$CaCl_2$(aq) concentrations of 1, 5, and 10 mM gave the following E values: 7.16 ± 0.04, 7.06 ± 0.11, and 7.21 ± 0.14 mV, respectively. These are the average values of the cell voltages over a 3-day period. The uncertainties are the standard deviations. The absence of hysteresis in current–voltage plots provided strong evidence that the cells were operating reversibly. The cells 5 and 10 mM in $CaCl_2$(aq) were also 0.4 mM in $MgCl_2$, because Mg^{2+} was reported[9] to inhibit the aragonite-to-calcite transformation. Analogous emf measurements on cells of the type (1) but with vaterite in place of aragonite gave the following E values: 19.01 ± 0.30 mV [1 mM $CaCl_2$(aq)] and 19.21 ± 0.14 mV [5 mM $CaCl_2$(aq) + 0.4 mM $MgCl_2$(aq)] over a 3-day period at 22 ± 1 °C. The above data yield for the aragonite-to-calcite transition at 22 °C, $E_{tr}° = 7.14 \pm 0.18$ mV and $\Delta\bar{G}_{tr}° = -330 \pm 8$ cal mol^{-1}, whereas for the vaterite-to-calcite transition we compute $E_{tr}° = 19.11 \pm 0.33$ mV and $\Delta\bar{G}_{tr}° = -881 \pm 15$ cal mol^{-1}. Since $\Delta\bar{V} = 2.936$ cm^3 mol^{-1} for the aragonite-to-calcite transition, we compute that the pressure at which aragonite and calcite are in equilibrium at 22 °C is 4.6 ± 0.1 kbar (the effect due to compressibility is negligible). Since $\Delta\bar{V} = -0.69$ cm^3 mol^{-1} for the vaterite-to-calcite transition, equilibrium is not possible between vaterite and calcite around room temperature, as noted by Turnbull.[4]

Data at 25 °C on aragonite and calcite from ref 10 yield $\Delta\bar{G}_{tr}° = -250$ cal mol^{-1}, $\Delta\bar{H}_{tr}° = 50$ cal mol^{-1}, and $\Delta\bar{S}_{tr}° = 1.0$ cal K^{-1} mol^{-1} (no error limits given for these quantities and no data given on vaterite). Kelley and Anderson report[11] $\Delta\bar{G}_{tr}° = -273$ cal mol^{-1}, $\Delta\bar{H}_{tr}° = 42$ cal mol^{-1}, and $\Delta\bar{S}_{tr}° = 1.06$ cal K^{-1} mol^{-1} at 25 °C. Buchan[12] reported $\Delta\bar{G}_{tr}° = -414 \pm 9$ (25 °C) from measurements on cells with liquid junction, but his reported cell stability was poor (~5 min). Kobayashi,[13] on the basis of heat capacity measurements, reported $\Delta\bar{G}_{tr}° = -311 \pm 23$ cal mol^{-1} (25 °C), in excellent agreement with our results. The ratio of the K_{sp} values at 25 °C for aragonite and calcite reported by Christ et al.[14] yield $\Delta\bar{G}_{tr}° = -218 \pm 109$ cal mol^{-1}, which is marginally consistent with our value of -330 ± 8 cal mol^{-1}. Values of the aragonite–calcite transition pressure are exceedingly difficult to determine directly around room temperature. Our calculated value of 4.6 ± 0.1 kbar is consistent with several values obtained by extrapolation of high temperature data,[15-19] namely, 3-5 kbar. On the basis of conductivity measurements of saturated aqueous solutions at high pressure Jamieson[20] reported $P_{tr} = 3.8$ kbar at 25 °C. From the results of extensive heat capacity measurements, Staveley and Linford[21] obtained $\Delta\bar{S}_{tr}° = 0.89 \pm 0.05$ cal K^{-1} mol^{-1} at 25 °C. Combination of our $\Delta\bar{G}_{tr}°$ value with $\Delta\bar{S}_{tr}° = 0.89$ yields $\Delta\bar{H}_{tr}° = -65 \pm 23$, which is in disagreement with the $\Delta\bar{H}_{tr}°$ values of Bäckström[22] (30 ± 20 cal mol^{-1} at 25 °C) and Roth and Chall[23] (48 cal mol^{-1} at 50 °C), obtained from heats-of-solution measurements. A possible source for this discrepancy can be found in the study of Rao et al.[24] on the effect of impurities on $\Delta\bar{H}_{tr}°$. They found that at 480 °C $\Delta\bar{H}_{tr}°$ increased from about 45 cal mol^{-1} for high purity aragonite and calcite to 230 cal mol^{-1} as the Sr^{2+} content was increased from >0.001 to 1%. The Sr^{2+} content in our samples was <0.005% (electron microprobe). Combination of Rao's $\Delta\bar{H}_{tr}° = 45 \pm 10$ cal mol^{-1} (480 °C) with Kobayashi's[13] heat capacity data yields $\Delta\bar{H}_{tr}° = -85 \pm 30$ cal mol^{-1} mol at 25 °C. Because $\Delta\bar{S}_{tr}°$ is positive, a negative value of $\Delta\bar{H}_{tr}°$ implies that aragonite and calcite cannot exist in equilibrium at 1 atm.

