

for evaluating the B compounds in many of their screens. The research at Emory University was made possible by the support of Dr. R. A. Day, Jr., Chairman of the Department of Chemistry at the time, and a generous research grant from Richardson-Merrell Inc., both of which are gratefully acknowledged.

### Synthesis of L-Dopa (3,4-Dihydroxyphenyl-L-alanine)

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*N*-Acetyl-3-(3,4-dimethoxyphenyl)-L-alanine (L-I) and *N*-acetyl-3-(3,4-methylenedioxyphenyl)-L-alanine (L-II) could be starting materials for the synthesis of L-dopa. A new chemical resolution method of *N*-acetyl-3-(3,4-dimethoxyphenyl)-DL-alanine (I) and *N*-acetyl-3-(3,4-methylenedioxyphenyl)-DL-alanine (II) by using *d*-ephedrine as a resolving reagent was adopted.

#### Experimental Section

***N*-Acetyl-3-(3,4-dimethoxyphenyl)-L-alanine-*d*-ephedrine Salt (*d*-Ephedrine-L-I Salt).**—*N*-Acetyl-3-(3,4-dimethoxyphenyl)-DL-alanine (DL-I) (53.4 g, 0.2 mole) and 33.0 g of *d*-ephedrine (0.2 mole) were dissd together in 130 ml of MeOH or in 200 ml of EtOH with warming at 55–60° for 1.0 hr, and the soln was kept in a refrigerator overnight. The colorless crystals that sepd were filtered off, washed with MeOH (ca. 30 ml), and dried, giving 37.9 g (87.8%) of the *d*-ephedrine-L-I salt: mp 147.5–149.5°,  $[\alpha]^{20}_D + 49.8^\circ$  (c 5, H<sub>2</sub>O). After recrystn from 3 vol of MeOH, the mp and  $[\alpha]_D$  became constant: mp 152–153°;  $[\alpha]^{20}_D + 54.5^\circ$  (c 5, H<sub>2</sub>O); yield, 28.4 g (68.1%). *Anal.* (C<sub>23</sub>H<sub>32</sub>N<sub>2</sub>O<sub>6</sub>) C, H, N.

***N*-Acetyl-3-(3,4-methylenedioxyphenyl)-L-alanine-*d*-ephedrine Salt (*d*-Ephedrine-L-II Salt).**—DL-II (90.4 g) and *d*-ephedrine (72.7 g) were dissd in 600 ml of MeOH or 900 ml of EtOH at 55–60° with stirring for 1.0 hr, cooled, and kept in a refrigerator overnight. The colorless crystals that sepd were filtered off, washed with MeOH (ca. 30 ml), and dried, giving 66.5 g (89.1%) of the *d*-ephedrine-L-II salt: mp 150.2–152.5°;  $[\alpha]^{20}_D + 48.2^\circ$  (c 5, H<sub>2</sub>O). Recrystn from 3 vol of MeOH gave 46.6 g (62.1%) of *d*-ephedrine-L-II: mp 156.3–158.6°;  $[\alpha]^{20}_D + 55.6^\circ$  (c 5, H<sub>2</sub>O). *Anal.* (C<sub>22</sub>H<sub>28</sub>N<sub>2</sub>O<sub>6</sub>) C, H, N.

***N*-Acetyl-3-(3,4-dimethoxyphenyl)-L-alanine (L-I) from the *d*-Ephedrine-L-I Salt.**—*d*-Ephedrine-L-I (20 g) was dissd in 50 ml of H<sub>2</sub>O, then this soln was added dropwise with 30% HCl with cooling and stirring, giving colorless crystals. After standing in a refrigerator overnight they were filtered off, washed with H<sub>2</sub>O (20 ml), and dried, affording 11.4 g (91.0%) of L-I: mp 149–150°;  $[\alpha]^{20}_D + 46.2^\circ$  (c 5, MeOH). *Anal.* (C<sub>13</sub>H<sub>17</sub>NO<sub>5</sub>) C, H, N.

***N*-Acetyl-3-(3,4-dimethoxyphenyl)-L-alanine (L-I) from the *d*-Ephedrine-L-I Salt.**—*d*-Ephedrine-L-I (20 g) was dissd in 50 ml of H<sub>2</sub>O, then this soln was added dropwise with 20% HCl with cooling and stirring, giving colorless crystals. After standing in a refrigerator overnight they were filtered off, washed with H<sub>2</sub>O (20 ml), and dried, affording 11.4 g (91.0%) of L-I: mp 149–150°;  $[\alpha]^{20}_D + 46.2^\circ$  (c 5, MeOH). *Anal.* (C<sub>13</sub>H<sub>17</sub>NO<sub>5</sub>) C, H, N. From the filtrate and washings of the acid (L-I), *d*-ephedrine-HCl was nearly quant recovered as colorless crystals; mp 217–218°;  $[\alpha]^{20}_D + 34.1^\circ$  (c 1, H<sub>2</sub>O).

