Scheme I

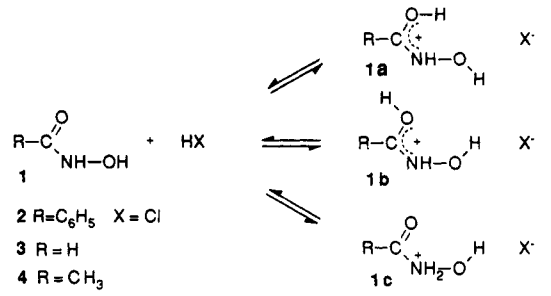


Table I. Gas-Phase Basicities of Hydroxamic Acid Derivatives and of Some Simple Amides (kcal mol^{-1})

entry	compound	GB[a]	experimental ΔG's[c]
4	$CH_3CONHOH$	197.3 (0.2)	diisopropyl ether, -1.09; tetrahydrothiophene, +0.55
5	$CH_3CON(CH_3)OH$	200.9 (0.3)	pyrimidine, -2.42; pyrrole, +0.32
6	$CH_3CONHOCH_3$	201.3 (0.1)	dimethylformamide, -1.84; pyrrole, +0.95
7	$CH_3CONHCH_3$	204.5 (0.4)	cyclopropylamine, -0.22; 2-fluoropyridine, +1.3; methylamine, -0.64
8	$CH_3CON(CH_3)_2$	208.4[b]	
9	$CH_3CONHC_2H_5$	206.2 (0.1)	cyclopropylamine, -0.61; methylamine, +0.77

[a] This work, unless otherwise stated. The uncertainties in parentheses are based on comparison of separate experiments with various reference compounds and are estimates of the reliability of the relative gas-phase basicities. absolute values may be uncertain by ±2 kcal, see ref 15. [b] Reference 15. [c] Gibbs energies of proton transfer to the indicated reference base, measured at 338 K. A positive value corresponds to a compound which is a stronger base than the reference.

acids are both stronger acids[6] and bases in the gas phase. Part of this effect may be due to the greater polarizability of the larger molecule.

The question of the site of protonation cannot be answered in a quite straightforward way from our results. Note that the similar problem of the site of deprotonation of 4 was investigated,[6] exploiting the compounds 5 and 6 as models, each containing only one of the two acidic H atoms. Similar model compounds are not possible for the protonation. We may only attempt to evaluate the substituent effects in more detail by referring always to alkyl-substituted amides with the same number of heavy atoms (Table I). In this way the polarizability effects are practically eliminated. The difference in basicity between 4 and 7 or between 5 and 8 is equal to 7.5 kcal but is reduced to 5 kcal in the case of the pair 6 and 9. For this reason we attribute the effect of 2.5 kcal to the hydrogen bond in 4 and 5, stabilizing the neutral species. The remaining 5 kcal are attributed to the electron-attracting effect of the oxygen atom, while the polarizability effect, due simply to the presence of an additional atom, is assumed to be equal as in amides, say 6 kcal. The whole picture is compatible with the assumption that all the compounds of the table are protonated at the same place, viz. on the carbonyl oxygen atom. If a protonation on the nitrogen should also take place, one could expect a strengthened basicity of the compound 5 which has the most basic nitrogen atom. By the same token, however, referring to the inductive effect of the next atom, one can predict that an N-protonation is not to be expected: when it has not been observed on amides, it is still less probable with hydroxamic acids.

In conclusion, the acid-base behavior of hydroxamic acids and their functional derivatives in the gas phase is consistent with understanding their structure as N-substituted amides with an adjoining electron-attracting substituent. The name "acid" seems to be obsolete.

Experimental Section

The compounds 4-6 were described previously;[6] compounds 7 and 9 as well as all reference compounds were commercial products.

Proton-transfer equilibria were monitored by Fourier transform ion cyclotron resonance (FT-ICR) as described in detail in a previous article.[18]

Acknowledgment. The Conseil Général des Alpes Maritimes is gratefully acknowledged for financial support.

