s, 5-H), 4.94 (2 H, br s, 16-H), 4.82 (1 H, s, 12-H), 3.61 (1 H, d, J = 16 Hz, 2′-H), 2.34 (1 H, d, J = 16 Hz, 3′-H). Gnidicin (**3**) afforded 12-hydroxydaphnetoxin (**5**) and methyl cinnamate on methanolysis and an acetonide **9** (mass spec, M^+ at m/e 668; nmr τ 8.53, br s, 6 H) under similar conditions to those used above. Gnidicin (**3**) may be the same as the compound isolated by Coetzer and Pieterse[11] from *Lasiosyphon burchellii* and characterized by its hydrolysis products.

It is noteworthy that 12-hydroxydaphnetoxin (**5**), which bears no ester function at C-12, shows no antileukemic activity. In contrast, the benzoate ester **6** [$C_{34}H_{34}O_{10}$; $[\alpha]^{26}\text{D}$ +64° (c 0.24, $CHCl_3$); uv(max) (EtOH) 231 nm (ϵ 18,400); mass spec m/e 602.2152 (M^+, calcd 602:2152), prepared by benzoylation of 12-hydroxydaphnetoxin 5,20-acetonide (**11**) followed by acid hydrolysis of **12**] shows antileukemic activity of the same order as the naturally occurring esters **1**, **2**, and **3**. The results to date support the hypothesis that the ester affixed at C-12 may act as a carrier moiety (*e.g.*, in processes concerned with cell penetration or selective molecular complex formation).[12] Investigations are in progress to determine the significance of the epoxide, the cyclopentenone, the orthoester, and of other structural features for the antileukemic activity of these diterpenoid esters and related compounds.

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(2) Supported by grants from the National Cancer Institute (CA 11718) and American Cancer Society (CI-102J) and a contract with the Division of Cancer Treatment, National Cancer Institute (N01-CM-12099).

(3) Roots were collected in Kenya in June, 1972. We thank Dr. R. E. Perdue, Jr., U.S.D.A., Beltsville, Md., for supplying the plant material.

(4) Antileukemic activity was assayed under the auspices of the National Cancer Institute, by the procedures described by R. I. Geran, N. H. Greenberg, M. M. McDonald, A. M. Schumacher, and B. J. Abbott, *Cancer Chemother. Rep., Part 3,* **3,** 1 (1972). Gnididin, gniditrin, and gnidicin showed potent antileukemic activity against P-388 leukemia in the mouse at the 20–100 μg/kg level.

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(10) We have found that mezerein (**4**) forms an acetonide **10** [$C_{41}H_{42}O_{10}$; mass spec m/e 694.2762 (M^+, calcd 694.2778)] under these conditions, indicating that the 4-phenylpentadienoyl side chain is attached at C-12 (*cf.* ref 8), and not at C-5 (*cf.* ref 7).

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(12) A similar proposal has been advanced for the role of the long aliphatic chain in the piscicidal activity of huratoxin; *cf.* ref 9.

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Consideration of a Report[1] on the Formulation of Monomeric Cobalt–Dioxygen Adducts. Continued Support for Co(III)–O_2^-

Sir:

In recent years there has been considerable interest in the 1:1 binding of dioxygen, O_2, to cobalt(II) complexes. The thermodynamics of the binding reaction have been explored, not only with solution complexes[2] but with cobalt porphyrin incorporated into hemoglobin and myoglobin.[3]

On the basis of the frozen solution epr spectra of dioxygen adducts of low-spin cobalt(II) Schiff base-complexes, it was concluded[4] that the majority (> 80%) of the spin density from the parent compound is transferred to dioxygen upon complexation. This fact, coupled with an observed O–O stretching frequency of ~1130 cm^{-1}, similar to that of O_2^-,[5] led to the formulation of the complexes as Co(III)–O_2^-; that is, that the best formal description is that of a superoxo complex of low-spin cobalt(III).[4] It was further suggested that the dioxygen is singly coordinate and exhibits a bent geometry (Pauling structure).[6] Studies[7] of oxygenated cobalt porphyrin systems, coboglobins, and other cobalt complexes give quite similar epr spectra, suggesting similar electronic and steric properties of all monomeric cobalt–dioxygen complexes.

