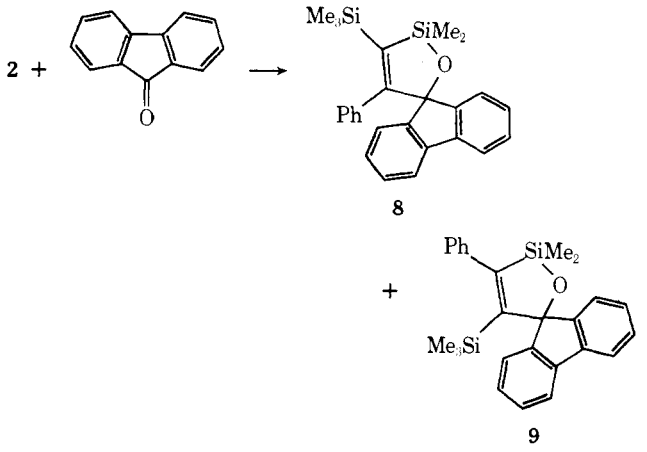
fluorenone reacts with **2** in the dark at room temperature to give **8** and **9** (**8**/**9** = 1/3) in 42–51% yield[14] after 30 min.

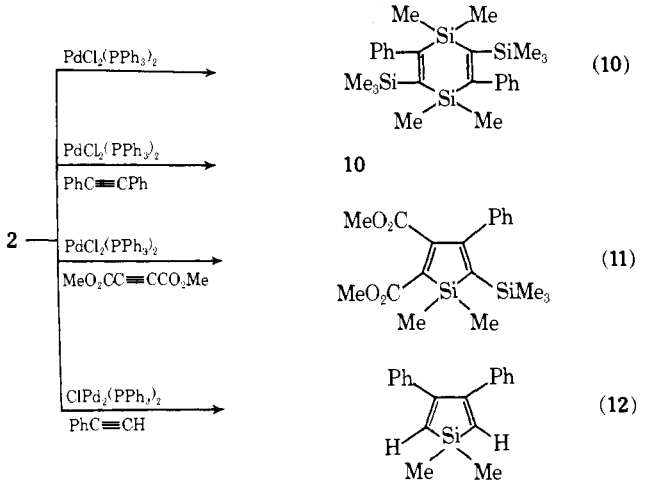


8

9

The reactivity of benzophenone is in between aliphatic ketones and fluorenone. Thus, a slow dark reaction gave **6c** and **7c** (**6c**/**7c** = 1/3) in 7.2% yield after 50 min. Irradiation of **2** and benzophenone through a Pyrex filter resulted in the formation of **6c** and **7c** (**6c**/**7c** = 1/1.4) in 42.4% yield.[14] Interestingly, the photochemical cycloaddition with benzophenone was completely suppressed by addition of piperylene, only the dark reaction being observed.

We have demonstrated that a strained Si–C bond of silacyclobutane can undergo palladium complex-catalyzed cycloaddition with acetylenes.[15] Naturally, the Si–C bond of **2** should be more prone to such a reaction. The course of the reaction was, however, affected dramatically by the structure of the acetylene, as shown by the following scheme.



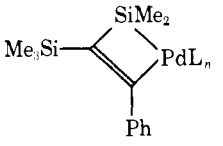
(10)

10

(11)

(12)

These reactions were carried out at 75 °C for 10–30 min, and yields are 30–50%.[14] Mechanisms of these reactions are not necessarily clear, but we believe that they probably involve a common intermediate such as silapalladacyclobutene (**13**).



13

In the absence of acetylenes or even in the presence of an unreactive actylene such as diphenylacetylene, **13** reacts with **2** leading to **10**, while with acetylene dicarboxylic ester the acetylene is incorporated in the product. Although the reaction with phenylacetylene is rather difficult to explain, presumably **13** changes to a silylene complex with extrusion of (trimethylsilyl)phenylacetylene before the reaction, and the silylene complex reacts with 2 mol of acetylene to give **12**.[16] We have evidence for the formation of a silylene complex that will be reported later.

