

1,8-dichloroanthracene. The 9-anthraldehyde was eluted from the column with THF: yield 9 g; mp 224–226° (THF). *Anal.* (C<sub>15</sub>H<sub>8</sub>Cl<sub>2</sub>O) C, H.

**1,5-Dichloro-9-anthraldehyde.** Formylation of 34.4 g of 1,5-dichloroanthracene with 20.2 g of  $\alpha,\alpha$ -dichloromethyl methyl ether as detailed in the preceding preparation yielded 3 g of the titled compound, mp 188–190° (PhH–heptane). *Anal.* (C<sub>15</sub>H<sub>8</sub>Cl<sub>2</sub>O) C, H, Cl.

**Acknowledgment.** The author wishes to express gratitude to Dr. R. E. Strube for the encouragement of this work and to the U. S. Army Medicinal Research and Development Command for their financial support. This work was performed under Contract No. DADA17-71-C-1038 and is Contribution No. 1217 from the Army Research Program on Malaria.

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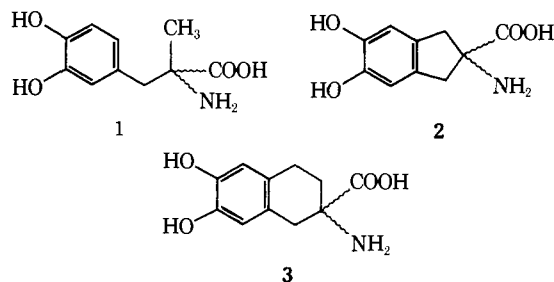
## Rigid Amino Acids Related to $\alpha$ -Methyldopa

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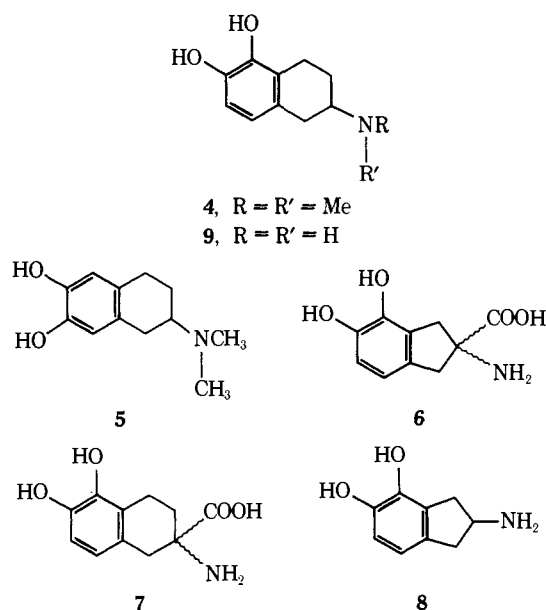
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Received December 17, 1973

The antihypertensive activity of  $\alpha$ -methyldopa (**1**) has prompted numerous workers to incorporate the salient features of this molecule into a rigid framework. Taylor, *et al.*,<sup>1</sup> prepared an indan derivative **2** and its dimethyl ether, both of which were inactive in an *in vivo* screen for hypotensive activity. The compounds were likewise inactive in *in vitro* screens against Dopa decarboxylase, and it was concluded that the rigidity and symmetry incorporat-

ed into this molecule (compared to  $\alpha$ -methyldopa) was the possible cause of the biological inactivity. Rastogi, *et al.*,<sup>2</sup> prepared an analogous tetralin amino acid **3** and found no hypotensive effect and no *in vitro* inhibition of Dopa decarboxylase. Neither the Taylor nor the Rastogi group described the Dopa decarboxylase inhibition test which was employed.



The dramatically high order and wide spectrum of biological effects produced by 2-dimethylamino-5,6-dihydroxytetralin (**4**),<sup>3,4</sup> as compared with the 6,7-dihydroxy system **5**,<sup>†</sup> suggested that molecular rigidity *per se* might not be the critical parameter for biological effect but that the arrangement of the OH functions on the aromatic ring is critical.



