

Synthesis of Novel Anionic Receptors with (Thio)urea and Amide Binding Sites and the Recognition Properties for Anions

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Two new neutral receptors (**1** and **2**) containing (thio)urea and amide groups were synthesized by simple steps in good yields. The binding properties for anions of **1** and **2** were characterized by UV-vis and fluorescence spectra. Receptor **1** had an excellent selectivity for AcO^- in comparison with other anions. The association constants of $1 \cdot \text{AcO}^-$ and $2 \cdot p\text{-NO}_2\text{PhPO}_3^{3-}$ were higher than those of other anions (Cl^- , Br^- , I^- , H_2PO_4^- and $p\text{-NO}_2\text{PhO}^-$). In particular, an obvious color change was observed from light yellow to golden yellow upon addition of AcO^- to the solution of **1** in DMSO. The results of non-linear curve fitting by UV-vis and fluorescence spectral data indicate that a 1:1 stoichiometry complex is formed between compound **1** or **2** and anions through a hydrogen bonding interaction.

Keywords neutral anion receptor, hydrogen binding, anionic recognition, synthesis

Introduction

Since more and more anions play an important role in biological and chemical processes, the design and synthesis of receptors for on-line and real time detection of biologically important anions, and for environmental monitoring of harmful anion pollutants have attracted particular attention in supramolecular chemistry.¹ The basic strategy for the construction of anion-binding receptors is to exploit the receptors that have electrostatic,² hydrogen bonding,³ or Lewis acidic central interaction.⁴ Among a variety of non-covalent interactions, hydrogen bonding interaction has been proven to be very efficient manner for anionic recognition. In numerous possible H-bonding donor groups, thiourea, urea and amide moieties have become the focus of the development of neutral anionic receptors, because the hydrogen bonding of these functional groups is directional in character and results in relatively strong complex with various biologically important anions such as carbonate, chloride, or phosphate.⁵

To our best knowledge, although some neutral anionic receptors containing urea or thiourea units have been reported in the last decades,^{5,6} the neutral receptors containing simultaneously both binding units of (thio)urea with

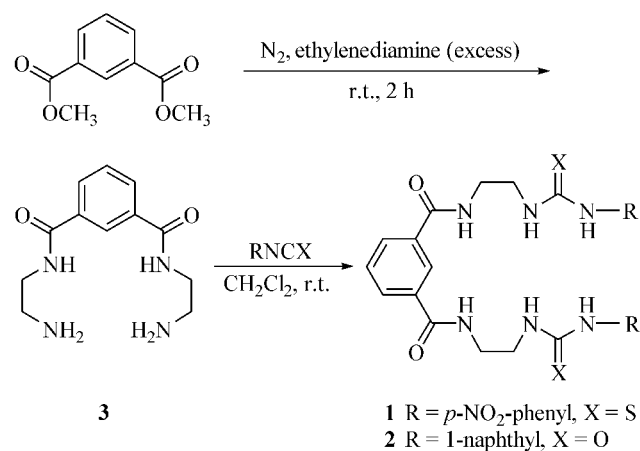
amide in a molecule have seldom been reported. The cooperative action of two functional groups for anion could enhance effectively selectivity in the recognition and the stability of the resultant complex. Herein, we report the synthesis and binding properties of two new neutral anionic receptors (**1** and **2**) containing thiourea with amide or urea with amide, respectively. The anionic recognition of receptors **1** and **2** has been investigated respectively by UV-vis absorption and fluorescence emission spectra.

Results and discussion

Synthesis

Receptors **1** and **2** which respectively contain thiourea with amide and urea with amide groups, were synthesized by the reaction of *p*-nitrophenylisothiocyanate or 1-naphthylisocyanate and 1,3-di(aminoethylenecarbamoyl) benzene (**3**) with almost quantitative yields (Scheme 1).

Scheme 1 Synthesis route of receptors **1** and **2**



Absorption and fluorescence spectra

The binding properties of receptor **1** with various an-

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Received May 26, 2003; revised July 18, 2003; accepted August 15, 2003.

