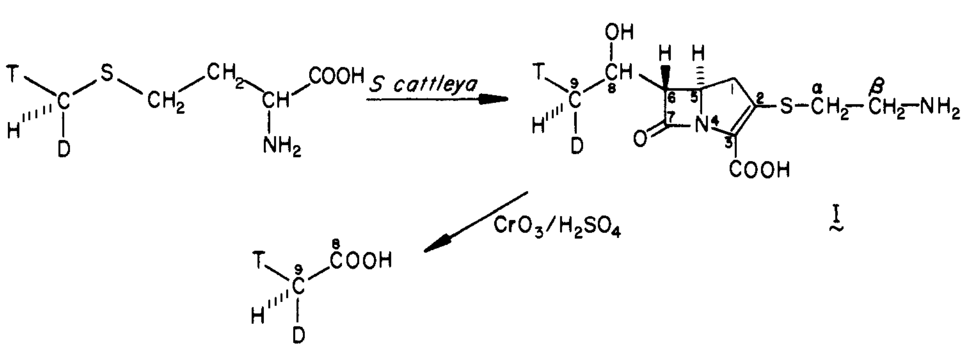
Scheme I



I

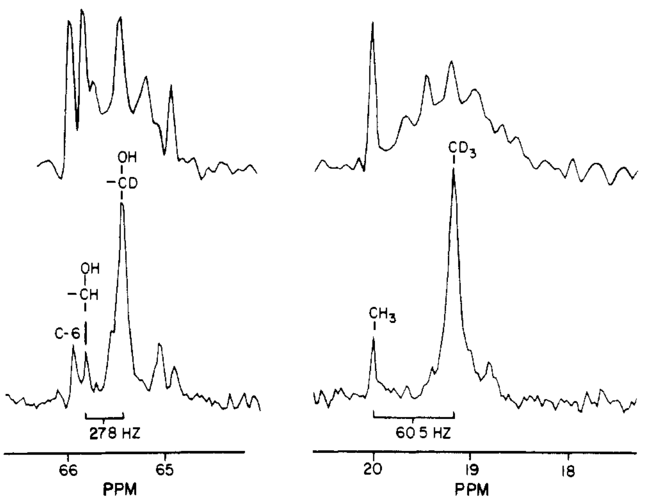


Figure 1. ^{13}C NMR spectrum of thienamycin biosynthesized from [methyl-^{13}C,^{2}H$_3$]methionine. Signals for C-8 (left) and C-9 (right) with broad-band ^{1}H decoupling (top tracings) and with broad-band ^{1}H and ^{2}H decoupling (bottom tracings).

degradation of I from (*methyl-R*)-methionine had an F value[10] of 69 indicating 66% ee R configuration of the thienamycin methyl group. Conversely, the acetate from the (*methyl-S*)-methionine experiment had $F = 35$ corresponding to 52% ee S configuration of the thienamycin methyl group. A complete repetition of the experiments confirmed these results.

The above results demonstrate that the biosynthesis of thienamycin involves transfer of a methyl group from methionine or, most likely, its activated form, *S*-adenosylmethionine[11] (AdoMet), to an acceptor carbon with net retention of configuration (Scheme I). This is in marked contrast to the findings with all other AdoMet-dependent methyltransferases studied to date which, without exception, have been found to catalyze methyl transfer with inversion of configuration. The 11 examples include enzymes catalyzing methyl transfer to oxygen,[12-14] nitrogen,[6,13,15,16] and sulfur[13] as well as to carbon.[6,13,17] This stereochemical uniformity has been interpreted to indicate a single transfer of the methyl group directly from the sulfur of AdoMet to the acceptor nucleophile in an S$_N$2 transition state.[12] Methyl transfer to C-8 of I could be followed by hydride migration from C-8 to C-6 and proton loss from the methyl group to give a C-9 methylene group, in analogy to the side-chain methylation of sterols.[13] Such a methylene group could be reduced to give either an R or an S methyl group. However, the full retention of three atoms of deuterium from [^{13}C,^{2}H$_3$]methionine at C-9 argues against this possibility. It seems more likely, then, that C-9 of I is derived by a mechanistically different methylation reaction involving two sequential methyl transfers, each proceeding with inversion. Since the thienamycin fermentation has been noted to have a cobalt requirement,[3] one may tentatively speculate that a corrin could serve as an intermediate carrier. This would have an analogy in the formation of methionine from 5-methyltetrahydrofolate by B$_{12}$-dependent methionine synthase, which we have recently shown to proceed with net retention of methyl group configuration.[18]

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Enhancement of Radioactivity of ^{14}C–^{12}C Mixtures via Partial Reduction

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Observable nuclear transmutation reactions have occupied an extremely important position in nuclear medicine, nuclear energy, and geological and anthropological dating. Further, the concentration of radioactive materials (enhancement of radioactivity) has grown to be very important in the treatment and storage of radioactive waste and in the development of techniques for reactivating spent nuclear fuel. These facts coupled with our observation[1] that the solution electron affinities of perdeuterated polyaromatics are less than that of the protiated materials led us to investigate the possibility of increasing the radioactivity of benzophenone-*carbonyl*-^{14}*C* (BZO-14C)–cold benzophenone (BZO-12C) mixtures via the partial reduction of these mixtures to the ketyls.

