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Synthesis and halochromism of new quinoxaline fluorescent dyes

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Abstract

New 6,7-bis-(3-methylbutoxyl)quinoxaline fluorescent dyes with groups of different electron-donating ability were synthesized by the condensation of [3-(diethoxyphosphoryl methyl)-6,7-bis-(3-methylbutoxy)-quinoxalin-2-yl methyl]-phosphonic acid diethyl ester **3** with arylaldehydes. The substituent effects of the donor moiety on the absorption and fluorescent properties in solution were correlated with the nature of the chromophoric systems.

Keywords: Chemical sensors; Spectral change; New quinoxaline fluorescent dye; Fluorescent sensors

1. Introduction

Fluorescent heterocyclic compounds are of interest as functional materials in the emitters of electroluminescence devices and in the molecular probes used for biochemical research, as well as in the traditional textile and polymer fields [1–3]. In particular, fluorescent dye materials whose fluorescence emission occurs at a longer wavelength in the red light region are expected to play a leading role in full color electroluminescence displays. Heterocyclic fluorophores are useful materials in the search for new biologically active compounds and diagnostic methods [4].

Fluorescent chromophores are generally known to have planar and rigid π-conjugation systems, and many fluorescent chromophores are based on rigid ring systems such as stilbene, coumarin, naphthalimide, perylene and rodamine. Our research group has been interested in the chemistry of nitrogen-containing heterocyclic molecules for many years. We have previously studied new fluorescent chromophores based on a pyrazine nucleus. New fluorescent compounds such as styrylpyrazines [5], pyrazinophthalocyanines [6] and pyrazinoheterocycles [7] have previously been reported.

In this study, we designed and synthesized some new 6,7-bis-(3-methylbutoxyl)quinoxaline derivatives with different electron-donating abilities. The chromophoric systems of these compounds, and the substituent effects on their absorption spectra in solution, were studied.

2. Results and discussion

*2.1. Reaction of [3-(diethoxyphosphoryl methyl)-6,7-bis-(3-methylbutoxy)-quinoxalin-2-yl methyl]-phosphonic acid diethyl ester **3** with 2 equivalents of arylaldehydes*

Quinoxalines are, in general, comparatively easy to prepare, and numerous derivatives have been designed and prepared for potential use as biologically active materials. The classical synthesis of quinoxalines involves the condensation of an aromatic 1,2-diamine with a 1,2-dicarbonyl compound. The reaction is facile and is the most widely used synthetic method for both quinoxaline itself and its derivatives.

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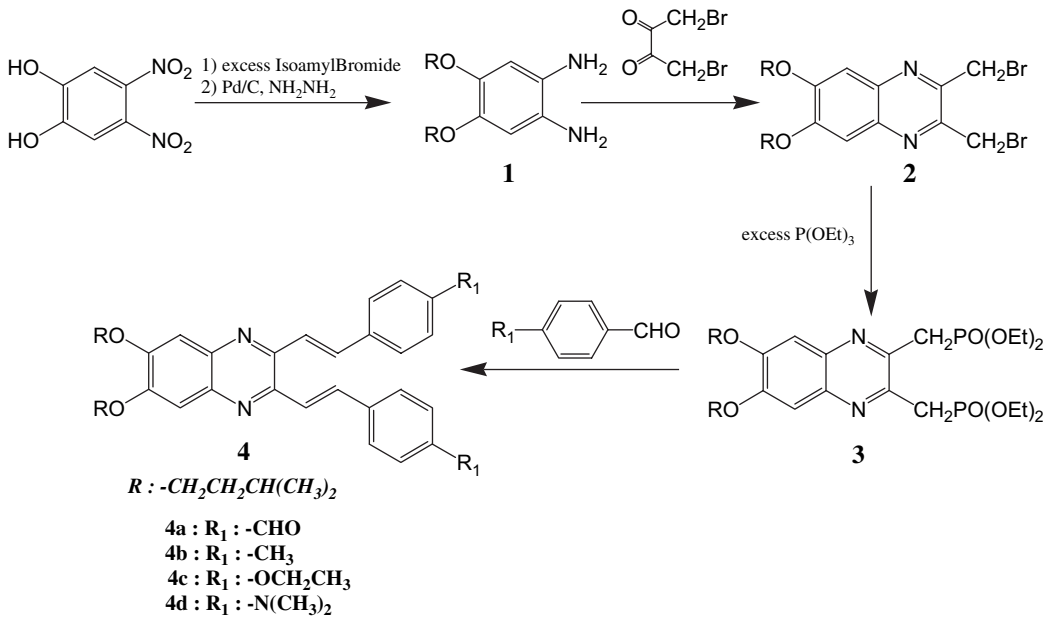

Scheme 1.