(1) Bauer, L.; Exner, O. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 376-384.
(2) Exner, O. *Collect. Czech. Chem. Commun.* **1956**, *21*, 1500-1512.
(3) Buglass, A. J.; Hudson, K.; Tillett, J. G. *J. Chem. Soc. B* **1971**, 123-126.
(4) Berndt, D. C.; Fuller, R. L. *J. Org. Chem.* **1966**, *31*, 3312-3314.
(5) Ahmad, A.; Socha, J.; Vecera, M. *Collect. Czech. Chem. Commun.* **1974**, *39*, 3293-3303.
(6) Decouzon, M.; Exner, O.; Gal, J.-F.; Maria, P.-C. *J. Org. Chem.* **1990**, *55*, 3980-3981.
(7) Bordwell, F. G.; Fried, H. E.; Hughes, D. L.; Lynch, T.-Y.; Satish, A. V.; Whang, Y. E. *J. Org. Chem.* **1990**, *55*, 3330-3336.
(8) Remko, M.; Mach, P.; Schleyer, P. v. R.; Exner, O., to be published.
(9) Kolasa, T. *Tetrahedron* **1983**, *39*, 1753-1759.
(10) Larsen, I. K. *Acta Crystallogr., Sect. B* **1988**, *44*, 527-533.
(11) Exner, O.; Kakac, B. *Collect. Czech. Chem. Commun.* **1963**, *28*, 1656-1663.
(12) Lindberg, B.; Berndtsson, A.; Nilsson, R.; Nyholm, R.; Exner, O. *Acta Chem. Scand. A* **1978**, *32*, 353-359.
(13) Lobo, A. M.; Prabhakar, S.; Fonseca, M. T. C.; Rodriguez, A. M. B. *Tetrahedron Lett.* **1977**, 3167-3170.
(14) Farkas, E.; Kiss, T.; Kurzak, B. *J. Chem. Soc., Perkin Trans. 2* **1990**, 1255-1257.
(15) Lias, S. G.; Bartmess, J. E.; Holmes, J. L.; Levin, R. D.; Liebman, J. F.; Mallard, W. G. *J. Phys. Chem. Ref. Data* **1988**, *Suppl. 1 to Vol. 17*. For the gas-phase basicities, see also: Lias, S. A.; Liebman, J. F.; Levin, R. D. *J. Phys. Chem. Ref. Data* **1984**, *13*, 695-808; additions and corrections, personal communication, 1987.
(16) Calculated protonation energies of methylamine and hydroxylamine suggest that the effect of the OH is much larger than in hydroxamic acids, as might be expected for the smaller charge-localized ion. See: Del Bene, J. E.; Frisch, M. J.; Raghavachari, K.; Pople, J. A. *J. Phys. Chem.* **1982**, *86*, 1529-1535.
(17) Exner, O.; Simon, W. *Collect. Czech. Chem. Commun.* **1965**, *30*, 4078-4093.
(18) Berthelot, M.; Decouzon, M.; Gal, J.-F.; Laurence, C.; Le Questel, J.-Y.; Maria, P.-C.; Tortajada, J. *J. Org. Chem.* **1991**, *56*, 4490-4494.

Synthesis of Optically Quadratic Nonlinear Phenylpyridylacetylenes

Koichi Kondo,* Noriaki Ohnishi, Kiichi Takemoto, Hidetsugu Yoshida,† and Kunio Yoshida†

Department of Applied Fine Chemistry, Faculty of Engineering, Institute of Laser Engineering, Osaka University, Suita, Osaka 565, Japan