It was speculated that the OH group disposition in **2** and **3** might be detrimental to maximal  $\alpha$ -methyldopa-like effects, and accordingly the indan and tetralin systems **6** and **7** were selected for preparation and biological study. These systems are, like **2** and **3**, rigid analogs of  $\alpha$ -methyldopa, but they represent different frozen rotamers of it. Attention was limited in the present work to *in vitro* effects of the amino acids on Dopa decarboxylase.

Compounds **6** and **7** were prepared from the corresponding ketones by literature modifications of the Strecker reaction. Preparation of the amines **8** and **9** (which are decarboxylation products of **6** and **7**) has been described in prior communications;<sup>3,5</sup> however, in the present work, the dimethyl ether of **9** was synthesized from the appropriate  $\beta$ -tetralone by conversion to its *O*-methyl oxime and reduction of this with diborane. Overall, this sequence represents a marked improvement over the literature one. Spectral (ir and nmr) data on all compounds

† J. P. Long, University of Iowa, unpublished data.

**Table I.** Inhibitors of Dopa Decarboxylase<sup>a</sup>

Inhibitor	% inhibition		
	$3 \times 10^{-4}$ M	$3 \times 10^{-3}$ M	$3 \times 10^{-2}$ M
Caffeic acid	33	66	100
<i>dl</i> - $\alpha$ -Methyldopa	33	66	100
3	0	33	100
6	0	100	100
7	0	100	100

<sup>a</sup>Incubations were conducted as described in the Experimental Section. All compounds listed in the table were preincubated with the enzyme and pyridoxal 5-phosphate for 15 min before L-Dopa ( $3 \times 10^{-3}$  M final concentration) was added to complete the reaction mixtures. Incubations were conducted for 30 min.

prepared were consistent with the proposed structures.

**Biological.** Aromatic L-amino acid decarboxylase (Dopa decarboxylase) was used to evaluate the ability of 3, 6, and 7 to serve either as substrates for the enzyme or as inhibitors of the enzymatic decarboxylation of L-dopa. When these  $\alpha$ -methyldopa analogs were incubated with the enzyme, none of the respective amine products<sup>3</sup> could be conclusively detected on chromatograms, while standard incubation mixtures converted 8.95  $\mu$ mol of L-dopa into dopamine in 1 hr. It had been anticipated that the rates of conversion of 3, 6, and 7 into their respective amines would be much slower than the conversion of L-dopa into dopamine; the rate of conversion of  $\alpha$ -methyldopa into  $\alpha$ -methyldopamine has been shown<sup>6</sup> to be approximately  $\frac{1}{200}$  that of L-Dopa. Enzyme incubations were conducted with 2, 10, and 20 times the standard amount of enzyme, and incubations were allowed to proceed with 3, 6, or 7 for as long as 24 hr, but no detectable amounts of the amine products resulted. It should be noted that *dl*-3, 6, and 7 were employed in the enzyme studies; racemic amino acids have been reported<sup>6</sup> to be substrates for aromatic L-amino acid decarboxylase. However, only the L enantiomers in these *dl* mixtures are decarboxylated by the enzyme.

Enzyme inhibitory actions of 3, 6, and 7 were compared with those of *dl*- $\alpha$ -methyldopa<sup>7</sup> and caffeic acid (3,4-dihydroxycinnamic)<sup>8</sup> (Table I).

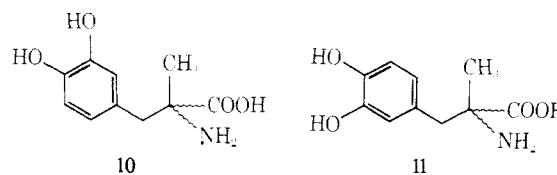
Caffeic acid and *dl*- $\alpha$ -methyldopa inhibited the conversion of L-Dopa to dopamine in all concentrations studied ( $10^{-2}$ ,  $10^{-3}$ , and  $10^{-4}$  M). The reaction was completely blocked by  $10^{-2}$  M concentrations of these compounds. Inhibition with either compound was observed when it was added to the enzyme preparation simultaneously with the L-Dopa substrate and when it was added to the preincubation mixtures. In contrast, 3, 6, and 7 were effective inhibitors only when they were preincubated with the enzyme and pyridoxal 5-phosphate.

