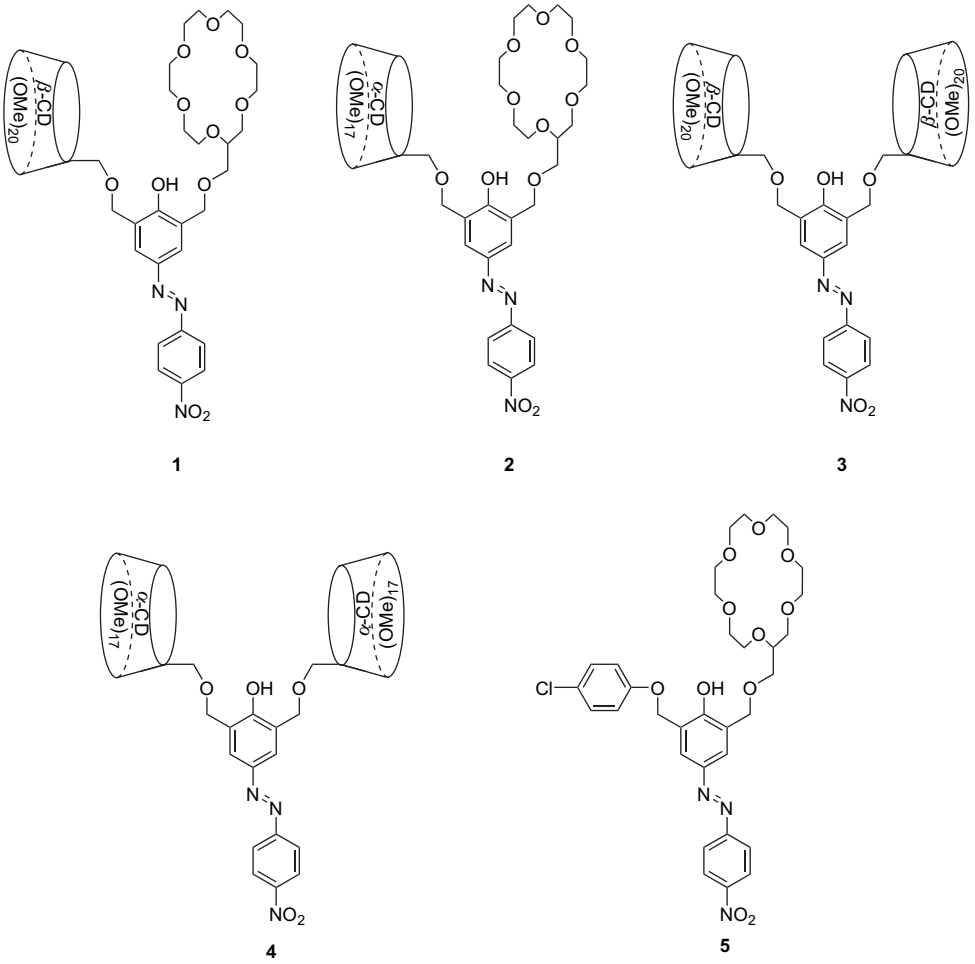


Figure 1. Chemical structures of **1**–**5**.

Table 1
Association constants and pK_a of the ligands **1**–**5** for various amines in $CHCl_3$[a]

Amine	1	2	3	4	5
n-Propylamine	4.6	4.45	2.01	1.71	2.04
n-Butylamine	4.72	4.6	2.04	1.79	2.09
n-Pentylamine	4.59	4.55	1.78	1.62	1.99
n-Hexylamine	4.45	4.3	1.62	1.59	2.05
n-Heptylamine	4.47	4.3	1.57	1.57	2.01
n-Octylamine	4.85	4.7	1.81	1.75	2.12
n-Decylamine	4.95	4.85	1.78	1.76	2.15
1,7-Diaminoheptane	4.25	4.19	1.72	1.67	2.05
Di-*n*-ethylamine	2.35	2.1	2.02	1.81	1.53
Di-*n*-propylamine	2.23	2.11	1.93	1.75	1.47
Di-*n*-butylamine	2.48	2.32	1.83	1.72	1.46
Di-*n*-hexylamine	2.2	2.14	1.76	1.74	1.46
Di-*n*-octylamine	2.19	2.17	1.77	1.75	1.45
Di-*n*-decylamine	2.37	2.2	1.85	1.8	1.5
Di-*n*-methyldiaminohexane	2.11	2.05	1.7	1.65	1.31
2,6-Dimethyl-piperidine	2.1	2.02	1.75	1.74	1.41
pK_a	5.45	5.75	5.91	5.99	7.30