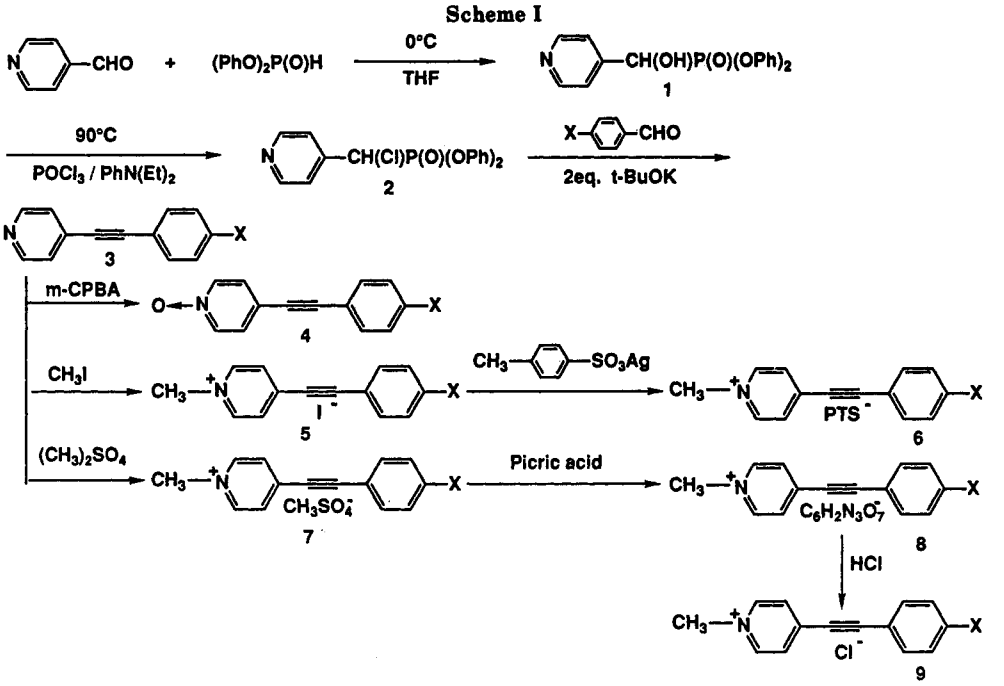
Received September 16, 1991

The nonlinear optical properties of organic compounds have been extensively studied in the last decade. Compounds with noncentrosymmetric crystal packing exhibit the quadratic optical phenomenon that is needed for second harmonic generation (SHG) by laser diodes as well as for theoretical treatment of molecular interactions.[1] The molecular framework that typically brings about SHG is a π-conjugated intramolecular donor-acceptor charge-

† Institute of Laser Engineering.

0022-3263/92/1957-1622$03.00/0 © 1992 American Chemical Society

Scheme I



transfer (ICT) system that occurs in *p*-nitroaniline derivatives such as 2-methyl-4-nitroaniline (MNA),[2] methyl [(2,4-dinitrophenyl)amino]propanoate (MAP),[3] and *N*-(4-nitrophenyl)-L-prolinol (NPP).[4] In addition, 3-methyl-4-nitropyridine *N*-oxide (POM)[5] has been shown to weaken dipole–dipole interaction, and the molecular salt 4-(dimethylamino-*N*-methyl-4-stilbazolium methylsulfate (DAMSM)[6] to enhance electrostatic interaction, both of which lead to noncentrosymmetric crystal packing. Substituted diphenylacetylenes are novel optically nonlinear candidates, as illustrated by 4-nitro-4′-methoxydiphenylacetylene.[7] Recently, optical nonlinearity in this molecularly linear rigid triple-bond system has been theoretically discussed, together with its crystal structure.[8]

Phenylpyridylacetylenes are interesting candidates for SHG activity since they should have not only linear rigid intramolecular charge-transfer character, but should also form *N*-oxides and salts similar to POM and DAMSM. However, the only synthetic route to such disubstituted diphenylacetylenes is the oxidative coupling of a copper(I) phenylacetylide with an iodobenzene, which is tedious and limited by the availability of suitable iodobenzenes.[9]

We here describe use of the modified Horner–Emmons reaction[10] for the synthesis of phenylpyridylacetylenes together with evaluation of their nonlinear optical character (SHG).

4-Pyridinecarboxaldehyde was reacted with diphenyl phosphite in THF at 0 °C for 1 h to produce diphenyl 1-hydroxy-1-(4-pyridyl)methanephosphonate (1) in 40% yield. Hydroxy compound 1 was converted into diphenyl 1-chloro-1-(4-pyridyl)methanephosphonate (2) by treatment with $POCl_3/PhN(Et)_2$ at 90 °C for 1 h. At the next step, 2 and the 4-substituted benzaldehyde in THF were treated with 2 equiv of *t*-BuOK at room temperature for 6 h to afford (4-substituted phenyl) 4-pyridylacetylenes 3 in 50–80% yield (Scheme I).

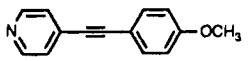
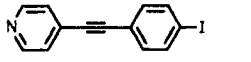
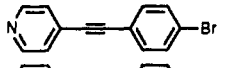
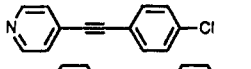
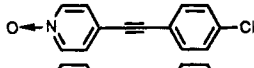
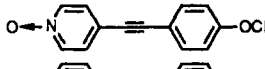
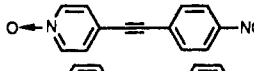
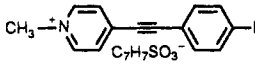
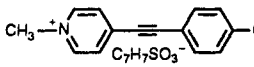
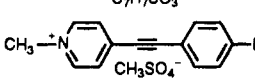
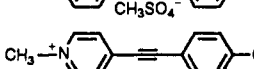
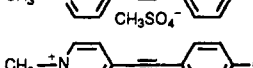
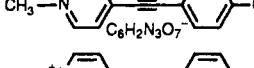
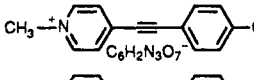
Treatment of 3 with excess 3-chloroperoxybenzoic acid (*m*-CPBA) in CH_2Cl_2 at 0 °C for 12 h afforded the *N*-oxides 4 in 30–54% yield. Acetylenes 3 were converted into the *N*-methylpyridinium iodides 5 (50% yield) or methyl sulfate salts 7 (75% yield) by treatment with excess CH_3I at 0 °C or dimethylsulfate at 100 °C. Further treatment of 5 or 7 with silver *p*-toluenesulfonate or picric acid in hot water led to the *p*-toluenesulfonates 6 or picrate salts 8. The chloride salts 9 were obtained by treatment of 8 with dilute aqueous hydrochloric acid.[11]

