of cytochrome c, and should the cytochrome c-flavodoxin complex be more stable than the porphyrin-cytochrome c complex, then addition of an equivalent of flavodoxin to the porphyrin-cytochrome c complex will displace ("unmix") the porphyrin and yield a mirror-image difference spectrum of that for complex formation. This proves to be so (Figure 1). The complete unmixing by a single flavodoxin equivalent places the boundaries on the porphyrincytochrome c stability to correspond to 0.05 μ M < K_d < 5 μ M.¹⁴

It is anticipated that this topographical mimicry may be of value in examination of the surface dynamics of complex formation, the exploration of analogous domains on other proteins, and the kinetics of electron transfer among these proteins. In this respect 1 may complement the smaller redox-inert metal complexes.¹³ Last, it provides a small yet satisfying vindication of the expectation that rational consideration of the structural elements of macromolecules may be used for the design of topographical mimics, as mechanistic principles now allow the design of mechanistic inhibitors.

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Supplementary Material Available: Experimental protocols and figures in support of the described experiments (4 pages). Ordering information is given on any current masthead page.

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Total Synthesis of (\pm) -4-Amino-4-deoxychorismic Acid: A Key Intermediate in the Biosynthesis of p-Aminobenzoic Acid and L-(p-Aminophenyl)alanine¹

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Chorismic acid (1), the branch-point metabolite of the shikimate pathway, is the biosynthetic precursor of both anthranilic acid (AA) and p-aminobenzoic acid (PABA).³ In the mid-1970's, Dardenne⁴ and Haslam^{3c} independently suggested that (a) AA



and PABA both originated from chorismate or (b) AA arose from chorismate and PABA from isochorismate (3) by parallel 1,5addition/elmination reactions of ammonia or glutamine (Scheme I). Amino enol pyruvates 2 and 4 were suggested as key "missing links". L-(p-Aminophenyl)alanine (L-PAPA), a microbial and plant precursor of chloramphenicol, could arise by the Claisen rearrangement of 4 to 5, an amino analogue of prephenic acid.⁴ These proposals gained support when we^{5a} and others^{5b} reported the conversion of 2 to AA by subunit I of anthranilate synthase (AS-I), purified from Serratia marescens. Here we describe the total synthesis of 4-amino-4-deoxychorismate (± -4) and 4amino-4-deoxyprephenate (5). Enzymic studies indicate that 4 and 5 are bona fide intermediates between chorismate and PABA and L-PAPA and that isochorismic acid apparently plays no part in the biosynthetic scheme.

Racemic trans-4-amino-3-hydroxy-1,5-cyclohexadiene-1carboxylic acid $(6)^6$ was smoothly N-protected with a BOC group



and then its sodium salt esterified (NaHCO₃/CH₃I/HMPA) to afford 7 in 46% overall yield. This substance was transformed to alkoxymalonate 8 [N₂C(CO₂CH₃)₂, Rh₂(OAc)₄, C₆H₆, 70 °C, 56%] and then alkylated with Eschenmoser's salt $[CH_2=N-$ (CH₃)₂I, CH₂Cl₂, Et₃N, 94%].⁷ The resulting Mannich base 9 was quaternized (CH₃I/CH₂Cl₂, room temperature) to ammonium salt 10 which, upon treatment with base (1 equiv of NaOH, THF/H₂O), furnished dimethyl ester 11 in 47% yield. Further saponification of 11 with 2.5 equiv of NaOH gave 12 in >90% yield after acidification with Amberlite IR-120-H resin. Deprotection of 12 in neat CF₃CO₂H (0 °C, 15 min) furnished the desired 4 as its TFA salt. Less polar aromatic impurities were removed by silica gel chromatography, thus affording pure (±)-4-TFA in 68% yield (mp 110-115 °C).8

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L-PAPA biogenesis.

Like 2, diene 4-TFA proved to be rather unstable.^{5a} Upon standing at room temperature, the olefinic signals in its 300-MHz NMR spectrum (room temperature, pure D₂O) gradually diminished while a new AB pattern emerged at δ 5.9, 6.1 (J = 12.2 Hz), highly characteristic of the Claisen rearrangement product 5 ($t_{1/2}$ = 5 days at 23 °C). Aqueous solutions of 5-TFA could readily be obtained in this fashion.9

p-Aminobenzoate synthase (PABS) is structurally and functionally similar to anthranilate synthase.¹⁰ The native enzyme consists of two subunits designated PABS-I and PABS-II. PABS-I can convert chorismate to PABA in the presence of NH_4^+ but requires an amidotransferase (PABS-II) in order to use glutamine as the nitrogen source. Recent biochemical and immunological studies further indicate that AS and PABS may both have evolved from a common ancestral gene.¹¹