Project supported by the National Natural Science Foundation of China (No. 20072029).

ions (AcO^- , H_2PO_4^- , $p\text{-NO}_2\text{PhOPO}_3^{2-}$, $p\text{-NO}_2\text{PhO}^-$, Cl^- , Br^- and I^-) were studied by UV-vis absorption spectra. Fig. 1 showed the absorption spectra of a mixture of receptor **1** (5×10^{-5} mol/L) with different concentration of AcO^- in DMSO. Receptor **1** displayed a maximum absorption at 360 nm. Gradually increasing the concentration of AcO^- , the intensity of absorption peak at 360 nm was decreased gradually, and a new absorption bond appeared with a maximum absorption at 477 nm, and an isobestic point was observed at 376 nm, demonstrating that **1** with AcO^- formed 1:1 complex.^{5a} The similar phenomenon appeared when H_2PO_4^- was added to the solution of **1** in DMSO. However adding hundreds of equivalent of Cl^- , Br^- or I^- to the solution of **1**, the absorption spectrum of **1** did not change at all. Fig. 2 showed the absorption spectra of a complexation of receptor **1** with $p\text{-NO}_2\text{PhOPO}_3^{2-}$ in DMSO. When the different concentrations of **1** were

added to the solution of the solutions of $p\text{-NO}_2\text{PhOPO}_3^{2-}$ (5×10^{-5} mol/L) in DMSO, the maximum absorption peak of $p\text{-NO}_2\text{PhOPO}_3^{2-}$ at 435 nm was decreased gradually until complete disappearing. It is confirmed that the complexation between receptor **1** and $p\text{-NO}_2\text{PhOPO}_3^{2-}$ had happened. The similar phenomenon also appeared when **1** was added to the solution of $p\text{-NO}_2\text{PhO}^-$ in DMSO.

In particular, it was remarkable that significant changes were observed while AcO^- was added into receptor **1** in DMSO. Upon the gradually increasing of the concentration of AcO^- , the color of solution of receptor **1** was changed from pale yellow to golden yellow, which could be observed by naked eyes. However, there was no similar color change upon adding other anions into receptor **1**. In the supramolecular system, the electronic excitation is mostly accompanied by a charge transfer from donor nitrogen of the thiourea to acceptor substituent ($-\text{NO}_2$) of the chromophore. Introducing electron-withdrawing substituent ($-\text{NO}_2$) can enhance the acidity of thiourea moiety, strongly stabilize the excited state, and result in a bathochromic shift in the absorption maximum, to produce a possible effective color change in aprotic media.^{5a,7} Among all anions studied, the phenomenon appeared only upon adding AcO^- into solution of **1**.

The binding property of **1** with AcO^- was further assessed by UV-vis spectroscopy titration.⁷ Because receptor **1** had many binding sites, a Job plot experiment was carried out to determine the complex ratio. Fig. 3(a) shows the Job plot of **1** with AcO^- at a total concentration of 0.1 mmol/L in DMSO. When the molar fraction of $[\text{1}]/([\text{1}] + [\text{AcO}^-])$ is about 0.5, the absorption gets to a maximum, which means the formation of 1:1 complex of **1** and AcO^- . Fig. 3(b) expressed the plot of absorption change of interaction of receptor **1** versus different equivalent of anion at 477 nm for AcO^- and H_2PO_4^- , or at 435 nm for $p\text{-NO}_2\text{PhO}^-$ and $p\text{-NO}_2\text{PhOPO}_3^{2-}$. The results of non-linear curve fitting confirmed that 1:1 stoichiometry complex was formed between **1** and anions.⁸

The fluorescence spectra of receptor **2** were studied from a solution (5×10^{-5} mol/L) of **2** in DMSO in the absence or the presence of various anions such as AcO^- , H_2PO_4^- , $p\text{-NO}_2\text{PhOPO}_3^{2-}$ and $p\text{-NO}_2\text{PhO}^-$. In each case the counter-ion was tetrabutylammonium except for ($p\text{-NO}_2\text{PhOPO}_3^{2-}$) Na_2^+ . As shown in Fig. 4(a), in the absence of anions, receptor **2** shows a strong emission at 384 nm. With increasing amounts of $p\text{-NO}_2\text{PhOPO}_3^{2-}$, the fluorescence intensity of **2** at 384 nm is gradually decreased until almost completely quenched. Complexation of **2** with $p\text{-NO}_2\text{PhO}^-$ results in similar quenching tendency of fluorescence intensity. In comparison with $p\text{-NO}_2\text{PhOPO}_3^{2-}$ and $p\text{-NO}_2\text{PhO}^-$, while AcO^- or H_2PO_4^- was added into the solution of **2** in DMSO, the phenomenon of fluorescence quenching was not obvious. When Cl^- , Br^- or I^- was added into the solution of **2** in DMSO, nothing happened. When host **2** and guest with strong

