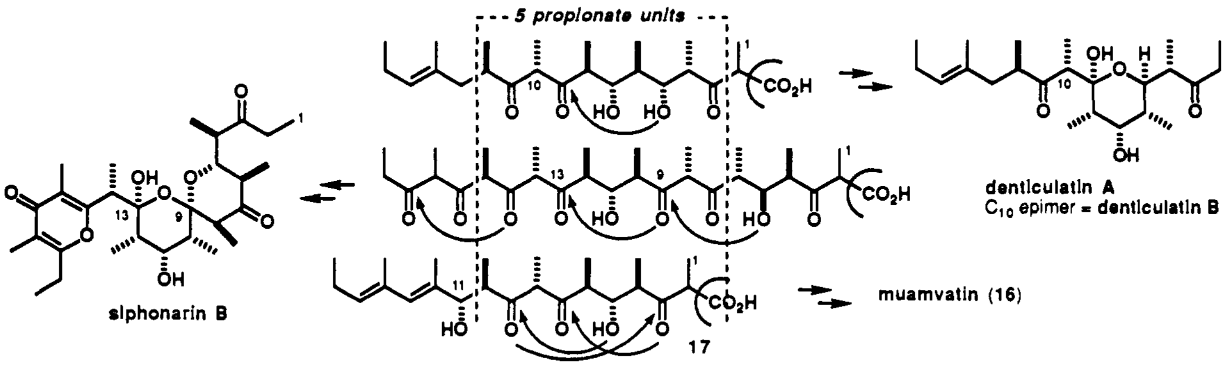
Scheme III. Configurational Model for Siphonariid Metabolites



IR) identical[10] to that reported by Ireland et al.,[1] thus establishing the C_{10} relative stereochemistry. Comparison of optical rotation, $[\alpha]^{20}_D = +84.4°$ (c 0.9, CH_2Cl_2) for **2** vs lit.[1] $[\alpha]^{20}_D = +50.2°$ (c 0.09, CH_2Cl_2), indicated that we had prepared[11] the correct enantiomer for completing a total synthesis of (+)-muamvatin.

The light-sensitive iodide **14** was prepared from the enyne **13**[12] by regioselective hydroboration by catecholborane, followed by treatment with in situ generated ICl.[13] Lithium-iodine exchange (^{n}BuLi) gave the corresponding dienyl lithium, which was then added to the aldehyde **2**. The resulting alcohol mixture (85% yield) was chromatographed (SiO_2, 5% Et_2O/CH_2Cl_2) to give predominantly 11-*epi*-muamvatin ($R_f = 0.19$) and a small amount (5%) of muamvatin ($R_f = 0.15$). ^{1}H NMR analysis of both the (R)- and (S)-MTPA esters of 11-*epi*-muamvatin showed that it had the 11R configuration, i.e., **15**.[14] This alcohol **15** could be oxidized to the corresponding dienone using catalytic $^nPr_4NRuO_4$,[15] followed by stereocontrolled reduction by DIBAL. This now gave (+)-muamvatin as the sole product, $[\alpha]^{20}_D = +62.0°$ (c 0.08, CH_2Cl_2) vs lit.[1] $[\alpha]^{20}_D = +61.1°$ (c 0.175, CH_2Cl_2), in 14 steps and 89% ds from (R)-**4**. The ^{1}H and ^{13}C NMR spectra were in full accord with the published data[1] and spectra provided by Professor Ireland. On the basis of the Mosher ester analysis on **15** and Felkin-Cram control operating in both the DIBAL reduction step and aldehyde addition (**14** + **2** → **15**), we assign the structure **16** (10R, 11S) to muamvatin.

The stereochemical homology between muamvatin and related siphonariid metabolites[3b,c] can be seen from the biogenetic configurational model[4b,16] in Scheme III, where a common pentapropionate section is apparent. The ready production of the trioxaadamantane skeleton by silica gel treatment suggests that muamvatin is probably an artifact of the chromatographic purification used in the natural product isolation.[17] On isolation, the cyclization mode is presumably under thermodynamic control and can be predicted[6] from the oxidation state of the carbons and the configuration of the hydroxyl and methyl groups in the associated acyclic precursor **17**.

Acknowledgment. We thank the SERC for support (Postdoctoral Award to M.V.P.; grant GR/F73458), Dr. J. M. Goodman (Cambridge) for the molecular modeling results, Dr. M. J. Garson (Queensland) for helpful discussions, Professor R. W. Hoffmann (Marburg) for the exchange of information, and Professor C. M. Ireland (Utah) for kindly providing spectra of muamvatin and the degradation product **2**.