On the basis of solubility measurements on vaterite and calcite, Turnbull has reported[4] a value of $\Delta\bar{G}_{tr}° = -790 \pm 25$ cal mol^{-1} for the vaterite-to-calcite transition. This result is in reasonable agreement with our directly measured value of -881 ± 15 cal mol^{-1}.

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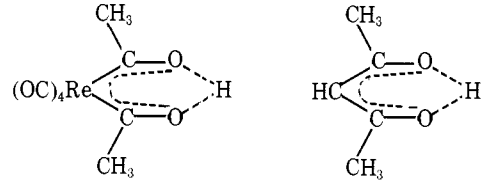
Reactions of Coordinated Molecules. V. Preparation of *cis*-$(OC)_4Re[C(CH_3)O\cdots H\cdots OC(CH_3)]$: the Enol Tautomer of a Metalloacetylacetone Molecule

Sir:

In a previous communication,[1] we reported the preparation of the first example of a "metalloacetylacetonate" anion and the complexation of this anion to a central aluminum ion forming a neutral tris-chelate complex. We now wish to report the preparation of the neutral molecule obtained from the protonation of a "metallo(acac)" anion. This molecule, **1**, is the metallo analogue of the enol tautomer of acetylacetone (**2**), where the methine group of **2** is replaced formally by the $Re(CO)_4$ group.



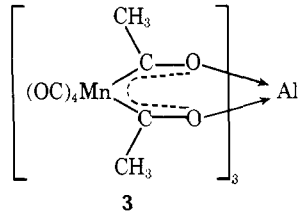


Table I. Bond Distances (Å) and Bond Angles (deg)

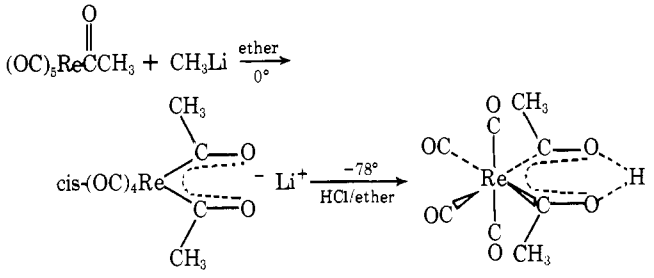
Re-C2	2.145 (17)	O1-C2	1.250 (19)	C1-C2	1.537 (20)
Re-C4	2.175 (15)	O2-C4	1.290 (19)	C3-C4	1.50 (2)
Re-C5	1.955 (19)	O3-C5	1.17 (2)	O1-O2	2.398 (15)
Re-C7	1.980 (18)	O6-C8	1.10 (2)		

