multiple bonding with its R′ ligand and/or the C(O) group is involved in multiple bonding with its R ligand (Table III).[22] None of the RC(O)NR′-ligands in these four cases are derived from parent organic amide functional groups.

Theoretical studies of amide group deformations[23] usually conclude that pyramidalization at nitrogen is energetically less demanding than pyramidalization at carbon or rotation about the C–N bond. It should be noted from Figure 5 that, in keeping with these studies, there is a much wider spread in $\chi_N$ values than in $\chi_C$ or $\bar{\tau}$ values. Amide nonplanarity has been considered previously for several metallo-N-amido groups which exhibit appreciable $\chi_N$ values.[20xxiv]

Complexes 3 and 4 are apparently the thermodynamically stable diastereomers as isomerization upon heating is not observed. The amide nitrogen lone pair, which in the planar amide ligand can be delocalized both onto the metal and the amide carbonyl group, is more available for π-donation to the metal in the nonplanar ligand. The amide nitrogen might also be expected to become a better σ-donor in the nonplanar form. In this context it is noteworthy that the geometries about the amide nitrogen atoms remain very close to trigonal planar when the amide is trans to the π-acceptor ligands suggesting that π-donation is present in these instances. The pyramidal distortions are larger for the amide ligands trans to phosphines (Table II). The $\nu_{CO}$(amide) bands for 4 are found at the same wavenumber value, and the amido groups have almost identical $\bar{\tau}$ values, whereas the two amido ligands for 3 have different $\nu_{CO}$(amide) bands and $\bar{\tau}$ values.

Metal–ligand bonding is probably greater with nonplanar N-amido ligands relative to the planar analogues. This conceivable increased bonding could be the principal compensating term to account for the substantial destabilization that is expected to accompany the loss of amide delocalization. We will present evidence in a subsequent paper to show that there is a significant increase in metal–ligand bonding for nonplanar N-amido ligands relative to planar N-amido ligands in these systems.

**Acknowledgment.** We acknowledge the Rohm and Haas Co., the Atlantic Richfield Corporation of America, and the National Science Foundation (Grants CHE-84-06198) for support of this work. T.T.F. thanks the Summer Undergraduate Research Fellowship Program of the California Institute of Technology for the award of a SURF. J.T.K. acknowledges SOHIO for the award of the SOHIO Fellowship in Catalysis, W.R. Grace for the award of the W.R. Grace Fellowship, and Shell for the award of the Shell Doctoral Fellowship. R.J.C. thanks the Exxon Education Foundation for postdoctoral support. We thank Dr. Richard E. Marsh for helpful discussions and Dr. B. Jean Westphal for assistance with the operation of the Cambridge crystallographic database programs. Operation of the Bruker WM-500 NMR spectrometer at the Southern California Regional NMR Facility was supported by NSF Grant CHE-79-16324. Upgrade of the X-ray diffraction facility was supported by NSF Grant CHE-82-19039 to the Division of Chemistry and Chemical Engineering.

**Registry No. 1**, 103191-18-0; **2**, 90791-57-4; **3**, 103191-19-1; **4**, 103191-20-4.

**Supplementary Material Available:** Listing of atomic coordinates, Gaussian amplitudes, bond lengths and angles, listings of structure factor tables, and complete listing of referenced compounds and torsion angle determinations (106 pages). Ordering information is given on any current masthead page.

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[22] The *cis*-diammineplatinum α-pyrrolidonato complex, $[Pt_4(NH_3)_8(C_4H_6NO)_4](NO_3)_{5.48}\cdot 3H_2O$, which is an apparent mixture of two tetranuclear species of different oxidation levels, shows several abnormally large $\chi_C$ (21, 25, 26, 30, −36, 45, −45°, there are two distinct molecules per unit cell) and $\chi_N$ (35, −39, −48°) parameters which are difficult to rationalize. This structure contains other abnormal bond parameters. For instance, C–C single bond distances vary from 1.36–1.90 Å. The points derived from this work by Matsumoto, Takahashi, and Fuwa are not included in Figure 5 (Matsumoto, K.; Takahashi, H.; Fuwa, K. *J. Am. Chem. Soc.* **1984**, *106*, 2049–2054). The related pyrrolidinato, mixed-valence, tetranuclear species, $[Pt_4(NH_3)_8(C_6H_6NO)_4](NO_3)_6\cdot H_2O$, has been the subject of two reports by Matsumoto and Fuwa and Matsumoto, Takahashi, and Fuwa, Matsumoto, K.; Fuwa, K. *J. Am. Chem. Soc.* **1982**, *104*, 897–898. Matsumoto, K.; Takahashi, H.; Fuwa, K. *Inorg. Chem.* **1983**, *22*, 4086–4090). In the former a trihydrate is claimed for which several $\chi_C$ values (−24, 39°) are extremely large. In the latter a dihydrate is claimed where one $\chi_C$ value is unreasonable (−74°), and another is at least inexplicably large (−28°). Presumably some atomic coordinates are inaccurate. The authors noted difficulties with this determination. The points for these structures are also excluded from Figure 5.

