and acylation[7] with 2-quinoxoyl chloride gave, following chromatography (silica gel) and recrystallization, des-*N*-tetramethyltriostin A (**1**) in a yield of 57%: mp 226–229 °C; TLC R_f ($CHCl_3$:MeOH:AcOH, 85:10:5) 0.60, R_f ($CHCl_3$:ethanol, 80:20) 0.69; amino acid analysis, Ala 1.08, Cys 0.87, Ser 1.06, Val 1.00; $[\alpha]^{25}_D$ −43° (*c* 1.5, $CHCl_3$); $\lambda_{max}^{CH_3CN}$ 315 nm (ϵ 1.13 × 10^4), 325 (ϵ 1.11 × 10^4); NMR ($CDCl_3$) δ 1.1 (q, 12 H, valyl methyl), 1.3 (d, 6 H, alanyl methyls), 2.5 (m, 2 H, valyl methines), 2.8 (d, 4 H, cystinyl methylenes), 4.4–5.1 (m, 10 H, seryl methylenes, 6 α-hydrogens), 5.6 (m, 2 H, α-hydrogens), 6.4 (d, 2 H, NH), 7.3 (d, 2 H, NH), 7.7–8.3 (m, 8 H, quinoxaline H_5–H_8), 8.5 (d, 2 H, NH), 8.7 (d, 2 H, NH), 9.6 (s, 2 H, quinoxaline H_3); M^+ 1031 (field desorption). The electron impact spectrum of **1** had peaks in the low mass region at *m/e* 102, 129, 157, 226, 297, 366, and 482; a similar fragmentation pattern was observed in the reported[1b] spectrum for the quinoxaline antibiotic echinomycin. Analysis[16] of **1** indicated 2% racemization of the alanine residues, which racemization likely occurred upon activation of the alanine carboxyl in the fragment coupling and cyclization procedures.

Des-*N*-tetramethyltriostin A (**1**) has been shown[17] to bind as a bifunctional intercalating agent to DNA. In contrast to triostin A (**2**), analogue **1** showed[17] no activity toward *Staphalococcus aureus*.

Acknowledgments. Appreciation is expressed to the National Institutes of Health (National Cancer Institute, Grant CA 10653) for support of this research, to Professor C. C. Sweely, Department of Biochemistry, Michigan State University, for providing mass spectral data, and to Professor M. J. Waring, Department of Pharmacology, University of Cambridge, for providing biological data.