4,5-Dinitrocatechol was reacted with 1-bromo-3-methylbutane (Cs_2CO_3, DMF, 100 °C) to afford 1,2-bis-(3-methylbutoxy)-4,5-dinitrobenzene (60%) [8]. The reduction of 1,2-bis-(3-methylbutoxy)-4,5-dinitrobenzene with Pd/C and NH_2NH_2 yielded 1,2-bis-(3-methylbutoxy)-4,5-diaminobenzene **1** (45%) [8], which was subsequently condensed with 1,4-dibromobutane-2,3-dione in the presence of a catalytic amount of *p*-toluenesulfonic acid in methanol to afford 2,3-bis-bromomethyl-6,7-bis-(3-methylbutoxy)quinoxaline **2** at a yield of 55%. The amyl ether moiety was chosen to improve the solubility of the resulting quinoxaline fluorescent dyes in common organic solvents. The reaction of **2** with an excess of triethylphosphite produced [3-(diethoxyphosphoryl methyl)-6,7-bis-(3-methylbutoxy)-quinoxalin-2-yl methyl]-phosphonic acid diethyl ester **3**. This crude product was used in the next step without purification. The reaction of **3** with 2 equivalents of arylaldehydes in the presence of 2.1 equivalents of sodium hydride in tetrahydrofuran gave the styryl derivatives **4** in moderate yield. The reaction and structures of the products are summarized in Scheme 1.

The formation of **4** was verified with ^{1}H NMR spectroscopy and elementary analysis. For example, the ^{1}H NMR spectra of **4d** indicated that the ethylene protons appeared as a doublet at 7.72 and 7.45 ppm and revealed a *trans*-configuration with a coupling constant of 15.6 Hz. The chemical shifts of the aromatic protons appeared as a doublet at 7.57 and 6.74 ppm, while those of the quinoxaline protons (H 5/8) and the protons of the terminal N–CH_3 appeared as singlets at 7.27 and 3.02 ppm, respectively.

2.2. Absorption and emission spectra (halochromism)

The substituent effects of the donor group on the visible and fluorescent spectra are summarized in Table 1. The electronic character of the substituents in dyes **4** strongly affects their absorption spectra producing a bathochromic shift to an extent which depends on their electron-donating ability. Dye **4a** absorbs at 420 nm and emits at 470 nm. As the electron-donating ability of the donor group increases from the aldehyde (**4a**) to the dimethylamine derivative (**4d**), the λ_{max} and F_{max} values show bathochromic shifts attaining the maximum values of 444 nm ($\Delta\lambda = 24$ nm) and 567 nm ($\Delta F = 97$ nm) for **4d**, respectively. The Stokes shift (SS) values for dyes **4** in $CHCl_3$/MeOH (10/1) are in the range of 50–123 nm. The big difference in their SS values indicates that **4d** looses more energy in the excited state (i.e. has a bigger SS value) than **4a**.

In an acidic medium, the absorption spectra of dyes **4** were dramatically changed. Thus, the original orange solution of **4d** became greenish blue as the concentration of *p*-toluenesulfonic acid was increased, returning to the original orange color upon the addition of triethylamine (Figs. 1 and 2). As the concentration of *p*-toluenesulfonic acid was increased, the absorption maximum of **4a** at 420 nm decreased while that of a new absorption band which appeared at 480 nm increased.

