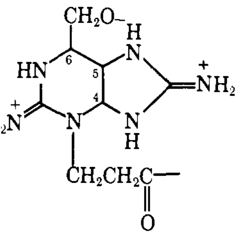
Mild alkaline oxidation of saxitoxin with 0.8% hydrogen peroxide at 25° led to the isolation in good yield and identification of the pyrimidopurine 1[2] which contains all but one each of the original complement of carbon and nitrogen atoms. As important as the product itself is the manner in which 1 was formed. Saxitoxin was readily oxidized over the pH range 3–12 to yield 1, consuming 1 mol of oxygen/mol of toxin when oxygen was used as the oxidant. The conclusion therefore can be drawn that saxitoxin contains a tetrahydropurine nucleus which gives rise to 1, and this is consistent with the conversion of saxitoxin to the pyrrolopyrimidine 3 upon treatment with phosphorus and hydriodic acid.[8] Both 1 and 3 contain a 3,6-dialkylpyrimidine although they were generated in totally different environments. These data are now summarized in structure 4 which is lacking only (a) the carbonyl terminus of the propionyl group[9] and (b) the single carbon and nitrogen atoms lost in the formation of 1.



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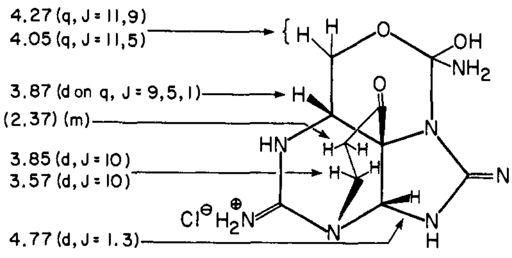
Since the propionyl residue is part of a ketone, the carbonyl must be bonded to C-4, -5, or -6. Analysis of the nmr spectra permits a unique assignment to C-5, based on the AMX type of splitting patterns for the C-6 H and the C-6 CH_2 as shown in structure 5.



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Also, the long-range 1.3-Hz diequatorial coupling between the C-4 and C-6 H's defines the cis ring fusion and the configuration at C-6 as shown.

Assignment of bonding to the remaining carbon and nitrogen must accommodate the facts that (a) the nitrogen must be at the ammonia level since there are no N–N or N–O bonds in the toxin, and (b) the carbon is at the oxidation level of carbon dioxide since all the C–H's in the nmr are accounted for and no further bonding to any of the carbons of 4 is possible. Therefore, this carbon and nitrogen must be bonded to each other, forming a carbamyl group.

Definitive placement of this carbamyl group follows from a detailed p*K* study. Saxitoxin has two p*K* values, 8.24 and 11.60,[4] in water. When the solvent is changed to 20% ethanol, the first p*K* increases to 8.50, and in 50% ethanol, it becomes 9.05. This behavior of significant decreasing dissociation with decreasing polarity of the solvent is characteristic of proton dissociation from oxygen rather than from positively charged nitrogen.[10] Thus, saxitoxin must contain a hydroxyl group of p*K* 8.24, the remaining p*K* being accounted for by the guanidinium ions.

These observations are accommodated by bonding the carbamyl group to the oxymethyl at C-6 to form a carbamate which exists as a cyclol[11] *via* interaction with the NH at position 7. The resulting urea hemiacetal group provides the acidic hydroxyl. Thus saxitoxin has the structure 5.

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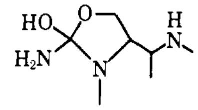
[8] W. Schuett and H. Rapoport, *J. Amer. Chem. Soc.*, 84, 2266 (1962).

[9] The carbonyl terminus of the propionyl residue at exocyclic N-2 in the pyrimidopurine 1 is of no structural significance since we have found that the purine propionic acid exits in solution at pH 9 and above and lactamizes to N-2 upon neutralization and evaporation to dryness. Thus, structural conclusions can be drawn only from the intermediate propionic acid.

[10] E. Grunwald and B. J. Berkowitz, *J. Amer. Chem. Soc.*, 73, 4939 (1951); B. Gutbezahl and E. Grunwald, *ibid.*, 75, 559 (1953).