Acknowledgment. We thank Toshiba Silicone Co., Ltd., for gifts of chlorosilanes.

References and Notes

(1) Chemistry of Organosilicon Compounds. 98.
(2) M. E. Volpin, Yu. D. Koreshkov, V. G. Dulova, and D. N. Kursanov, *Tetrahedron*, **18**, 107 (1962).
(3) R. West and R. E. Bailey, *J. Am. Chem. Soc.*, **85**, 2871 (1963).
(4) (a) R. T. Conlin and P. P. Gaspar, *J. Am. Chem. Soc.*, **98**, 3715 (1976); (b) D. Seyferth, D. C. Annarelli, and S. C. Vick, *ibid.*, **98**, 6382 (1976).
(5) H. Sakurai, Y. Kamiyama, and Y. Nakadaira, *J. Am. Chem. Soc.*, **98**, 7424 (1976).
(6) H. Sakurai and M. Yamagata, *Chem. Commun.*, 1144 (1970).
(7) Irradiation of the solution with a 160-W low-pressure mercury arc lamp required 24 h to complete the reaction.
(8) **3a** and **3b** were separated by silica gel TLC, and the stereochemistry was determined by the nuclear Overhauser effect between vinylic hydrogen and methyl groups on silicon. Other products reported in this paper were also isolated by silica gel TLC.
(9) The course of the reaction was not affected by the addition of acetic acid, piperylene, and *m*-xylene, but was completely suppressed by a Pyrex filter. Benzophenone did not sensitize the reaction with a Pyrex filter. These facts suggest that the silacyclopropene may arise from the singlet excited state of **1**.
(10) The Si–Me signals of both **2** and **4** at δ 0.39 overlap each other in benzene, but can be separated in other solvents.
(11) Although the silacyclopropene (**2**) could be isolated by fractional distilation or by VPC from the reaction mixture, separation of **2** from the isomeric acetylene (**1**) was not easy. We hope to succeed in the purification of **2** with a large scale experiment. However, the chemistry of **2** can be done perfectly with the mixture as described in the text since both **1** and **4** are inactive in the reactions.
(12) (a) R. L. Lambert, Jr., and D. Seyferth, *J. Am. Chem. Soc.*, **94**, 9246 (1972); (b) for a review, see D. Seyferth, *J. Organomet. Chem.*, **100**, 237 (1975).
(13) D. Seyferth and D. C. Annarelli, *J. Organomet. Chem.*, **117**, C51 (1976).
(14) Yields are based on the amount of **1**. Since the photochemical ejection of dimethylsilylene accompanies the reaction, the product mixture always contains **4**. Yields are affected by the amount of **4**, but conversion of **2** to the product appears quantitative.
(15) H. Sakurai and T. Imai, *Chem. Lett.*, 891 (1975).
(16) H. Okinoshima, K. Yamamoto, and M. Kumada, *J. Organomet. Chem.*, **86**, C27 (1975).

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Templated Syntheses of Cyclic Acetylacetone Hosts, Their Affinities for Divalent Ions, and an Example of a Slow Proton Transfer from Enol to Hydroxide Ion[1]

Sir:

We report here the first β-diketone-templated syntheses of macrocycles from acac, the effects of gathering and orienting the units on their affinities for ten different metal dianions, and a surprisingly slow proton transfer from C–OH to OH^- which is on the human time scale.[2,3]