[23] See, for example: (a) Dunitz, J. D.; Winkler, F. K. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1975**, *31*, 251–263. (b) Ramachandran, G. N.; Lakshminarayanan, A. V.; Kolaskar, A. S. *Biochim. Biophys. Acta* **1973**, *303*, 8–13. (c) Kolaskar, A. S.; Lakshminarayanan, A. V.; Sarathy, K. P.; Sasisekharan, V. *Biopolymers* **1975**, *14*, 1081–1094.

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# *Communications to the Editor*

## Demonstration of Heteroaromaticity via d-Orbital Overlap in a Cyclic Conjugated Sulfone: NMR, Crystallography, and ab Initio Calculation[1]

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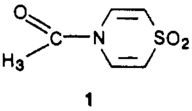
Questions regarding the nature of the interaction between second-row elements such as sulfur and carbon π-electron systems, including the relative merits of p(C)–d(S) vs. p(C)–p(S) overlap, have been the subject of extensive investigation and sometimes heated controversy.[3,4]

In this paper we exploit the extreme sensitivity of electronic energy of cyclic π-electron species to the number of π electrons associated with the ring in order to assess the possible existence and magnitude of sulfur π-system overlap.

The system we have chosen to investigate is the sulfone heterocycle 4,4-dioxy-4-thia-1-acetyl-1,4-dihydropyridine (**1**).[5,6] We shall show how a combination of NMR line-shape analysis, X-ray crystallography, and ab initio calculations implicates p–d bonding unequivocally and for the first time.



**1**

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[1] Abstracted in part from: Finklestein, H. Ph.D. Thesis, The Ohio State University, 1983.

[2] Current addresses: (a) Lubrizol Corp., Cleveland, OH. (b) Monsanto Chemical Co., St. Louis, MO. (c) Aldrich Boranes, Sheboygan, WI.

[3] Gavaraghi, G.; Pagani, P. *J. Chem. Soc., Perkin Trans. 2* **1978**, 50.

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[5] Prepared by acylating 4*H*-1,4-thiazine 1,1-dioxide,[6] with acetyl chloride and anhydrous $Na_2CO_3$ in acetone: Wong, S. Ph.D. Thesis, The Ohio State University, 1978.

[6] Noland, W. E.; Demaster, R. D. *Org. Synth.* **1972**, *52*, 135.

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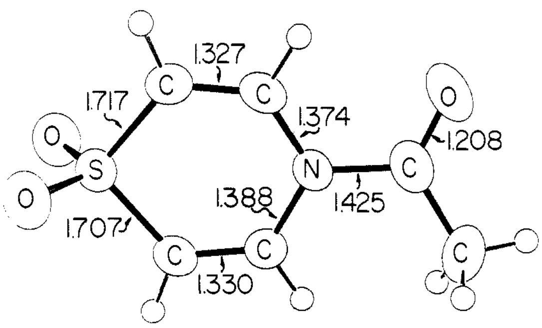
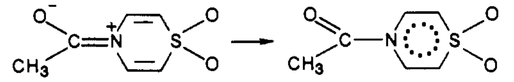


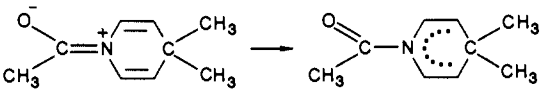
**Figure 1.** Bond distances compound **1**.

Consider rotation about the carbonyl carbon–nitrogen bond of **1**.



