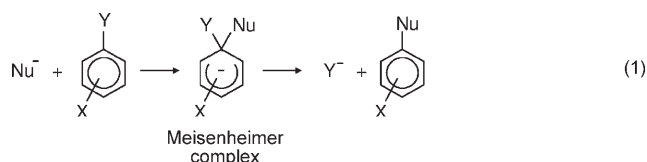


Meisenheimer Complexes Positively Characterized as Stable Intermediates in the Gas Phase**

Barbara Chiavarino, Maria Elisa Crestoni, Simonetta Fornarini,* Francesco Lanucara, Joel Lemaire, and Philippe Maître

Anionic σ complexes, also referred to as “Jackson–Meisenheimer” or “Meisenheimer” complexes, are key intermediates in the S_NAr mechanism of aromatic nucleophilic substitution reactions [Eq. (1)].^[1] They are formed by the covalent addition of nucleophiles (Nu^-) to aromatic substrates bearing electron-withdrawing substituents (X) and have been characterized as stable or transient species by X-ray crystallography, NMR, and UV/Vis spectroscopy in condensed phases.^[2]

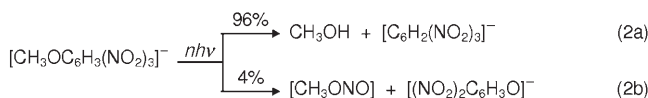


As compared with the wealth of kinetic and thermodynamic studies on Meisenheimer complexes in solution, relatively few studies are concerned with their gas-phase chemistry.^[3] In a recent report, the exceedingly fast reaction of fluoride ion with nitrobenzene was ascribed to a potential-energy profile where the anionic *ipso* complex is a transition state rather than a stable species lying in a local energy minimum.^[4] A transition towards an energy profile displaying an anionic σ complex intermediate is predicted by DFT calculations, as the *para* position with respect to the NO_2 leaving group ($Y = NO_2$) is substituted by an electron-withdrawing group.^[5] Gas-phase thermochemical data for the equilibria involving the addition of anions to substituted benzenes have been obtained by high-pressure mass spec-

trometry, thereby providing information on the stabilities of the complexes though not directly on their structures.^[6] Indeed, depending on the nature of the substituents on the benzene ring and the nature of Nu^- , various stable structures can occur and structural assignments have relied largely on calculations.^[4–7]

The structural elucidation of prototypical Meisenheimer complexes in the gas phase is reported herein. To this end, a spectroscopic methodology is applied that is based on the coupling of the radiation output of an IR free-electron laser (FEL) at the CLIO (Centre Laser Infrarouge d'Orsay) European facility with a Paul-type ion-trap mass spectrometer,^[8] thus exploiting the potential emerging from the combination of mass spectrometry with an IR FEL radiation source.^[9] The IR features of a gaseous ion may be disclosed in the IR multiphoton dissociation (IRMPD) spectrum, which reports the resonance-enhanced photofragmentation process following multiple-photon absorption in correspondence with the IR active modes of the sampled species. Among the several recent achievements, IRMPD spectra have been reported for few inorganic negative ions, including complexes of halide ions,^[10] iron carbonyl clusters,^[11] and vanadium oxide cluster anions.^[12]

When a basic methanol solution of 1,3,5-trinitrobenzene (TNB) is subjected to electrospray ionization (ESI) in the negative-ion mode, the adduct ion incorporating the anion of the solvent, $[CH_3OC_6H_3(NO_2)_3]^-$, is the major ionic species observed.^[13] The structural assay of the so-formed species is gained by IRMPD spectroscopy, whereby the ion is isolated in the ion trap and allowed to interact with the IR FEL radiation.^[14] A wavelength-dependent dissociation process leads to a major product ion formally corresponding to deprotonated TNB [Eq. (2a)], implying loss of a methanol molecule. These products are thermodynamically favored with respect to the alkoxide ion and neutral TNB pair, owing to the higher acidity of nitrobenzene relative to primary alcohols.^[15] A second, minor dissociation pathway [Eq. (2b)] occurs by formal loss of neutral methyl nitrite, leading to 2,4-dinitrophenoxide as the likely product ion in a process involving substantial bonding rearrangement.