References and Notes

(1) (a) W. Keller-Schierlein, M. L. Mihailovic, and V. Prelog, *Helv. Chim. Acta*, **42**, 305 (1959); (b) A. Dell, D. H. Williams, H. R. Morris, G. A. Smith, J. Feeney, and G. C. K. Roberts, *J. Am. Chem. Soc.*, **97**, 2497 (1975); (c) D. A. Martin, S. A. Mizsak, C. Biles, J. C. Stewart, L. Baczynskyi, and P. A. Meulman, *J. Antibiot.*, **28**, 332 (1975); (d) H. Otsuka and J. Shōji, *Tetrahedron*, **23**, 1535 (1967); (e) H. Otsuka, J. Shōji, K. Kawano, and Y. Kyogoku, *J. Antibiot.*, **29**, 107 (1976).
(2) J. I. Shōji and K. Katagiri, *J. Antibiot., Ser. A*, **14**, 335 (1961).
(3) S. Matsuura, *J. Antibiot., Ser. A*, **18**, 43 (1965).
(4) M. Waring and A. Makoff, *Mol. Pharmacol.*, **10**, 214 (1974); G. G. Gauze, Jr., N. P. Loshkareva, and I. B. Zbarsky, *Biochim. Biophys. Acta*, **166**, 752 (1968).
(5) M. J. Waring and L. P. G. Wakelin, *Nature (London)*, **252**, 653 (1974); L. P. G. Wakelin and M. J. Waring, *Biochem. J.*, **157**, 721 (1976).
(6) W. Chen, M. Hsu, and R. K. Olsen, *J. Org. Chem.*, **40**, 3110 (1975).
(7) H. C. Koppel, I. L. Honigberg, R. H. Springer, and C. C. Cheng, *J. Org. Chem.*, **28**, 1119 (1963); S. Gerchavok and H. P. Schultz, *J. Med. Chem.*, **12**, 141 (1969).
(8) Satisfactory combustion analyses and ^1H NMR spectral data were obtained for all compounds reported in this synthesis.
(9) B. Marinier, Y. C. Kim, and J. M. Navarre, *Can. J. Chem.*, **51**, 208 (1973).
(10) D. F. Verber, J. D. Milkowski, S. L. Varga, R. G. Denkewalter, and R. Hirschmann, *J. Am. Chem. Soc.*, **94**, 5456 (1972).
(11) J. C. Sheehan, P. A. Cruickshank, and G. L. Boshart, *J. Org. Chem.*, **26**, 2525 (1961).
(12) W. Konig and R. Geiger, *Chem. Ber.*, **103**, 788 (1970).
(13) G. W. Anderson, J. E. Zimmerman, and F. M. Callahan, *J. Am. Chem. Soc.*, **89**, 5012 (1967).
(14) J. Halstrom and H. Klostermeyer, *Justus Liebigs Ann. Chem.*, **715**, 208 (1968); W. Konig and R. Geiger, *ibid.*, **727**, 125 (1969).
(15) B. Kamber, *Helv. Chim. Acta*, **54**, 927 (1971).
(16) Determined by hydrolysis (6 N HCl, 110 °C, 24 h) of **1** followed by derivatization (*N*-trifluoroacetylation and esterification) and analysis on a capillary column coated with an optically active stationary phase (*N*-lauroyl-L-valyl-*tert*-butylamide)[18] that clearly separates the D- and L-alanine derivatives.
(17) The biological data, obtained by methods reported in ref 5, were kindly provided by Professor M. J. Waring.
(18) B. Feibush, *Chem. Commun.*, 544 (1971).

Thomas L. Ciardelli, Richard K. Olsen*
Department of Chemistry and Biochemistry
Utah State University
Logan, Utah 84322
Received October 18, 1976

The He I Photoelectron Spectrum of 3,7-Dimethyl-*p*-quinodimethane. A Non-Koopmans Theorem Effect

Sir:

Interpretations of observed bands of photoelectron spectra are most frequently cast in terms of Koopmans' approximation.[1] This has come to be the case in spite of the unrealistic restriction which this method places on the wave functions for the ionic states and the dependency of the whole procedure on the fortuitous cancellation of the errors due to correlation and electronic reorganization.[2] The adoption of such a scheme implies all pertinent information for highly excited ionic states is given through the orbital approximation as it is applied to the neutral ground state molecule, which seems a somewhat drastic assumption.[3]

We have previously reported[4] our observation of the PE spectrum of *p*-quinodimethane (**1**) by flash vacuum pyrolysis of 2,2-paracyclophane.[5] The most interesting feature of this study was the apparently low energetic position and intensity of the third band. We rationalized this observation as being a manifestation of the interaction between ionic structures (b_{2g}^0, b_{2g}^1) derived from the quinoid **1** and diradical **1a** contributors to the ground state. The purpose of this paper is to discuss the spectrum of the 3,7-dimethyl derivative **2** which confirms the previous assignment and appears to establish a strong effect outside of those encompassed through the Koopmans' approximation procedure.