Compounds 6 and 7 completely inhibited the reaction at concentrations of  $10^{-3}$  M, while a concentration of  $10^{-2}$  M of 3 was required for complete inhibition. Results obtained with control enzyme incubations containing the various inhibitors and equivalent amounts of KOH demonstrated that the observed inhibitions were functions of concentrations of 3, 6, or 7 and not of possible changes in the pH of the medium. Rates of Dopa decarboxylase mediated reactions are dependent upon pyridoxal 5-phosphate concentrations.<sup>9,10</sup> Christenson, *et al.*,<sup>9</sup> established that concentrations of pyridoxal 5-phosphate higher or lower than the optimum ( $10^{-5}$  M) resulted in a decrease in the rate of the enzyme reaction. The possibility was considered that the rigid  $\alpha$ -methyldopa analogs produced their observed inhibitory effect by removal of pyridoxal 5-phosphate from participation in the reaction *via* Schiff

base formation. Accordingly, controlled experiments were conducted in which an additional 0.215  $\mu$ mol of pyridoxal 5-phosphate was added, either to standard preincubation mixtures containing inhibitor or to the preincubated enzyme with L-Dopa substrate. Results with these controlled experiments were identical with those obtained previously with the  $\alpha$ -methyldopa analogs, which seem to eliminate the possibility of the observed inhibitory effects involving simple inactivation of pyridoxal. However, the exact nature of the inhibition of Dopa decarboxylase caused by 3, 6, and 7 remains to be determined by more sophisticated enzyme kinetic studies.

## Discussion

On the basis of the data on Dopa decarboxylase inhibition, it is concluded that the pattern of ring oxygenation in 6 and 7 is conducive to enzyme inhibitory activity, as compared to 2 and 3. It is therefore appealing to speculate that, as has been proposed<sup>3,11</sup> for dopamine, apomorphine, and for the biologically active dihydroxylated 2-aminotetralins, there is a common stereochemical arrangement—a single favored conformation—for  $\alpha$ -methyldopa-like inhibitors of Dopa decarboxylase. The conformer of  $\alpha$ -methyldopa which seems likely to be involved in enzyme inhibition is 10 rather than its rotamer 11.



Thus, it appears that maximal dopaminergic agonist effects and maximal Dopa decarboxylase antagonist effect require the same steric disposition of the 3,4-OH groups with respect to the side chain at the 1 position on the ring. This may reasonably suggest a great stereochemical similarity between dopaminergic receptors and the active catalytic site of L-amino acid decarboxylase.

## Experimental Section

Melting points were determined in open glass capillaries using a Thomas-Hoover Uni-Melt apparatus and are uncorrected. All boiling points are uncorrected. IR spectra were determined with Beckman IR5-A and IR-10 spectrophotometers. Nmr spectra were recorded with a Varian Associates T-60 spectrometer ( $\text{Me}_4\text{Si}$ ). Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn., and by the Microanalytical Service, College of Pharmacy, University of Iowa. Where analyses are indicated by symbols of the elements, the analytical results were within  $\pm 0.4\%$  of the theoretical values.

**4,5-Dimethoxy-2-amino-1-indanol Hydrochloride (12).** 4,5-Dimethoxy-2-amino-1-indanone hydrochloride<sup>3</sup> (5.0 g, 0.002 mol) in 500 ml of 95% EtOH was hydrogenated for 3 days in a Parr shaker at room temperature with 2.1 g of 10% palladium on charcoal at a maximum pressure of 40 psig. The solution was filtered and evaporated under reduced pressure to give a white powder which was recrystallized from EtOH-Et<sub>2</sub>O to give 3.8 g (76%) of product, mp 162–164°. *Anal.* ( $\text{C}_{11}\text{H}_{16}\text{ClNO}_3$ ) C, H, N.