[11] Equilibrium between the cyclol 5 and the cyclol involving N-1 *via* the carbamate accounts for the interconvertible saxitoxin's A and B seen on countercurrent distribution which revert to a single form in acid.[12] A firm choice between cyclol 5 and cyclol 6 is not possible at this time, although 6 appears sterically less favorable.



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[12] J. D. Mold, J. P. Bowden, D. W. Stanger, J. E. Maurer, J. M. Lynch, R. S. Wyler, E. J. Schantz, and B. Riegel, *J. Amer. Chem. Soc.*, 79, 5235 (1957).

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Transition Metal Catalyzed Valence Isomerizations. The Role of the Ligand[1]

Sir:

The transition metal catalyzed valence isomerizations of highly strained cyclobutane compounds have been shown to vary with the metal or metal complex utilized.[2] In such systems, Rh(I) complexes bring about cleavages of a cyclobutane to diolefin, whereas the noncomplexed Ag(I) and the complex $PdCl_2(C_6H_5CN)_2$ bring about cyclobutane–dicyclopropane isomerizations. Our initial study showed that the 1,1′-bishomocubane system 1 readily rearranged to the dicyclopropane isomer 2 in the presence of Ag(I).[3] Continued study of this strained system using transition metal complexes has shown that rearrangement to the dienes 3 and 4 can be achieved. For these rearrangements, *i.e.*, to 2 or to 3 and 4, it has been found that both the combination of the polarizability and the σ donor–π acceptor ability of the ligands of such complexes as well as the σ electron acceptor ability of the

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[1] This work was supported by the National Science Foundation, Grant No. GP-8700.

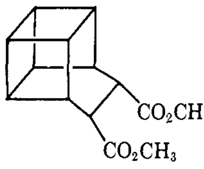
[2] (a) L. Cassar, P. E. Eaton, and J. Halpern, *J. Amer. Chem. Soc.*, 92, 3515, 6366 (1970); (b) J. Wristers, L. Brener, and R. Pettit, *ibid.*, 92, 7499 (1970); (c) K. L. Kaiser, R. F. Childs, and P. M. Maitlis, *ibid.*, 93, 1270 (1971); G. F. Koser, *Chem. Commun.*, 388 (1971).

[3] W. G. Dauben, M. G. Buzzolini, C. H. Schallhorn, and D. L. Whalen, *Tetrahedron Lett.*, 787 (1970); W. G. Dauben, C. H. Schallhorn, and D. L. Whalen, *J. Amer. Chem. Soc.*, 93, 1446 (1971).

Table I. Products from Metal-Catalyzed Rearrangements of 1,1′-Bishomocubane **1**[a]

Expt no.	Catalyst	Solvent	Temp, °C	Reaction time	% **2**	% **3**	% **4**
1	$Rh(Ph_3P)_3Cl$	$CDCl_3$	50–55	15 days	0	33	67
2	$Rh(Ph_3P)_2COCl$	$CDCl_3$	50–55	12 days	0	23	76
3	$Rh(Ph_3P)_2COBr$	$CDCl_3$	50–55	70 hr	0	23	76
4	$Rh(Ph_3P)_2COI$	$CDCl_3$	50–55	41 hr	0	23	76
5	$[Rh(NOR)Cl]_2$[b]	$CDCl_3$	50–55	69 hr	0	22	77
6	$PdCl_2(Ph_3P)_2$	$CDCl_3$	50–55	12 hr	41	23	35.5
7	$PdI_2(Ph_3P)_2$	$CDCl_3$	50–55	$t_{1/2}$ = 7 days	4	34	61
8	$PdCl_2(Ph_3As)_2$	$CDCl_3$	50–55	6 hr	61.5	9.5	29
9	$PdI_2(Ph_3As)_2$	$CDCl_3$	50–55	60 hr	6	39.5	54
10	$PdCl_2(Ph_3Sb)_2$[c]	$CDCl_3$	50–55	8 days	100	0	0
11	$PdI_2(Ph_3Sb)_2$	$CDCl_3$	50–55	4 hr	23	22.5	54
12	$PdCl_2[P(OCH_3)_3]_2$	$CDCl_3$	RT	28 days	67	8	24
13	$PdBr_2[P(OCH_3)_3]_2$	$CDCl_3$	50–55	46 hr	25	25	50
14	$PdI_2[P(OCH_3)_3]_3$[c]	$CDCl_3$	50–55	$t_{1/2}$ = 13 days	11	32	56
15	$PdCl_2[P(OPh)_3]_2$	$CDCl_3$	50–55	4 hr	94	2	4
16	$PdI_2[P(OPh)_3]_2$	$CDCl_3$	50–55	6 days	36.5	18	45.5
17	$PdCl_2(pyr)_2$[d]	$CHCl_3$	Reflux	$t_{1/2}$ = 10 days	100	0	0
18	$PdCl_2(NOR)$[b]	$CDCl_3$	45–50	10 days	100	0	0
19	$PdI_2(NOR)$	$CDCl_3$	50–55	72 hr	86	4	9
20	$PdCl_2(PhC{\equiv}N)_2$	$CDCl_3$	RT	28 days	100	0	0
21	$PdI_2(PhC{\equiv}N)_2$	$CDCl_3$	50–55	19 hr	95	1	4
22	$PdCl_2$[e]	Aq CH_3OH	RT		100	0	0
23	$AgNO_3$[e]	Aq CH_3OH	RT		100	0	0