**1a** **1b**

In the ground state substantial conjugation of the nonbonding electrons, formally associated with nitrogen, into the carbonyl group leaves four $\pi$ electrons in the six-membered ring while in the twisted transition state, **1b**, six $\pi$ electrons are associated with the ring. The reference compound used is $N$-acetyl-4,4-dimethyl-1,4-dihydropyridine (**2**), with minimal interaction between the ends of the $\pi$-loop.[7] To the extent that sulfur overlaps with the $\pi$ system in **1**, one would expect the ground state **1a** to be destabilized compared to **2a** and twisted state **1b** to be stabilized vs. **2b**. Hence the barrier to amide rotation in **1** should be lower than that in **2**.

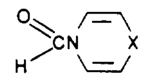


**2a** **2b**

Proton NMR, 300 MHz, acetone solution, of **1** at −73 °C and **2**, 17 °C, reveals all ring hydrogens to be magnetically nonequivalent, implying planarity or near planarity around the amide function and slow amide rotation, relative to the NMR time scale. NMR line shape analysis[9] of the ring proton NMR at higher temperatures yields $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for amide rotation in sulfone **1** of 11.7 kcal (1 cm$^3$, −0.997) and 1 eu, while for the model compound **2** the values are respectively 17.2 kcal and 1 eu (1 cm$^3$, −0.999), typical of many tertiary amides. The latter activation parameters for the reference compound are quite typical of barriers to rotation[10] in amides generally. Hence the unusually low barrier in sulfone **1** is most likely due to the interaction of sulfone with the $\pi$-system.

Signs of a destabilized ground state of sulfone **1a** come from the IR with carbonyl stretch at 1735 cm$^{-1}$, closer to a ketone value than for an amide, 1700 cm$^{-1}$ in reference compound.[7] Crystals of **1**, clear colorless rods, were grown from a solution of acetone. The space group is monoclinic, $P2_1/c$, with a unit cell of dimensions $a$ = 10.790 (2) Å, $b$ = 8.999 (2) Å, $c$ = 7.911 (1) Å, and $\beta$ = 98.59 (1)°, $Z$ = 4, $V$ = 760 Å$^3$, and $\rho_c$ = 1.51 g cm$^{-3}$. Intensities were measured by the $\theta$–$2\theta$ scan method out to $2\theta$ = 55° with a Syntex P$\bar{1}$ diffractometer equipped with graphite-monochromated Mo K$\alpha$ radiation. The final refinement on the 1192 unique reflections with $F_o^2 > 3\sigma(F_o^2)$ yielded an $R$ index (on $F$) of 0.042 for the 100 variables (anisotropic non-hydrogen atoms and fixed hydrogen atoms). The ring itself is approximately planar, Figure 1, with the dihedral angle between the atom planes C–N–C in the six-membered ring and C–C–O around the acetyl moiety of 10.0°. However, the carbonyl carbon nitrogen bond is 1.425 Å, noticeably longer than the ca 1.36 Å found for most amides,[11] more like the single C–N bond in dimethylamine, 1.456 Å.[12] Consistently 1.208 Å found for carbonyl resembles a ketone more than an amide, usually 1.22 Å. All these results point to a significantly destabilized ground state, **1a** vs. reference **2a**.

**Table I.** Calculations of Energies of $N$-Formyldehydropyridines



**3** or **4**

| X | state | basis set | energy, au |
|---|---|---|---|
| SO$_2$, **3a** | planar | 3G* | −858.321 427 727 |
| SO$_2$, **3b** | twisted[a] | 3G* | −858.303 407 290 |
| CH$_2$, **4a** | planar | 3G | −355.953 494 431 |
| CH$_2$, **4b** | twisted | 3G | −355.929 332 069 |

[a] 90° about $C_{CO}$–N bond.

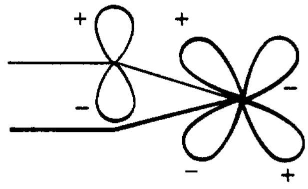


**Figure 2.** 3d$_{xz}$(S) overlap to the $\pi$-system in **1**.

Further insight into the sulfur $\pi$ system interaction comes from ab initio calculations of amide barriers using the Gaussian 80 series of programs at the STO 3G* level of approximation, including 3d orbitals of sulfur.[13] To simplify this calculation we simulate acetyl as formyl, **3**, otherwise use the crystallographic parameters for **1a**, and then, for **1b** just twist the amide dihedral angle by 90°. This results in a barrier of 11.3 kcal for **3**, well within the error of the NMR line-shape measurement of 11.7 kcal.