**4,5-Dimethoxy-2-indanone (13).** A variation of a method of Thrift<sup>12</sup> was employed. A solution of 10.0 g (0.052 mol) of 12 in 400 ml of concentrated HCl was extracted with 1 l. of  $\text{C}_6\text{H}_6$  for 24 hr in a liquid-liquid extractor. The  $\text{C}_6\text{H}_6$  layer was evaporated under reduced pressure and the residue was recrystallized from petroleum ether (bp 30–68°) to give 4.5 g (60%) of 13: mp 89–90°; ir (KBr) 1740  $\text{cm}^{-1}$  (C=O). *Anal.* ( $\text{C}_{11}\text{H}_{12}\text{O}_3$ ) C, H.

**Spiro(4,5-dimethoxyindan)-2,5-hydantoin (14).** Compound 13 (3.5 g, 0.019 mol), 3.1 g (0.062 mol) of NaCN, 16.0 g of ammonium carbonate, and 80 ml of EtOH-H<sub>2</sub>O (3:2) were heated at 55–60° for 6 hr. The mixture was then refluxed for 1.5 hr, and the volume was reduced to 40 ml and neutralized with concentrated HCl. On cooling, a solid separated which was recrystallized from EtOAc to give 3.5 g (73%) of 14: mp 189–190°; ir (KBr) 3300–3200

(NH), 1770–1690  $\text{cm}^{-1}$  (C=O). *Anal.* ( $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}_4$ ) C, H, N.

***dl*-2-Amino-4,5-dimethoxyindan-2-carboxylic Acid (15).** Compound 14 (1.0 g, 0.004 mol) and 4.0 g of  $\text{Ba}(\text{OH})_2$  in 60 ml of  $\text{H}_2\text{O}$  and 5 ml of EtOH were heated in a bomb at 160° for 3 hr. The cooled solution was filtered and the filtrate was treated with excess ammonium carbonate and then was filtered. Evaporation of this filtrate gave a solid which recrystallized from EtOH– $\text{H}_2\text{O}$  to give 0.67 g (75%) of white needles: mp 275–277°; ir (KBr) 1500–1620  $\text{cm}^{-1}$  (COO<sup>-</sup>); nmr ( $\text{D}_2\text{O}$ -AcOD)  $\delta$  2.80–3.81 (m, 4 H,  $-\text{CH}_2-$ ), 3.82 (s, 6 H,  $-\text{OCH}_3$ ), 7.0 (s, 2 H, arom H). *Anal.* ( $\text{C}_{12}\text{H}_{15}\text{NO}_4$ ) C, H, N.

***dl*-2-Amino-4,5-dihydroxyindan-2-carboxylic Acid Hydrobromide (6).** Compound 15 (0.5 g, 0.0017 mol) in 8 ml of 48% HBr was heated under  $\text{N}_2$  at 150–160° for 1.5 hr. Evaporation of the dark violet solution under reduced pressure (steam bath) left a brown residue which was recrystallized twice from 2-PrOH– $\text{Et}_2\text{O}$  to afford 0.360 g (60%) of a white solid, mp 262° dec. On exposure to air, this material turned brown. *Anal.* ( $\text{C}_{10}\text{H}_{12}\text{BrNO}_4$ ) C, H, N.

**1,2,3,4-Tetrahydro-5,6-dimethoxy-1-naphthalenol (16).** 3,4-Dihydro-5,6-dimethoxy-1(2*H*)-naphthalenone<sup>13</sup> (20.0 g, 0.097 mol) in 500 ml of 95% EtOH was stirred with 1.5 g (0.032 mol) of  $\text{NaBH}_4$  for 6 hr, then 0.75 g (0.016 mol) of additional  $\text{NaBH}_4$  was added, and stirring was continued for a total of 10 hr.  $\text{H}_2\text{O}$  (100 ml) was added, the volatiles were removed under reduced pressure, and the residue was extracted several times with  $\text{C}_6\text{H}_6$ . The combined extracts were washed with  $\text{H}_2\text{O}$ , 10% HCl, and finally with  $\text{H}_2\text{O}$  and were dried ( $\text{MgSO}_4$ ).  $\text{C}_6\text{H}_6$  was removed under reduced pressure and the resulting oil was distilled at 135–140° (0.025 mm) to give 17 g (85%) of a clear liquid. *Anal.* ( $\text{C}_{12}\text{H}_{16}\text{O}_3$ ) C, H.

