Synthesis and Characterization of a New Fluorescent Zwitterionic Spirocyclic Meisenheimer Complex of 1,3,5-Trinitrobenzene

Rabih O. Al-Kaysi,*[a][‡] Gonzalo Guirado,*[a,b] and Edward J. Valente[c]

Dedicated to Professor David Creed on the occasion of his retirement[‡‡]

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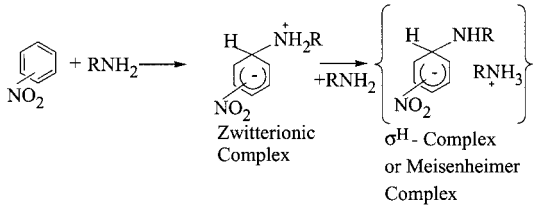
In this communication we present the first stable zwitterionic spirocyclic Meisenheimer compound based on an N→N rearrangement in the reaction between picric acid and diisopropylcarbodiimide. The structure was confirmed by single-crystal X-ray diffraction. Furthermore, this compound exhibits interesting fluorescence properties (φ_f = 0.4–0.5), not shared with a typical Meisenheimer complex, and a fluorescence lifetime (τ = 9.1 ns) in dichloromethane.

Introduction

Nucleophilic aromatic substitution is one of the most thoroughly studied reactions because of its use in the synthesis of numerous novel and natural product compounds.[1] When a nucleophile attacks an aromatic ring substituted with two or more nitro (NO_2) groups, it is well established that this reaction involves Meisenheimer complex intermediates in its key step.[2] The spectroscopic (UV/Vis, IR, NMR) [3] and electrochemical properties[4] of these complexes have recently and extensively been reported. It is thought that when amines are used as nucleophiles, a precursor intermediate to the Meisenheimer complex is formed. These intermediates are commonly known as zwitterionic complexes (Scheme 1).[1–5] However, in some cases these zwitterionic complexes are stable enough to be isolated and fully characterized.[6]



Scheme 1. Reaction of an alkylamine with polynitrobenzene to yield a Meisenheimer complex

Results and Discussion

In this communication we present the synthesis and photophysical properties of the zwitterionic spiro Meisenheimer complex **1**, which is formed from the reaction of picric acid and diisopropylcarbodiimide (**2**). Another compound **3** is formed as well. Note that an N→N rearrangement occurs that leads to the substituted spirocyclic ring system **1** (Scheme 2). This type of zwitterionic intermediates based on N→N rearrangement has been proposed several times in the literature, but has rarely been isolated or fully characterized.[7,8] Compound **1** is stable indefinitely in methanol, chlorinated solvents, and methanol/water mixtures. The unusual stability of the reactive iminium ion of **1** in methanol and water could be due to the steric effect of the isopropyl group on the weak nucleophiles. A possible mechanism (Scheme 3) could account for the formation of compounds

[a] University of Rochester, Department of Chemistry, Rochester, NY 14627, USA
Fax: (internat.) + 1-585-506-0205
E-mail: alkaysi@chem.rochester.edu
[b] NanoScience Group (GNS) Centre d'Elaboration de Materiaux et Etudes Structurales, (CEMES-CNRS), 29, rue Jeanne Marvig, 31055 Toulouse, France
Fax: (internat.) + 33-5-62257999
E-mail: guirado@cemes.fr
[c] Mississippi College, Department of Chemistry and Biochemistry, Clinton, MS 39058, USA
Fax: (internat.) + 1-601-925-3933
E-mail: valente@mc.edu
[‡] Previous address: Department of Chemistry and Biochemistry, The University of Southern Mississippi, Hattiesburg, MS 39406, USA
[‡‡] After researching and educating people in polymer chemistry and photochemistry for over 25 years (Department of Chemistry and Biochemistry, University of Southern Mississippi, Hattiesburg, MS, USA)