[a] Experiments were performed in nmr tubes with molar ratios of **1** to a catalyst of approximately 20:1 except as indicated. Products were formed quantitatively from **1** and were identified by comparison of spectral properties and vpc retention times of known compounds. See ref 3. Catalysts were prepared by literature methods. [b] (NOR) is norbornadiene. [c] Molar ratio was greater than 20:1 due to low solubility of catalyst. [d] Molar ratio approximately 2.5:1; (pyr) is pyridine. [e] Reaction was performed for product analysis only.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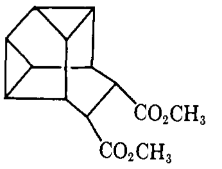
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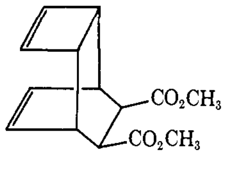
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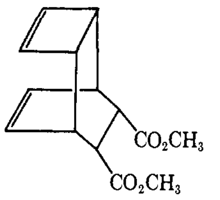
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transition metal complex guides the course of the reaction. The results of this present study are summarized in Table I.

When **1** was allowed to react with a series of Rh(I) complexes,[4] only the dienes **3** and **4** were found (experiments 1–5), a result in contrast to the Ag(I) catalyzed rearrangement of **1** to the dicyclopropyl isomer **2** (experiment 23). Since both of the above metals are capable of good dπ bonding (the so-called class "b" metals)[5] the related Pd(II) series was studied.

It was found that formation of dienes **3** and **4** predominated with Pd(II) complexes which contained ligands which were both good σ donors and π acceptors (experiments 6–11), for example, complexes containing triphenylphosphine, triphenylarsine, and triphenylstibine.[6] In this series the phosphine derivative, being the best σ donor and π acceptor, gave the largest percentages of **3** and **4**. With complexes having ligands which are very strong π acceptors but weak σ donors, *i.e.*, the phosphites[6] (experiments 12–16), a smaller percentage of **3** and **4** was observed; the triphenyl phosphites, being the strongest π acceptor and the weakest σ donor of this group, gave the smallest percentage of the dienes. It was also found that by increasing the polarizability of the ligands on the transition metal by varying the halogens from chlorine to iodine[7] increased amounts of **3** and **4** were obtained (experiments 7, 9, 11 13, 14, 16, 19, 21).

Transition metal complexes containing ligands which are weak σ donors and π acceptors and which are not polarizable[6–8] act in the same manner as the uncomplexed metal ion and give exclusively the dicyclopropyl derivative **2** (experiments 17, 18, 20, 22). This type of rearrangement process can be viewed as the transition metal interacting, edge-on, with a strained carbon–carbon σ bond, the metal acting as a strong σ acceptor,[9] to yield an intermediate with an electron-deficient center (*i.e.*, a carbonium ion like intermediate) which goes on to the product.[10] The present results are in agreement with such a postulate.[11] Furthermore,

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[4] Private communication from Professor J. Halpern initially informed us that $[Rh(NOR)Cl]_2$ brought about a rearrangement to dienes.