[a] The K_a [M^{-1}] values were obtained by using the ENZFITTER program based on the 1:1 complexation phenomena between receptor and respective amines.

listed in Table 1 and Table S1 (Supplementary data). Among these receptors, **1** responded markedly to the 1° and 2° amines, exhibiting distinct color changes from orange (complementary to the absorption of 380 nm) to blue (complementary to the absorption of 580 nm, Figs. 2 and 3 and Fig. S1 (Supplementary data)) for 1° amines and red (complementary to the absorption of 510 nm, Figs. 2 and 3, and Fig. S1 (Supplementary data)) for 2° amines, with an isosbestic point at 439 nm. This bathochromic shift is caused by the amine based-deprotonation of the azophenol, inducing a photo-induced charge transfer (PCT).[15] In addition, the selectivity of **1** toward the type of amines is closely related to comparable H-bonding interactions between the crown ring of **1** and the protons of the ammonium ion as well as to a critical role of the adjacent β-CD, which can interact with the lipophilic alkyl chain of the amine by a hydrophobic interaction (vide infra). On the other hand, addition of 3° amines to **1** gave no color change. The lack of color change of **1** toward 3° amines is presumably due to a steric hindrance between the alkyl chain of the 3° amine and the β-CD.

The color change of **2** upon the addition of amines was quite similar to that of **1** (Fig. 3 and Fig. S2 (Supplementary data)). However, bathochromic shifts of **2** with 1° and 2° amines were slightly smaller than those of **1**. The reason for this lesser shift is not clear. It may be attributed to steric hindrance between the α-CD moiety and alkyl chain of amine, despite the fact that the binding affinity of the α-CD for alkylamines is much stronger than that of the β-CD.[16,17]

To gain an insight into the role of the hydrophobic interaction between the CD moiety and the alkyl chain of amine, we measured ^{1}H NMR spectrum of **2** upon the addition of the amine. The NMR spectrum of the **1**·*n*-heptylamine complex (Fig. S3 (Supplementary data)) showed that the protons of the crown loop and C_1–H of the α-CD underwent a high-field shift. This observation is consistent with the formation of H-bonds between the H atoms of the ammonium and the crown ring of **2** as well as with the development of hydrophobic interactions with the target amine.

Upon addition of *n*-octylamine, the intensity of the ~380 nm absorption band of **1** and **2** decreased with concomitant increase of a new band centered at ~580 nm with only one isosbestic point at ~460 nm, providing solid evidence of formation of a 1:1 complex (Figs. S1 and S4 of Supplementary data). To confirm the complexation ratio, we performed FAB mass spectroscopy for the **2**·*n*-heptylamine complex. A 1:1 complexation ratio (1886.12 *m*/*e*, Fig. 4) is evident for **2**·*n*-heptylamine complex.

The log K_a values of **1** for 1° and 2° amines are 4.25–4.95 and 2.10–2.48, respectively, as listed in Table 1. The selectivity of **1** between 1° and 2° amines was calculated to be 60–720. These results also indicate that the number of H-bonds formed between the

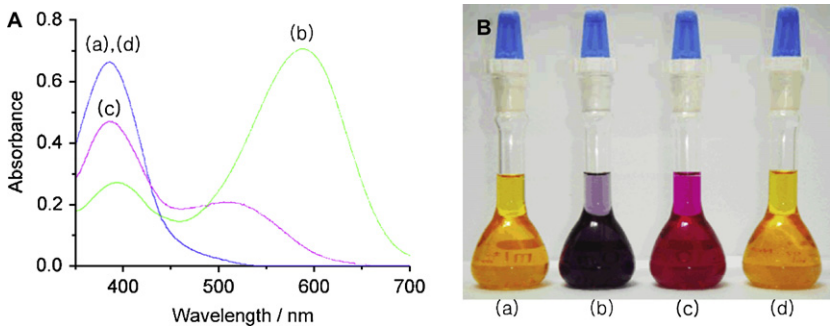


Figure 2. (A) UV–vis spectra and (B) photograph of **1** with amines in $CHCl_3$: (a) **1**, (b) **1**+*n*-octylamine (1000 equiv), (c) **1**+di-*n*-butylamine (1000 equiv), and (d) **1**+tri-*n*-butylamine (1000 equiv).