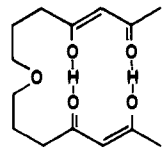
Treatment of acac in THF successively with NaH,[4] BuLi,[4] and either diethylene glycol ditosylate or 1,3-bis(bromomethyl)benzene at 0 °C gave, after 20 h at 20 °C and acidification, **1** (70%)[5] or **2** (95%),[5] respectively. Treatment of **1** under N_2 with CaH_2 gave its calcium salt. The calcium salt in a solution of THF and HMPA was added to lithium diisopropylamide in THF followed by diethylene glycol ditosylate (20 h, 20 °C, solution 0.01 M). Acidification of the mixture and separation of the products by gel permeation chromatography gave macrocycle **3** (16%),[5] mp 32–34 °C, and the dimer of **3** (2%), polymer (3.5%), and recovered **1** (75%). When the Mg^{2+} complex of **1** (Mg turnings plus **1**) was simi-

Table I. Formation Constant Data for Acetylacetone (acac) and Derivatives

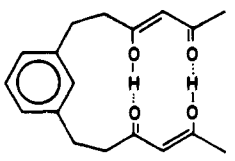
Log K^f	Cu^{2+}	UO_2^{2+}	Co^{2+}	Zn^{2+}	Pb^{2+}	Mg^{2+}	Cd^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}
acac	9.5	8.7	6.3	6.1	5.5	4.5	4.0	3.1	2.7	2.5
1	12.0	11.8	9.2	8.8	8.6	7.1	7.0	7.0	5.3	5.2
3	12.1	12.5	9.7	9.5	9.1	7.2	7.4	7.4	5.6	5.4
2	11.8	11.4	8.8	8.4	8.1	6.6	6.8	6.3	4.7	4.3
4	12.0	11.2	8.6	9.0	9.0	5.5	7.5	4.1	2.8	2.5
pH range	0.5–2.5	0.5–2.5	3.0–6.0	3.0–7.0	3.5–7.5	7–12	4.0–8.0	7–12	7–12	7–12
$\Delta \log K^f_{av}$[a]										
1 − acac	2.5	3.1	2.9	2.7	3.1	2.6	3.0	3.9	2.6	2.7
2 − acac	2.3	2.7	2.5	2.3	2.6	2.1	2.8	3.2	2.0	1.8
3 − 1	0.1	0.7	0.5	0.7	0.5	0.1	0.4	0.4	0.3	0.2
4 − 2	0.2	−0.2	−0.2	0.6	0.9	−1.1	0.7	−2.2	−1.9	−1.8

[a] Log K^f_{av} for one compound *minus* log K^f_{av} for a second.

larly treated, only polymer and the dimer of **3** (15%) were produced. Treatment of **2** with Mg turnings in dry THF (I_2 crystal and trace of MeOH) gave its magnesium salt, which in dry THF-HMPA under N_2 was added at 0 °C to lithium diisopropylamide in THF followed by 1,3-bis(bromomethyl)-benzene (solution 0.01 M). After 20 h at 20 °C, the reaction mixture was acidified, and the products were separated by gel permeation chromatography to give polymer (12%), *dimer* of cycle **4** (12%), cycle **4** (13%) as a glass, and recovered **2** (35%). When the Ca salt of **2** was used, only polymer and *dimer* of cycle **4** (16%) were produced. Cycle **3** was produced from the Ca but not from the Mg salt of **1**, and **4** was generated from the Mg but not the Ca salt of **2**. The disodium salt of **2** even under high dilution gave only polymer. These facts indicate the cyclization reactions are templated. Gram quantities of **1–4** were prepared by these methods.



1



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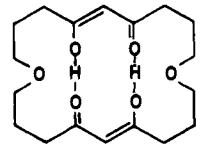

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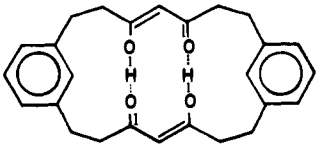

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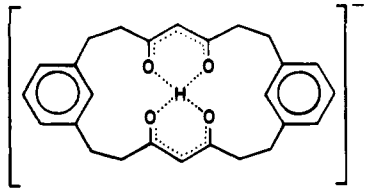

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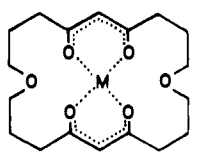