Re-C4-O2	123.1 (11)	Re-C7-O5	176.6 (16)
Re-C2-O1	124.0 (11)	C2-Re-C5	178.2 (8)
Re-C4-C3	123.9 (12)	C5-Re-C8	90.0 (9)
Re-C2-C1	124.2 (13)	C6-Re-C7	170.6 (6)
Re-C5-O3	174.8 (21)	C2-Re-C4	86.5 (6)

To 0.50 g (1.36 mmol) of acetylpentacarbonylrhenium dissolved in 10 ml of ether was added 0.66 ml of a 2.06 M methyllithium solution (1.36 mmol, in ether) at 0° over a 10-min period. During this addition any solid that was present dissolved and the solution became yellow. The reaction solution was stirred at 0° for an additional 45 min, and then it was cooled to −78°.

To this solution was added dropwise 0.34 ml of a 4.2 M HCl solution (1.43 mmol, in ether) over a 5-min period. During this addition a white solid precipitated. The reaction mixture was stirred at −78° for an additional 5 min, and then stirred at 0° for 1 h. The solvent was removed at reduced pressure affording a pale yellow solid which was extracted with 25 ml of hexane at 25°. Filtration under nitrogen gave a colorless filtrate. Removal of the solvent at reduced pressure afforded 0.40 g (77%) of the crude title compound which was crystallized from hexane solution at −78° as colorless needles: mp 66-68 °C, ir (C_6H_{12}, in cm^{-1}) ν(CO) 2095 (m), 2005 (s, sh), 1990 (vs), 1965 (s), ν(C=O) 1520 (m); ^1H NMR (CS_2 vs. Me_4Si) τ 7.22 (s, 6, 2 CH_3), −11.79 (br s, 1, enol H); MS, P (*m/e* 386), ligand fragments predominately with loss of methyl and acetyl radicals and methane to give $Re(CO)_5^+$, base peak (*m/e* 43, CH_3CO^+).[2]

Anal. Calcd for $C_8H_7O_6Re$: C, 24.94; H, 1.83; Re, 48.32. Found: C, 24.85; H, 1.59; Re, 48.62.



1

Since complex **1** is a direct analogue to acetylacetone and may exhibit a similar extensive reaction chemistry, we obtained, commercially, an x-ray structure determination which was performed as a technical service.[3] Crystal data: $Re(CO)_4[C(CH_3)O\cdots H\cdots OC(CH_3)]$; mol wt = 385.34; monoclinic; a = 6.264 (1), b = 17.510 (4), c = 10.036 (6) Å; $\alpha = \gamma = 90$; β = 96.18 (2)°; Z = 4; d_{calcd} = 2.333 g/cm^3; space group $P2_1/n$. Intensity data were collected on a Syntex P$\bar{1}$ computer-controlled diffractometer using Mo Kα radiation. In the refinement of the structure, 1285 reflections having $F_o^2 > 3\sigma(F_o^2)$ were used. Anisotropic refinement of all nonhydrogen atoms gave the final agreement factors R_1 = 0.051 and R_2 = 0.062. An ORTEP view of the molecular structure of **1** is shown in Figure 1 and pertinent bond distances and bond angles are given in Table I. See paragraph at the end of paper regarding supplementary material.

The idealized molecular structure belongs to the symmetry point group C_{2v}. The chemically interesting structural features

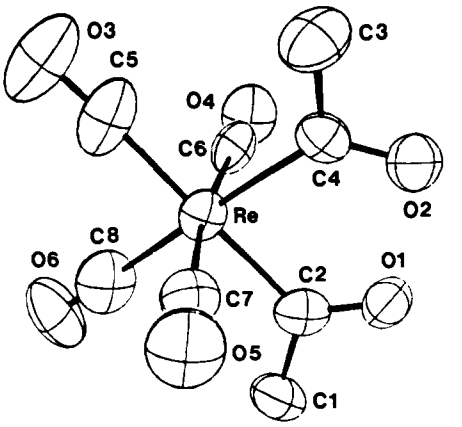


Figure 1. An ORTEP view of *cis*-$(OC)_4[ReC(CH_3)O\cdots H\cdots OC(CH_3)]$ showing the atomic numbering scheme. The sizes and shapes of the atoms are determined by their final thermal parameters and their perspective view.