**5,6-Dimethoxy-3,4-dihydronaphthalene (17).** Compound 16 (20.0 g, 0.096 mol) was heated for 5 min in the presence of a crystal of  $\text{KHSO}_4$  and then the viscous oil was distilled at 95–99° (0.025 mm) to afford 16.6 g (90%) of product; nmr ( $\text{CDCl}_3$ )  $\delta$  2.05–3.00 (m, 4 H,  $-\text{CH}_2-$ ), 3.80, 3.84 (s, 6 H,  $-\text{OCH}_3$ ), 5.75–6.55 (m, 2 H,  $-\text{CH}=\text{CH}-$ ), 6.75 (s, 2 H, arom H). *Anal.* ( $\text{C}_{12}\text{H}_{14}\text{O}_2$ ) C, H.

**1,2,3,4-Tetrahydro-5,6-dimethoxy-2(1*H*)-naphthalenone (18).** To a chilled, stirred solution of 17.5 g (0.090 mol) of 17 in 125 ml of  $\text{CHCl}_3$  was added over 0.5 hr a suspension of 25 g (0.145 mol) of *m*-chloroperbenzoic acid in 175 ml of  $\text{CHCl}_3$ . The resulting mixture was stirred in the cold for an additional 2 hr. It was then filtered and the filtrate was extracted several times with cold 10% NaOH and finally with  $\text{H}_2\text{O}$ . The  $\text{CHCl}_3$  was removed under reduced pressure (steam bath) to give an oil which was dissolved in 150 ml of EtOH and 100 ml of 2 *N* HCl. This solution was heated for 1 hr on a steam bath. The deep red solution was cooled and extracted with  $\text{C}_6\text{H}_6$ ; volatiles were removed from this extract under reduced pressure to leave a dark red oil which was shaken vigorously with a solution of 75 g (0.40 mol) of  $\text{NaHSO}_3$  in 150 ml of  $\text{H}_2\text{O}$  and 50 ml of EtOH. The voluminous bisulfite addition product which separated was collected on a filter and was washed with EtOH and then with  $\text{Et}_2\text{O}$ . It was dissolved in a solution of 172 g (0.60 mol) of  $\text{Na}_2\text{CO}_3$  in 500 ml of  $\text{H}_2\text{O}$ . The ketonic product was extracted with  $\text{C}_6\text{H}_6$ ; the extract was washed with 10% HCl and then with  $\text{H}_2\text{O}$  and was dried ( $\text{MgSO}_4$ ), and volatiles were removed under reduced pressure. The residue was crystallized from cyclohexene to give 13.5 g (71%) of white needles: mp 64–65°; ir (KBr) 1700  $\text{cm}^{-1}$  (C=O); nmr ( $\text{CDCl}_3$ )  $\delta$  2.45, 3.15 (t, 4 H,  $-\text{CH}_2-$ ), 3.45 (s, 2 H,  $-\text{CH}_2-$ ), 3.80, 3.84 (s, 6 H,  $-\text{OCH}_3$ ), 6.85 (s, 2 H, arom H). *Anal.* ( $\text{C}_{12}\text{H}_{14}\text{O}_3$ ) C, H.

**Spiro(5,6-dimethoxy-1,2,3,4-tetrahydronaphthalene)-2,5'-hydantoin (19).** The procedure was that used for 14, using 1.5 g (0.0073 mol) of 18, 1.6 g (0.03 mol) of NaCN, 8.0 g of ammonium carbonate, and 80 ml of EtOH– $\text{H}_2\text{O}$  (3:2). The product was recrystallized from EtOAc (charcoal) to afford 1.40 g (72%) of a white solid, mp 235–236°. *Anal.* ( $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_4$ ) C, H, N.