This view of the properties of Co–O_2 was supported by the X-ray study[8] of a cobalt(II) dioxygen adduct, in which Co–O–O is nonlinear and with an O–O bond length similar to that of a superoxide anion. Further confirmation was obtained in studies[9,10] employing ^{17}O labeled O_2, where the spin density on oxygen is found to be close to 100%. The formulation Co(III)–O_2^- is also in accord with the observation[2d] that the oxygen uptake of cobalt(II) Schiff base chelates increases with the ease of oxidation of the chelates and with increasing solvent polarity.

Carbon monoxide and alkyl isocyanide complexes of cobalt(II) porphyrins have also been reported.[11] Carbon monoxide binds weakly, and will not bind to a five-coordinate Co(II) porphyrin;[7d] however, CO will act as a fifth ligand to a four-coordinate Co(II) porphyrin. The epr spectra obtained are characteristic of a low-spin Co(II) adduct, quite different from spectra of corresponding Co–O_2 complexes.[11]

In view of this large body of accumulated data, we were surprised to read a recent report[1] that the high-spin, five-coordinate cobalt(II) Schiff base Co^{II}(salMeDPT)[12] bound O_2, CO, and CH_3NC and that the CO adduct gave identical and the CH_3NC adduct similar epr spectra to that of the O_2 adduct. Previous studies[7a,13] of high-spin Co^{II}(salHDPT), the unmethylated analog of Co(Me), had not explored CO binding. Furthermore, it was reported[1] that for Co(Me) binding either O_2 or CO produced similar changes in the nmr spectra. It seemed to us highly improbable that CO should bind to the five-coordinate Co(Me) and even more improbable that an adduct, if formed, should show an *identical* epr and similar nmr spectrum to that of the O_2 adduct. Admittedly Co(Me) is high spin, unlike most systems previously studied, and so it was not possible to dismiss this recent report *a priori*. We have therefore examined the question of O_2, CO, and RNC binding to both Co(Me) and Co(H).

The chelate compounds Co(Me) and Co(H) were prepared following published procedures[14] and showed satisfactory elemental analyses. Solvents (toluene and CH_2Cl_2) were distilled from appropriate drying agents and stored under N_2. The CO was passed through an aminated silica-gel trap[15a,b] (−78°) to remove CO_2, Ridox[15c] (Fisher Scientific) to remove O_2, and 4A molecular sieves to remove H_2O. The chelate Co(H) was studied in either toluene or CH_2Cl_2; Co(Me) was examined in CH_2Cl_2 and in a 50/50 (v/v) toluene-CH_2Cl_2 mixture in order to reproduce the conditions of ref 1. Epr samples were prepared under rigorously anaerobic conditions, and the absence of oxygen contamination was verified by epr. Neither Co(Me) nor Co(H) in degassed, dilute solution shows a signal at room temperature; both show a broad high-spin signal (with $g_{\perp}$ ~4.3) when frozen to 77°K (Figure 1A).

To these solutions was then added CO at a pressure of 960 Torr with the sample either (a) in a toluene slush

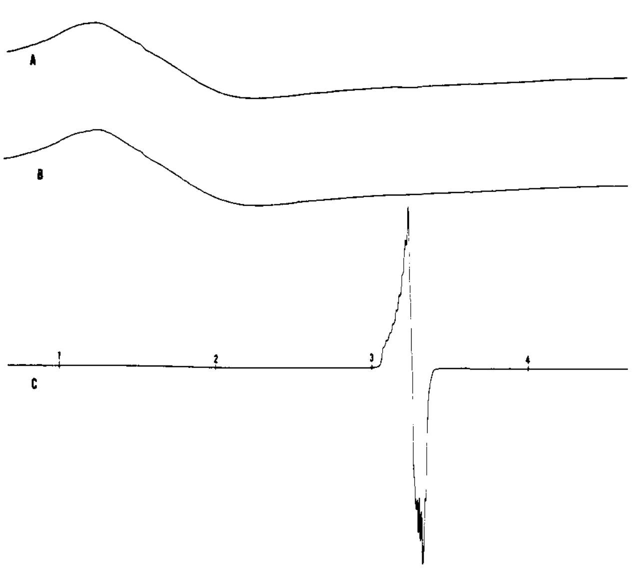

Figure 1. Epr spectrum of Co(Me) in 1/1 (v/v) CH_2Cl_2-toluene at 77°K: (A) degassed; (B) equilibrated with 960 Torr of CO; (C) with CO removed and 960 Torr O_2 added. Intensity in (C) is times 1/10. Field calibration, in kG, indicated in (C).