Supplementary Material Available: Listing of spectroscopic and physical data for all numbered compounds (5 pages). Ordering information is given on any current masthead page.

(10) In (+)-**2**, the ^{13}C NMR resonances for the acetal carbons appear at δ 103.1, 102.9, and 97.3, whereas these are reported[1] at δ 105.4, 103.1, and 97.2. Professor Ireland informs us that δ 105.4 is an error and there are two signals at 103.1 and 102.9 ppm. Otherwise, the NMR data were identical. In our hands, (+)-**2** was obtained as a crystalline solid, mp 153-154 °C (pentane).

(11) We initially prepared the enantiomer of aldehyde **2**, which had $[\alpha]_D^{20} = -80°$ (c 0.05, CH_2Cl_2), by using the (S) ketone corresponding to **4**.

(12) Prepared in two steps from (E)-2-methyl-2-pentenal in 58% yield by: (i) PPh_3, CBr_4, CH_2Cl_2, 0 °C; (ii) ^{n}BuLi, THF, -78 → 20 °C, MeI, -78 → 20 °C. Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.

(13) Kabalka, G. W.; Sastry, K. A. R.; Somyaji, V. *Heterocycles* **1982**, *18*, 157.

(14) (a) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092. (b) Dale, J. A.; Mosher, H. S. *J. Am. Chem.* **1973**, *95*, 512. (c) Sullivan, G. R.; Dale, J. A.; Mosher, H. S. *J. Org. Chem.* **1973**, *38*, 2143.

(15) Griffith, W. P.; Ley, S. V.; Whitcombe, G. P.; White, A. D. *J. Chem. Soc., Chem. Commun.* **1987**, 1625.

(16) For similar configurational models for macrolide and polyether polyketides, see: (a) Celmer, W. D. *J. Am. Chem. Soc.* **1965**, *87*, 1801. (b) Cane, D. E.; Celmer, W. D.; Westley, J. W. *J. Am. Chem. Soc.* **1983**, *105*, 3594.

(17) This may also be true for other siphonariid metabolites,[3,8f] where the actual natural products are more closely related to the open-chain polypropionate precursors.

Base Properties of CH_3NC: Interactions with HCl and H^+ and Comparisons with CH_3CN

Janet E. Del Bene

Department of Chemistry, Youngstown State University Youngstown, Ohio 44555

Received October 29, 1992

In a recent paper, Legon, Lister, and Warner reported an elegant study of the hydrogen-bonded complex formed between CH_3NC and HCl.[1] On the basis of the rotational spectra of three isotopomers, they determined that the complex $CH_3NC\cdots HCl$ has C_{3v} symmetry with an intermolecular C-Cl distance of 3.404 Å, which is longer than the experimental N-Cl distance of 3.291 Å in $CH_3CN\cdots HCl$.[2] From their data they also suggested that these two complexes might have similar stabilities even though the proton affinity of CH_3NC is significantly greater than that of CH_3CN.[3]

The methodological dependence of the structures and binding energies of acid-base complexes has been a subject of continuing interest in this laboratory. As part of that study, the structures and binding energies of a series of hydrogen-bonded complexes including $CH_3CN\cdots HCl$ were investigated at a high level of ab initio theory, and good agreement between computed and experimental data was found.[4] In the present communication, this same level of theory will be used to investigate the complex $CH_3NC\cdots HCl$. Comparisons will be made of the structures and binding energies of $CH_3NC\cdots HCl$ and $CH_3CN\cdots HCl$ and of the proton affinities of the isomers CH_3CN and CH_3NC.

(1) Legon, A. C.; Lister, D. G.; Warner, H. E. *J. Am. Chem. Soc.* **1992**, *114*, 8177.

(2) Legon, A. C.; Millen, D. J.; North, H. M. *J. Phys. Chem.* **1987**, *91*, 5210.

(3) Knight, J. S.; Freeman, C. G.; McEwan, M. J. *J. Am. Chem. Soc.* **1986**, *108*, 1404.

(4) Del Bene, J. E. *Int. J. Quantum Chem., Quantum Chem. Symp.* **1992**, *26*, 527.