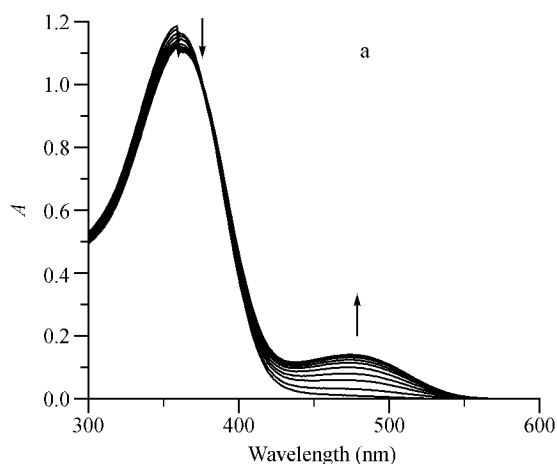


Fig. 1 UV-vis absorption spectra of **1** (5×10^{-5} mol/L) in the presence of various amounts of AcO^- in DMSO, Equivalent of $\text{Bu}_4\text{N}^+(\text{AcO}^-)$: 0, 0.1, 0.2, 0.4, 0.6, 0.8, 1.0, 1.4, 1.8 and 2.4.

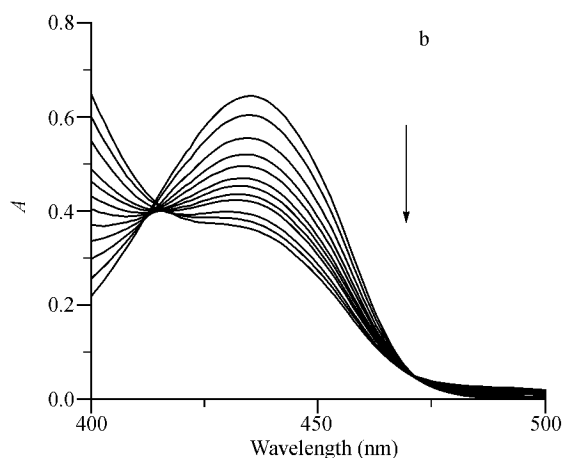


Fig. 2 UV-vis absorption spectra of $p\text{-NO}_2\text{PhOPO}_3^{2-}$ (5×10^{-5} mol/L) in the presence of various amounts of **1** in DMSO, Equivalent of **1**: 0, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 1.0, 1.2 and 1.4.