***N*-Acetyl-3-(3,4-methylenedioxyphenyl)-L-alanine (L-II) from the *d*-Ephedrine-L-II Salt.**—*d*-Ephedrine-L-II salt (58.8 g) was dissd in 150 ml of H<sub>2</sub>O and added dropwise to 20% HCl under cooling and stirring, giving colorless crystals. After standing in a refrigerator overnight they were filtered off, washed with 50 ml of cold H<sub>2</sub>O, and dried, affording 33.7 g (95.0%) of L-II based on the

L-II of *d*-ephedrine-L-II used: mp 179.6–180.8°;  $[\alpha]^{20}_D + 46.5^\circ$  (c 5, MeOH). *Anal.* (C<sub>12</sub>H<sub>13</sub>NO<sub>5</sub>) C, H, N.

**L-Dopa (L-III) from L-I.**—A mixt of 26.8 g (0.1 mole) of L-I, 69.8 ml (0.6 mole) of 47% HBr, and 28 ml (0.32 mole) of PhOH was heated under stirring and reflux for 6 hr, and the resulting slight brown soln was evapd to a reddish syrup. This was dissd in 30 ml of *n*-BuOAc and extd twice with 30 ml and 10 ml of H<sub>2</sub>O. The 2 aq exts were combined and adjusted to pH 5.0 with 25% NH<sub>4</sub>OH soln contg a little NaHSO<sub>3</sub>, whereupon colorless crystals sepd. After standing in a refrigerator overnight the crystals were filtered off, washed with H<sub>2</sub>O, and dried, giving 19.6 g (99.5%) of crude L-dopa: mp 266–269°;  $[\alpha]^{15}_D - 11.6^\circ$  (c 5, 1 N HCl). Recrystn from 800 ml of H<sub>2</sub>O contg a little NaHSO<sub>3</sub> gave 15.6 g (79.5%) of L-dopa as colorless minute leaflets: mp 277–278° dec;  $[\alpha]^{15}_D - 13.3^\circ$  (c 5, N-HCl). *Anal.* (C<sub>9</sub>H<sub>11</sub>NO<sub>4</sub>) C, H, N.

**L-Dopa from L-II.**—L-II (30 g) and PhOH (30 g) were heated in 300 ml of 20% HCl under reflux and stirring for 20.0 hr, and the resulting soln was evaporated to the reddish syrup. This was worked up as in the preceding expt: yield, 22.6 g (95.6%); mp 268–270°,  $[\alpha]^{17}_D - 11.8^\circ$  (c 5, N-HCl); after recrystn 16.4 g (82.0%) of L-dopa, mp 277.2–278.2° dec,  $[\alpha]^{15}_D - 13.2^\circ$  (c 5, 1 N HCl). *Anal.* (C<sub>9</sub>H<sub>11</sub>NO<sub>4</sub>) C, H, N.

### Evaluation of Carbazoles as Antifungal Agents

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Some complex carbazole alkaloids have been reported to possess antifungal activity.<sup>1</sup> In a search for similar agents, a group of simple derivatives were prepared<sup>2</sup> and evaluated against *Candida albicans*.<sup>3</sup> None of the results are sufficiently high to recommend these compounds for further testing.

TABLE I  
ANTI-*Candida* ACTIVITY

No.	Carbazole <sup>a</sup>	Concn, mg/ml	Activity zone size, mm <sup>b</sup>
1	1-OH	0.1	12
2	1-OH-3-Me	0.1	11
3	3-MeO-6-Me	0.1	12
4	1,3-(MeO) <sub>2</sub> -6-Me	0.1	11
5	2,3-(MeO) <sub>2</sub> -6-Me	0.1	11
6	2,4-(MeO) <sub>2</sub> -6-Me	1.0	c
7	2,3-(OH) <sub>2</sub> -6-Me	0.1	10
8	<i>N</i> -Me-2,3-(MeO) <sub>2</sub> -6-Me	1.0	c
9	Glycozolidine <sup>d</sup>	1.0	c

<sup>a</sup> All new compds had satisfactory anal. (C, H, N) and spectral values. <sup>b</sup> In an agar diffusion cup-plate assay, where the cup diameter itself is 8 mm. <sup>c</sup> The zone was not larger than that produced by the diluent (ethylene glycol-EtOH, 4:1). <sup>d</sup> D. P. Chakraborty and B. P. Das, *Sci. Cult.*, **32**, 181 (1966).

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(1) K. C. Das, D. P. Chakraborty, and P. K. Bose, *Experientia*, **21**, 340 (1965).

(2) K. C. Das and B. Weinstein, unpublished data.

(3) We thank Dr. John W. Westley, Hoffman-LaRoche, Nutley, N. J., for furnishing the test report.