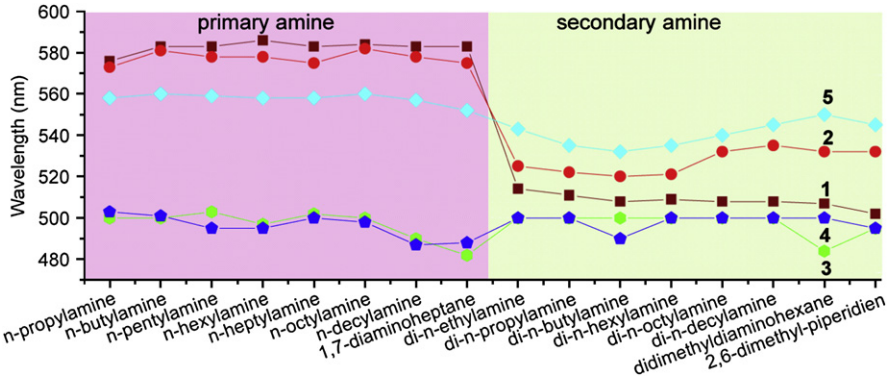


Figure 3. Absorption maxima of **1**–**5** with amines (1000 equiv) in chloroform.

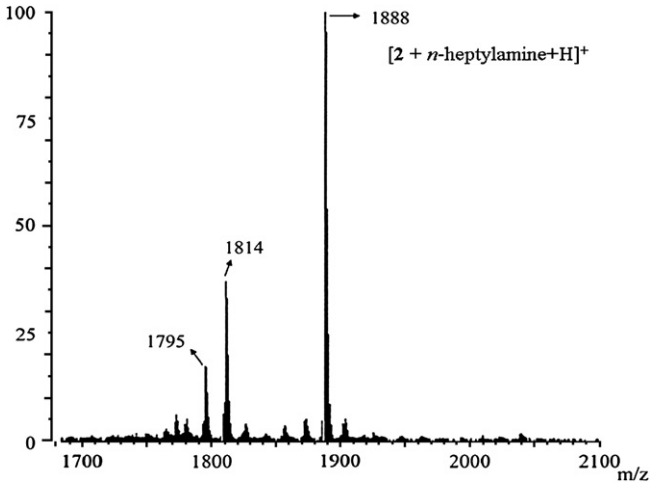


Figure 4. FAB mass spectrum of **2**+*n*-heptylamine (1000 equiv) in $CHCl_3$.

crown ring of **1** and the protons of the ammonium ion is of critical importance for discrimination between the amines. The log K_a of **2** with amines is slightly smaller than that of **1**. We think that the slightly smaller log K_a is probably due to the steric hindrance between 6-methyl groups of permethylated α-CD and the alkyl chain of amine. Also, the log K_a is dependent on the acidity (pK_a) of **1** or **2**. In conclusion, probably the slightly smaller log K_a of **2** with primary amines is probably due to the two factors (steric hindrance and pK_a) mentioned above.

Compounds **3** and **4**, which contained no 18-crown-6 ether moiety, were synthesized to investigate the influence of the crown unit on the amine selectivity. Unlike the case of **1**, addition of 1° and 2° amines to the chloroform solutions of **3** or **4** changed the color from yellow (380 nm) to pink (500 nm) (Table S1 and Figs. S5–S8 of Supplementary data, respectively), but with no selectivity. On the other hand, addition of 3° amines to **3** or **4** gave no color change. Thus, the crown unit in **1** or **2** plays an important role in discriminating among the types of amines.