of the molecule are: (i) the "metallo(acac)" backbone (atoms Re, C2, C4, O1, O2) is essentially planar (maximim deviation from planarity is atom C2 of +0.08 Å) with atoms C1 and C3 being displaced on the same side of the ring by 0.21 and 0.36 Å, respectively; (ii) and oxygen atoms, O1 and O2, are syn relative to the Re-C4 and Re-C2 bonds, thus being in the position of closest contact;[4] (iii) although the Re-C4 and Re-C2 bond lengths (2.16 Å average) are 0.34 Å longer than the corresponding Mn-C distance found in tris(*cis*-diacetyltetracarbonylmanganate)aluminum (**3**),[1] the internal angles centered at Re, C2, and C4 decrease by 6.5, 4.5, and 3.5°, respectively, relative to the corresponding values found in complex **3**, thus permitting the O1-O2 "bite" distance of **1** to be only 2.40 Å whereas the same distance in complex **3** is 2.74 Å. The structural features observed within the ligand ring of complex **1** are directly analogous to those found for the symmetrical dienol tautomer of tetraacetylethane.[6] Although the enol protons were not located in the x-ray structure of tetraacetylethane, the O-O "bite" distance is 2.42 Å and the internal angle centered at the 3-position is only 117.9°, whereas the average value of this angle in six acetylacetonate complexes is 124.6°.[6] This decrease of 6.7° is very similar to the decrease of 6.5° observed for the corresponding angle in the metallomolecules **1** and **3**.

Although the hydrogen atoms of the methyl groups and the enol hydrogen atom were not located in the x-ray structure determination of **1**, the above structural features and spectroscopic data are consistent only with the formulation of complex **1** as the symmetrical enol tautomer of a metalloacetylacetone molecule.

The chemical shift of the enol proton of **1**, τ − 11.79, is 9.4 ppm downfield from the resonance of the hydroxyl proton in the hydroxycarbenoid complex, $(CH_3)(HO)CCr(CO)_5$,[7] and is more similar to the chemical shift of an enol proton of a

1,3-diketone containing a substituent on the methine carbon atom which can effectively stabilize a negative charge.[8] It is very reasonable to assume that the $Re(CO)_4$ group would stabilize a negative charge very effectively. Adding a drop of methanol-d_4 to the ^1H NMR solution of **1** in CS_2 leads to no change in the methyl resonance while the enol resonance completely disappears.

The acidity of the enol proton is qualitatively similar to that of acetylacetone. Although complex **1** is very soluble in hexane, it dissolves also in potassium carbonate–water, pyridine–ether, and sodium hydride–ether media with the appearance of the characteristic pale yellow color of the "metallo(acac)" anion. An ether solution of complex **1** does not evolve carbon dioxide from sodium bicarbonate, but spontaneously evolves hydrogen when placed over sodium hydride.

The keto tautomer of complex **1** is less favored, presumably, because this tautomer would be a seven-coordinate rhenium(III)–hydride complex, and the only complexes of this type which have been prepared have contained a η^5-cyclopentadienyl ligand. The ^1H NMR resonance of the hydride ligand in these complexes occurs at τ 12 or above.[10]

The investigation of the similarities in the organic reaction chemistry of complex **1** to the known reactions of 1,3-dicarbonyl molecules is being pursued.

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Supplementary Material Available: A listing of data, structure factor amplitudes, refinement procedures, least-squares planes, interatomic bond distances and angles, and positional and thermal parameters (18 pages). Ordering information is given on any current masthead page.