SHG activity of the phenylpyridylacetylenes was evaluated by the Kurtz powder method[12] (75–100-μm particle size) using Nd:YAG laser (1064-nm) irradiation. The SHG intensity relative to urea at 532 nm is summarized in Table I, together with the cutoff wavelength determined at 95% transmittance for a 1 mmol acetonitrile solution. The presence of the less electron donating and accepting group at the 4-position of the benzene ring gave rise to high SHG relative to urea as observed in (4-iodophenyl)(4-pyridyl)-acetylene (15 times) and (4-methoxyphenyl)(4-pyridyl)-acetylene (5 times). As for the *N*-oxides and salts, (4-chlorophenyl)(4-methylpyridiniumyl)acetylene methyl sulfate was fairly high (7 times), indicating noncentrosymmetric crystal packing controlled by the counter anion.

All these SHG-active compounds also had low cutoff wavelengths, which could be useful for blue-green wavelength generation in laser diodes. In addition, the extent of ICT in phenylpyridylacetylenes could be estimated from the cutoff wavelength, which varied from 320 nm for the weak donor–acceptor to 410 nm for the powerful elec-

(1) *Nonlinear Optical Properties of Organic Molecules and Crystals*; Chemla, D. S., Zyss, J., Eds; Academic Press: Orlando, 1987; Vol. 1, p 679.
(2) Lipscomb, G. F.; Garito, A. F.; Narang, R. S. *Appl. Phys. Lett.* **1981**, *38*, 663.
(3) Ouda, J.; Hieple, R. *J. Appl. Phys.* **1977**, *48*, 2699.
(4) Zyss, J.; Nicoud, J. F.; Coquillay, M. *J. Chem. Phys.* **1984**, *81*, 4160.
(5) Zyss, J.; Chemla, D. S. *J. Chem. Phys.* **1981**, *74*, 4800.
(6) *Nonlinear Optical Properties of Organic and Polymeric Materials*; ACS Symp. Ser. No. 233, 1983, p 27.
(7) Kurihara, T.; Tabei, H.; Kaino, T. *J. Chem. Soc., Chem. Commun.* **1987**, 959. Wang, Y.; Tam, W.; Stevenson, S. H.; Clement, R. A.; Calabrese, J. *Chem. Phys. Lett.* **1988**, *148*, 136.
(8) Graham, E. M.; Miskowski, V. M.; Perry, J. W.; Coulter, D. R.; Stiegman, A. E.; Schaefer, W. P.; Marsh, R. E. *J. Am. Chem. Soc.* **1989**, *111*, 8771.
(9) *Organic Functional Group Preparations*; Sandler, S. R.; Karo, W., Eds.; Academic Press: New York, 1968; Vol. 1, p 65.
(10) Zimmer, H.; Bercz, P. J.; Maltenieks, O. J.; Moore, M. W. *J. Am. Chem. Soc.* **1965**, *87*, 2777. Zimmer, H.; Hickey, K. R.; Schumacher, R. J. *Chimia* **1974**, *28*, 656.
(11) Michaelis, L.; Hill, E. S. *J. Am. Chem. Soc.* **1933**, *55*, 1481.
(12) Kurtz, S. K.; Perry, T. T. *J. Appl. Phys.* **1968**, *39*, 3798.

Table I. Relative SHG Powder Efficiency of Phenyl Pyridyl Acetylene Compounds

structure	SHG (x urea)	cut-off (nm)	mp (°C)	yield[a] (%)
	5.1	345	98	81
	15.0	352	196	78
	2.0	320	143	76
	1.0	320	123	79
	<0.1	361	174	39
	<0.1	377	100	54
	0	410	218	40
	<0.1	380	>300	61
	<0.1	378	250	74
	1.0	383	198	71
	7.0	380	212	69
	<0.1	478	203	76
	<0.1	478	141	74
	0	370	186	52

[a] At the final step.

tron-withdrawing group at the 4-position. The cutoff wavelength for the picrates (478 nm) indicates an important contribution from the counter anion.