The corresponding calculation of the barrier in 1-formyl-1,4-dihydropyridine (**4**) is 15.2 kcal, see Table I. Inspection of the upper occupied orbitals of twisted state **3b** reveals a significant bonding contribution from 3d$_{xz}$(S)–2p$_z$(C) overlap, no 2p$_z$(C)–2p$_z$(S) interaction and neither effects are seen in bonding MO's of the ground state **3a**. Interestingly this d,p overlap in the twisted state of sulfone **3b** is between 3d$_{xz}$ of carbon and one side of the sulfur 3d$_{xz}$ which bisects the ring of **1b** along its principle axis, $x$, Figure 2.[14]

Also these calculations show remarkably little variation in atom charges comparing ground and twisted states of respectively **3** and **4** as well as among all four states together. This argues against a significant contribution to sulfone behavior from inductive-field effects.

In sum, the gratifying confluence of theory and experiment provides the first clear evidence for cycloconjugation around a six-$\pi$-electron sulfone species, here the twisted state of compound **1**.

**Acknowledgment.** This research was partly supported by the National Science Foundation, Grant 8304636, as was purchase of the high-field NMR equipment. We thank Dr. Charles Cottrell, Central Campus Instrumentation Center, as well as Dr. Michael

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(14) Higher order calculations of this and related systems are in progress.

(15) For ground, g, and twisted, t, forms, the charges are proceeding from N to the para atom, 3g −0.2833, +0.0761, −0.0929, +0.3614; 3t −0.2922, +0.0800, −0.0916, +0.3617; 4g −0.02963, +0.0537, −0.0718, −0.1105; 4t −0.3138, +0.0571, −0.0848, −0.1072.

J. Geckle, Bruker Instruments, for assistance with NMR technology.

**Registry No.** 1, 23863-20-9; 2, 67402-84-0; 3, 103025-32-7; 4, 103025-33-8.

**Supplementary Material Available:** Atomic coordinates and tables of relevant details of X-ray crystallography (8 pages). Ordering information is given on any current masthead page.

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## Surface-Specific Phosphate Cleavage of a Substrate-Functionalized Vesicular Surfactant

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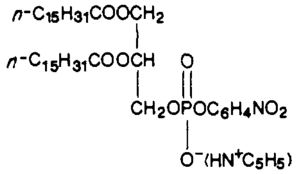
One goal of vesicular chemistry is the control of reaction locus, for example, by the development of reactions specific to exo- or endovesicular surfaces.[1] Not only are such reactions intrinsically interesting, but they differentiate these surfaces, creating further opportunities for locus-specific chemistry. Examples involving reactions of functional surfactant vesicles include diazo coupling,[2] imine formation,[3] viologen reduction,[4] stilbene bromination,[5] and fluorescamine labeling.[6]

The hydrolytic or nucleophilic cleavage of esters or phosphates, an extensively studied reaction in aggregate chemistry,[1d,7] has not been successfully surface-restricted,[8] although two kinetically distinct, competitive cleavages were observed in the aminolysis of *p*-nitrophenyl laurate in polymeric vesicles[9] and in the hydrolysis of clustered or dispersed ester-functionalized, azobenzene surfactants in dialkyldimethylammonium ion vesicles.[10] Here we report the first example of a surface-specific vesicular hydrolytic reaction, one that is dependant on the maintenance of a substantial pH gradient[11] by the vesicle.

1,2-Dipalmitoyl-3-glyceryl *p*-nitrophenyl phosphate (**1**, DPGPNPP) was prepared by reaction of *p*-nitrophenyl phosphorodichloridate (Aldrich) with 1,2-dipalmitoyl-*rac*-glycerol (Sigma) in ether/pyridine (4 h, 25 °C), followed by hydrolysis ($H_2O$, pyridine, 1 h, 25 °C). The product was isolated as its pyridinium salt in 80% yield, mp 68–70 °C, after several recrystallizations from EtOAc, and was characterized by NMR spectroscopy and elemental analysis. Treatment of a sample with ethanolic KOH released the theoretical quantity of *p*-nitrophenoxide ion ($PNPO^-$).