(−93°), (b) Dry Ice–ethanol slush (−78°), or (c) at room temperature. After 15 min, a spectrum was taken at room temperature and 77°K. The sample was then thawed and shaken in the sealed epr tube in order to promote dissolution of CO, reequilibrated at one of the three temperatures, frozen, and reexamined. Samples were then left under 960 Torr of CO for up to 1 week, and examined as above. No sample of Co(H) or Co(Me), in any solvent or solvent combination, using any equilibration techniques, showed *any* evidence of forming a CO adduct (Figure 1B). *No* sign of an epr spectra similar to those exhibited by a Co–O_2 adduct, either at 77°K or at room temperature, was produced by addition of CO. As verification of the procedures used, Co(TPP)–CO was prepared, and found to give an epr spectrum identical with that reported by Wayland.[11]

In contrast, removal of CO and addition of O_2 gave very intense spectra of $Co(H)O_2$ and $Co(Me)O_2$ (Figure 1C), as observed, respectively, in ref 7a and 1. In addition some diamagnetic μ-peroxo bridged species is formed.[13b]

We have also examined the ^1H nmr of Co(H) and Co(Me) in $CDCl_3$; the former was originally reported in an unpublished thesis.[13b] Although ref 1 discusses resonances less than 50 ppm from TMS, these high-spin compounds in fact exhibit resonances spread over ca. 900 ppm (−64°). *No* change is observed, even at −64°, upon addition of CO. Addition of O_2 causes the slow appearance of a new species with a much smaller span of resonances (<10 ppm). These studies, to be published later,[16] confirm the absence of any adduct formation with CO by these high-spin Co(II) Schiff bases; the new species is not the paramagnetic 1:1 dioxygen adduct, as claimed in ref 1, but appears to be the diamagnetic μ-peroxo-bridged complex.[13,16] The nmr spectrum of the 1:1 adduct appears to be unobservable.

An experiment was also performed using C_2H_5NC.[17] With 20% (v/v) of ligand added to a CH_2Cl_2 toluene solution of Co(Me), a new signal with low intensity appears, with superhyperfine splittings from a single ^{14}N and the spin-Hamiltonian parameters (g_z = 2.02, $g_x \sim g_y$ = 2.20; $A_{\perp}{}^{Co} \approx 40$, $A_{\parallel}{}^{Co} = 64$, $A_{\parallel}{}^{N} = 12.5$ G). The spectrum, corresponding to a low-spin Co(II) complex, is similar to those for six-coordinate Co(II) porphyrins[7c,d] and is probably Co(Me)(C_2H_5NC), with splitting from the apical nitrogen. The spectrum is wholly distinguishable and different from those of oxygen adducts.[4,7,1d]

In summary, there is no evidence for any coordination of CO by Co(Me) and Co(H); the adduct formed upon addition of RNC is typical of low-spin cobalt(II) complexes, not Co–O_2 adducts. It must be concluded that the observations of ref 1 are artifacts caused by the presence of O_2, and therefore their conclusions must be dismissed. Thus, the evidence for spin transfer to O_2 and for the formal description of Co–O_2 adducts as Co(III)–O_2^- adducts remains secure.

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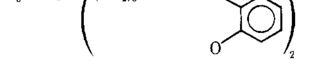
(12) Abbreviations: $salMeDPT^{2-}$ =



$salHDPT^{2-}$ = above with H in place of CH_3, Co(salMeDPT) = Co(Me), Co(salHDPT) = Co(H).

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(17) The C_2H_5NC was a generous gift of Dr. B. L. Haymore.

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Stereochemistry of the Hydroxypalladation of Cyclooctadiene

Sir:

The stereochemical course of the reaction of olefin–transition metal complexes may be considered the result of two distinct mechanistic processes.[1] Reactions in which the addend or nucleophile is coordinated to the metal and transfers directly from the metal to an olefinic carbon proceed by cis addition in an anti-Markovnikov direction. Those reactions in which the nucleophile is solvated but not coordinated and forms a bond with an olefinic carbon by external nu-