Experimental Section

THF was distilled over sodium wire and $LiAlH_4$ and stored over sodium wire before use.

Diphenyl 1-Hydroxy-1-(4-pyridyl)methanephosphonate (1). To 50 mL of a THF solution of diphenyl phosphite (27.0 g, 115 mmol) was added 4-pyridinecarboxaldehyde (12.4 g, 116 mmol) over 1 h at 0 °C. The precipitate was filtered and recrystallized from ethanol to give the product in 40% yield, mp 146 °C.

IR (solid/KBr): ν (cm^{-1}) 3250 (OH), 1240 (P=O), 1060, 1020, 960 (P–O). ^1H NMR (100 MHz, $CDCl_3$): δ 8.62 (d, 2 H), 7.55 (d, 2 H), 7.45–6.95 (m, 10 H), 5.33 (d, 1 H, J = 12.5 Hz), 3.70 (s, 1 H). Anal. Calcd for $C_{18}H_{16}NO_4P$: C, 63.34; H, 4.73; N, 4.11; P, 9.07. Found: C, 63.44; H, 4.60; N, 4.07; P, 9.02.

Diphenyl 1-Chloro-1-(4-pyridyl)methanephosphonate (2). 1 (7.8 g, 23 mmol) was treated with 25 mL of $POCl_3$ in the presence of 2 mL of diethylaniline for 1 h at 90 °C. After evaporation, the residue was added to ice–water, neutralized with aqueous potassium carbonate solution, extracted with CH_2Cl_2, and dried over $MgSO_4$. The organic layer was removed and recrystallized from ethanol to give the product in 80% yield, mp 102 °C.

IR (solid/KBr): ν (cm^{-1}) 1270 (P=O), 1070, 1020, 1000 (P–O); ^1H NMR (100 MHz, $CDCl_3$) δ 8.70 (d, 2 H), 7.55 (d, 2 H), 7.50–6.95 (m, 10 H), 5.25 (d, 1 H, J = 15 Hz). Anal. Calcd for $C_{18}H_{15}O_3PCl$: C, 60.10; H, 4.20; N, 3.89; Cl, 9.85. Found: C, 60.03; H, 4.15; N, 3.91; Cl, 9.89.

(4-Iodophenyl)(4-pyridyl)acetylene (3, X = I). 2 (1.4 g, 3.9 mmol) and 4-iodobenzaldehyde (1 g, 4.3 mmol) were treated with t-BuOK (0.92 g, 8.2 mmol) in THF (20 mL) for 3 h at room temperature. After evaporation, water (20 mL) was added to the residue, which was extracted with CH_2Cl_2 and dried over $MgSO_4$. The organic layer was removed and recrystallized from ethanol–chloroform (1:1) to give the product in 22% yield, mp 196 °C.

IR (solid/KBr): ν (cm^{-1}) 2225 (C≡C). ^1H NMR (90 MHz, $CDCl_3$); δ 8.60 (d, 2 H), 7.73 (d, 2 H), 7.36 (d, 2 H), 7.26 (d, 2 H). Anal. Calcd for $C_{13}H_8NI$: C, 51.17; H, 2.64; N, 4.59; I, 41.59. Found: C, 51.06; H, 2.60; N, 4.57; I, 41.36.

(4-Bromophenyl)(4-pyridyl)acetylene (3, X = Br). 2 (7.0 g, 19.4 mmol) and 4-bromobenzaldehyde (3.81 g, 20.6 mmol) were treated with t-BuOK (4.83 g, 43.0 mmol) in THF (100 mL) for 3 h at room temperature. The workup was conducted as above. Recrystallization from ethanol–chloroform (1:1) gave the product in 76% yield, mp 143 °C.

IR (solid/KBr): ν (cm^{-1}) 2225 (C≡C). ^1H NMR (60 MHz, DMSO-d_6): δ 8.63 (d, 2 H), 7.6 (overlapping d, d, 2 H), 7.47 (d, 2 H). Anal. Calcd for $C_{13}H_8NBr$: C, 60.49; H, 3.12; N, 5.42; Br, 30.96. Found: C, 59.87; H, 3.13; N, 5.37; Br, 30.98.

(4-Chlorophenyl)(4-pyridyl)acetylene (3, X = Cl). 2 (8.15 g, 22.7 mmol) and 4-chlorobenzaldehyde (3.4 g, 24.1 mmol) were similarly treated with t-BuOK (5.16 g, 46.0 mmol) in THF (100 mL) to give the product in 80% yield, mp 123 °C.