Table I. Computed MP2/6-31+G(d,p) Distances (Å) Involving the Cyano and Isocyano C and N Atoms

	CH_3CN	CH_3CNH^+	$CH_3CN\cdots HCl$[a]
C≡N	1.179	1.158	1.177
C—C	1.461	1.448	1.460
N—H		1.010	2.035
N—Cl			3.316
	CH_3NC	CH_3NCH^+	$CH_3NC\cdots HCl$[a]
N≡C	1.186	1.157	1.183
C—N	1.425	1.443	1.425
C—H		1.075	2.126
C—Cl			3.411

[a] The H—Cl bond length in the monomer is 1.269 Å.

The structures of the monomers CH_3CN, CH_3NC, and HCl, the protonated ions CH_3CNH^+ and CH_3NCH^+, and the complexes $CH_3CN\cdots HCl$ and $CH_3NC\cdots HCl$ were fully optimized using many-body second-order Møller–Plesset perturbation theory [MBPT(2) = MP2][5-10] with the 6-31+G(d,p) basis set,[11-14] with all electrons correlated. Vibrational frequencies were computed to confirm that the optimized structures are equilibrium structures (no imaginary frequencies) and to evaluate zero-point (ZPE) and thermal vibrational energies. Single-point calculations in which the valence electrons were correlated at full fourth-order Møller–Plesset perturbation theory (MP4) were then carried out to evaluate binding energies. The basis set used for the MP4 calculations was that recommended in ref 4, namely, the Dunning correlation-consistent polarized valence triple-split basis set[15] for H, C, and N atoms, augmented with diffuse s and p functions on C and N, with exponents of 0.04 and 0.06, respectively. The chlorine atom was described by the McLean–Chandler (12,9) basis set contracted to (6,5).[16] This basis was also augmented with a set of diffuse s and p functions, two sets of d polarization functions, and a single set of f functions, with exponents taken from the 6-31+G(2df,2pd) basis set.[17] All calculations were done using the Gaussian 90[18] and Gaussian 92[19] systems of computer programs.

Selected bond lengths from the MP2/6-31+G(d,p) optimized structures are reported in Table I. The monomers, hydrogen-bonded complexes, and protonated ions all have C_{3v} symmetry. Hence, hydrogen bond formation and protonation occur at the lone pairs on N and C in CH_3CN and CH_3NC, respectively. The computed C–Cl hydrogen-bond distance in $CH_3NC\cdots HCl$ is 3.411 Å, in excellent agreement with the experimental value of 3.404 Å.[1] These values are greater than the corresponding computed and experimental N–Cl distances of 3.316[4] and 3.291 Å,[2] respectively, in $CH_3CN\cdots HCl$. As is evident from Table I, hydrogen bonding has little effect on the intramolecular coordinates of the proton acceptor molecules, the largest change being a decrease of 0.002 and 0.003 Å in C–N triple-bond distances. The electronic MP4 binding energies, the zero-point vibrational energy (ZPE) contributions to the binding of these complexes, and the binding enthalpies at 298 K (ΔH^{298}) are reported in Table II. These data show that CH_3NC and CH_3CN are comparable as proton acceptors in hydrogen-bonded complexes with HCl, with ΔH^{298} values of −5.0 and −4.8 kcal/mol, respectively, for $CH_3NC\cdots HCl$ and $CH_3CN\cdots HCl$. Thus, these results support the suggestion of Legon et al.[1] that "the n-pairs on isocyano C and cyano N have an essentially identical propensity to interact with the nonperturbing proton donor HCl in the hydrogen-bonded complexes". The complex $CH_3NC\cdots HCl$, which has a slightly greater binding energy, also exhibits a larger increase in the H–Cl bond length and decrease in the H–Cl stretching frequency. The MP2/6-31+G(d,p) H–Cl stretching frequencies are 3121, 2953, and 2887 cm^{-1} in HCl, $CH_3CN\cdots HCl$, and $CH_3NC\cdots HCl$, respectively.

Legon measured vibrational parameters associated with the intermolecular stretching modes of these complexes.[1,2] For $CH_3NC\cdots H^{35}Cl$ and $CH_3C^{15}N\cdots H^{35}Cl$, the intermolecular stretching mode ν_σ occurs at 100.6 and 97 cm^{-1} respectively, with similar force constants of 11.45 and 10.68 N/m, respectively. It was on the basis of the similarity in force constants that Legon concluded that the binding energies of these complexes are similar. The computed MP2/6-31+G(d,p) intermolecular stretching vibrations for $CH_3NC\cdots H^{35}Cl$ and $CH_3CN\cdots H^{35}Cl$ occur at 111 and 117 cm^{-1}, respectively, with computed force constants of 7.2 and 8.1 N/m, respectively. The computed frequencies and force constants correlate with the intermolecular distances, but once again, the differences between these two complexes are very small. Hence, they also suggest that the binding energies of these two complexes are similar.