Conceivable structures for the sampled adduct ion, $[CH_3OC_6H_3(NO_2)_3]^-$, and for its dissociation products have

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been examined by theoretical calculations by using hybrid density functional theory (DFT) at the B3LYP/6-311++G-(d,p) level. Besides the anionic σ complex, the possible presence of noncovalent species was considered. Discriminating between noncovalent and covalent adducts in the gas phase is not a trivial task to be solved by mass spectrometry. Optimized geometries of $[\text{CH}_3\text{OC}_6\text{H}_3(\text{NO}_2)_3]^-$ isomers are presented in Figure 1, and they illustrate the covalent anionic

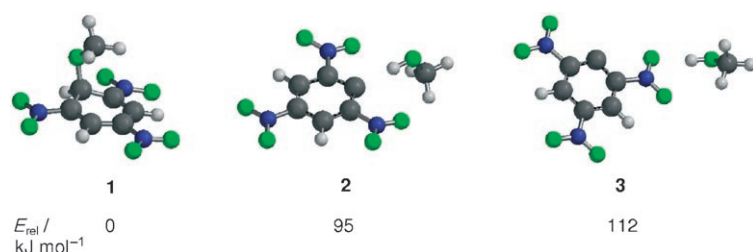


Figure 1. Geometries and relative energies for exemplary $[\text{CH}_3\text{OC}_6\text{H}_3(\text{NO}_2)_3]^-$ species calculated at the B3LYP/6-311++G(d,p) level. C gray, N blue, O green, H white.

σ complex (**1**) together with two noncovalent complexes whereby a hydrogen bond is established between neutral methanol and the 2,4,6-trinitrophenyl anion, engaging either the negatively charged carbon atom (in **2**) or one of the nitro groups where the negative charge is largely delocalized (in **3**). As shown by the relative energies at 0 K reported in Figure 1, both **2** and **3** are markedly less stable than **1**, by 95 and 112 kJ mol^{-1} , respectively. Though reasonably lying on the reaction coordinate for the dissociation path of Equation (2a), these species are bound by only 44–27 kJ mol^{-1} relative to the separated fragments.

The dependence of the IRMPD yield R ($R = -\ln\{I_{\text{parent}}/(I_{\text{parent}} + \sum I_{\text{fragment}})\}$, obtained from the relative abundances of the parent and fragment ions, I_{parent} and I_{fragment}) on the radiation wavenumber is plotted as profile (a) in Figure 2, which also displays the computed IR spectra for **1–3**. The matching observed between the experimental IRMPD spectrum of $[\text{CH}_3\text{OC}_6\text{H}_3(\text{NO}_2)_3]^-$ ions and the IR spectrum calculated for ion **1** is remarkably good. As expected, the noncovalent complexes **2** and **3** do not contribute appreciably to the sampled ion population, their brightest vibrational modes appearing at a wavenumber where IRMPD activity is practically absent. Rather, the experimental IRMPD spectrum shows a remarkably good agreement with the IR spectrum of the Meisenheimer complex **1** both in terms of wavenumbers and of relative intensities of the observed features. In particular, the prominent band at 1253 cm^{-1} in the IRMPD spectrum is accounted for by the two modes at 1245 and 1261 cm^{-1} standing out in the calculated spectrum of **1**. Also the relatively large bandwidth (fwhm = 60 cm^{-1}), compared with a typical value of 25 cm^{-1} for IRMPD spectra taken under comparable experimental conditions,^[8] is consistent with a composite feature. The overall remarkable agreement provides an unambiguous spectroscopic characterization of a gaseous Meisenheimer complex, thus proving its existence as a stable species in the isolated state.^[16]