IR (solid/KBr): ν (cm^{-1}) 2225 (C≡C). ^1H NMR (60 MHz, DMSO-d_6) δ 8.57 (d, 2 H), 7.60 (d, 2 H), 7.46 (d, 2 H), 7.40 (d, 2 H). Anal. Calcd for $C_{13}H_8NCl$: C, 73.08; H, 3.77; N, 6.55; Cl, 16.59. Found: C, 72.51; H, 3.82; N, 6.45; Cl, 16.45.

(4-Methoxyphenyl)(4-pyridyl)acetylene (3, X = OCH_3). 2 (7.50 g, 20.8 mmol) and 4-methoxybenzaldehyde (3.0 g, 22.0 mmol) were similarly treated with t-BuOK (5.10 g, 45.4 mmol) in THF (100 mL) to give the product in 81% yield, mp 98 °C.

IR (solid/KBr): ν (cm^{-1}) 2215 (C≡C). ^1H NMR (90 MHz, DMSO-d_6): δ 9.00 (d, 2 H), 8.24 (d, 2 H), 7.76 (d, 2 H), 7.61 (d, 2 H), 4.32 (s, 3 H). Anal. Calcd for $C_{14}H_{11}NO$: C, 80.36; H, 5.30; N, 6.70. Found: C, 80.05; H, 5.18; N, 6.71.

Di-4-pyridylacetylene. 2 (2.3 g, 6.4 mmol) and 4-pyridine carboxaldehyde (0.8 g, 7.4 mmol) were treated with t-BuOK (1.65 g, 14.7 mmol) in THF (30 mL) for 3 h at room temperature. After evaporation, the residue was extracted with ether and washed with water. The ether layer was dried over $MgSO_4$ and then removed to give the product in 60% yield.

IR: inactive for $\nu_{C\equiv C}$. ^1H NMR (60 MHz, $CDCl_3$) δ 8.64 (d, 4 H), 7.40 (d, 4 H). Anal. Calcd for $C_{12}H_8N_2$: C, 79.98; H, 4.48; N, 15.55. Found: C, 79.11; H, 4.66; N, 14.89.

(4-Chlorophenyl)(4-pyridyl)acetylene *N*-Oxide (4, X = Cl). To 30 mL of a CH_2Cl_2 solution of (4-chlorophenyl)(4-pyridyl)-acetylene (0.21 g, 1.0 mmol) was added 10 mL of a CH_2Cl_2 solution of 3-chloroperoxybenzoic acid (0.26 g, 1.5 mmol) at 0 °C over 1 h, and the mixture was stirred for 12 h at room temperature. After washing with aqueous potassium carbonate solution, the organic layer was dried over $MgSO_4$ and evaporated, and the residue was recrystallized from ethanol to give the *N*-oxide in 40% yield, mp 174 °C.

IR (solid/KBr) ν (cm^{-1}): 2220 (C≡C), 1260 (NO). ^1H NMR (60 MHz, DMSO-d_6) δ 8.20 (d, 2 H), 7.58–7.48 (m, 6 H). Anal. Calcd for $C_{13}H_8NOCl$: C, 67.98; H, 3.51; N, 6.10; Cl, 15.44. Found: C, 67.71; H, 3.15; N, 5.88; Cl, 15.33.

(4-Methoxyphenyl)(4-pyridyl)acetylene *N*-Oxide (4, X = OCH_3). (4-Methoxyphenyl)(4-pyridyl)acetylene (1.06 g, 5.06 mmol) was similarly treated with 3-chloroperoxybenzoic acid (1.1 g, 6.37 mmol) and recrystallized from ethanol to give the product in 54% yield, mp 100 °C.

IR (solid/KBr) ν(cm^{-1}): 2210, 2180 (C≡C), 1210 (NO). ^1H NMR (90 MHz, DMSO-d_6) δ 8.32 (d, 2 H), 7.9 (m, 2 H), 7.6 (m, 2 H), 7.02 (d, 2 H), 3.85 (s, 3 H). Anal. Calcd for $C_{14}H_{11}NO_2$: 74.65; H, 4.92; N, 6.22. Found: C, 74.24; H, 4.71; N, 6.10.

(4-Chlorophenyl)(4-methylpyridiniumyl)acetylene Iodide (5, X = Cl). 30 mL of an iodomethane solution of (4-chlorophenyl)(4-pyridyl)acetylene (4.38 g, 20.5 mmol) was heated to 40 °C to complete solution. After cooling, the preciptate was filtered and dried to give the product in 50% yield, which was used for the next reaction without further purification.

Anal. Calcd for $C_{14}H_{11}NClI$: C, 47.29; H, 3.12; N, 3.94. Found: C, 47.06; H, 3.04; N, 3.86.