In addition, **5** with a *p*-chlorophenyl unit instead of the CD was prepared to elucidate the role of the CD in the amine selectivity. Addition of 1° and 2° amines to the chloroform solution of **5** changed the color from yellow (λ_{max}=380 nm) to pale blue (λ_{max}=~560 nm) and to pink (λ_{max}=~540 nm), respectively, with an isosbestic point at 445 nm (Table S1 and Figs. S9–S11 of (Supplementary data). As with **1**, no color change was noted with the addition of 3° amines. However, both binding affinity and selectivity of **5** toward the tested amines were much lower than those of **1** and **2**. Therefore, the less selective interaction and low sensitivity are related to the hydrophobic interaction between the CD moiety and the alkyl chain of the amine. A single isosbestic point appeared in the spectrum of **5** with *n*-octylamine in $CHCl_3$, indicating the formation of a 1:1 complex (Fig. S11 of Supplementary data).

Acidity, pK_a, is also an important determinant of the selectivity and sensitivity of the acidic ligands toward the target guest molecules. The pK_a values of azophenols **1**–**5** in solutions of H_2O/1,4-dioxane (9:1 v/v) were determined to be in the range from 5.45 to −7.30. The pK_a value of **1** was much higher than those of **2**–**5** and thus, the sensitivity of **1** toward amines greatly exceeded that of compounds **2**–**5**. It is noteworthy that **1** and **2** can be easily deprotonated to give rise to the phenoxide anion, which develops the photo-induced charge transfer through the *p*-nitrodiazophenol to provide its bathochromic shift.

According to UV–vis, NMR, and mass spectra of the complex, we proposed the complex structures of **1**·amine or **2**·amine in Figure 5. Previously Kaneda et al., investigating the H-bonding interactions between the crown ring of a macrocyclic chromophore and amines through XRD study,[16,17] reported that 1° amines formed three-pointed perching H-bonds between the oxygen atoms of 18-crown-6 and the H atoms of the ammonium ion while a 2° amine participated only through two-pointed H-bonding interaction.

By utilizing a competition experiment, we measured the changes of the absorption intensity upon the addition of the 1° amine (*n*-propylamine) to the chloroform solution of **1** containing 2000 equiv of the 3° amine (triethylamine). Addition of even a small amount of the *n*-propylamine under these conditions resulted in a marked increase in absorption intensity at 585 nm (Fig. 6). In the reverse case, after addition of 3° amine to the solution (**1**+1° alkylamine), no spectral changes were observed. These findings predict that **1** could selectively recognize a 1° amine, even in the presence of an excess of 3° amine.

3. Conclusions

Amine receptors based on CD/18-crown-6-appended azophenol (compounds **1** and **2**) were synthesized. The main factors contributing to the high selectivity of **1** and **2** toward amines are: (i) the formation of efficient H-bond interactions between the oxygen atoms of the crown loop and the H atoms of the ammonium ion of the amines; (ii) the hydrophobic interaction between the CD and the lipophilic tail of the amine; and (iii) the acidity of the host

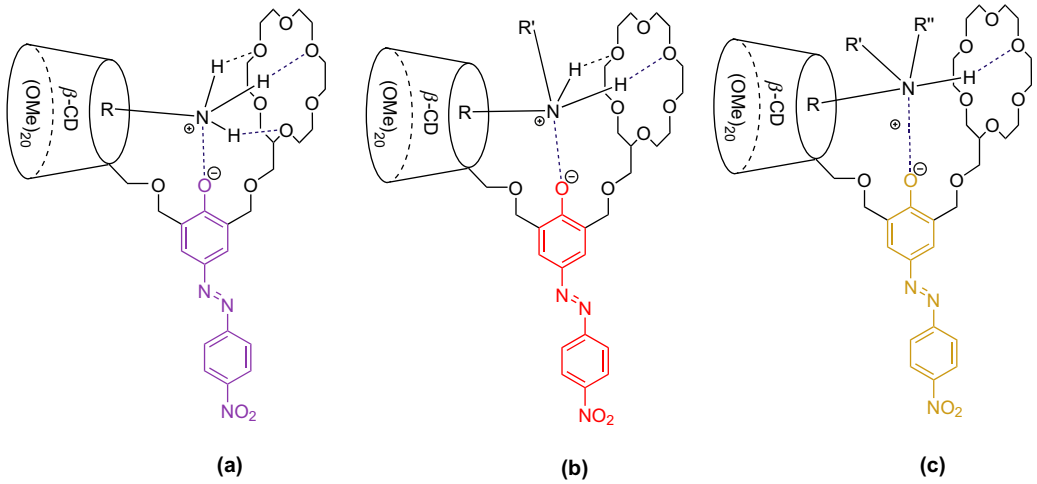


Figure 5. Proposed structures for complex formation of **1** with (a) 1° amine, (b) 2° amine, and (c) 3° amine.