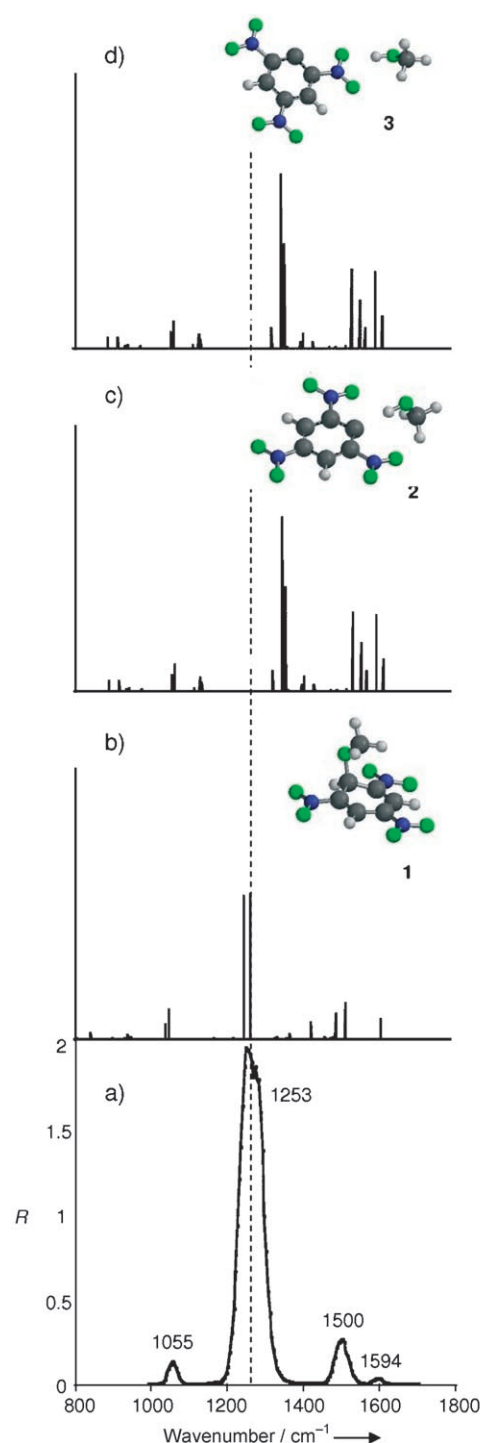


Figure 2. IRMPD spectrum of mass-selected $[\text{CH}_3\text{OC}_6\text{H}_3(\text{NO}_2)_3]^-$ ions (a) and calculated IR spectra for **1–3** (b–d). The dashed line is meant to guide the eye; see text for R notation.

To test the generality of the observed conclusion, a higher homologue was produced by ESI of an ethanolic solution of TNB. Incidentally, the parent Meisenheimer complex isolated in 1902 was the ethoxy adduct of 2,4,6-trinitroanisole [Eq. (1); $\text{Nu}^- = \text{EtO}^-$, $\text{Y} = \text{MeO}$, $\text{X} = 2,4,6-(\text{NO}_2)_3$].^[1] Upon irradiation, the so-formed $[\text{C}_2\text{H}_5\text{OC}_6\text{H}_3(\text{NO}_2)_3]^-$ complex undergoes a fragmentation process by exclusive loss of neutral ethanol

when the infrared light is tuned to a resonance. The ensuing IRMPD spectrum is displayed in Figure 3a together with the calculated IR spectrum for the optimized structure of the covalent σ complex (**4**; Figure 3b), showing a remarkably

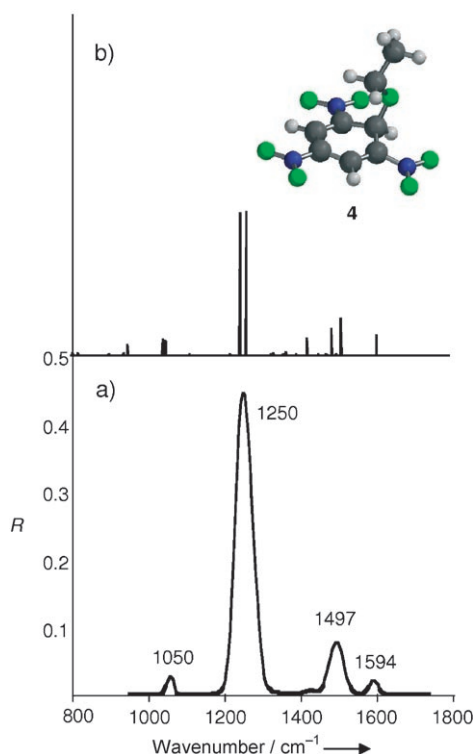


Figure 3. IRMPD spectrum of $[\text{C}_2\text{H}_5\text{OC}_6\text{H}_3(\text{NO}_2)_3]^-$ (a) and calculated IR spectrum for **4** (b).