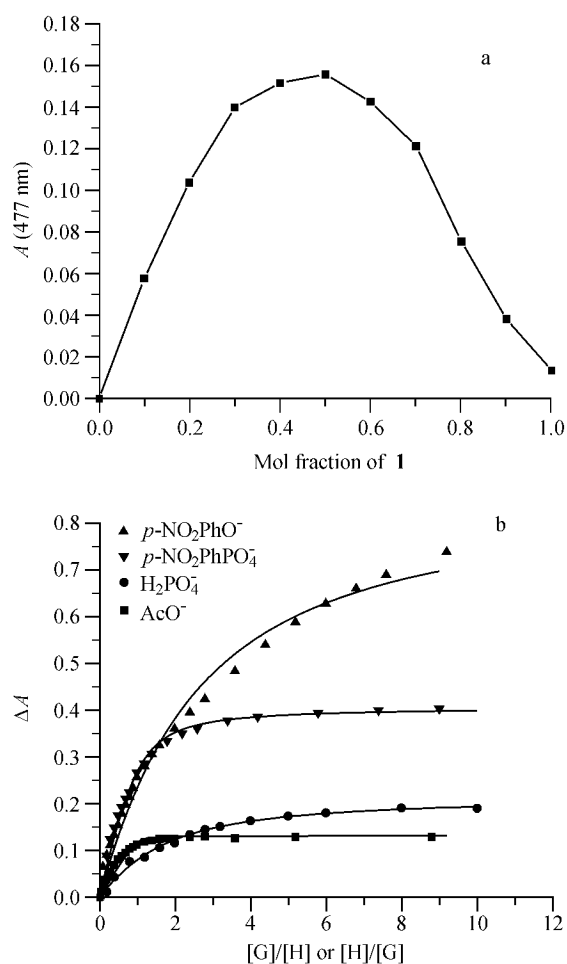


Fig. 3 (a) Job plot of **1** and AcO^- at a total concentration of 0.1 mmol/L in DMSO; (b) Plots of absorption change versus equivalent of anions added, the lines are fitting curves. AcO^- or H_2PO_4^- was added into the solution of **1** (5×10^{-5} mol/L) in DMSO at 477 nm, $\Delta A = A - A_0$; for other anions, the various concentration of **1** was added into the solutions of anions (5×10^{-5} mol/L) in DMSO at 435 nm, $\Delta A = A - A_0$.

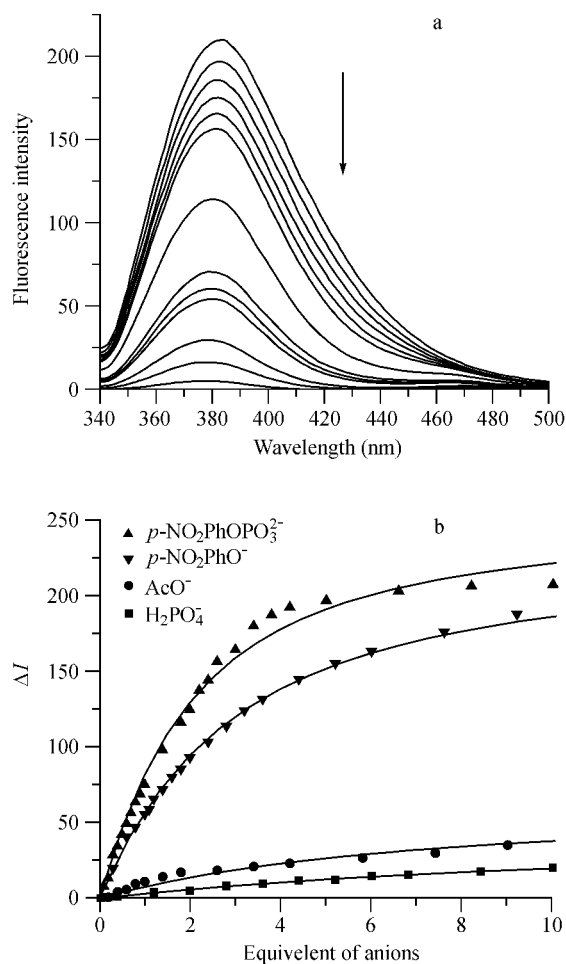


Fig. 4 (a) Fluorescence spectra of **2** (5×10^{-5} mol/L, DMSO) in the presence of various amounts of $p\text{-NO}_2\text{PhOPO}_3^{2-}$ in DMSO, $\lambda_{\text{ex}} = 320$ nm, equivalent of $p\text{-NO}_2\text{PhOPO}_3^{2-}$: 0, 0.2, 0.4, 0.6, 0.8, 1.0, 1.4, 1.8, 2.0, 2.2, 3.4, 4.2, 6.6; (b) Plots of fluorescence change versus equivalent of anions added [**2**]: 5×10^{-5} mol/L, the lines are fitting curves. For all anions, $\Delta I = I_0 - I$.

electron-withdrawing groups (-nitro) interacted, it could be hypothesized that the fluorescence quenching was due to an electron transfer process. The interaction between receptor **2** and $p\text{-NO}_2\text{PhOPO}_3^{2-}$ (or $p\text{-NO}_2\text{PhO}^-$) resulted in nitro group and photo-excited naphthyl fragments at an effective distance, and orbital overlapping and efficient electron transfer occurred.⁹ The fitting curves [Fig. 4(b)] proved the formation of 1:1 stoichiometry complex.⁸

Determination of the association constants (K_{ass}) of the complexes

For the complex of 1:1 stoichiometry, according to the following relation:¹⁰

$$X = X_0 + (X_{\text{lim}} - X_0) / 2 \left\{ c_{\text{H}} + c_{\text{G}} + 1/K_{\text{ass}} - \left[(c_{\text{H}} + c_{\text{G}} + 1/K_{\text{ass}})^2 - 4c_{\text{H}}c_{\text{G}} \right]^{1/2} \right\}$$