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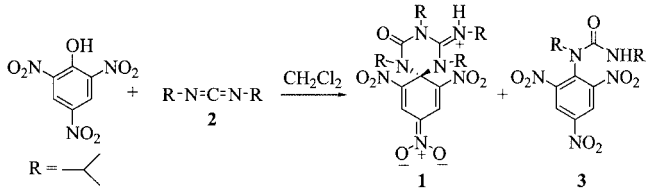
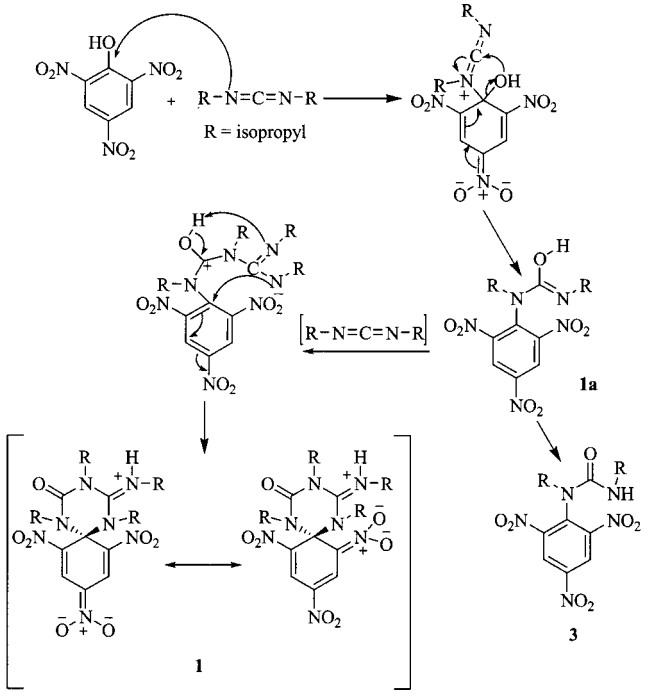
1 and **3**; however, it was challenging to prove the N→N rearrangement. The nitrogen atom of the carbodiimide can nucleophilically attack the substituted position (1-OH) thereby leading to a zwitterionic intermediate. Displacement of the hydroxy group (by an addition/elimination mechanism) would then lead to **1a**. The intermediate **1a** can easily evolve to compound **3**, its most stable tautomeric form, or can further react with excess carbodiimide to give compound **1**. This step was effected by slowly adding a dilute solution of diisopropylcarbodiimide **2** in dichloromethane (DCM) to a solution of picric acid. The resulting product is mainly **3** with traces of **1**. Reverse addition of a picric acid solution to a concentrated fivefold excess of **2** in DCM results in compounds **1** and **3** in almost similar chemical yields. There was no apparent reaction between **3** and excess diisopropylcarbodiimide. A solution of **1** or **3** in hydroxylic solvents like NaOH/MeOH is unstable; it reacts to give nonfluorescent blood-red products characteristic of the formation of Meisenheimer complexes, which have not been isolated and characterized, in the reaction mixture.[9]



Scheme 2. Reaction of picric acid with diisopropylcarbodiimide



Scheme 3. Possible mechanism for the formation of compounds **1** and **3**

Several techniques, such as NMR and UV/Vis spectroscopy and elemental analysis, have been used to characterize **1**. Definitive confirmation of **1** was achieved by X-ray diffraction (Figure 1).