The absorption and fluorescence maxima of dyes **4** in an acidic medium were observed in the regions 480–600 nm and 574–602 nm, respectively. The observed color change is considered to be due to the protonation of the nitrogen atom in the quinoxaline ring. It has been reported

Table 1
Visible and fluorescence spectra of quinoxalines **4**

Compound	λ_{max}[a] (nm)	ε_{max}[b]	λ_{max}[c] (nm)	F_{max}[d] (nm)	F_{max}[e] (nm)	SS[f]
4a	420	137,708	480	470	574	50
4b	422	112,361	494	474	560	52
4c	430	109,869	514	490	591	60
4d	444	106,202	600	567	602	123

[a] In $CHCl_3/CH_3OH$ (10/1).
[b] At λ_{max}[a] value.
[c] In acidic condition.
[d] Fluorescence maximum excited at λ_{max}[a] value.
[e] Fluorescence maximum excited at λ_{max}[c] value.
[f] Stokes shift (F_{max}[d] − λ_{max}[a]).

that the protonation of the nitrogen atom of heteroaromatic poly(arylene) in acidic media sometimes leads to a bathochromic shift of the absorption peak [9,10].

The UV–visible spectra of the synthesized novel quinoxalines in chloroform/methanol (10/1) were measured by varying the mole ratio of quinoxaline/*p*-toluenesulfonic acid (PTC). Both quinoxaline derivatives showed bathochromic shifts as the proportion of PTC was increased. The UV–visible spectra of **4a** showed a maximum shift of the absorption band at a mole ratio of 1:32, while the absorption band of **4d** shifted dramatically as the mole ratio was increased from 1:0 to 1:7, but did not shift at mole ratios of above 1:7. This result was attributed to the electron-donating abilities of the substituents. In the case of **4d**, it is supposed that the 1,4-position nitrogen atoms in the quinoxaline ring were easily saturated with electrons and thus able to be protonated by less PTC than those of **4a**, and that subsequently the electron density of the protonated nitrogen decreased and the electron-withdrawing ability of quinoxaline increased. Fig. 3 shows the ^{1}H NMR spectra of the unprotonated and

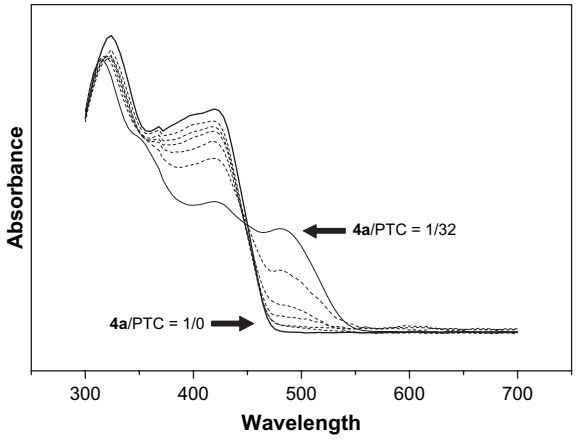

Fig. 1. The effect of *p*-toluenesulfonic acid (PTC) on the absorption spectra of **4a** in $CHCl_3/CH_3OH$ (10/1).

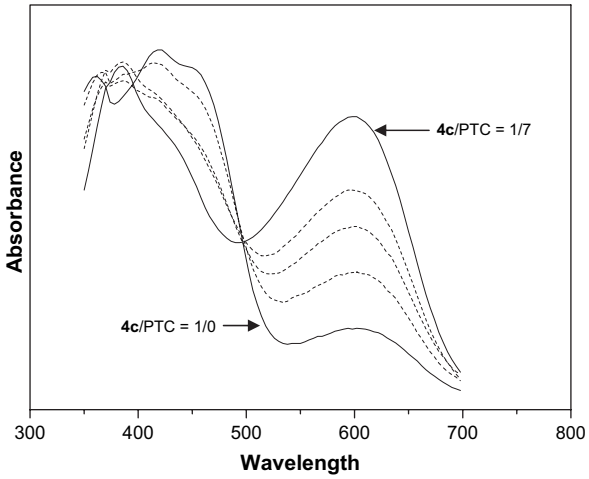

Fig. 2. The effect of *p*-toluenesulfonic acid (PTC) on the absorption spectra of **4d** in $CHCl_3/CH_3OH$ (10/1).

protonated forms of **4d**. This was verified by the shift of the proton signal in the quinoxaline ring from 7.27 to 7.32 ppm in the ^{1}H NMR spectra when trifluoroacetic acid was added. This result corresponds well with the values obtained from the observed optical properties.