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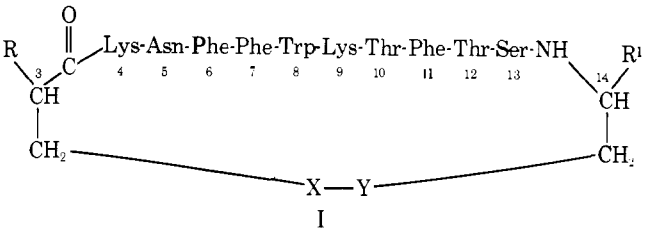
Nonreducible Cyclic Analogues of Somatostatin

Sir:

Since the isolation, characterization,[1] and synthesis[2] of the peptidal release inhibiting factor, somatostatin (Ia), the question concerning the biological activities of the cyclic and linear (reduced) forms has not been resolved, because the systems used to measure biological activities both in vitro and in vivo do not preclude interconversion of the cyclic (disulfide) and linear (dithiol) forms of somatostatin. The very low activity of [Ala^{3,14}]somatostatin[3,4] does not clarify the question of activity of dihydrosomatostatin since replacement of the two sulfurs by hydrogen may produce more consequences than the obvious ring opening. (See ref 4 for further discussion of these problems.) Convincing evidence that a cyclic form can possess intrinsic activity and that sulfhydryls are not required for activity would be obtained through the synthesis of a highly active cyclic analogue of somatostatin which cannot be cleaved by biological reduction. We have, therefore, undertaken the syntheses of somatostatin analogues in which one or both of the sulfur atoms have been replaced by methylene groups.[5] We report herein our initial findings with two analogues of somatostatin having both sulfur atoms replaced by methylene groups. A simplification of the synthetic objective was suggested by the observation that des(Ala^1,Gly^2)-desamino-[Cys^3]somatostatin (Ib) is highly active.[3,6] We therefore synthesized des(Ala^1,Gly^2)-desamino[Cys^3]dicarba^{3,14}-somatostatin (Ic) as a model of a nonreducible, cyclic somatostatin C-terminal analogue. In a further modification designed to test the requirement for the carboxyl group, we also synthesized des(Ala^1,Gly^2)-desamino[Cys^3]descarboxy-[Cys^{14}]dicarba^{3,14}-somatostatin (Id).



I

Ia, R = H-Ala-Gly-NH-; R^1 = CO_2H; X = Y = S (somatostatin)
b, R = H; R^1 = CO_2H; X = Y = S
c, R = H; R^1 = CO_2H; X = Y = CH_2
d, R = R^1 = H; X = Y = CH_2

The synthetic routes to Ic and Id are outlined in Scheme I. It should be noted that the amino terminal sequence of the intermediates VII corresponds to positions 8-13 of somatostatin. Cyclization forms the amide bond required to convert these intermediates to a sequence equivalent to that of somatostatin.

The common intermediates, II and Va, were synthesized sequentially in solution as well as by solid phase methods. They were characterized by NMR and uv spectroscopy and amino acid analysis (Table I).

Toward the synthesis of Ic, the aminosuberic acid residue was incorporated by condensation of α-*tert*-butyl ω-*p*-nitrophenyl N^{α}-Boc-D,L-α-aminosuberate (XII) with the tetrapeptide IIb to give III. The selectively protected α-aminosuberic acid derivative XII was prepared as shown in Scheme II from ω-methyl-D,L-α-aminosuberate (IX).[9a,b] Both the Boc and *tert*-butyl ester protecting groups of III were removed by the action of trifluoroacetic acid. Coupling[10] of III with Vc gave VIIa, which was purified by gel filtration (Sephadex G-25, 50% acetic acid). VIIb was prepared by condensation of VI (via the azide) with IIb and purified in the same manner as VIIa. The ester VI was prepared by condensation of methyl ω-aminoheptanoate with Vc.

The undecapeptides VII were converted to hydrazides by the action of hydrazine in methanol, and the Boc protecting group was removed by HCl in ethyl acetate using mercaptoethanol as scavenger. The hydrazides were then converted to azides under acidic conditions.[10] Dilution of the resulting aminoazides to a concentration of 1 mg/ml with DMF at −20° and neutralization to pH 7.5 (as measured on moistened narrow range indicator papers) by the addition of diisopropylethylamine allowed cyclization to proceed. The crude VIII generated in this reaction was partially purified by precipita-