***dl*-2-Amino-5,6-dimethoxy-1,2,3,4-tetrahydronaphthalene-2-carboxylic Acid (20).** The procedure was the same as for 15, using 1.0 g (0.0036 mol) of 19, a reaction time of 5 hr, and reaction temperature of 160°. The product was recrystallized from EtOH– $\text{H}_2\text{O}$  to afford 0.65 g (72%) of white needles: mp 292–295° dec; ir (KBr) 1500–1620  $\text{cm}^{-1}$  (COO<sup>-</sup>); nmr ( $\text{D}_2\text{O}$ -AcOD)  $\delta$  2.20–3.30 (m, 6 H,  $-\text{CH}_2-$ ), 3.80, 3.84 (s, 6 H,  $-\text{OCH}_3$ ), 6.90 (s, 2 H, arom H). *Anal.* ( $\text{C}_{13}\text{H}_{17}\text{NO}_4$ ) C, H, N.

***dl*-2-Amino-5,6-dihydroxy-1,2,3,4-tetrahydronaphthalene-2-carboxylic Acid Hydrobromide (7).** The procedure was that employed for 6, using 0.500 g (0.0049 mol) of 20, a reaction time of 3 hr, and reaction temperature of 150–160°. The product was recrystallized twice from EtOH– $\text{Et}_2\text{O}$  to afford 0.45 g (75%) of a

white solid, mp 235–240° dec. *Anal.* ( $\text{C}_{11}\text{H}_{14}\text{BrNO}_4$ ) C, H, N.

**1,2,3,4-Tetrahydro-5,6-dimethoxy-2(1*H*)-naphthalenone *O*-Methyl Oxime (21).** Compound 18 (6.64 g, 0.0322 mol) was melted over a steam bath, then 5.33 g (0.0644 mol) of methoxyamine hydrochloride was added, followed by 2.57 g (0.0644 mol) of NaOH in 32.2 ml of  $\text{H}_2\text{O}$ . The resulting mixture was shaken over a steam bath for 0.25 hr, then was shaken in a closed container on a mechanical shaker and was gently heated with an infrared lamp for 0.5 hr, and then was shaken at room temperature for a total of 24 hr. The reaction mixture was extracted several times with  $\text{Et}_2\text{O}$ , the combined extracts were dried ( $\text{MgSO}_4$ ) and filtered, and  $\text{Et}_2\text{O}$  was removed from the filtrate to leave an oil which was distilled, bp 165–169° (0.05 mm), to afford 4.0 g (52%) of product. *Anal.* ( $\text{C}_{13}\text{H}_{17}\text{NO}_3$ ) C, H, N.

**2-Amino-5,6-dimethoxy-1,2,3,4-tetrahydronaphthalene Hydrochloride (22).** The method of Feuer and Braunstein<sup>14</sup> was employed. To a cooled (0°) mixture of 3.8 g (0.0161 mol) of 21 and 20 ml of tetrahydrofuran was slowly added with stirring 12.4 ml (0.0124 mol) of 1 *M* diborane in tetrahydrofuran (Aldrich Chemical Co.) under  $\text{N}_2$ . The resulting mixture was stirred at 0° for 1 hr and then was refluxed for 2 hr. The reaction mixture was again cooled to 0° and 10 ml of  $\text{H}_2\text{O}$  was added, followed by 10 ml of 20% KOH. This mixture was refluxed under  $\text{N}_2$  for 1 hr and then was permitted to stand overnight under  $\text{N}_2$ . It was then transferred to a separatory funnel and was extracted three times with  $\text{Et}_2\text{O}$  in a  $\text{N}_2$  atmosphere. The combined  $\text{Et}_2\text{O}$  extracts were dried ( $\text{Na}_2\text{SO}_4$ ) and filtered, and the filtrate was treated with excess ethereal HCl. The resulting white solid was washed several times with anhydrous  $\text{Et}_2\text{O}$  and then with hexane and was recrystallized from MeOH– $\text{Et}_2\text{O}$  to afford 1.35 g (35%) of crystals, mp 272–274° (lit.<sup>9</sup> mp 270–272°).