In contrast to the strong fluorescence of dyes **4** in a non-acidic solution, the addition of *p*-toluenesulfonic

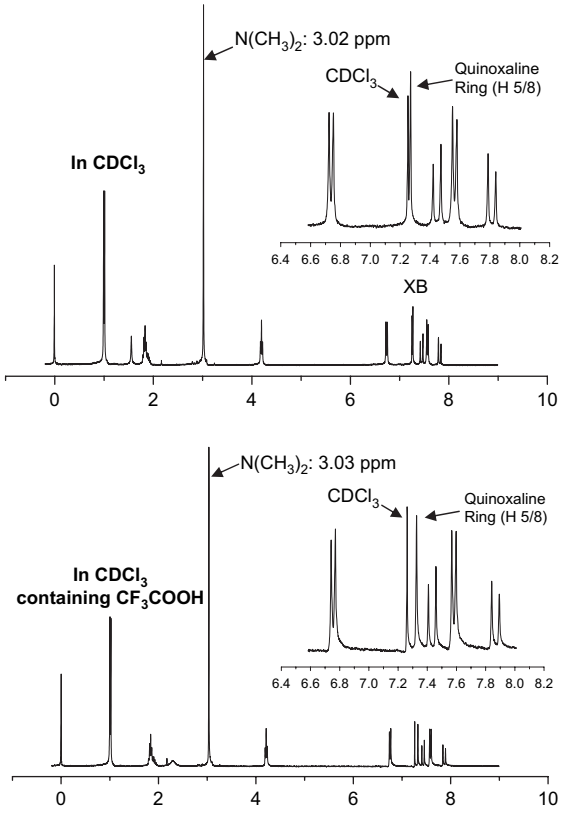

Fig. 3. 300 MHz ^{1}H NMR spectra of **4d**.

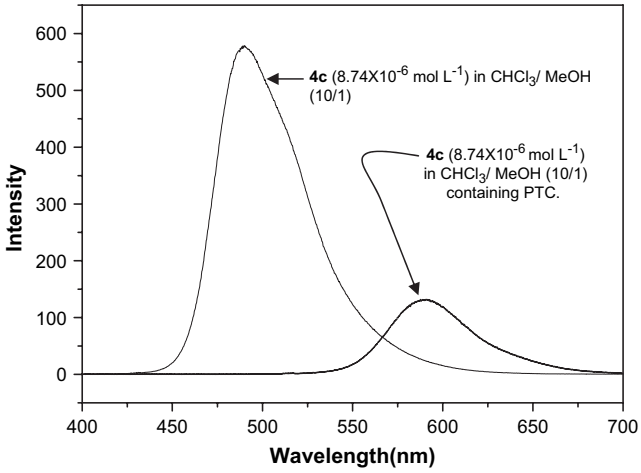

Fig. 4. The effect of *p*-toluenesulfonic acid (PTC) on the emission spectra of **4c** (8.74×10^{-6} mol L^{-1}) in $CHCl_3/CH_3OH$ (10/1).

acid to a $CHCl_3$/MeOH (10/1) solution of **4** leads to a continuous decrease in the intensity of the fluorescence. The protonation of the imine nitrogen(s) of **4** seems to change the electronic state(s) of the dyes and/or the process by which the fluorescence is generated (Fig. 4).

2.3. Photonic sensing properties

On the other hand, dye **4** showed absorption spectra changes depending on the extent of photo-irradiation. When a solution of dye **4** in chloroform was exposed to UV light (230–400 nm), the absorption spectra came to resemble that of its protonated form. This phenomenon may be due to the photo-induced structure of the quinoxaline moiety. The structural analysis of the photo-induced product will be determined in the near future and the results will be reported in due course. In conclusion, it is expected that the quinoxaline derivatives with different electron-donors will have different sensitivities and absorption spectra under acidic conditions (Fig. 5).