Where X represented the absorption or the fluorescence intensity, and c_{H} and c_{G} are the corresponding concentrations of host and anion guest. The association constants and correlation coefficients (R) obtained by a non-linear least-squares analysis of X versus c_{H} and c_{G} are listed in Table 1. The data show that receptor **1** has an excellent selectivity for AcO^- over other anions, and the selectivity is in the order of $\text{AcO}^- \gg p\text{-NO}_2\text{PhOPO}_3^{2-} > \text{H}_2\text{PO}_4^- > p\text{-NO}_2\text{PhO}^- \gg \text{Cl}^-$, Br^- and I^- . Table 1 also shows that receptor **2** has a selectivity in the order of $p\text{-NO}_2\text{PhOPO}_3^{2-} > p\text{-NO}_2\text{PhO}^- > \text{AcO}^- > \text{H}_2\text{PO}_4^- \gg \text{Cl}^-$, Br^- and I^- , but the selectivity of **1** for anions is better than that of **2**. All correlation coefficients (R) obtained are larger than 0.99. It is also illustrated the formation of 1:1 stoichiometry complex between receptor **1** or **2** and anion. The association constants of receptor **1** for anions are larger than those of similar neutral receptors only containing thiourea¹¹ or amide¹² groups reported formerly. It is

Table 1 Association constants K_{ass} (L/mol) of receptors **1** and **2** with guest anions

Anion	Receptor 1		Receptor 2	
	K_{ass} (L/mol) ^d	Correlation coefficient (R)	K_{ass} (L/mol) ^d	Correlation coefficient (R)
AcO ^{-a}	$(1.63 \pm 0.19) \times 10^6$	0.9970	$(3.08 \pm 0.32) \times 10^3$	0.9920
H ₂ PO ₄ ^{2-a}	$(1.85 \pm 0.16) \times 10^4$	0.9974	$(1.61 \pm 0.10) \times 10^3$	0.9991
<i>p</i> -NO ₂ PhO ^{-a}	$(1.01 \pm 0.11) \times 10^4$	0.9930	$(8.57 \pm 0.27) \times 10^3$	0.9987
<i>p</i> -NO ₂ PhOPO ₃ ^{2-b}	$(1.92 \pm 0.16) \times 10^4$	0.9957	$(1.36 \pm 0.12) \times 10^4$	0.9953
Cl ⁻ , Br ⁻ and I ^{-a}	f		f	

^a The anions were used as their tetrabutylammonium salts. ^b The anion was used as its disodium salt. ^c The data were calculated from UV-vis titration in DMSO. ^d All error values were obtained by the results of non-linear curve fitting. ^e The data were calculated from fluorescence titration in DMSO. ^f The change of the spectrum was too small to calculate the association constant accurately.

approved that the cooperative action of thiourea and amide groups in binding for anion by multiple hydrogen bonding interactions and the electron-withdrawing substituents in receptor **1** play important roles.⁸

Conclusion

The neutral anion receptors **1** and **2** were synthesized by an easy method with high yields. Receptor **1** or **2** can form 1:1 complex with anions by multiple hydrogen bonding interactions. The selectivity of **1** for anions is better than that of **2**. Receptor **1** has an excellent selectivity recognition to AcO⁻ by comparison with other anions, and there is an observable color change by naked eyes, which is promising to be used as optical chemosensors for acetate anion.

Experimental

General methods

Melting points were measured on a Reichert 7905 melting-point apparatus (uncorrected). The infrared spectra were performed on a Testscan Shimadzu FT-IR spectrophotometer. The mass spectra were recorded on a ZAB-HF-3F spectrometer. Elemental analyses were determined by a Perkin-Elmer 204B elemental autoanalyzer. ¹H NMR spectra were recorded on a Varian Mercury VX-300 MHz spectrometer. UV-vis spectra were taken on a TU-1901 spectrometer. Fluorescence spectra were obtained on a Shimadzu RF-5301 spectrometer.