6

Unlike the previously prepared cyclic β-diketones,[3] **1–4** are completely in the enol form in $CDCl_3$ at 40 °C (^1H NMR), and isotopic exchange of the vinyl protons is slow (24 h in CD_3OD–D_2O). The pK_as of acac and of **1–4** were determined by titration in 1:1 (v:v) purified dioxane-water at 24 °C with $HClO_4$ and NaOH solutions with a Corning glass electrode against a calomel electrode (Beckman Model H 2 pH meter). Acetylacetone gave pK_a of 9.5; **1**, 9.5 and 12.6; **2**, 9.8 and 11.8; **3**, 9.9 and 13.0; **4**, 10.6 and 13.2. The collection of two acetylacetone units into open-chain compounds **1** and **2** increases the pK_a of the second unit by about 2 pK_a units over the first. The organization of two acetylacetone units into cycles **3** and **4** increases the pK_as of *both* the first and second protons. In going from open-chain compound **2** to cycle **4**, pK_a^1 increases by 0.8 unit, and pK_a^2 by 0.4 unit. Corey-Pauling-Koltun (CPK) molecular models of **4** indicate a partially enforced organization of the system in which two enolized acetylacetone units hydrogen bond one another in a complementary way. More striking is the fact that, in the titration of **4** with NaOH solution, the ionization rate in passing from the monoanion to the dianion was easily observable on the pH meter. The rate constant was $\sim 4 \times 10^{-4}$ s^{-1}, which indicated the reverse reaction was close to diffusion controlled. Proton transfer rates from oxygen to oxygen rarely are on the human time scale.[6] CPK models of the monoanion of **4** indicate the proton can be locked in a tetrahedrally arranged cage of four oxygens carrying one negative charge (structure **5**). A similar cage formed from **3** is much more flexible and less sterically enveloped.

The formation constants for complexes from **1–4** and acac and ten divalent cations (as nitrates) were determined under N_2 in 1:1 water-dioxane (v:v) at 24 °C (titration with NaOH, K^f_{av} at $\bar{n} = 1$ in Bjerrum curves).[7,8] In calculations of K^f_{av}, 2 mol of acac was treated as equivalent to 1 mol of **1–4**. Equilibration was essentially instantaneous. Table I reports the results.

The values of $\Delta \log K^f_{av}$ for **1** − acac and **2** − acac of Table I provide a rough measure of the effects on binding ability of ligand collection and loose molecular organization. The values range from a high of 3.9 for Ca·**1** to a low of 1.8 for Ba·**2**. Compound **1** contains a potentially usable ether oxygen ligand absent in **2**, and **1** is more adaptable than **2** with regard to ligand placement.

The values of $\Delta \log K^f_{av}$ for **3** − **1** and **4** − **2** measure the effects on binding power of the spatial constraints caused by ring formation (Table I). Cycle **3** is a better binder than **1** for all ions by factors that range from 0.7 log K^f_{av} units for the larger ions Zn^{2+} and UO_2^{2+}, to only 0.1 for the smaller Cu^{2+} and Mg^{2+} ions. Molecular models (CPK) of UO_2·**3** and Zn·**3** suggest that all of the oxygens of **3** might be utilized in the complex. The higher value for Ca^{2+} (0.4) than for Mg^{2+} (0.1) correlates with the fact that Ca^{2+} templates the ring-closing reaction leading from **1** to **3** and Mg^{2+} does not. The high value for Zn^{2+} (0.7) suggests that use of this ion as a templating agent would give a better yield in preparing **3**. Cycle **4** is a better binder than precursor **2** for Pb^{2+} (by 0.9 units), Cd^{2+} (0.7), Zn^{2+} (0.6), and Cu^{2+} (0.2), but is a poorer binder for Ca^{2+} (−2.2), Sr^{2+} (−1.9), Ba^{2+} (−1.8), Mg^{2+} (−1.1), UO_2^{2+} (−0.2) and Co^{2+} (−0.2). The fact that the value for Mg^{2+} (−1.1) is less negative than that for Ca^{2+} (−2.2) correlates