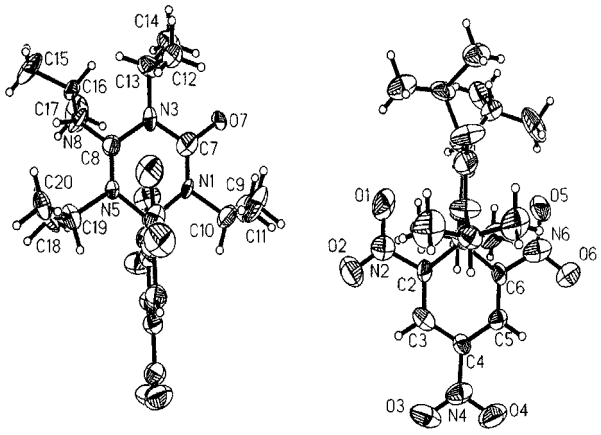


Figure 1. Thermal ellipsoid plot (50% boundaries) for **1**

Note that the *ortho*-nitro groups are slightly twisted from the cyclohexadienyl ring plane. A careful examination of the electron density map reveals that the iminium H atom is surrounded by isopropyl groups and does not engage in intermolecular hydrogen bonding. These structural properties, which are not common in other Meisenheimer or zwitterionic Meisenheimer complexes, might contribute to the unusual stability and photophysical properties of this compound. It was thought that these complexes do not exhibit fluorescence due to the presence of electron-withdrawing groups. However, preliminary investigations performed by Taylor,[10] under different environmental conditions, showed that the 1,1,-dihydro-2,4,6-trinitrocyclohexadienate anion fluoresces in acetonitrile with an emission maximum at about 670 nm., but the fluorescence quantum yield was very poor at about 0.09.[11] Fluorescence studies carried out on **1** gave a fluorescence quantum yield around 0.4−0.5 in dichloromethane and a fluorescence lifetime of 9.1 ns. The absorption spectrum of **1** in dichloromethane shows two absorption maxima at 406 and 526 nm (Figure 2, a). The emission spectrum in several solvents is also reported and shows emission maxima at 549, 561 and 577 nm in heptane, dichloromethane, and methanol, respectively (Figure 2, b).

Conclusion

The zwitterionic and fluorescent nature of **1** enables it to be used in multiple and different applications. These types of compounds can be used as fluorescent biomarkers for biochemical applications.[10] They can also be used in environmental applications, for instance, for the detection of polluting agents such as 2,4,6-trinitrotoluene and picric acid with the use of colorimetric tests. It is important to note that in a large family of cheap dyes, we can use this synthetic approach to obtain these types of zwitterionic complexes. Finally, further reactions of **1** could lead to novel heterocyclic compounds. Theoretical aspects of the fluorescence of this compound and a logical extension of this

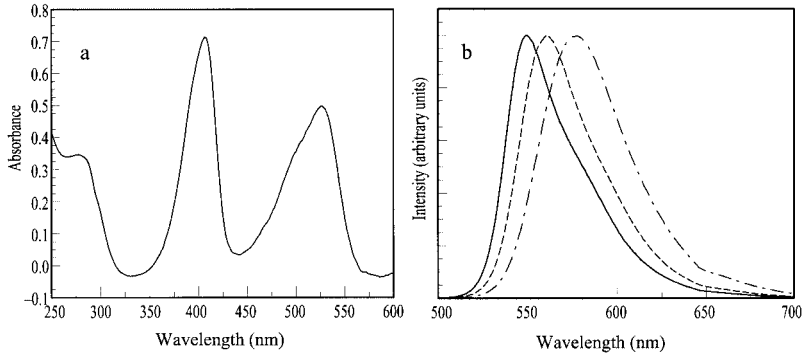


Figure 2. (a) Absorption spectrum of 3.1×10^{-5} M solution of **3** in dichloromethane, $\lambda_{max.}$ = 406, 526 nm; (b) normalized emission spectra of 1.9×10^{-5} M of **3**, (– – –) in heptane, where $\lambda_{max.\ emission}$ = 549 nm; (– – –) in dichloromethane, where $\lambda_{max.\ emission}$ = 561 nm; (– - – - – -) in methanol, where $\lambda_{max.\ emission}$ = 577 nm

work to other nitroaromatic compounds will be investigated in the near future. In addition, electrochemical experiments will be performed so as to establish the electrochemical oxidation/reduction mechanism of these Meisenheimer zwitterionic intermediates.