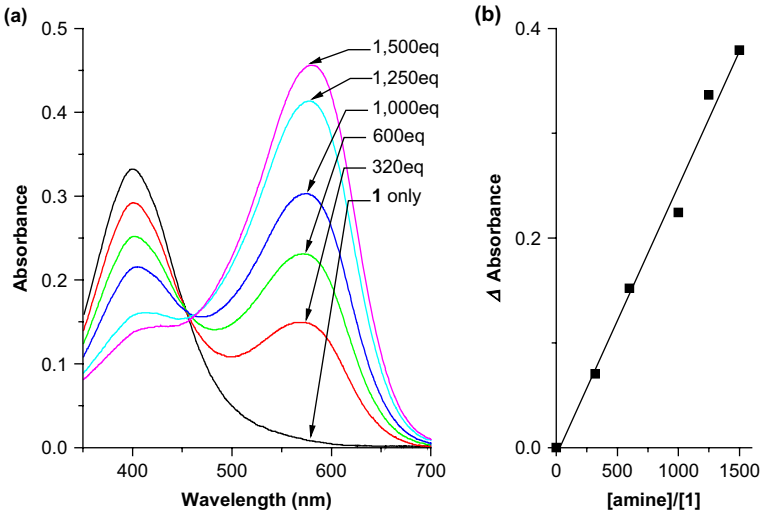


Figure 6. Wavelength changes of **1** (0.03 mM) upon the addition of *n*-octylamine in the presence of triethylamine (2000 equiv) in $CHCl_3$.

molecule. Hence, molecules **1** and **2** reported here can be considered as an innovative tool in the discrimination of the 1°–3° amines. This simple and straightforward qualitative analysis, using the synthesized novel compounds herein, can be considered a new innovative tool for discriminating 1°–3° amines as an alternative to the historical Hinsberg test.

4. Experimental

4.1. Synthesis

Compounds **6** and **7** were prepared by adaptation of procedures previously reported.[12,13]

4.2. Compound 8

Under N_2 atmosphere, a solution of **6** (0.5 g, 0.412 mmol) and 2-bis(bromomethyl)-1,4-dimethoxybenzene (0.4 g, 1.23 mmol) in dry THF (10 mL) was slowly added to a suspension of NaH (0.138 g) in dry THF (1 mL), and the reaction mixture was refluxed for 21 h. After the reaction mixture was cooled to 0 °C, a small portion of chilled water was added to the reaction mixture to quench the excess NaH. The solvent was removed under reduced pressure and the residue was extracted with $CHCl_3$. The combined extracts were washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by LC (eluting with methanol) provided 0.32 g of **8** in 75% yield. Mp 102.7 °C. FTIR (KBr): 3015, 2980, 1585, 1521, 1480, 1047 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): 6.90 (s, 1H), 6.82 (s, 1H), 5.09–5.04 (m, 7H), 4.78 (d, 2H), 4.72 (s, 2H), 3.82–3.15 (m, 108). MS (*m*/*z*): 1678.7 [M+Na^+]. Anal. Calcd for $C_{72}H_{121}BrO_{37}$: C, 52.14; H, 7.35. Found: C, 53.07; H, 7.21.

4.3. Compound 9

Compound **9** was prepared by a similar method as mentioned above in 75% yield. Mp 102.7 °C. FTIR (KBr): 3010, 2983, 1579, 1520, 1480, 1045 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): 6.91 (s, 1H), 6.80 (s, 1H), 5.09–5.04 (m, 6H), 4.82 (d, 2H), 4.73 (s, 2H), 4.73 (s, 2H), 3.82–3.15 (m, 91). MS (*m*/*z*): 1475 [M+Na^+]. Anal. Calcd for $C_{63}H_{105}BrO_{32}$: C, 52.03; H, 7.28. Found: C, 53.05; H, 7.20.

