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 porphyrin-cytochrome *c* stability to correspond to $0.05\ \mu M < K_d < 5\ \mu M$.[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.

Acknowledgment. This research is supported by the National Institute of General Medical Sciences. We further acknowledge fellowships from the University of Minnesota (J.F.) and the UOP Foundation (K.C.F.). Don Hirsh and Mohamed Ruyan are thanked for their contributions to the early stages of this problem. Lastly, J.F. thanks Seymour Cohen for sharing his persuasive arguments for the use of macromolecule structure in molecular design.[15]

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 (±)-4-Amino-4-deoxychorismic Acid: A Key Intermediate in the Biosynthesis of *p*-Aminobenzoic Acid and L-(*p*-Aminophenyl)alanine[1]

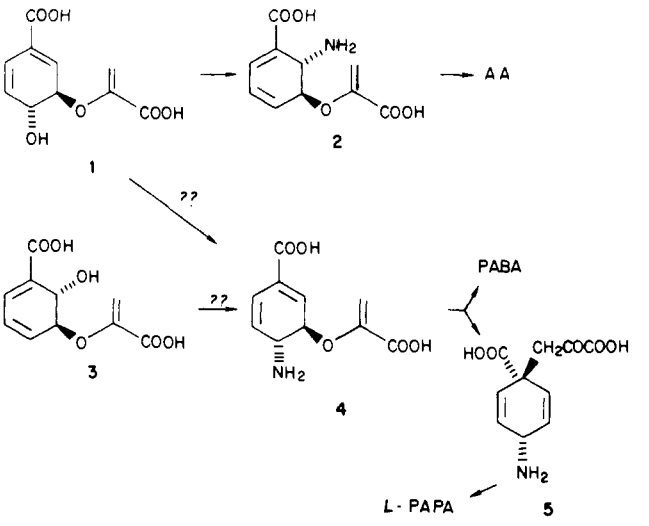
Chia-Yu P. Teng,[2a] Bruce Ganem,*[2a] Stella Z. Doktor,[2b] Brian P. Nichols,[2b] Raj K. Bhatnagar,[2c] and Leo C. Vining[2c]

Department of Chemistry, Baker Laboratory Cornell University, Ithaca, New York 14853
Laboratory for Cell, Molecular and Developmental Biology, Department of Biological Sciences University of Illinois at Chicago Chicago, Illinois 60680
Department of Biology, Dalhousie University Halifax, Nova Scotia, Canada B3H 4J1

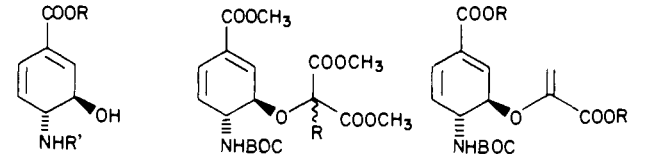
Received January 28, 1985

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, Dardenne[4] 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 1,5-addition/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 4-amino-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.

Scheme I



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



6, R; R'=H
7, R=CH_3; R'=BOC
8, R=H
9, R=$CH_2N(CH_3)_2$
10, R=$CH_2N(CH_3)_3I$

and then its sodium salt esterified ($NaHCO_3/CH_3I$/HMPA) to afford **7** in 46% overall yield. This substance was transformed to alkoxymalonate **8** [$N_2C(CO_2CH_3)_2$, $Rh_2(OAc)_4$, C_6H_6, 70 °C, 56%] and then alkylated with Eschenmoser's salt [$CH_2{=}N(CH_3)_2I$, CH_2Cl_2, Et_3N, 94%].[7] The resulting Mannich base **9** was quaternized (CH_3I/CH_2Cl_2, room temperature) to ammonium salt **10** which, upon treatment with base (1 equiv of NaOH, THF/H_2O), 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 CF_3CO_2H (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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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 D_2O) 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 (±)-**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 μM). By comparison, chorismate and NH_4^+ formed PABA with a V_{max} of 52 (pmol/min)/unit enzyme (K_M = 12 μM). 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 ((±)-**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 preparations[16] were unstable, even in the cold, and required added glutamine to convert chorismate to L-PAPA at pH 8.5 (50 μM Tris-HCl buffer, 20 μM $MgCl_2$, 5 μM 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_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-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 reveal other fascinating similarities between AA, PABA, and L-PAPA biogenesis.

Acknowledgment. We thank the National Institutes of Health (grants to B.G., B.P.N.), the NSERC of Canada (grants to L. C.V.) and the Killam Trust (fellowship to R.K.B.) for generous financial assistance. We also thank Matthew Gande (Cornell) for preparing a sample of isochorismic acid and Dr. Morris Laycock (NRC-Canada) for performing L-PAPA aminoacid analyses. Support of the Cornell Nuclear Magnetic Resonance Facility by the NSF (CHE 7904825; PCM 8018643) and NIH (RR-02002) is gratefully acknowledged.

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; $CH_2{=}N^+Me_2I^-$, 15956-28-2; $N_2C(CO_2Me)_2$, 6773-29-1.

(8) NMR (methanol-d_4, 300 MHz) δ 6.85 (br s, H-2), 6.50 (d, H-6, J = 9.5 Hz), 5.90 (d, H-5, J = 9.5 Hz), 5.49 (d, one OC=CH, J = 2 Hz), 5.06 (d, H-3, J = 14 Hz), 4.7-4.8 (HOD plus the other OC=CH), 4.30 (d, H-4, J = 14 Hz); IR ν_{max} (KBr) 3430, 2930, 2860, 1680, 1645, 1445 cm^{-1}; UV λ_{max} 272 nm (ϵ 5230, H_2O).

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The Multiply Bonded Octachlorodiosmate(III) Anion $[Os_2Cl_8]^{2-}$. The First Example of a Homoleptic Halide Complex of This Type for the Platinum Metals

Phillip E. Fanwick,[1a] M. Kathleen King,[1a]
Stephen M. Tetrick,[1b] and Richard A. Walton*[1b]

Department of Chemistry, University of Kentucky
Lexington, Kentucky 40506
Department of Chemistry, Purdue University
West Lafayette, Indiana 47907

Received April 1, 1985

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 metal-metal 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 $Os_2(\mu\text{-}O_2CR)_4Cl_2$ (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-workers[5]

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