[5] S. Ahrland, J. Chatt, and N. R. Davies, *Quart. Rev., Chem Soc.*, 12, 265 (1958); S. Ahrland, *Struct. Bonding (Berlin)*, 1, 207 (1966).

[6] (a) F. A. Cotton, *Inorg. Chem.*, 3, 702 (1964); (b) R. P. Stewart and P. M Treichel, *ibid.*, 7, 1942 (1968); (c) C. A. Tolman, *J. Amer. Chem. Soc.*, 92, 2953 (1970); G. Henrici-Olivé and S. Olivé, *Angew. Chem., Int. Ed. Engl.*, 10, 105 (1970), and references therein.

[7] R. G. Pearson, *J. Chem. Educ.*, 45, 581 (1968).

[8] The relative importance of σ and π components of the bonding in $PdCl_2(NOR)$ is uncertain: see F. R. Hartley, *Chem. Rev.*, 69, 799 (1969).

[9] See H. W. Quinn and J. H. Tsai (*Advan. Inorg. Chem. Radiochem.*, 12, 217 (1969)) for the importance of σ acceptor ability of Ag(I) compared to other transition metals.

[10] A similar carbonium ion like intermediate has been suggested; however, oxidative addition of Ag(I) has been proposed as the initial step: see J. E. Byrd, L. Cassar, P. E. Eaton, and J. Halpern, *Chem. Commun.*, 40 (1971).

[11] In similar transition metal catalyzed rearrangements of strained carbon bonds the role of the σ acceptor ability of the transition metal which results in a carbonium ion like intermediate has been suggested. See (a) L. A. Paquette, *Accounts Chem. Res.*, 4, 280 (1971); (b) P. G.

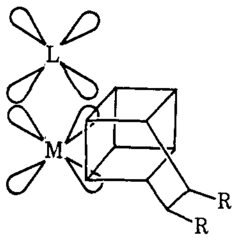
Table II. Solvent Effects of $PdCl_2(Ph_3P)_2$-Catalyzed Rearrangements of 1,1′-Bishomocubane **1**[a]

Solvent	% **2**	% **3**	% **4**
$CDCl_3$	41	23	35.5
CH_2Cl_2	43	20	37
$CH_3C{\equiv}N$	55	13	31.5
$CD_3C(=O)CD_3$	55.5	13	31.5
$CD_3S(=O)CD_3$	71	9	19.5
$HOCH_2CH_2OH$	85	4	11
CH_3OH	86	4	9.5

[a] Reactions were performed similarly to those in Table I. There was no rate comparison due to varying solubility of catalysts in solvents.

as shown in Table II, it has been found in the $PdCl_2[P(C_6H_5)_3]_2$-catalyzed rearrangement of **1** that as the solvent was changed the amount of the dicyclopropyl rearrangement product increased with the carbonium ion stabilizing ability of the solvent.

The results from this study of the ligand effect upon the rearrangement of the strained bishomocubane system to the dienes **3** and **4** are in agreement with the suggestion that the rearrangement process proceeds *via* a bidentate interaction of the strained carbon system with the transition metal complex[12,13] (I). The



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orbital symmetry and the geometry of the metal d orbitals make the d_{xz} orbital an effective π acceptor from the organic substrate and make the d_{yz} orbital an effective donor to the σ^* orbital of the substrate.[12] The bidentate interaction is equivalent to an oxidative addition[14] and the results reported in this study show a good correlation between those ligands which enhance the oxidative addition of a transition metal[14] and those ligands on Pd(II) which favor formation of dienes **3** and **4**. The results of Rh(I) giving only dienes **3** and **4** are also in line with the greater oxidative addition ability of Rh(I) relative to Pd(II).[14,15] It has previously been pointed out that in highly strained ring systems where there is a large energy release upon isomerization, a continuum very likely exists between the stepwise oxidative addition process and a more concerted process.[12]

The present results demonstrate for the first time in the transition metal complex catalyzed rearrangement of a strained cage compound that by variation of the ligand a change in product distribution has resulted. The extent of the two rearrangement courses to **2** and to **3** and **4** followed is controlled by the σ electron acceptor ability of the complex and by the σ donor π acceptor ability, and polarizability, of the ligands in the transition metal complex.