4.4. Compound 10

Under N_2 atmosphere, a solution of *p*-chlorophenol (0.63 g, 4.90 mmol) and 2-bis(bromomethyl)-1,4-dimethoxybenzene (2.0 g, 6.17 mmol) in dry THF (80 mL) was slowly added to a suspension of NaH (6.7 g) in dry THF (20 mL), and the reaction mixture was refluxed for overnight. After the reaction mixture was cooled to 0 °C, a small portion of chilled water was added to the reaction mixture to quench the excess NaH. The solvent was removed under reduced pressure and the residue was extracted with $CHCl_3$. The combined extracts were washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by LC (eluting with chloroform) provided 0.45 g of **10** in 20% yield. Mp 159.7 °C. FTIR (KBr): 3012, 2985, 1580, 1520, 1475, 1050 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): 6.98–6.80 (m, 6H), 5.14 (s, 2H), 4.34 (s, 2H), 3.84 (s, 3H), 3.70 (s, 3H). MS (*m*/*z*): 393 [M+Na^+]. Anal. Calcd for $C_{16}H_{16}ClBrO_3$: C, 51.71; H, 4.34; Cl, 9.54; Br, 21.50. Found: C, 52.00; H, 4.37; Cl, 9.52; Br, 21.51.

4.5. Compound 11

Under N_2 atmosphere, a solution of **8** (0.4 g, 0.24 mmol) and (2-hydroxymethyl)18-crown-6 (0.14 g, 0.417 mmol) in dry THF (3 mL) was slowly added to a suspension of NaH (0.16 g, 4.17 mmol) in dry THF (1 mL), and the reaction mixture was refluxed for 20 h. After the reaction mixture was cooled to 0 °C, a small portion of chilled water was added to the reaction mixture to quench the excess NaH. The solvent was removed under reduced pressure and the residue was extracted with $CHCl_3$. The combined extracts were washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by LC (eluting with methanol) gave **11** in 66.7% yield. Mp 115.2 °C. FTIR (KBr): 3015, 2982, 1585, 1510, 1473, 1048 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): 6.92 (s, 1H), 6.85 (d, 1H), 5.08–5.04 (m, 7H), 4.62 (d, 2H), 4.51 (s, 2H), 3.80–3.11 (m, 133H). FABMS (*m*/*z*): 1893.0 [M+*m*-nitrobenzoic acid]. Anal. Calcd for $C_{85}H_{146}O_{44}$: C, 54.53; H, 7.86. Found: C, 53.05; H, 7.95.

4.6. Compound 12

Yield: 50%. Mp 110.5 °C. FTIR (KBr): 3010, 2980, 1587, 1520, 1480, 1050 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): 6.80 (s, 2H), 5.09–5.04 (m, 6H), 4.82 (d, 2H), 4.73 (s, 2H), 3.82–3.15 (m, 118H). MS (*m*/*z*): 1697 [M+Na^+]. Anal. Calcd for $C_{76}H_{130}O_{39}$: C, 54.73; H, 7.86. Found: C, 54.70; H, 7.85.

4.7. Compound 13

Yield: 70%. Mp 150.2 °C. FTIR (KBr): 3012, 2983, 1581, 1515, 1472, 1050 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): 7.00–6.80 (m, 6H), 5.17 (s,

2H), 4.30 (s, 2H), 3.80 (s, 3H), 3.70–3.20 (m, 28H). MS (*m*/*z*): 607.2 [M+Na^+]. Anal. Calcd for $C_{29}H_{41}ClO_{10}$: C, 59.53; H, 7.06; Cl, 6.06; Br, 27.35. Found: C, 59.00; H, 7.07; Cl, 6.12.

4.8. Compound 14

A solution of **13** (0.36 g, 0.79 mmol) in CH_3CN (1 mL) was added to a solution of ceric ammonium nitrate (0.340 g, 0.79 mmol) in CH_3CN (1 mL) and H_2O (0.5 mL). The mixture was then stirred for 2 h at room temperature. After the reaction mixture was cooled to 0–5 °C, water was added to the mixture. The mixture was extracted with $CHCl_3$ and the combined extracts were washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by LC (eluting with methanol) gave **14** in 85% yield. Mp 115.6 °C. FTIR (KBr): 3015, 2980, 1640, 1582, 1517, 1480, 1050 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): 6.75 (s, 1H), 6.57 (s, 1H), 5.05 (m, 7H), 4.47 (s, 2H), 4.25 (s, 2H), 3.85–3.14 (m, 129H). MS (*m*/*z*): 1849.9 [M+Na^+]. Anal. Calcd for $C_{83}H_{140}O_{44}$: C, 54.12; H, 7.66. Found: C, 54.25; H, 7.55.