When 0.6–5.0-mmol samples of a radioactive (0.02–0.16 μCi)[2] mixture of BZO-14C and BZO-12C are reduced with deficient amounts of sodium metal in liquid ammonia (20–40 mL), the concentrations of the cold and hot anion radicals and neutral molecules are controlled via reaction 1.

$$\text{BZO-12C}^{\bullet-} + \text{BZO-14C} \rightleftharpoons \text{BZO-12C} + \text{BZO-14C}^{\bullet-} \quad (1)$$

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(1) Stevenson, G. R.; Espe, M. P.; Reiter, R. C. *J. Am. Chem. Soc.* **1986**, *108*, 532.

(2) Pure BZO-14C has 0.0624 Ci/mmol.

If the equilibrium constant for reaction 1 sufficiently deviates from unity, the reaction should provide a means of separation of the two benzophenones containing the different isotopes of carbon in the carbonyl position, since the physical and chemical properties of the ketyls are very different from those of the neutral benzophenones. Indeed, the equilibrium constant for reaction 1 was found to be less than one and the separation of the hot and cold benzophenones was realized.

The deep blue ammonia solutions were exposed to high vacuum at −78 °C until all of the ammonia was evaporated leaving the solid organometallic salt $[Na^+(NH_3)BZO^{\bullet-}]$[3] together with neutral benzophenone. The neutral hot and cold benzophenones could then be sublimed from this mixture by simply heating the sample to 130 °C under high (10^{-6} torr) vacuum. Alternatively, dry ether could be added to the solid ketyl–ketone mixture. As only the neutral ketone is soluble in the ether, this effects a separation of the ketyl and neutral material. The benzophenones recovered from the reaction mixture were recrystalized from methanol–ether and stored under vacuum to ensure complete removal of solvent.

Accurately weighed samples (about 12 mg) of the recovered neutral hot and cold benzophenones were dissolved in toluene containing Omniflour as the scintillation solvent. The radioactivity associated with each sample was determined by using a Packard Tri-carb 460C-460D liquid scintillation system. Comparison of the radioactivity of the recovered samples to that of the original unreacted mixture showed the benzophenones recovered from the anion radical mixture to be enhanced in radioactivity. The original mixture (used as the radioactivity standard) of BZO-14C + BZO-12C yields $(2.676 \pm 0.002) \times 10^5$ dpm/mmol, while a mixture recovered from a reaction of 1.43 mmol of this standard with 0.66 mmol of sodium yielded 2.97×10^5 dpm/mmol. Further enhancement of the radioactivity can be achieved by simply reducing the recovered materials with sodium in liquid ammonia and working up this reaction mixture in the same manner.

The specific activity of the standard in disintegration per minute/millimole (dpm[S]) can be utilized with that of the recovered material (dpm[R]) to estimate the equilibrium constant for reaction 1. This is true since the decompositions/minute of pure BZO-14C (dpm[14]) is related to that of the standard and the concentration of BZO-14C and BZO-12C in the standard, eq 2, and a similar relationship holds for the dpm[R] and the

$$\mathrm{dpm[S]} = \mathrm{dpm[14][BZO\text{-}14C]_S/([BZO\text{-}14C]_S + [BZO\text{-}12C]_S)} \quad (2)$$

concentrations of the benzophenones in the recovered material ($\mathrm{[BZO\text{-}14C]_R}$) and ($\mathrm{[BZO\text{-}12C]_R}$), eq 3. Dividing eq 2 by eq

$$\mathrm{dpm[R]} = \mathrm{dpm[14][BZO\text{-}14]_R/([BZO\text{-}14C]_R + [BZO\text{-}12C]_R)} \quad (3)$$

3 and remembering that $\mathrm{[BZO\text{-}14C]_S - [BZO\text{-}14C]_R = [BZO\text{-}14C^{\bullet-}]}$ and using the analogous expression for BZO-12C yields eq 4.

$$\mathrm{dpm[R]/dpm[S]} = \frac{K_{\mathrm{eq}} + \mathrm{[BZO\text{-}12C]_R/[BZO\text{-}12^{\bullet-}]}}{1 + \mathrm{[BZO\text{-}12C]_R/[BZO\text{-}12^{\bullet-}]}} \quad (4)$$