(4-Chlorophenyl)(4-methylpyridiniumyl)acetylene *p*-Toluenesulfonate (6, X = Cl). To 50 mL of a water solution of (4-chlorophenyl)(4-methylpyridiniumyl)acetylene iodide (1.07

g, 3.0 mmol) was added 25 mL of a water solution of silver *p*-toluenesulfonate (0.87 g, 3.0 mmol), and the mixture was heated to 100 °C for 30 min. After cooling, the precipitate (AgI) was filterd off, the filtrate was condensed, and the residue was recrystallized from ethanol to give the product in 74% yield, mp 250 °C.

IR (solid/KBr) ν (cm^{-1}): 2220, 2190 (C≡C). Anal. Calcd for $C_{21}H_{18}NO_3SCl$: C, 63.07; H, 4.54; N, 3.50. Found: C, 62.96; H, 4.45; N, 3.54.

(4-Chlorophenyl)(4-methylpyridiniumyl)acetylene Methyl Sulfate (7, X = Cl). 25 mL of a dimethyl sulfate solution of (4-chlorophenyl)(4-pyridyl)acetylene (4.0 g, 18.8 mmol) was heated to 100 °C to complete solution. After cooling, the precipitate was filtered and recrystallized from methanol to give the methyl sulfate in 69% yield, mp 212 °C.

IR (solid/KBr) ν (cm^{-1}): 2230, 2200 (C≡C), 1260 (SO). ^1H NMR (270 MHz, DMSO-d_6) δ 9.001 (d, 2 H, pyridyl-3′,5′), 8.257 (d, 1 H, pyridyl-2′,6′), 7.756 (d, 2 H, phenyl-3,5), 7.630 (d, 2 H, phenyl-2,6), 4.328 (s, 3 H, NCH_3), 3.382 (s, 3 H, $CH_3SO_4^-$). Anal. Calcd for $C_{15}H_{14}NO_4SCl$: C, 53.02; H, 4.15; N, 4.12. Found: C, 52.46; H, 4.08; N, 4.10.

(4-Chlorophenyl)(4-methylpyridiniumyl)acetylene Picrate (8, X = Cl). 15 mL of a water solution of (4-chlorophenyl)(4-methylpyridiniumyl)acetylene methyl sulfate (0.69 g, 2.03 mmol) was warmed to complete solution. To the solution was added 10 mL of a water solution of picric acid (0.50 g, 2.2 mmol), and it was cooled. The precipitate was filtered and recrystallized from water–ethanol (3:1) to give the picrate in 76% yield, mp 212 °C.

IR (solid/KBr) ν(cm^{-1}): 2220, 2190 (C≡C). Anal. Calcd for $C_{20}H_{13}N_4O_7Cl$: C, 52.58; H, 2.87; N, 12.27; Cl, 7.76. Found: C, 51.97; H, 2.75; N, 12.01; Cl, 7.54.

(4-Chlorophenyl)(4-methylpyridiniumyl)acetylene Chloride (9, X = Cl). 25 mL of a water solution of (4-chlorophnyl)(4-methylpyridiniumyl)acetylene picrate (0.5 g, 1.1 mmol) was warmed to complete solution. To the solution was added 1 N hydrochloric acid (10 mL), and it was extracted with toluene and ether to remove picric acid. After the aqueous layer was condensed, the residue was recrystallized from methanol to give the chloride in 52% yield, mp 186 °C.

IR (solid/KBr) ν (cm^{-1}) 2210 (C≡C). Anal. Calcd for $C_{14}H_{11}NCl_2$: C, 63.65; H, 4.20; N, 5.30; Cl, 26.84. Found: C, 63.82; H, 4.11; N, 5.09; Cl, 26.53.

SHG Measurement. The compounds were ground in a mortar, meshed to 75–100 μm, and fixed on a glass slide by tape. The slide was irradiatd by a Nd:YAG laser (wavelength 1064 nm, pulse width 350 ps, power density 5 GW/cm^2, spot size 0.8 mm), and the intensity of SHG light (532 nm) was monitored by a photo diode and compared with the SHG intensity of urea.