4.9. Compound 15

Yield: 52%. Mp 107.6 °C. FTIR (KBr): 3020, 2985, 1650, 1587, 1517, 1480, 1050 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): 6.48 (s, 2H), 5.10–5.03 (m, 6H), 4.82 (d, 2H), 4.73 (s, 2H), 3.82–3.15 (m, 112H). MS (*m*/*z*): 1660 [M+Na^+]. Anal. Calcd for $C_{74}H_{124}O_{39}$: C, 54.27; H, 7.63. Found: C, 54.25; H, 7.55.

4.10. Compound 16

Yield: 65%. Mp 145.5 °C. FTIR (KBr): 3010, 2985, 1635, 1588, 1517, 1472, 1050 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): 7.10–6.85 (m, 6H), 5.15 (s, 2H), 4.30 (s, 2H), 3.78 (s, 3H), 3.80–3.15 (m, 28H). MS (*m*/*z*): 577.5 [M+Na^+]. Anal. Calcd for $C_{27}H_{35}ClO_{10}$: C, 58.43; H, 6.36; Cl, 6.39. Found: C, 58.45; H, 6.35; Cl, 6.35.

4.11. Compound 1

To a solution of **14** (0.13 g, 0.070 mmol) in EtOH (1 mL), a solution of (4-nitrophenyl)hydrazine (0.022 g, 0.14 mmol) and two drops of concd H_2SO_4 in EtOH (1 mL) were added. The reaction mixture was allowed to stir overnight. The mixture was extracted with $CHCl_3$ and the combined extracts were washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by LC (eluting with methanol) gave 0.03 g of **1** in 25% yield. Mp 125.7 °C. FTIR (KBr): 3020, 2985, 1730, 1587, 1517, 1480, 1450, 1050 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): 8.47 (s, 1H), 8.37 (d, 2H), 7.95 (d, 2H), 7.86 (s, 1H), 7.84 (s, 1H), 5.22–5.10 (m, 7H), 4.82 (s, 2H), 4.73 (s, 2H), 3.82–3.15 (m, 127H). MS (*m*/*z*): 1998.5 [M+Na^+]. Anal. Calcd for $C_{89}H_{145}O_{45}N_3$: C, 54.04; H, 7.39; N, 2.13. Found: C, 54.28; H, 7.18; N, 2.07.

4.12. Compound 2

Yield: 30%. Mp 115.7 °C. FTIR (KBr): 3020, 2985, 1730, 1587, 1517, 1480, 1450, 1050 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): 8.47 (s, 1H), 8.37 (d, 2H), 7.95 (d, 2H), 7.85 (s, 2H), 5.09–5.04 (m, 6H), 4.82 (d, 2H), 4.73 (s, 2H), 3.82–3.15 (m, 112H). MS (*m*/*z*): 1795 [M+Na^+]. Anal. Calcd for $C_{80}H_{129}O_{40}N_3$: C, 54.20; H, 7.33; N, 2.37. Found: C, 51.95; H, 7.20; N, 2.22.

4.13. Compound 3

Compound **3** was prepared as described previously. Mp 205–207 °C. FTIR (KBr): 3253, 3010, 2973, 1585, 1521, 1485, 1050 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): 8.37 (d, 2H), 8.35 (s, 1H), 7.96 (d, 2H), 7.86 (s, 2H), 5.08 (m, 7H), 4.95–4.82 (dd, 4H), 3.82–3.15 (m, 212H). MS (*m*/*z*): 3130.5 [M+Na^+]. Anal. Calcd for $C_{138}H_{229}O_{73}N_3$: C, 53.50; H, 7.45; N, 1.36. Found: C, 53.87; H, 7.41; N, 1.35.