The only assumption made in eq 4 is that the total amount of BZO-14C is much less than that of BZO-12C. The concentration of the anion radical and the exact amount of distilled sodium used in the reduction were obtained by reacting the leftover anion radical salt with water and titrating the resulting solution with standardized HCl. Such treatment leads to a K_{eq} of about 0.7. There might be considerable error in this value, since the relative concentrations of the anions and neutral molecules in reaction 1 may deviate drastically from their equilibrium values in dilute solution during the process of evaporation of the solvent (ammonia). The ^{14}C-depleted benzophenones left in the reaction vessel in the form of $Na^+(NH_3)BZO^{\bullet-}$ can be recovered by simply adding a solution of I_2 in tetrahydrofuran to the solid salt.[4] Further, there is no theoretical limit as to how much the radioactivity of the sample can be enhanced by passing ^{14}C-enhanced material through this process consecutively, up to the point where the pure carbon-14 compound is obtained.

On the basis of the Raman and IR studies carried out upon the neutral molecules and anion radicals of tetracyanoethylene and tetracyanoquinone, the effect of an added electron is best characterized as a strengthening of single bonds and a weakening of multiple bonds with a net reduction in molecular bond energies.[5] It is this zero point energy effect that lowers the electron affinity of benzophenone when the carbonyl carbon is replaced with the heavier radioactive isotope.

Acknowledgment. We thank NSF (Grant CHE-841127) for support of this work.

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Synthesis and X-ray Crystal Structure of a Novel Bimetallic Bis(η^5-dicarbollide) Aluminum Sandwich Complex

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In the course of our investigation of the coordination chemistry of *closo*-3-C_2H_5-3,1,2-$AlC_2B_9H_{11}$ (**1**),[2] we sought to examine the reaction, if any, of **1** with carbon monoxide. Upon stirring a benzene solution of **1** under an atmosphere of CO at ambient temperature, what proved to be a CO-catalyzed reaction occurred which produced in high yield a previously unknown aluminacarborane species.[3] This species could be isolated as a colorless to slightly reddish, air-sensitive, crystalline solid. As the nature of this species could not be elucidated fully from spectroscopy alone, an X-ray structure determination was undertaken.[4] This species was shown to be the novel aluminacarborane sandwich complex, *commo*-3,3′-Al[(*exo*-8,9-(μ-H)$_2$Al(C_2H_5)$_2$-3,1,2-$AlC_2B_9H_9$)(3′,1′,2′-$AlC_2B_9H_{11}$)] (**2**), an ORTEP representation of which is shown in Figure 1.

In **2**, the planar bonding faces of the two dicarbollide ligands are nearly parallel, making an angle of 2.6° to one another and they are η^5-coordinated to a single aluminum atom in the same

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(1) Recipient of a University of California, Los Angeles, Graduate Division Research Grant Award, 1984.

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(3) Compound **1**, *closo*-3-C_2H_5-3,1,2-$AlC_2B_9H_{11}$ (500 mg, 2.64 mmol), was dissolved in 30 mL of dry, freshly distilled benzene in a nitrogen-filled glovebox. Carbon monoxide was passed through a 3 × 30 cm column filled with P_4O_{10} and then through a liquid-N_2-cooled trap and was bubbled through benzene prior to being introduced into the reaction flask containing the solution of **1**. After purging the reaction flask with a flow of CO for 20 min, the solution was stirred under an atmosphere of CO for 12 h. After this time, CO and solvent were removed in vacuo. Recrystallization of the residue from toluene/heptane afforded 465 mg (1.23 mmol, 93% yield) of **2** (mp 147 °C, sealed tube, uncorrected) after drying for 12 h under vacuum.

(4) Crystallographic data: Suitable crystals of **2** ($C_8H_{32}B_{18}Al_2$) were grown from benzene/pentane. Crystals were sealed in 0.5-mm capillary tubes under dry N_2. Data collection was carried out at 24 °C, using a modified Picker FACS-1 automated diffractometer, Mo K_α radiation. The space group is $P2_1/n$ with $a = 7.122$ (2) Å, $b = 27.668$ (8) Å, $c = 11.629$ (3) Å, $\beta = 96.246$ (5)°, $V = 2288$ Å^3. 2335 reflections which measured $I > 3\sigma(I)$ were used for structure solution using MULTAN 78 and locally written refinement programs. The last cycle of least-squares refinement gave residuals of $R = 0.065$, $R_w = 0.075$, and GOF = 2.39.

0002-7863/86/1508-5367$01.50/0