The 3,7-dimethyl derivative[6] **2** was chosen for these studies because of the predictions of the simple structure representation[7] (SR) procedure of the effects of the added methyl groups. In this (SR) procedure, the shifts due to methyl or methylene substitution are attributed *entirely* to hyperconjugation. The parameters associated with the interaction in the ionic states were determined from studies of other alkylated olefins.[8] The calculated shifts (Table I) of the first, second, and fourth (zero order) II ionic states are significant while the third is predicted to be unaffected by 3,7-dimethyl substitution. Huckel wave functions and the INDO[9] Koopmans approximation methods (Table I) give similar results. All three criteria indicate that 3,7-dimethyl substitution would uncover a (weak) band near 9.8 eV if our original rationalization were correct. The SR

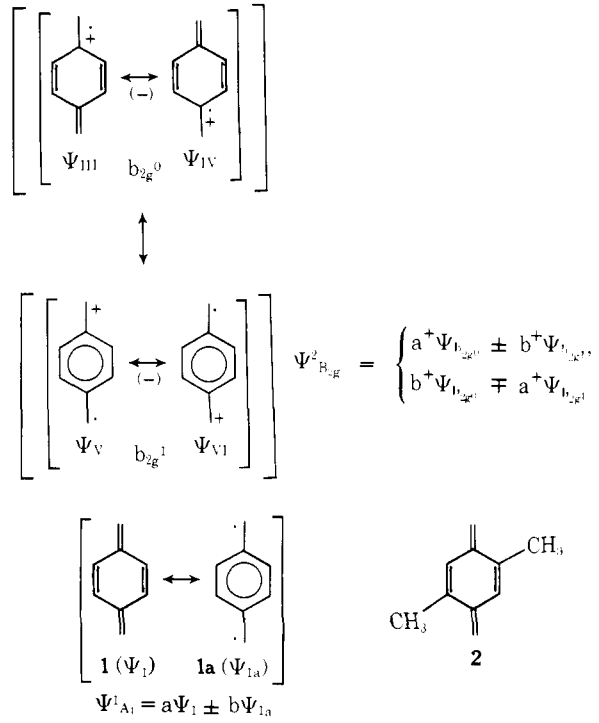


Table I. Calculated Shifts[c] in PE Band Positions by 3,7-Dimethyl Substitution

Band (Π)	D_{2h} State sym	Position (eV)	C_{2h} State sym[a]	ΔCH₃(SR) (eV)	ΔCH₃(HMO)[b] (eV)	ΔCH₃(INDO) (eV)	Δobsd[c]
1	$^2B_{3u}$	7.87	^2A_u	−0.11	−0.10	−0.28	−0.3
2	$^2B_{1g}$	9.7	^2B_g	−0.63	−0.52	−1.69	−0.7
3	$^2B_{2g}$	9.8	^2B_g	−0.03	−0.08	−0.20	0
4	$^2B_{3u}$	?	^2A_u	−0.39	−0.53	−4.98	*a*

[a] The SR method, including σ-bands in the basis set suggests that the fourth band may be σ. [b] Using the relationship of J. Eland and C. Danby, *Z. Naturforsch.*, **239**, 355 (1968). [c] Calculated shifts due to methylation without consideration of configuration interaction or its equivalent. None of the calculational methods would give degeneracy of the second and third bands indicated in column 3.

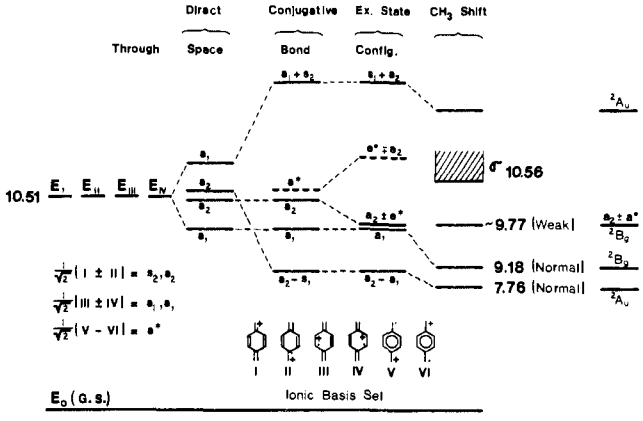


Figure 1.

predictions are shown graphically as Figure 1 where the "non-Koopmans" interaction has been included.