Experimental Section

Synthesis of Compounds 1 and 3: Picric acid (3.0 g, 13.0 mmol) in dichloromethane (35.0 mL) was added slowly to a solution of diisopropylcarbodiimide (8.0 g, 63.5 mmol, 4.8 equiv.) in dichloromethane (20 mL). The reaction mixture was stirred under a blanket of argon for 3 h. After the dichloromethane was removed under reduced pressure, the crude product was dissolved in boiling methanol (120 mL). Water (80 mL) was added to this mixture, and the solution was cooled to 0 °C. The crude orange crystals (1.9 g) were recovered by filtration and consisted of a mixture of **3** and **1**. The products were separated by column chromatography (silica gel; ethyl acetate/hexane, 30:70). The first eluting component was **3**, which upon removal of the solvent gave yellow crystals (yield 0.8 g, 15.8%). **3:** M.p. 156–158 °C. IR (KBr): $\tilde{\nu}$ = 723, 912, 1360, 1555, 1611, 1655, 2864, 2940, 3102, 3320 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.15 (d, *J* = 6.3 Hz, 6 H), 1.17 (d, *J* = 6.6 Hz, 6 H), 3.92–4.03 (m, 1 H), 4.22 (sept, *J* = 6.9 Hz, 1 H), 4.36 (d, *J* = 7.5 Hz, 1 H), 8.87 (s, 2 H) ppm. $C_{13}H_{17}N_5O_7$ (355.3): calcd. C 43.95, H 4.82, N 19.71; found C 43.86, H 4.70, N 19.92. The second eluting component was recovered after removing the solvent under reduced pressure to give red crystals of **1** (yield 1.1 g, 15.5%). M.p. 203 °C with decomposition. Compound **1** was further purified by addition of hexane to a saturated ethyl acetate solution; the crystalline product was recovered by filtration. **1:** IR (KBr): $\tilde{\nu}$ = 1081, 1202, 1279, 1491, 1530, 1593, 1715, 2985, 3441 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.22 (d, *J* = 6.9 Hz, 6 H), 1.33 (d, *J* = 7.2 Hz, 6 H), 1.45 (d, *J* = 6.3 Hz, 6 H), 1.72 (d, *J* = 6.6 Hz, 6 H), 3.14 (sept, *J* = 6.9 Hz, 1 H), 3.87 (sept, *J* = 7.2 Hz, 1 H) 3.95–4.10 (m, 1 H), 4.18 (sept, *J* = 6.6 Hz, 1 H), 4.30 (d, *J* = 9.0 Hz, 1 H), 9.01 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.90, 22.01, 23.11, 24.10, 51.05, 51.10, 53.12, 58.40, 82.28, 120.13, 125.54, 130.83, 145.01, 154.71 ppm.. $C_{20}H_{31}N_7O_7$ (481.5): calcd. C 49.91, H 6.44, N 20.38; found, C 49.86, H 6.51, N 20.09.

X-ray Crystallographic Data: Crystal data for **1**: $C_{20}H_{31}N_7O_7$, *M* = 481.52, orthorhombic, *Pna*2_1 (no. 33), with *a* = 24.119(40) Å, *b* = 9.011(19) Å, *c* = 10.868(21) Å, *V* = 2373(7) $Å^3$ for *Z* = 4, *T* = 293(2) K, reflections collected/unique 3612/3612, final R_{int} [*I* > 2F(*I*)] R_1, wR_2 = 0.098, 0.192.[12] CCDC-201161 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk].

Photophysical Measurements: Determination of the fluorescence lifetime of **1** in dichloromethane (τ = 9.1 ns) was performed with the time-resolved single-photon-counting technique. A Coherent Antares A76s Neodymium:YLF cw-modelocked laser with a fundamental frequency of 1053 was frequency doubled in a KTP (potassium tytanil phosphate) crystal to give a 527 nm 76 MHz reprate, the pulse width was in the order of 100 ps. The fluorescence quantum yield of **1** in dichloromethane was determined relative to the fluorescence quantum yield of a standard, in this case 9,10-diphenylanthracene (φ_f = 0.90) in cyclohexane.[13] Two dilute solutions of the standard in cyclohexane ($od_{400\ nm}$ = 0.050) and **1** in dichloromethane ($od_{400\ nm}$ = 0.050) were accurately prepared and degassed with argon ensuring the absorbance at the excitation wavelength (400 nm) is the same or within 0.1% error. The φ_f of **1** was determined according to the formula $\varphi_{f(\mathbf{1})} = [(Fn^2)/(F_o n_o^2)]\cdot\varphi_{fo}$, where *F* and F_o are the integrated emission area across the band of **1** and the standard, $\varphi_{f(\mathbf{1})}$ and φ_{fo} are the fluorescence quantum yields of **1** and the standard, *n* and n_o are the indices of refraction of the solvents containing **1** and the standard, respectively.

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