**Enzyme Studies. Materials.** Aromatic L-amino acid decarboxylase from hog kidney cortex was obtained from Worthington Co. (Lot No. E-E2JA, 47 units of activity/mg of protein). One unit of activity is defined as the amount of enzyme which converts 1 nmol of L-Dopa to dopamine per minute under prescribed assay conditions.<sup>1</sup> The enzyme was stable at –20° for several months. Sources of the following chemicals are as indicated: *dl*- $\alpha$ -methyl-dopa, L-Dopa, and pyridoxal 5-phosphate (Sigma); dopamine (Aldrich). Deionized  $\text{H}_2\text{O}$  for buffers was redistilled from all-glass apparatus.

**Enzyme Incubation Procedure.** The procedure was essentially that described by Christenson, *et al.*<sup>9</sup> Incubations were conducted in 7-dram snap-cap vials which were agitated in the air at 37° in a New Brunswick G-76 water bath-shaker. The standard enzyme incubation mixture consisted of 0.1 ml (5 mg of protein) of the enzyme preparation which was preincubated for 15 min with 2.4 ml of a 0.1 *M* potassium–sodium phosphate buffer (pH 6.8), containing 0.21  $\mu\text{mol}$  of pyridoxal phosphate. After preincubation, 0.5 ml of phosphate buffer containing 8.95  $\mu\text{mol}$  of L-Dopa was added, and the incubations were continued with shaking for 10–30 min. Enzyme reactions were terminated by quick-freezing in an acetone–Dry Ice bath, and the frozen samples were lyophilized and prepared for thin-layer chromatography.

Inhibition studies with rigid  $\alpha$ -methyl-dopa analogs and with *dl*- $\alpha$ -methyl-dopa and caffeic acid were performed in two ways: by adding the inhibitor candidate and L-Dopa simultaneously to the preincubated enzyme; or by incubating the enzyme preparation with the inhibitor candidate for 15 min prior to addition of the L-Dopa substrate. Complete reaction mixtures were then incubated as previously described. The results of all enzyme incubations were compared with those obtained with the standard incubation mixture containing L-Dopa.

**Tlc Analysis of Enzyme Reactions.** Samples of enzyme reaction mixtures were examined semiquantitatively by tlc. Lyophilized samples were suspended in 1.0 ml of anhydrous EtOH and these solutions were spotted (60  $\mu\text{l}$ ) on silica gel GF254 tlc plates and were developed in pyridine–AcOH–1-butanol– $\text{H}_2\text{O}$  (8:12:60:20).<sup>15</sup> In this system, the  $R_f$  values of L-Dopa and dopamine were 0.25 and 0.51, respectively. 3, 6, and 7 and their respective amine decarboxylation products also separated well in this system. Developed tlc plates were visualized by quenching of 254-nm-induced fluorescence and by spraying with freshly prepared 1%  $\text{FeCl}_3$  in  $\text{H}_2\text{O}$ –MeOH (1:1). The lower limit of detection of dopamine with the  $\text{FeCl}_3$  reagent was approximately 1  $\mu\text{g}$ , which would represent the equivalent of a 2% enzymatic conversion of L-Dopa to dopamine in the standard incubation system. Estimation of the amount of dopamine formed in enzyme reaction mixtures was based on colorimetric evaluation of the blue-black color produced with  $\text{FeCl}_3$  reagent relative to standard amounts of reference compounds.

**Acknowledgment.** This work was supported by Grant NS-04349, National Institute of Neurological Diseases and Stroke.

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## Book Reviews

**Aromatic and Heteroaromatic Chemistry.** Vol. 1. C. W. Bird and G. W. H. Cheeseman, Senior Reporters. The Chemical Society, Burlington House, London. 1973. xvi + 445 pp. 22 × 14 cm. £11.00.