Synthesis and Structure of 4,10-Diaza-5′-nitro-2,3-dibenzo-12-crown-4

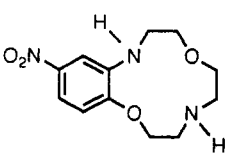
Richard A. Bartsch,*,† Thomas W. Robison,† Dhimant H. Desai,† Jan Krzykawski,† N. Kent Dalley,‡ and Weiming Jiang‡

Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, Texas 79409, and Chemistry Department, Brigham Young University, Provo, Utah 84602

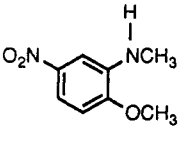
Received September 13, 1991

Introduction

Small-ring, mixed oxygen and nitrogen donor macrocycles interact strongly with a variety of heavy metal cations.[1] As part of a general program of mixed-donor macrocycle synthesis, we have prepared 4,10-diaza-5′-nitro-2,3-benzo-12-crown-4 (**1**). This ligand possesses a benzo-12-crown-4 ring system in which two oxygen donor atoms are replaced by nitrogens. For ligands derived from **1**, reduction of the nitro group would provide a potential attachment site for a chromogenic group[2] or modification for coupling with a monoclonal antibody.[3]



1



2

The ^1H NMR spectrum of **1** was unusual in that the chemical shift for the alkylarylamine hydrogen was further downfield than anticipated. To probe the reason for this anomaly, acyclic model compound **2** was synthesized and the crystal structure of **1** was determined. The synthetic routes to **1** and **2**, their ^1H NMR spectra, and the solid-state structure of **1** are now reported.

Results and Discussion

Synthesis. The preparation of macrocycle **1** in four steps from commercially available 2-amino-4-nitrophenol is shown in Scheme I. Reaction of 2-amino-4-nitrophenol with $TsOCH_2CH_2NHTs$[4] and K_2CO_3 in DMF gave tosyl amide **3** in 36% yield. Substitution of *N*-tosylaziridine[5] as the alkylating agent gave the same yield of **3**. For conversion of **3** into ditosyl amide **4**, reaction with tosyl chloride and pyridine in dichloromethane gave a good yield (69%) and easier workup than when pyridine was utilized as both the base and solvent. Cyclization of ditosyl amide **4** with the dimesylate of diethylene glycol and K_2CO_3 in DMF was achieved in 67% yield. This cyclization yield is appreciably higher than that obtained when the ditosylate of diethylene glycol was utilized. Deprotection of **4** by heating in concentrated H_2SO_4 at 100 °C gave a higher yield (60%) of mixed-donor macrocycle **1** than did the alternative deprotection method of heating with 30% HBr in acetic acid and phenol at reflux[6] (50% yield).

Although **2** is a known compound, it was previously isolated in low yield as a minor product from the exhaustive methylation of 2-amino-4-nitrophenol.[7] Reaction of 2-amino-4-nitrophenol with tosyl chloride and pyridine in dichloromethane gave a 77% yield of 4-nitro-2-(*p*-toluenesulfonamido)phenol (**6**) which was subsequently dimethylated with iodomethane and K_2CO_3 in DMF to provide *N*-methyl-4-nitro-2-(*p*-toluenesulfonamido)anisole (**7**) in 91% yield. Deprotection of **7** by heating in concentrated sulfuric acid at 100 °C produced a 91% yield of model compound **2**.

The structures of all new compounds were verified by IR, ^1H NMR spectra, and elemental analysis.

^1H NMR Spectra. Absorptions for the amine hydrogens in macrocycle **1** in deuteriochloroform appeared as broadened singlets at δ 1.86 and 6.15.[8] Ordinarily the chemical shift for a dialkylamine hydrogen occurs in the range of δ 0.5–3.0 and for an aromatic amine hydrogen at

† Texas Tech University.
‡ Brigham Young University.

(1) Lindoy, L. F. *Cation Binding by Macrocycles*; Inoue, Y.; Gokel, G. W.; Eds.; Marcel-Dekker: New York, 1990, p 599–629.
(2) Takagi, M.; Nakamura, H.; Ueno, K. *Anal. Lett.* **1977**, *10*, 1115.
(3) Moi, M. K.; Yanuck, M.; Deshpande, S. V.; Hope, H.; Denardo, S. J.; Meares, C. F. *Inorg. Chem.* **1987**, *26*, 3458.
(4) Hope, D. B.; Horncastle, K. *J. Chem. Soc. C* **1966**, 1090.
(5) Martin, A. E.; Ford, M. T.; Bulkowshi, J. E. *J. Org. Chem.* **1982**, *47*, 412.
(6) Haskell, E.; Bowlus, S. P. *J. Org. Chem.* **1976**, *41*, 159.
(7) Ingold, C. K.; Ingold, E. H. *J. Chem. Soc.* **1926**, 1310.
(8) The chemical shift values were not concentration dependent.

0022-3263/92/1957-1625$03.00/0 © 1992 American Chemical Society