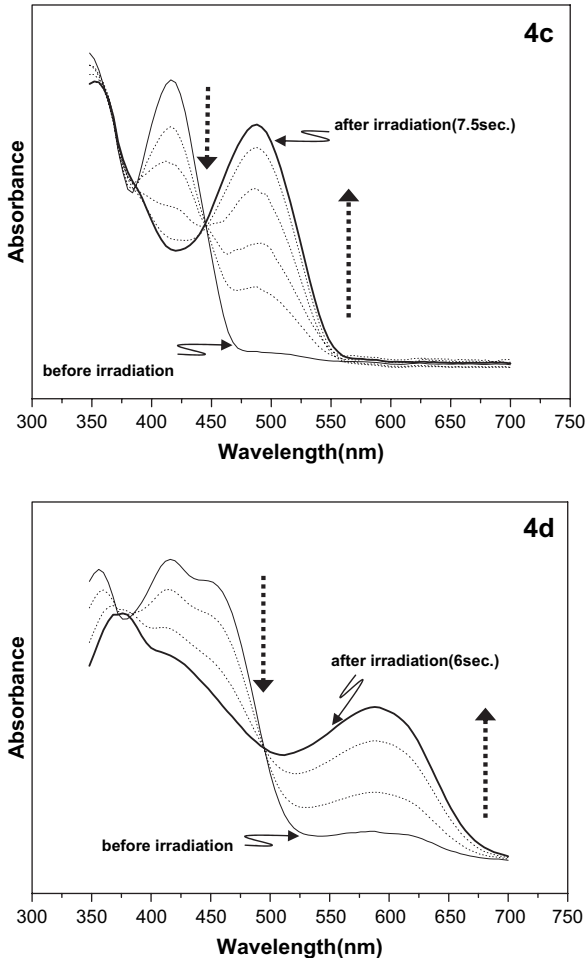

Fig. 5. Absorption spectral changes of **4c** and **4d** in $CHCl_3$ irradiated at 230–400 nm.

3. Experimental

3.1. General

All reactions were carried out under N_2 atmosphere unless otherwise noted. Flash chromatography was performed with Merck-EM Type 60 (230–400 mesh) silica gel (flash). Melting points were obtained with a capillary melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker DRX-300 FT-NMR spectrometer using TMS as internal standard. Elemental analyses were performed on a CE, EA 1110. The visible and fluorescence spectra were measured on UNICAM 8700 and SHIMADZU RF-5301PC spectrophotometer.

3.2. 2,3-Bis-bromomethyl-6,7-bis-(3-methylbutoxy)quinoxaline **2**

The reaction mixture of 1,4-dibromobutane-2,3-dione (18 g, 70 mmol), an equivalent amount of 1,2-bis-(3-methylbutoxy)-4,5-diaminobenzene, and a catalytic amount of *p*-toluenesulfonic acid in methanol (50 mL) was refluxed for 2 h under nitrogen atmosphere. After the reaction was complete, the reaction mixture was cooled to room temperature and the precipitate was filtered off. The crude product was purified by flash chromatography (silica gel, EtOAc:hexane = 1:4) to give **2** in 55% yield as a white solid. M.p. 66–67 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99 (d, 12H, $J = 6.0$, CH_3), 1.81 (m, 6H, CH and CH_2), 4.18(t, 4H, $J = 6.3$, OCH_2), 4.88 (s, 4H, CH_2Br), 7.30 (s, 2H, ArH).

Elem anal. Calcd. for $C_{20}H_{28}N_2O_2Br_2$: C, 49.20; H, 5.78; N, 5.74. Found: C, 49.35; H, 5.88; N, 5.70.

3.3. Typical procedure to synthesize **4**

A mixture of **2** (24.4 g, 50 mmol) and triethylphosphite (41.5 g, 250 mmol) was refluxed for 16 h. After cooling, the excess triethylphosphite was removed in vauco to leave a brown residue. This crude product **3** was used in the next step without purification.