4.14. Compound 4

Compound **4** was prepared as described previously.[6] Mp 199–200 °C. FTIR (KBr): 3250, 3015, 2980, 1585, 1520, 1485, 1050 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): 8.37 (d, 2H), 8.34 (s, 1H), 7.97 (d, 2H), 7.86 (s, 2H), 5.08 (m, 6H), 4.95–4.82 (dd, 4H), 3.82–3.15 (m, 196H). MS (*m*/*z*): 2917.3 [M+Na^+]. Anal. Calcd for $C_{129}H_{213}O_{68}N_3$: C, 53.54; H, 7.42; N, 1.45. Found: C, 53.87; H, 7.41; N, 1.39.

4.15. Compound 5

Yield: 21%. Mp 125.5 °C. FTIR (KBr): 3225, 3017, 2985, 1730, 1585, 1520, 1480, 1450, 1050 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): 8.37 (d, 2H), 8.17 (s, 1H), 7.97 (d, 2H), 7.72 (s, 2H), 7.23 (d, 2H), 6.96 (d, 2H), 5.22 (s, 2H), 4.92 (s, 2H), 3.95–3.52 (br m, 25H). MS (*m*/*z*): 711 [M+Na^+]. Anal. Calcd for $C_{33}H_{40}O_{11}N_3Cl$: C, 57.43; H, 5.84; N, 6.09; Cl, 5.14. Found: C, 56.95; H, 5.60; N, 6.02; Cl, 5.20.

Acknowledgements

This work was supported by Korea Research Foundation Grant (KRF-2005-070-C00068) and KOSEF (2008-01014).

Supplementary data

UV–vis spectra of **1**–**5** with amines in $CHCl_3$. Photographs for color changes of **2**–**5** with amines. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.05.013.

References and notes

1. Fiorilli, S.; Onida, B.; Macquarrie, D.; Garrone, E. *Sens. Actuators, B* **2004**, *100*, 103.
2. Absalan, G.; Soleimani, M.; Asadi, M.; Ahmadi, M. *Anal. Sci.* **2004**, *20*, 1433.
3. Lau, K.; Edwards, S.; Diamond, D. *Sens. Actuators, B* **2004**, *98*, 12.
4. Mohr, G.; Demuth, G.; Spichiger-Keller, U. *Anal. Chem.* **1998**, *70*, 3868.
5. Hinsberg, O. *Chem. Ber.* **1890**, *23*, 2962.
6. Jung, J. H.; Lee, S. J.; Kim, J. S.; Lee, W. S.; Sakata, Y.; Kaneda, T. *Org. Lett.* **2006**, *8*, 3009.
7. Kim, J. S.; Lee, S. J.; Jung, J. H.; Hwang, I.-C.; Singh, N. J.; Kim, S. K.; Lee, S. H.; Kim, H. J.; Keum, C. S.; Lee, J. W.; Kim, K. S. *Chem.—Eur. J.* **2007**, *13*, 3082.
8. Cram, D. J.; Cram, J. M. *Acc. Chem. Res.* **1978**, *11*, 8.
9. Stoddart, J. F. *Chem. Soc. Rev.* **1979**, *8*, 85.
10. Mock, W. L.; Shih, N.-Y. *J. Org. Chem.* **1986**, *51*, 4440.
11. Hayward, R. C. *Chem. Soc. Rev.* **1983**, *12*, 285.
12. Jung, J. H.; Takehisa, C.; Sakata, Y.; Kaneda, T. *Chem. Lett.* **1996**, 147.
13. Fujimoto, T.; Uejima, Y.; Imaki, H.; Kawarabayashi, N.; Jung, J. H.; Sakata, Y.; Kaneda, T. *Chem. Lett.* **2000**, 564.
14. Connors, K. A. *Binding Constants*; Wiley: New York, NY, 1987.
15. Cobben, P. L. H. M.; Egberink, R. J. M.; Bomer, J. G.; Bergveld, P.; Verboom, W.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1992**, *114*, 10573.
16. Kaneda, T. *Crown Ethers and Analogous Compound*; Hiraoka, M., Ed.; Elsevier: New York, NY, 1992; Chapter 6.
17. Kaneda, T.; Umeda, S.; Ishizaki, Y.; Kuo, H.-S.; Misumi, S.; Kai, Y.; Kanehisa, N.; Kasai, N. *J. Am. Chem. Soc.* **1989**, *111*, 1881.