good match. The spectra show only minor differences with respect to the ones pertaining to the methoxy adduct as conceivable, owing to the relatively small perturbation effected by the additional methylene unit. The dominant bands in the spectrum arise from vibrational modes involving symmetric NO stretching of the nitro groups. These characteristics are obviously common to both the methoxy and ethoxy anionic σ complex. In conclusion, both species, representing prototypical Meisenheimer complexes, are characterized as stable, covalent intermediates in the gas phase, and thus a highly diagnostic spectroscopic technique has been exploited. The same IRMPD spectroscopic tool has been exploited to positively characterize arenium ions or cationic σ complexes, namely the cationic counterparts of Meisenheimer complexes.^[17]

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[1] J. March, *Advanced Organic Chemistry. Reactions, Mechanisms, and Structure*, 4th ed., Wiley, New York, **1992**, chap. 13.

- [2] a) F. Terrier, *Chem. Rev.* **1982**, 82, 77–152; b) E. Buncel, J. M. Dust, F. Terrier, *Chem. Rev.* **1995**, 95, 2261–2280.
- [3] a) S. Ingemann, N. M. M. Nibbering, S. A. Sullivan, C. H. DePuy, *J. Am. Chem. Soc.* **1982**, 104, 6520–6527; b) S. M. J. Briscese, J. M. Riveros, *J. Am. Chem. Soc.* **1975**, 97, 230–231; c) I. L. Freriks, L. J. De Koning, N. M. M. Nibbering, *J. Am. Chem. Soc.* **1991**, 113, 9119–9124; d) S. L. VanOrden, R. M. Pope, S. W. Buckner, *Org. Mass Spectrom.* **1991**, 26, 1003–1007; e) H. Chen, H. Chen, R. G. Cooks, *J. Am. Soc. Mass Spectrom.* **2004**, 15, 998–1004; f) I. Cotte-Rodriguez, Z. Takats, N. Talaty, H. Chen, R. G. Cooks, *Anal. Chem.* **2005**, 77, 6755–6764.
- [4] T. Giroldo, L. A. Xavier, J. M. Riveros, *Angew. Chem.* **2004**, 116, 3672–3674; *Angew. Chem. Int. Ed.* **2004**, 43, 3588–3590; .
- [5] H. Sun, S. G. DiMagno, *Angew. Chem.* **2006**, 118, 2786–2791; *Angew. Chem. Int. Ed.* **2006**, 45, 2720–2725; .
- [6] a) G. W. Dillow, P. Kebarle, *J. Am. Chem. Soc.* **1988**, 110, 4877–4882; b) G. J. C. Paul, P. Kebarle, *J. Am. Chem. Soc.* **1991**, 113, 1148–1154; c) K. Hiraoka, S. Mizuse, S. Yamabe, *J. Phys. Chem.* **1987**, 91, 5294–5297; d) K. Hiraoka, S. Mizuse, S. Yamabe, *J. Chem. Phys.* **1987**, 86, 4102–4105.
- [7] a) M. N. Glukhovtsev, R. D. Bach, S. Laiter, *J. Org. Chem.* **1997**, 62, 4036–4046; b) Y.-J. Zheng, R. L. Ornstein, *J. Am. Chem. Soc.* **1997**, 119, 648–655; c) E. Buncel, R. M. Tarkka, J. M. Dust, *Can. J. Chem.* **1994**, 72, 1709–1721.
- [8] L. Mac Aleese, A. Simon, T. B. McMahon, J.-M. Ortega, D. Scuderi, J. Lemaire, P. Maître, *Int. J. Mass Spectrom.* **2006**, 249–250, 14–20.
- [9] a) J. Oomens, A. J. A. Van Rooij, G. Meijer, G. von Helden, *Astrophys. J.* **2000**, 542, 404–410; b) J. Lemaire, P. Boissel, M. Heninger, G. Mauclaire, G. Bellec, H. Mestdag, A. Simon, S. Le Caer, J. M. Ortega, F. Glotin, P. Maître, *Phys. Rev. Lett.* **2002**, 89, 273002–273004; c) J. J. Valle, J. R. Eyler, J. Oomens, D. T. Moore, A. F. G. van der Meer, G. von Helden, G. Meijer, C. L. Hendrickson, A. G. Marshall, G. T. Blakney, *Rev. Sci. Instrum.* **2005**, 76, 023103.
- [10] a) T. D. Fridgen, T. B. McMahon, P. Maître, J. Lemaire, *Phys. Chem. Chem. Phys.* **2006**, 8, 2483–2490; b) N. L. Pivonka, C. Kaposta, G. von Helden, G. Meijer, L. Woste, D. M. Neumark, K. R. Asmis, *J. Chem. Phys.* **2002**, 117, 6493–6499; c) M. J. Nee, A. Osterwalder, D. M. Neumark, C. Kaposta, C. Cibrian Uhalte, T. Xie, A. Kaledin, J. M. Bowman, S. Carter, K. R. Asmis, *J. Chem. Phys.* **2004**, 121, 7259–7268.
- [11] D. T. Moore, J. Oomens, J. R. Eyler, G. Meijer, G. von Helden, D. P. Ridge, *J. Am. Chem. Soc.* **2004**, 126, 14726–14727.
- [12] K. R. Asmis, G. Santambrogio, M. Brümmer, J. Sauer, *Angew. Chem.* **2005**, 117, 3182–3185; *Angew. Chem. Int. Ed.* **2005**, 44, 3122–3125.
- [13] a) W. Danikiewicz, T. Bienkowski, K. Wojciechowski, *Tetrahedron Lett.* **2004**, 45, 931–934; b) W. Danikiewicz, T. Bienkowski, D. Poddebniak, *J. Am. Soc. Mass Spectrom.* **2004**, 15, 927–933.
- [14] The experiments were run with a Bruker Esquire 3000 instrument appropriately modified to admit the IR laser beam from the FEL source, as described elsewhere.^[8] The ions of interest were obtained by ESI of a methanol solution of TNB (0.1 mM) and NH_3 (0.2 M) infused at a rate of 5 $\mu\text{L min}^{-1}$. The ions were mass-selected and exposed to irradiation by three macropulses of the IR beam. The electron energy was set to 42 MeV and the average IR power was 700–800 mW. The calculations were performed using hybrid density functional theory at the B3LYP/6-311++G(d,p) level, and a scaling factor of 0.98 was applied to calculated harmonic frequencies prior to deriving IR spectra and zero-point vibrations.
- [15] E. P. Hunter, S. G. Lias, *Proton Affinity Evaluation in NIST Chemistry WebBook*, NIST Standard Reference Database Number 69 (Eds.: P. J. Linstrom, W. G. Mallard) National Institute of Standards and Technology: Gaithersburg, MD, **2005** (<http://webbook.nist.gov>).