To a mixture of *N*,*N*-(dimethyl)amino benzaldehyde (0.957 g, 4 mmol) and sodium hydride (0.083 g, 4.2 mmol) in tetrahydrofuran (THF, 10 mL) was added **3** (1.205 g, 2 mmol) dissolved in THF(20 mL), and the mixture was refluxed for 2 h. The concentration of the mixture under reduced pressure afforded a crude product, which was purified by flash chromatography (silica gel, EtOAc:hexane = 1:3) to provide 2,3-bis-[2-(4-dimethylaminophenyl)ethenyl]-6,7-bis-(3-methylbutoxy)quinoxaline **4d** (0.7 g, 59%) as a yellow solid. For analytic data, the solid was recrystallized from methanol to give **4d** as a yellow solid. M.p. 137–138 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.01 (d, 12H, $J = 6.3$, CH_3), 1.83–1.91 (m, 6H, CH and CH_2), 3.02 (s, 12H, NCH_3), 4.21 (t, 4H, $J = 6.3$, OCH_2), 6.74 (d, 4H, $J = 7.8$, ArH), 7.27 (s, 2H, quinoxaline), 7.45 (d, 2H, $J = 15.6$ Hz, ethylene), 7.57 (d, 4H, $J = 7.8$, ArH), 7.72 (d, 2H, $J = 15.6$ Hz, ethylene).

Elem anal. Calcd. for $C_{38}H_{48}N_4O_2$: C, 76.99; H, 8.16; N, 9.45. Found: C, 76.56; H, 8.20; N, 9.28.

3.4. 2,3-Bis-[2-(4-formylaminophenyl)ethenyl]-6,7-bis-(3-methylbutoxy)quinoxaline **4a**

For analytic data, the solid was recrystallized from methanol to give **4a** as a yellow solid. M.p. 197–198 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 ppm (d, 12H, CH_3), 1.82–1.90 ppm (m, 6H, CH and CH_2), 4.14 ppm (t, 4H, OCH_2), 7.32 ppm (s, 2H, quinoxaline), 7.76 (d, 2H, $J = 15.6$ Hz, ethylene), 7.81 (d, 4H, $J = 6.9$ Hz, ArH), 7.93 (d, 4H, $J = 6.9$ Hz, ArH), 7.96 (d, 2H, $J = 15.6$ Hz, ethylene), 9.98 ppm (s, 2H, CHO).

Elem anal. Calcd. for $C_{36}H_{38}N_2O_4$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.99; H, 6.95; N, 4.85.

3.5. 2,3-Bis-[2-(4-methylphenyl)ethenyl]-6,7-bis-(3-methylbutoxy)quinoxaline **4b**

For analytic data, the solid was recrystallized from methanol to give **4b** as a yellow solid. M.p. 171–172 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 ppm (d, 12H, CH_3), 1.82–1.86 ppm (m, 6H, CH and CH_2), 2.4 ppm (s, 6H, CH_3), 4.22 ppm (t, 4H, OCH_2), 7.22 (d, 4H, $J = 7.8$ Hz, ArH), 7.30 ppm (s, 2H, quinoxaline), 7.56 (d, 4H, $J = 7.8$ Hz, ArH), 7.58 (d, 2H, $J = 15.6$ Hz, ethylene), 7.84 ppm (d, 2H, $J = 15.6$ Hz, ethylene).

Elem anal. Calcd. for $C_{36}H_{42}N_2O_2$: C, 80.86; H, 7.92; N, 5.24. Found: C, 81.02; H, 7.99; N, 5.19.

3.6. 2,3-Bis-[2-(4-ethoxyphenyl)ethenyl]-6,7-bis-(3-methylbutoxy)quinoxaline **4c**

For analytic data, the solid was recrystallized from methanol to give **4c** as a yellow solid. M.p. 159–160 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 ppm (d, 12H, CH_3), 1.45 ppm (t, 6H, CH_3), 1.83–1.87 ppm (m, 6H, CH and CH_2), 4.11 ppm (q, 4H, OCH_2), 4.22 ppm (t, 4H, OCH_2), 6.94 (d, 4H, $J = 8.7$ Hz, ArH), 7.27 ppm (s, 2H, quinoxaline), 7.52 (d, 2H, $J = 15.6$ Hz, ethylene), 7.61 (d, 4H, $J = 8.7$ Hz, ArH), 7.84 ppm (d, 2H, $J = 15.6$ Hz, ethylene).

Elem anal. Calcd. for $C_{38}H_{46}N_2O_4$: C, 76.73; H, 7.80; N, 4.71. Found: C, 76.91; H, 7.89; N, 4.68.

Acknowledgements

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