Materials

Methanol and CH₂Cl₂ were dried and distilled before using according to the standard procedure. All other commercially available reagents were used without further purification. Tetrabutylammonium salts were used as anionic substrates except the disodium salt was used as *p*-NO₂PhOPO₃²⁻ substrate. 1-*β*-Di(*aminoethylenecarbamoyl*)benzene (**3**) was synthesized according to the reported

method in literature.¹³

Synthesis

1-*β*-Di(*aminoethylenecarbamoyl*)benzene (**3**)

In nitrogen atmosphere, ethylenediamine (8.98 g, 149.0 mmol) and 1-*β*-di(methoxycarbonyl)benzene (3.96 g, 20.4 mmol) were dissolved in 300 mL of absolutely dry methanol, and the reaction mixture was stirred at room temperature for 2 h. After filtration, the filtrate was collected, and then both the solvent and the excess ethylenediamine was removed entirely by evaporation under reduced pressure to give **3** (4.52 g) as a white solid in 88.6% yield, which was used in the next step without further purification. m.p. 168–171 °C; ¹H NMR (CDCl₃, 300 MHz) δ: 2.77 (t, *J* = 5.4 Hz, 4H, NCH₂), 3.18 (b, 4H, NH₂, diminished after adding D₂O), 3.25 (t, *J* = 5.4 Hz, 4H, CONCH₂), 7.48 (t, *J* = 8.1 Hz, 1H, ArH), 7.95 (d, *J* = 8.1 Hz, 2H, ArH), 8.32 (s, 1H, ArH), 8.58 (s, 1H, CONH), 8.78 (s, 1H, CONH); IR (KBr) ν: 3488, 3405, 1655 cm⁻¹.

1-*β*-Di(*p*-nitrophenylthioureidoethylenecarbamoyl)benzene (**1**)

To a solution of *p*-nitrophenylisothiocyanate (0.72 g, 4.0 mmol) in dry CH₂Cl₂ (25 mL), **3** (0.5 g, 2.0 mmol) in dry CH₂Cl₂ (25 mL) was added slowly at room temperature. After stirring for 2 h, the precipitate was filtered off, and dried in vacuum to obtain **1** (1.15 g) as light yellow solid in 94.3% yield. m.p. 158–160 °C; ¹H NMR (DMSO-*d*₆, 300 MHz) δ: 3.42 (t, *J* = 5.1 Hz, 4H, NCH₂), 3.65 (t, *J* = 5.1 Hz, 4H, CONCH₂), 7.77–8.17 (AA'BB', 8H, ArH), 7.48 (t, *J* = 7.8 Hz, 1H, ArH), 7.95 (d, *J* = 7.8 Hz, 2H, ArH), 8.32 (s, 1H, ArH), 8.39 (s, 2H, NHCS), 8.70 (s, 2H, CONH), 10.12 (s, 2H, ArNHCS); IR (KBr) ν: 3256, 3283, 1633, 1597, 1547, 1510, 1330, 1303, 1261, 847, 723 cm⁻¹; MS *m/z* (%): 611 (M⁺ + 1, 15). Anal. calcd for C₂₆H₂₆N₈O₆S₂: C 51.13, H 4.30, N 18.35; found C 51.22, H 4.20, N 18.25.

1 *β*-Di(1-naphthylureidoethylenecarbamoyl)benzene (2)

To a solution of naphthylisocyanate (0.85 g, 5.0 mmol) in dry CH₂Cl₂ (20 mL), **3** (0.63 g, 2.5 mmol) in dry CH₂Cl₂ (20 mL) was added slowly at room temperature. After stirring 2 h, the precipitate was filtered off, and dried under vacuum to obtain **2** (1.3 g) as a white solid in 87.8% yield. m.p. > 210 °C; ¹H NMR (DMSO-*d*₆, 300 MHz) δ: 3.42–3.48 (m, 8H, CONCH₂-CH₂N), 6.68 (s, 2H, NHCO), 7.35–8.37 (m, 18H, ArH), 8.53 (s, 2H, CONH), 8.65 (s, 2H, ArNHCO); IR (KBr) ν: 3309, 1638, 1547, 780 cm⁻¹; MS *m/z* (%): 589 (M⁺ + 1, 68). Anal. calcd for C₃₄H₃₂N₆O₄: C 69.36; H 5.49; N 14.28; found C 69.21, H 5.52, N 14.40.

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(E0305261 SONG, J. P.; ZHENG, G. C.)