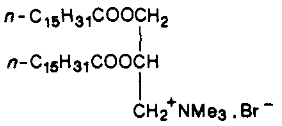


$$\begin{array}{l} n\text{-}C_{15}H_{31}COOCH_2 \\ n\text{-}C_{15}H_{31}COOCH \\ CH_2OP(=O)(OC_6H_4NO_2)O^-(HN^+C_5H_5) \end{array}$$

**1**(DPGPNPP)

$(n\text{-}C_{16}H_{33})_2{}^+NMe_2 . Br^-$

**2**



$$\begin{array}{l} n\text{-}C_{15}H_{31}COOCH_2 \\ n\text{-}C_{15}H_{31}COOCH \\ CH_2{}^+NMe_3 . Br^- \end{array}$$

**3**

Vesicles of **1** were created at pH 5.5 by sonication (immersion probe, 80 W, 55–60 °C, 15 min), cooling to 25 °C, and filtration through a 0.8 μM Millipore filter. Dynamic light scattering[12] revealed vesicles of 1500-Å diameter at pH 11.8 (under reaction conditions, see below.) Differential scanning calorimetry[12,13] detected a phase transition ($T_c$) at 29.5 °C, with $\Delta H$ = 14.8 kcal/mol.

Vesicular **1** is *anionic* and resistant to phosphorolytic cleavage at pH 8. At pH 11.8, however, it releases 48–50% of the theoretical $PNPO^-$ in a pseudo-first-order process characterized by $k_\psi = 4.68 \times 10^{-4}\ s^{-1}$ (Table I, run 1),[14] appropriate to vesicular cleavage of an anionic phosphate.[15] A more significant observation is the *partial* nature of $PNPO^-$ cleavage, even after 24 h. If, however, the vesicles are "damaged" by the addition of excess cetyltrimethylammonium chloride (CTACl), the residual $PNPO^-$ is released within 6 min (Figure 1, curve 1).[16a]

Partial $PNPO^-$ cleavage of DPGPNPP vesicles persists at 35 °C, above $T_c$ (run 2), and is unaffected by added $K^+$ or hydrophobic $Bu_4N^+$ cations (runs 3 and 4). However, incorporation of cationic CTACl during vesicle formation at pH 5.5 profoundly affects subsequent behavior at pH 11.8 (runs 5–11). When [DPGPNPP] > [CTACl] (run 5), $k_\psi^f$ is enhanced, but still only ~55% of the $PNPO^-$ is cleaved. When [CTACl] slightly exceeds [DPGPNPP] (run 6; Figure 1, curve 2), the reaction becomes kinetically biphasic, with a slow, pseudo-first-order process, $k_\psi^s$ accounting for the residual ~45% of $PNPO^-$ over ~22 h. When [CTACl] exceeds [DPGPNPP] by 1.6 times or more (runs 7–11; Figure 1, curve 3), all the $PNPO^-$ cleaves in *one* exponential process and $k_\psi^f$ increases with increasing [CTACl].[16b]

The results point to moderately fast exovesicular $PNPO^-$ cleavage from vesicular **1**, whereas native vesicles are not attacked at endovesicular sites. However, such cleavage does occur in the presence of cationic CTACl, which also charge neutralizes anionic **1**, enhancing $k_\psi$ due to $OH^-$ attack. CTACl could either convert the vesicles to micelles, thus exposing all the *p*-nitrophenyl phosphate head groups, or it could "insert" into the vesicle providing regions permeable to $OH^-$, facilitating endovesicular attack.

We favor the latter explanation because (1) dynamic light scattering shows that 2000-Å species persist under conditions corresponding to run 9, Table I; (2) quantitative, single-exponential $PNPO^-$ release occurs from *covesicles* of **2** and DPGPNPP, where surfactant **2** is structurally related to CTACl (run 12); (3) the fluorescence at 530 nm of entrapped riboflavin[11a] in vesicular DPGPNPP is maintained for at least 5 h at pH 11.8 but is quenched by $OH^-$ immediately upon the addition of excess CTACl; and (4) vesicles of **2** and analogues are readily permeable to hydroxide[8] and other anions.[12,17]

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(16) (a) A typical rate constant for CTACl-induced cleavage of residual $PNPO^-$ was $55 \times 10^{-4}\ s^{-1}$ at [CTACl] = $3.6 \times 10^{-4}$ M. (b) The similarity of the preceding rate constant[16a] and that of run 8, Table I, suggests that $OH^-$ transit of CTACl-damaged vesicles is not rate-limiting and that $PNPO^-$ cleavage occurs at comparable rates at exo- or endovesicular sites; see below.

0002-7863/86/1508-5341$01.50/0