Figure 2 (bottom) shows the observed spectrum of **2** obtained by the flash vacuum pyrolysis of the corresponding paracyclophane (Figure 2 top). The positions and intensities of the first three bands are in very good agreement with the predictions of Figure 1. The low apparent intensity[10] of the third band is particularly indicative of the non-Koopmans' effect proposed and suggests strong mixing of the b_{2g}^0 and b_{2g}^1 structural representations.

The effect described above in terms of structures has good precedent in the MO-CI theory of electronic excitation, particularly of doublet species. In MO-CI language, the *formal* counterpart to the mixing of the wave function associated with **1** and **1a** is configuration interaction between $\Psi(1b_{3u}^2 1b_{2g}^2 1b_{1g}^2 2b_{3u}^2)$ and $\Psi(1b_{3u}^2 1b_{2g}^2 1b_{1g}^2 2b_{2g}^2)$, i.e., between the zero order ground state and the lowest configuration with two-electron promotion, similar to the description of Michl.[11] For the doublet[12] (radical cation) species, the $\chi_{m-2,m}(1b_{3u}^2 1b_{2g}^1 1b_{1g}^2 2b_{3u}^2)$ and $\chi_{m,m+1}(1b_{3u}^2 1b_{2g}^2 1b_{1g}^2 2b_{2g}^1)$ configurations are both b_{2g}, and the transition energy and intensity is dependent on the extent to which they are mixed. The low apparent intensity of the third band can be qualitatively recognized to result from an appreciable contribution from a configuration in which one electron is photodetached and a second has been promoted from the highest occupied to the lowest unoccupied MO to the total $^2B_{1g}$ stationary state. Such a transition is forbidden to a very high order with single determinant representations.

The present results suggest relatively little configurational

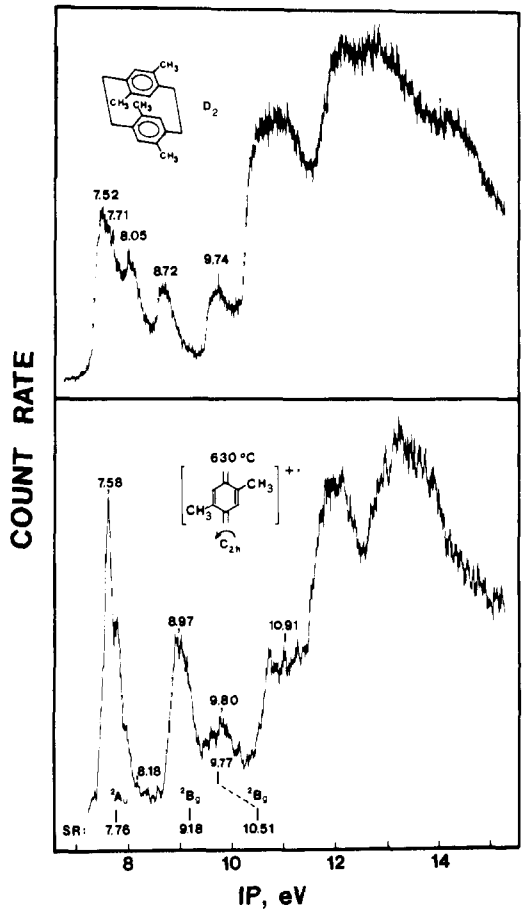


Figure 2.

mixing in the ground state compared to the strong mixing in the $^2B_{1g}$ ionic state.[13] The apparent success of the Koopmans' theorem procedure in the majority of cases is important. However, we believe the present results are important in illustrating the fundamental conceptual error in the Koopmans' procedure and hope they will serve as a stimulus for the application of better calculational methods for the ionization process in large molecules than single determinant representations can give.

Acknowledgment. We are grateful to the National Science Foundation for financial support of this work.