with the fact that Mg^{2+} templates the conversion of **2** to **4** and Ca^{2+} does not. The high value for Pb^{2+} (0.9) suggests this ion should be used as the templating agent for preparation of **4.** The overall log K^{f}_{av} values for **4** − **2** vary much more (from 0.9 to −2.2) than do the values for **3** − **1** (from 0.7 to 0.1). This fact correlates with the much greater difference in rigidity of ligand organization induced by cyclization of acac units through m-$CH_2C_6H_4CH_2$ vs. $CH_2CH_2OCH_2CH_2$ connecting units. However, CPK models of complexes of the smaller ions indicate **3** or **4** can form two different Macac rings with either square planar or tetrahedral arrangements of oxygens.

Comparisons of log K^{f}_{av} values for cycles **3** and **4** are particularly interesting. Toward all ions but Cd^{2+}, **3** is a better binder than **4.** However, the more rigid **4** shows more selectivity toward the ions than does **3** (or acac, **1,** or **2**). Thus log K^{f}_{av} values for **4** complexing the ten ions vary by 9.5, whereas for **3** the values vary by 6.7. Particularly noteworthy are the relatively high log K^{f}_{av} values that result from encircling with **3** to give neutral complexes of the physiologically important ions Cu^{2+} (12.1), Co^{2+} (9.7), Zn^{2+} (9.5), Ca^{2+} (7.4), and Mg^{2+} (7.2). Since Na^{+} was the reference ion, it complexes powers of ten less well than these ions.

References and Notes

(1) This research was supported by ERDA Contract AT(04-3)34, P. A. 218.
(2) Acetylacetone (acac) complexes most metal ions: (a) F. Bonati, *Organomet. Chem. Rev.*, **1,** 379 (1966); (b) R. M. Pike, *Coord. Chem. Rev.*, **2,** 163 (1967); (c) D. Gibson, *Coord. Chem. Rev.*, **4,** 225 (1969).
(3) Less efficient syntheses of macrocyclic β-diketones have been reported previously: A. H. Alberts and D. J. Cram, *J. Chem. Soc. Chem. Commun.*, 958 (1976). M. M. Coombs and R. P. Houghton were the first to incorporate β-diketone units in macrocycles (*J. Chem. Soc.*, 5015 (1961)).
(4) D. Seebach and V. Ehrig, *Angew. Chem.*, **86,** 446 (1974).
(5) (a) Carbon and hydrogen analyses were within 0.30% of theory; (b) ^1H NMR spectra in $CDCl_3$ were as expected; (c) 70 eV mass spectra gave M^+.
(6) R. P. Bell, "The Proton in Chemistry", Cornell University Press, Ithaca, N.Y., 1959, p 120.
(7) (a) M. Calvin and R. Wilson, *J. Am. Chem. Soc.*, **67,** 2003 (1945); (b) F. J. C. Rossotti and H. Rossotti, "The Determination of Stability Constants", McGraw-Hill, New York, N.Y., 1961; (c) L. G. van Uitert, W. C. Fernelius, and B. E. Douglas, *J. Am. Chem. Soc.*, **75,** 451, 457, 2736 (1953).
(8) Degassed stock solutions (0.02 M) of the metal nitrates that were 0.02 M in $HClO_4$ and 0.05 M in $NaClO_4$ were used in 25-mL aliquots. Compounds **1**–**4** (0.60 mmol) in 0.3 mL of dioxane (0.024 M) or 1.20 mmol of acetylacetone were added. The solutions were titrated with 1.00 N aqueous NaOH solutions.

