range of electronegativity. Analogous trends for some of the coupling constants were already reported for various compounds in the series of ortho-[18,19] and para-disubstituted[20,21] benzenes. It was however, impossible from those data to dissect the observed effect into contributions surely attributable to each substituent separately. It may be interesting to report that by direct interpolation of the experimental data, the following values of the coupling constants for the protons of benzene are obtained: $J_{ortho} = 7.72, 7.65$ cps $[J_{12}, (J_{12} + J_{34})/2]$; $J_{meta} = 1.38, 1.46$ cps $[(J_{13} + J_{24})/2, (J_{13} + J_{24} + J_{15})/3]$; $J_{para} = 0.60$ cps $[J_{14}]$.

It is difficult, on the basis of current theories alone, to explain the observed trend of $J_{ortho-meta}$ or for that matter, those of all the other coupling constants with the electronegativity of the substituent in the series of monosubstituted benzenes. Our experimental results establish, however, that, as far as the magnitude of the coupling constants is concerned, the perturbation introduced by the substituent attenuates rapidly and is not appreciable beyond the ortho carbons as expected for an inductive effect. The algebraic variations observed for the $J_{ortho-meta}$ coupling constants are, however, of opposite sign to the ones that would have been predicted from the results obtained in the series of monosubstituted ethanes and ethylenes. Any correct formulation of the mechanism of the coupling between vicinal protons should take into account and explain this alternating effect of the electronegativity of the substituents. Perhaps the real clue toward the solution of this problem is furnished by the observation that, by decreasing the electronegativity of the substituent in the series of monosubstituted benzenes, the magnitudes of all the coupling constants move consistently and unambiguously toward the corresponding values found in pyridine. In view of the isoelectronic character of the phenyl anion and pyridine, this convergence of the experimental results appears quite natural in retrospect. The possibility of formulating quantitative correlations in this direction is presently under study.

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Biosynthesis of the Cinchona Alkaloids.
The Incorporation of Geraniol-3-^{14}C into Quinine[1]

Sir:

It has been suggested[2] that quinine (6) and related alkaloids found in Cinchona species are derived from a corynantheine-type indole alkaloid (3) as indicated briefly in Figure 1. Loss of a carbon atom at C_{16}, bond cleavage between N_4 and C_5, and bond formation between C_{17} and N_4 affords the carbon skeleton of the alkaloid cinchonamine (5). Finally ring expansion of the indole moiety of cinchonamine involving the side

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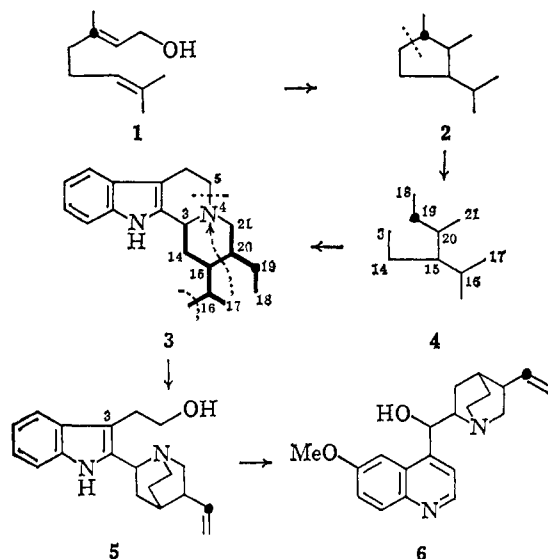
Figure 1. Biosynthesis of quinine (^{14}C indicated with a heavy dot).

chain at C_3 yields the quinoline nucleus present in quinine. Our previous tracer experiments[3] have supported the latter part of this scheme relating to the origin of the quinoline ring. The origin of the 10-carbon atom unit indicated with heavy lines in formula 3 has been the subject of much discussion and speculation. However it has recently been established[4-7] that this unit and related structures found in the indole alkaloids of Vinca rosea are derived from geraniol (1). The pattern of labeling found in these alkaloids was consistent with the intermediate formation of a cyclopentano monoterpene (2) which then underwent bond cleavage to the unit 4 as suggested 5 years ago by Thomas[8] and Wenkert.[9]

We have now tested this hypothesis for the origin of the quinuclidine ring of quinine by feeding geraniol-3-[14]C[7] (1, 17.6 mg, 75 μcuries), emulsified in water with Tween 80, to three 2-month-old Cinchona succirubra plants by means of cotton wicks inserted in the stems. After 3 weeks the plants were harvested and radioactive quinine (8.1 × 10^4 dpm/mmole) isolated without dilution by chromatography of the crude alkaloids on alumina followed by thin layer chromatography on silica gel.[10] Dihydroquinine (7.5 × 10^4 dpm/mmole), obtained on hydrogenation of the vinyl group, was subjected to a Kuhn–Roth oxidation affording a mixture of acetic and propionic acids. These acids were separated on silicic acid,[11] assayed as their α-naphthylamides,[12] and had specific activities of 7.5 and 7.9 × 10^4 dpm/mmole, respectively. A Schmidt reaction on the acetic acid afforded carbon dioxide collected as barium carbonate having an activity of

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7.4 × 10⁴ dpm/mmole. This degradation thus established that essentially all the activity of the quinine was located at the position indicated with a heavy dot in formula **6**, a result which is consistent with the previously discussed hypothesis.