References and Notes

(1) T. Koopmans, *Physica (Utrecht)*, **1**, 104 (1934).
(2) G. Richards, *Int. J. Mass Spec. Ion Phys.* **2**, 149 (1969).
(3) The topic of Koopmans' theorem breakdown in small molecules has received attention from several authors. See M. Okuda and N. Jonathan, *J. Electron Spectrosc. Relat. Phenom.*, **3**, 19 (1974); A. Potts and T. Williams, *ibid.*, **3**, 3 (1974); L. Cedarbaum, *Chem. Phys. Lett.*, **25**, 562 (1974); L. Cedarbaum, *J. Phys. B*, **8**, 290 (1975); L. Cedarbaum, W. Doncke, and W. von Niessen, *Chem. Phys. Lett.*, **34**, 60 (1975); M. Morrell, R. Parr, and M. Levy, *J. Chem. Phys.*, **62**, 549 (1975); R. DeKock, *Chem. Phys. Lett.*, **27**, 297 (1974); T. Chen, W. Smith, and J. Simons, *ibid.*, **26**, 296 (1974), and references therein.
(4) T. Koenig, R. Wielesek, W. Snell, and T. Balle, *J. Am. Chem. Soc.*, **97**, 3225 (1975).
(5) J. Pearson, H. Six, D. Williams, and M. Levy, *J. Am. Chem. Soc.*, **93**, 5034 (1971).
(6) D. Longone and H. Chow, *J. Am. Chem. Soc.*, **92**, 994 (1970).
(7) W. Simpson and C. W. Looney, *J. Am. Chem. Soc.*, **76**, 6285, 6793 (1954).
(8) T. Koenig and H. Longmaid, *J. Org. Chem.*, **39**, 560 (1974); R. Wielesek and T. Koenig, *Tetrahedron Lett.*, 2429 (1974).
(9) J. A. Pople, D. Beveridge, and P. Dobosh, *J. Chem. Phys.*, **47**, 2026 (1967).
(10) The overlap between bands makes accurate area ratios impossible to determine. The ratio of areas of the first three bands is crudely estimated as 1:0.85:0.50.
(11) Michl and co-workers have given the CI coefficients for these two a_{1g} configurations as 0.88 and 0.36. C. Flynn and J. Michl, *J. Am. Chem. Soc.*, **96**, 3280 (1974). See ref 13.
(12) Configuration interaction as it applies to the excited states of doublets is discussed by Salem, "Molecular Orbital Theory of Conjugated Systems", W. A. Benjamin, Reading, Mass., 1966, pp 435–443.
(13) The published wave function of Michl[11] gives an unrealistically large contribution from $\Psi(1b_{3u}^{2}1b_{2g}^{2}1b_{1g}^{2}2b_{2g}^{2})$ to the closed shell ground state because of the assumption of benzene ring geometry. His wave function implies $\Psi_{^2B_{2g}} \simeq 0.32\chi_{m-2,m} - 0.95\chi_{m,m+1}$ assuming positive interaction constants in the CI matrix.[14]
(14) Professor Michl has informed us of the results of a new CI treatment of **1** using polyene geometry. This wave function and the approximate intensity ratio found here gives $\Psi_{^2B_{2g}} \simeq 0.55\chi_{m-2,m} - 0.84\chi_{m,m+1}$. The change in the wave functions with geometry is in the expected direction although the estimated character of $\chi_{m,m+1}$ suggests it may have a lower configurational energy than that of (Koopmans' theorem configuration) $\chi_{m-2,m}$.
(15) National Science Foundation Undergraduate Research Participant, 1975.