PABS-I was obtained from a plasmid-containing strain of E. coli BN116 which produced ca. 50-fold greater concentrations of the enzyme.¹² From a fluorescence assay similar to that for AS-I,^{5,13} freshly prepared (\pm) -4-TFA was found to be an effective substrate for PABS-I. In the absence of NH_4^+ , 4-TFA was converted to PABA with a V_{max} of 667 (pmol/min)/unit enzyme.¹⁴ With added $(NH_4)_2SO_4$ (33 mM), V_{max} increased to 788 $(pmol/min)/unit enzyme (K_M = 16 \mu M)$. By comparison, chorismate and NH_4^+ formed PABA with a V_{max} of 52 (pmol/ min)/unit enzyme ($K_{\rm M} = 12 \,\mu M$). These data appear to establish 4 as an intermediate between chorismate and PABA. However, no PABA was formed by the action of the enzyme (plus NH_4^+) on synthetic isochorismic acid $((\pm)-3)$.¹⁵

Yields of PABA from 4 never exceeded ca. 10% and product formation was nonlinear with time and enzyme concentration. Controls showed that buffered solutions of 4 were rearranging nonenzymically to 5, pure samples of which effectively blocked the conversion of either 1 or 4 to PABA. This observation was strickingly reminiscent of the enzymatic chemistry of 2 with AS-I.^{5a}

The multistep biosynthesis of L-PAPA from 1 in Streptomyces venezuelae is catalyzed by the enzyme system arylamine synthase.¹⁶ Partially purified enzyme preparations¹⁶ were unstable, even in the cold, and required added glutamine to convert chorismate to L-PAPA at pH 8.5 (50 μ M Tris-HCl buffer, 20 μ M MgCl₂, 5 μ M NAD⁺). Gratifyingly, both 4–TFA and 5–TFA were readily converted to L-PAPA in the absence of glutamine, although substrate concentration ranges were too low in relation to apparent $K_{\rm M}$ values to give meaningful kinetic parameters.¹⁷ Controls with boiled and precipitated protein clearly indicated that product formation was enzyme catalyzed. It was noteworthy that aged samples of arylamine synthase continued to form L-

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PAPA from 5-TFA long after all catalytic activity toward 1 was lost. Future efforts to purify the component enzymes and make accurate kinetic measurements on our synthetic intermediates may

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reveal other fascinating similarities between AA, PABA, and

Registry No. (±)-4, 97279-79-3; (±)-4.TFA, 97293-82-8; (±)-5, 97279-80-6; (±)-5.TFA, 97279-88-4; (±)-6, 97279-81-7; (±)-6.Na (BOC derivative), 97279-82-8; (±)-7, 97279-83-9; (±)-8, 97279-84-0; (±)-9, 97279-85-1; (±)-10, 97279-86-2; (±)-11, 97279-87-3; (±)-1, 97293-81-7; PABA, 150-13-0; L-PAPA, 943-80-6; CH₂=N⁺Me₂I⁻, 15956-28-2; $N_2C(CO_2Me)_2$, 6773-29-1.

The Multiply Bonded Octachlorodiosmate(III) Anion [Os₂Cl₈]²⁻. The First Example of a Homoleptic Halide **Complex of This Type for the Platinum Metals**

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Central to the development of the field of metal-metal multiple bond chemistry has been the isolation of, structure determination of, study of the bonding in, and reactivity studies of the homoleptic halide anions of the type $[M_2X_8]^{n-}$ (X = Cl, Br, or I).²⁻⁴ These species contain metal-metal bonds of orders 3.5 or 4 and have been encountered previously only for the cases where M = Mo, W. Tc, or Re.²⁻⁴ We can now report an important extension of this chemistry to the platinum metals, through the isolation and structural characterization of the octachlorodiosmate(III) anion, the first example of such a halide complex to contain a metalmetal triple bond. The existence of this novel species is of importance both from the point of view of heralding a new chapter in the expansion of multiple-bond chemistry and in the discovery of a hitherto unknown class of complex halo anions of the platinum metals.

The diosmium(III) carboxylates of the type $Os_2(\mu - O_2CR)_4Cl_2$ $(R = CH_3, C_2H_5, n-C_3H_7, or CH_2Cl)$ constitute an important group of triply bonded complexes that have short Os-Os bonds.^{5,6} These species have been described as possessing a ground state that can be represented as having contributions from the $\sigma^2 \pi^4 \delta^2 \delta^{*2}$ and $\sigma^2 \pi^4 \delta^2 \pi^{*1} \delta^{*1}$ configurations,^{5,7} although, more recently, a description involving only the triplet state $\sigma^2 \pi^4 \delta^2 \pi^{*1} \delta^{*1}$ has been advocated.⁸ Previously, Wilkinson, Stephenson, and co-workers⁵

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