(13) Alfred P. Sloan Foundation Fellow.
(14) Public Health Service Predoctoral Fellow, 1965–1966.

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The Molecular Configuration of π-Cyclopentadienyl-cis-1,2-bis(trifluoromethyl)ethanedithionecobalt

Sir:

In the recent report of the synthesis of a π-cyclopentadienylcobalt dithietenyl complex, $C_5H_5CoS_2C_4F_6$,[1] King proposed a sandwich-type structure of six-coordinate cobalt(III) with coordination to two sulfur atoms and the double bond of the ethylenic linkage and with the usual threefold coordination to the π-cyclopentadienyl ring. This structure reasonably accounts for the observed diamagnetism of the compound and for the shift of the C=C stretching frequency from 1621 cm⁻¹ in bis(trifluoromethyl)dithietene, $(CF_3)_2C_2S_2$,[2] to 1480
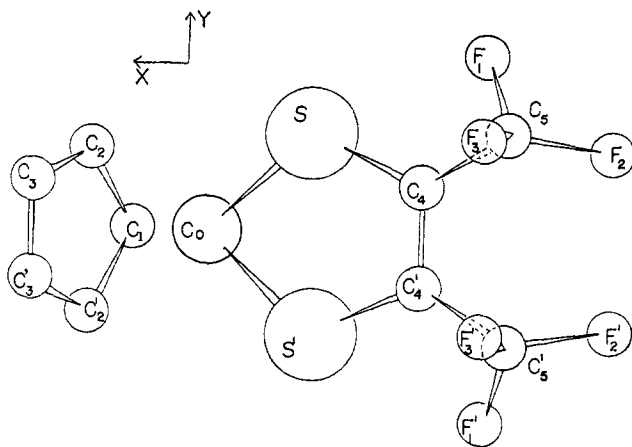

Figure 1. [001] molecular projection of $C_5H_5CoS_2C_4F_6$.

cm⁻¹. However, a structure involving a dithioketone ligand and Co(I) could achieve the effective atomic number of 36 and leave the CoS_2C_4 fragment planar. The planar metal-S_2C_4 moieties have been found recently in several related metal-dithiolate complexes (*e.g.*, the square-planar[3–8] and the trigonal prismatic[9–11]

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dithiolate–metal systems). From the results of a three-dimensional X-ray analysis on $C_5H_5CoS_2C_4F_6$, we present here evidence for a transition metal–dithioketonic complex.

Purple crystals suitable for X-ray analysis were kindly supplied by Dr. R. B. King. Weissenberg and precession photographs taken with Zr-filtered Mo Kα radiation showed the crystals to be orthorhombic with lattice parameters $a = 9.24$, $b = 12.24$, $c = 10.62$ A. Systematic absences showed the probable space groups to be Pn2₁a and Pnma. A piezoelectric test[12] gave negative results and the solution and refinement of the structure subsequently confirmed the choice of the centric space group. The calculated density of 1.92 g/cm³ for four monomeric molecules per unit cell agrees well with the observed value of 1.93 g/cm³ obtained by the flotation method. The centric space group thus demands that the molecule contain a crystallographic mirror plane.

X-Ray intensity data were collected by the Weissenberg multiple-film technique and were estimated visually. Proceeding through three-dimensional Patterson functions, three-dimensional electron density calculations, and least-squares refinement, the structure analysis has yielded the molecular configuration. The present reliability index, R_1, is 14.0% for 419 independent reflections. One fluorine atom has a large isotropic thermal parameter even though the atom clearly appears in the electron density maps at a reasonable distance from the methyl carbon. All other thermal parameters are reasonable. It is felt that anisotropic least-squares refinement is needed, and this will be carried out when more data are processed.

The centers of the seven atoms of the CoS_2C_4 moiety (Co, S, S′, C_4, C_4′, C_5, C_5′) are within 0.033 A of a plane which is perpendicular to the π-bonded cyclopentadienyl ring. The molecular geometry is shown in Figure 1. The bond distances of particular significance are 2.08 A for Co–S, 1.74 A for S–C_4, and 1.48 A for C_4–C_4′. The related bond angles are 92.2° for S–Co–S′, 108.0° for Co–S–C_4, 115.8° for S–C_4–C_4′, and 120.6° for S–C_4–C_5. Comparison of the Co–S bond distance with the sum of the single bond radii (2.20 A)[13] and with the average Co–S distance of 2.16 A in $Co_2S_8C_8$-$(CF_3)_8$[7] suggests that there is multiple Co–S bonding in $C_5H_5CoS_2C_4F_6$ as expected. Part of the Co–S π bonding will be due to back-donation of charge from the cobalt atom into antibonding orbitals of the dithione ligand leading to a carbon–sulfur bond of order less than 2. The C–S distance of 1.74 A is close to the value of 1.71 A which has been assigned as the distance for a C–S bond of order 1.22[14] and is to be compared with the values of 1.60 A for C=S[14,15] and 1.81 A[13,16] for singly bonded C–S. If one uses the π molecular orbitals reported for dithioglyoxal[17] and takes the

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