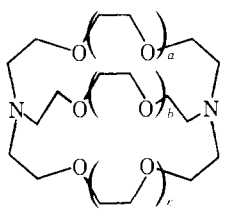
T. Koenig,* S. Southworth[15]
Department of Chemistry, University of Oregon
Eugene, Oregon 97403

Received November 18, 1976

The Acid Catalyzed Dissociation of Metal Cryptate Complexes

Sir:

The ability of synthetic macrobicyclic ligands, such as those of the type **1–3** (cryptands) described by Lehn and co-workers,[1] to form stable complexes with alkali and alkaline earth cations has resulted in many studies of their chemical properties. However, although a considerable amount of thermodynamic data on the metal complexes (cryptates) exists,[2-4] very few kinetic data are available, despite the potential information on the mechanism of complex formation that could come from such studies. This presumably results, at least in part, from the lack of significant visible or ultraviolet (>250 nm) spectral changes associated with complex formation, and also from the difficulty of avoiding effects from competitive protonation of



1, $a = 1$; $b = c = 0$ (2,1,1)
2, $a = b = 1$; $c = 0$ (2,2,1)
3, $a = b = c = 1$ (2,2,2)

Table I. Reaction of HCl with $K(2,2,2)^+$ Cryptate.

T/°C	10^3[2,2,2]/ mol dm^{-3}	10^3[KNO_3]/ mol dm^{-3}	10^3[HCl]/ mol dm^{-3}	k_e/s^{-1} [a]
10.0	0.109	1.06	2.40	1.2_7
10.0	0.0272	0.265	0.47	1.2_4
17.9	0.109	1.06	2.40	3.2_8
17.9	0.109	1.06	1.15	3.1_6
17.9	0.109	2.12	1.15	3.1_3
17.9	0.109	0.53	1.15	3.1_7
17.9	0.109	4.24	1.15	3.1_6
17.9	0.0272	0.265	0.60	3.2_9
17.9	0.0272	0.265	0.29	3.3_1
24.5	0.109	1.06	2.40	7.1_6
24.5	0.0272	0.265	0.60	7.2_1
30.4	0.109	1.06	2.40	$15._0$
30.4	0.0272	0.265	0.60	$16._0$

[a] Each value represents an average of at least three determinations. k_e values ±4%.

the strongly basic nitrogen centers. With the exception of a stopped flow study of the kinetics of formation of Ca cryptates,[5] existing rate data have come from NMR line broadening techniques,[6-8] and in the most comprehensive study,[6] are limited to measurements on (2,2,2) cryptates at the coalescence temperature.

We wish to report results of a method of apparent general applicability to the measurement of dissociation rates of metal cryptates in aqueous solution, involving the observation of conductance changes following the addition of excess acid to the cryptates. We have also found in the course of these studies, that in many cases the dissociation rates are *acid catalyzed*, and the significance of this is discussed.

When excess acid is added to a solution containing a metal cryptate ($MCry^{n+}$), the overall reaction is as shown in eq 1.

$$MCry^{n+} + 2H^+ \xrightarrow{k_e} CryH_2^{2+} + M^{n+} \quad (1)$$

However, if the reaction proceeds via the free cryptand, as in eq 2 and 3,[9]

$$MCry^{n+} \underset{k_f}{\overset{k_d}{\rightleftharpoons}} M^{n+} + Cry \quad (2)$$

$$Cry + H^+ \xrightarrow{k} CryH^+ \quad (3)$$

it can be readily shown that, provided the rate of protonation of the cryptand is significantly greater than the rate of formation of the metal cryptate, the observed rate law is given by eq 4;

$$-d\frac{[MCry^{n+}]}{dt} = k_d[MCry^{n+}] \quad (4)$$

i.e., the observed rate constant corresponds to the rate constant for the dissociation of the cryptate. Under these conditions, the observed rate constant should be independent of both the acid and metal ion concentrations. The reactions can be conveniently followed by observing the rate of change of conductance (the observed decrease in conductance resulting primarily from the loss of H^+) either using conventional techniques for slow reactions, or stopped-flow with conductance detection for rapid reactions. Any competitive protonation of the cryptand prior to the addition of the acid used to initiate the reaction has no effect on the observed kinetics (other than to reduce the amplitude of the conductance change occurring during the reaction). The formation rates can of course be readily obtained from the dissociation rates via the stability constants.

Table I lists results obtained for the K^+,(2,2,2) system at various temperatures, using the stopped flow technique to