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Gassman and T. J. Atkins, *J. Amer. Chem. Soc.*, **93**, 4597 (1971); (c) M. Sakai, H. H. Westberg, H. Yamaguchi, and S. Masamune, *ibid.*, **93**, 4611 (1971).

[12] (a) F. D. Mango, *Tetrahedron Lett.*, 505 (1971); (b) F. D. Mango and J. H. Schachtschneider, *J. Amer. Chem. Soc.*, **93**, 1123 (1971).

[13] An edge-on insertion into one carbon–carbon σ bond is also a possibility to be considered. However, this is comparable to and indistinguishable from the face-on insertion since initially it is a matter of small differences in metal atom positions. In the final stage of the rearrangement for both cases the metal atom would be symmetrically coordinated to the dienes before leaving to give free diene products.

[14] J. P. Collman and W. R. Roper, *Advan. Organometal Chem.*, **7**, 53 (1968); J. P. Collman, *Accounts Chem. Res.*, **1**, 136 (1968); J. Halpern, *ibid.*, **3**, 386 (1970), and references therein.

[15] Preliminary results using $PtCl_2(Ph_3As)_2$ and $PtCl_2(Ph_3Sb)_2$ showed a mixture of **2**, **3**, and **4** were formed also in line with the oxidative addition ability of Pt(II).

Direct Measurement of a First-Order Rate Constant for an Elementary Electron Transfer Step[1]

Sir:

Most kinetic studies of oxidation–reduction reactions, whether of the inner-sphere or the outer-sphere class, provide second-order rate constants for the overall reaction. One notable exception is afforded by the $Co(NH_3)_5L\text{–}Fe^{2+}$ system (L = nitrilotriacetate anion)[2] where the precursor complex was detected and the first-order rate constant for electron transfer within the binuclear inner-sphere unit was determined. In view of the importance of obtaining quantitative information about the elementary steps of redox reactions, we have started an investigation of the reduction of various tripositive cobalt(III) complexes by the hexacyanoferrate(II) anion. The choice of highly oppositely charged reactants was based on the expectation[3] that outer-sphere complex formation by the reactants would be substantial at relatively low concentrations. This expectation has been fulfilled in the $Co(NH_3)_5OH_2{}^{3+}\text{–}Fe(CN)_6{}^{4-}$ system, and we wish to report what we believe to be the first measurement of a first-order rate constant for an electron-transfer process within a binuclear, outer-sphere complex.

When aqueous solutions of $[Co(NH_3)_5OH_2](ClO_4)_3$ and $Na_4[Fe(CN)_6]$ are mixed at $10^{-4}\text{–}10^{-3}$ *M* concentrations, a precipitate [presumably cobalt(II) hexacyanoferrate(II) and/or cobalt(II) hexacyanoferrate(III)] forms within a few seconds, and therefore homogeneous kinetic measurements are precluded. However, when disodium dihydrogen ethylenediaminetetraacetate is added to the solution to complex the cobalt(II) formed, no precipitate is produced, and therefore all kinetic measurements reported here have been carried out in the presence of H_2EDTA^{2-}, the stoichiometry of the reaction being represented by[4]

$$Fe(CN)_6{}^{4-} + Co(NH_3)_5OH_2{}^{3+} + H_2EDTA^{2-} + 3H^+ = Fe(CN)_6{}^{3-} + CoEDTA^{2-} + 5NH_4{}^+ + H_2O$$

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[1] This work was supported by the National Science Foundation under Grant GP-9669.

[2] R. D. Cannon and J. Gardiner, *J. Amer. Chem. Soc.*, **92**, 3800 (1970).

[3] Outer-sphere complex formation between $Co(en)_3{}^{3+}$ and $Fe(CN)_6{}^{4-}$ has been reported by R. Larsson, *Acta Chem. Scand.*, **21**, 257 (1967).

[4] The addition of H_2EDTA^{2-} causes a slight complication because of the $CoEDTA^{2-}\text{–}Fe(CN)_6{}^{3-}$ reaction: D. H. Huchital and R. G. Wilkins, *Inorg. Chem.*, **6**, 1022 (1967). However, under the conditions of our experiments, the $CoEDTA^{2-}\text{–}Fe(CN)_6{}^{3-}$ reaction proceeds only to a small extent (*ca.* 20%) and is extremely rapid compared to the