This title is one of the expanding series of Specialist Periodical Reports published by the Chemical Society, London. This series, now approaching its full complement of 35 separate titles, offers extensive reviews of the chemical literature divided into major areas of research. Most of these reviews are published on an annual basis and are conveniently keyed to volumes of *Chemical Abstracts*.

The current publication is the initial one in the "Aromatic and Heteroaromatic Chemistry" series and is based on the contents of Vol. 75 and 76 of *Chemical Abstracts*. The material is arranged by reaction type, rather than by ring system, thus allowing a more concise and extensive literature coverage. The potential disadvantage of this organizational mode is a difficulty in gathering information on any particular ring system. Because of this, a book's usefulness as a pure reference text could be limited. The editors have remained cognizant of this problem, however, and through the use of subheadings have largely overcome it.

The work is very well organized into 15 chapters, as follows. Chapter 1 presents extensive coverage of ring systems of topical interest and novel structural features, with the emphasis on further understanding of the nature of aromatic systems and aromaticity in general. Chapters 2-5 consider general synthesis of aromatic ring systems, subdivided into the areas of intramolecular and intermolecular cyclizations, cycloaddition reactions, and ring interconversions. Chapters 6-11 cover reactions of ring systems, including electrophilic and nucleophilic substitution on carbon, electrophilic substitution on heteroatoms, substitution by electron-deficient species, addition reactions, and ring-cleavage reactions. Chapter 12 is dedicated to side chain reactions, while the remaining three chapters cover selected natural products, including porphyrins and oxygen heterocycles. No coverage is given to those systems covered by other Specialist Periodical Reports, such as alkaloids, terpenoids, and steroids.

Each chapter is further subdivided into general ring types or, in some cases, more specific reaction type (e.g., Chapter 6, Electrophilic Substitution on Carbon, is divided into subheadings treating replacement by hydrogen, metalation, reactions with groups IV, V, VI, and VII electrophiles, and direct substituent replacement). This further classification adds a great deal to the usefulness of the book by serving as a generalized index and, thus, effectively combines the advantages of both organization by reaction type and by ring type.

The work is quite extensive in its coverage, yet is easily read. It is generally written from a synthetic viewpoint and is thus extremely useful to anyone interested in synthetic organic chemis-

try. Being very well documented, with a particularly useful author index, it is a useful addition to any library.

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**Experimental Organic Chemistry.** By Arnold J. Krubsack. Allyn and Bacon, Boston, Mass. 1973. xvi + 445 pp. \$9.95.

The preface states the author's intent to construct a format for an organic chemistry laboratory manual which is a compromise between the "cookbook" approach and the "honors" approach in which the student is given a minimum amount of laboratory information and is required to utilize his own ingenuity and initiative to develop details for the experiment. To a remarkable degree, the volume is successful in this respect.

Early chapters deal with fundamental techniques in a highly readable style: melting points, extraction procedures, recrystallization, distillation, chromatography, use of the chemistry library. Chapters on infrared, ultraviolet, and mass spectroscopy and nuclear magnetic resonance are pitched at a reasonable and proper level for beginning organic chemistry students, and they are clear and readable. This entire portion of the book is designed as a reference resource for the experimental section which comprises the latter half.

This "reactions" portion surveys some of the principal types of organic reactions: formation of alkyl halides, organometallics, oxidations, Friedel-Crafts reactions, reductive methods (including catalytic hydrogenation), the Wittig reaction, Birch reduction, carbene formation and reactions, hydroboration, enamines, and heterocyclic ring formation. Each chapter contains excellent introductory theoretical material which helps make the experiment meaningful; useful techniques such as preparative tlc are integrated as a part of experimental procedures.

The book seems unusually well written and free from errors. This reviewer would highly recommend it as the laboratory manual for beginning organic chemistry courses. Indeed, many first-year graduate students might find it useful as a rapid, easily read reference for basic information on techniques and procedures to which they have been exposed, but which they have never really mastered.

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