- [16] Another isomeric possibility may be discarded, namely the one resulting from an *ipso* attack of a methoxide ion at a carbon atom bearing a nitro substituent, although this attack is not favored by any *ortho/para* relationship with the other two nitro groups that would enable conjugative delocalization of the negative charge. Calculations show that the ensuing species displays the features of a loose complex of nitrite ion with 3,5-dinitroanisole, of comparable stability as the other two noncovalent complexes, **2** and **3**. Its calculated IR spectrum differs significantly from the one calculated for **1**. Full details will be reported in a forthcoming paper. We thank a reviewer for his input on this point.
- [17] a) W. Jones, P. Boissel, B. Chiavarino, M. E. Crestoni, S. Fornarini, J. Lemaire, P. Maitre, *Angew. Chem.* **2003**, *115*, 2103–2105; *Angew. Chem. Int. Ed.* **2003**, *42*, 2057–2059; ; b) O. Dopfer, N. Solcà, J. Lemaire, P. Maitre, M. E. Crestoni, S. Fornarini, *J. Phys. Chem. A* **2005**, *109*, 7881–7887; c) B. Chiavarino, M. E. Crestoni, S. Fornarini, J. Lemaire, L. Mac Aleese, P. Maitre, *ChemPhysChem* **2005**, *6*, 437–440; d) O. Dopfer, J. Lemaire, P. Maitre, B. Chiavarino, M. E. Crestoni, S. Fornarini, *Int. J. Mass Spectrom.* **2006**, *249–250*, 149–154.
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