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A Crown Ether NAD(P)H Mimic. Complexation with Cations and Enhanced Hydride Donating Ability toward Sulfonium Salts

Sir:

The ability of crown ethers to associate with a variety of charged and uncharged substrates[1] bears resemblance to the initial step in reactions catalyzed by enzymes. In developing enzyme mimics one may hope that by using correctly designed crown ethers bearing the proper functional groups both a high degree of substrate selectivity and reactivity could be attained. The feasibility of this idea has been illustrated recently by Chao and Cram[2] with a crown ether model capable of mimicking reactions catalyzed by the enzyme trypsin. We describe here the first, to the best of our knowledge, report of the reactions of a NAD(P)H mimic formed from the union of a Hantzsch 1,4-dihydropyridine segment (**1a**) and a polyethylene glycol chain.[3]

The dihydropyridines (**1**) donate hydride only sluggishly or not at all to unactivated carbonyl compounds.[4] Enhanced rates

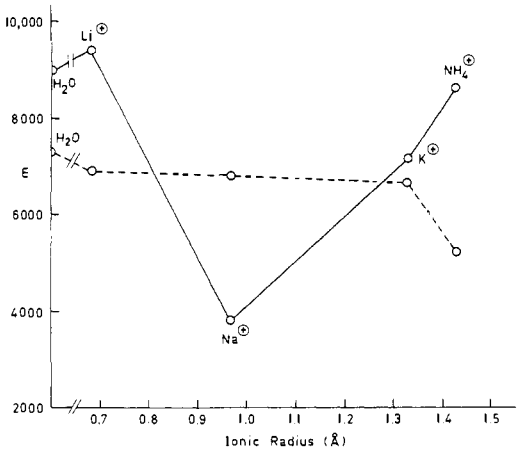
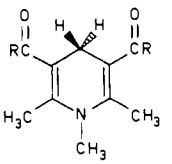


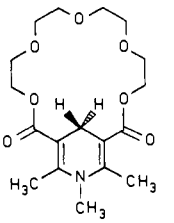
Figure 1. UV maxima for **2** (solid lines) at 270 nm and **1b** (dashed line) at 268 nm in 1.6 M aqueous M^+, Cl^- solution.

of reaction with **1** can be achieved by activating carbonyl substrates by chelation with a metal ion[5] or by hydrogen bonding;[6] similar effects are probably involved in hydrogenase enzymes.[7] The complexing ability of the crown in **2,** the synthesis of which has been described recently,[8] offers in principle the opportunity to have the hydride donor, a possible catalytic site, and a substrate in a single complex. For activation two



1

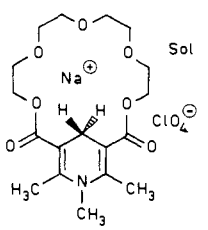
a) R = −O−
b) R = $-OC_2H_5$



2

types of complexes come to mind: (a) a *ternary* complex consisting of **2,** a (metal) ion, and a substrate and (b) a *binary* complex of **2** with a (positively charged) substrate capable of accepting hydride. We have isolated (unproductive) examples of the former and have obtained evidence for enhanced rates of hydride transfer with examples of the latter.

Spectroscopic (UV, and ^1H and ^{13}C NMR) measurements gave evidence that **2** associates with positive ions. For example in the UV spectrum of **2** in 1.6 M aqueous M^+, Cl^- solution the intensity of absorption at 270 nm depends strongly on the radius of M^+; this effect is absent with **1b** (Figure 1).[9] Na^+ ions give the strongest effect. When **2** (mp 90–92 °C) and $NaClO_4$ are mixed in the appropriate solvent (indicated in the formulation by Sol, one molecule of which cocrystallized) the complexes **3a** (mp 176–180 °C), **b** (mp 172.5–175 °C), and **c** (mp 169.5–171.5 °C) are isolated in 62–94% yield.[10] These materials are stable at ambient temperature but decompose in



3

a) Sol = H_3CCN
b) Sol = H_3CCOCH_3
c) Sol = $H_3CCO_2CH_3$