By comparison, the interaction of the isocyano C and cyano N with H^+ is quite different. Protonation of CH_3NC and CH_3CN leads to decreases of 0.029 and 0.021 Å, respectively, in the triple-bond C–N distances, as shown in Table I. However, protonation lengthens the single-bond C–N distance in CH_3NCH^+ by 0.018 Å but decreases the single-bond C–C distance in CH_3CNH^+ by 0.013 Å. The proton affinities of these two isomers are also significantly different. As is evident from Table II, the proton affinity of CH_3NC is about 14 kcal/mol greater than that of CH_3CN at absolute zero and at room temperature. The computed $-\Delta H^{298}$ values of 200.1 and 186.1 kcal/mol, respectively, for the proton affinities of CH_3NC and CH_3CN are in agreement with the experimental values[3] of 201.7 and 188.3 kcal/mol, respectively. This difference reflects differences in the isomerization energies of the neutral cyano and isocyano compounds and of the corresponding protonated ions. As is evident from Table II, CH_3NC is less stable than CH_3CN by 25 kcal/mol. However, CH_3NCH^+ is less stable than CH_3CNH^+ by only 11 kcal/mol. Thus, protonation has a greater stabilizing effect on the less stable isomer, and this gives rise to the greater proton affinity of CH_3NC.

Table II. Computed Reaction Energies (kcal/mol)

	MP4 Electronic	ZPE	ΔH^{298}
	Hydrogen Bonding		
$CH_3CN\cdots HCl$	−5.9	1.3	−4.8
$CH_3NC\cdots HCl$	−6.1	1.4	−5.0
	Protonation		
CH_3CNH^+	−191.7	6.9	−186.1
CH_3NCH^+	−205.8	7.1	−200.1
	Isomerization		
$CH_3NC \rightarrow CH_3CN$	−24.8	−0.2	−25.1
$CH_3NCH^+ \rightarrow CH_3CNH^+$	−10.7	−0.4	−11.0

Acknowledgment. The calculations reported here were carried out on the Cray Y-MP8/864 at the Ohio Supercomputer Center (OSC). A generous grant of supercomputer time from the OSC is gratefully acknowledged.

(5) Bartlett, R. J.; Silver, D. M. *J. Chem. Phys.* **1975**, *62*, 3258; **1976**, *64*, 1260, 4578.
(6) Binkley, J. S.; Pople, J. A. *Int. J. Quantum Chem.* **1975**, *9*, 229.
(7) Pople, J. A.; Binkley, J. S.; Seeger, R. *Int. J. Quantum Chem., Quantum Chem. Symp.* **1976**, *10*, 1.
(8) Krishnan, R.; Pople, J. A. *Int. J. Quantum Chem.* **1978**, *14*, 91.
(9) Purvis, G. D.; Bartlett, R. J. *J. Chem. Phys.* **1978**, *68*, 2114.
(10) Bartlett, R. J.; Purvis, G. D. *Int. J. Quantum Chem.* **1978**, *14*, 561.
(11) Hariharan, P. C.; Pople, J. A. *J. Chem. Phys.* **1975**, *62*, 2921.
(12) Dill, J. D.; Pople, J. A. *J. Chem. Phys.* **1975**, *62*, 2921.
(13) Spitznagel, G. W.; Clark, T.; Chandrasekhar, J.; Schleyer, P. v. R. *J. Comput. Chem.* **1982**, *3*, 3633.
(14) Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. v. R. *J. Comput. Chem.* **1983**, *4*, 294.
(15) Dunning, T. H., Jr. *J. Chem. Phys.* **1989**, *90*, 1007.
(16) McLean, A. D.; Chandler, G. S. *J. Chem. Phys.* **1980**, *72*, 5639.
(17) Frisch, M. J.; Pople, J. A.; Binkley, J. S. *J. Chem. Phys.* **1984**, *80*, 3265.
(18) Frisch, M. J.; Head-Gordon, M.; Trucks, G. W.; Foresman, J. B.; Schlegel, H. B.; Raghavachari, K.; Robb, M. A.; Binkley, J. S.; Gonzalez, C.; Baker, J.; Martin, R. L.; Kahn, L. R.; Steward, J. J. P.; Topiol, S.; Pople, J. A. *Gaussian 90*; Gaussian, Inc.: Pittsburgh, PA, 1990.
(19) Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. *Gaussian 92*; Gaussian, Inc.: Pittsburgh, PA, 1992.