

thus preventing the checking of the enantiomeric purity of (-) and (+)-3 by this method.

(-)-*c*-2-Methyl-*r*-5-[(dimethylamino)methyl]-1,3-oxathiolane *c*-3-Oxide Methiodide ((-)-1). An excess of MeI (1 mL) was added to a solution of (-)-3 (0.3 g) in anhydrous ether (20 mL), and the reaction mixture was left at room temperature overnight. The white solid obtained was crystallized from absolute ethanol: yield 90%; mp 195–196 °C (lit.<sup>5</sup> mp 172–174 °C for the racemate);  $[\alpha]^{20}_D$  -48.4° (EtOH); CD (EtOH)  $\lambda$  245 nm,  $\Delta\epsilon$  = -0.153. The IR and <sup>1</sup>H NMR spectra are identical with those of the racemate.

In the same way, starting from (+)-3, we obtained (+)-1: yield 90%; mp 194–195 °C;  $[\alpha]^{20}_D$  +48.2° (EtOH); CD (EtOH)  $\lambda$  245 nm,  $\Delta\epsilon$  = +0.132. The IR and <sup>1</sup>H NMR spectra are identical with those of the enantiomer.

(2*R*,3*R*,5*R*)-*c*-2-Methyl-*r*-5-[(dimethylamino)methyl]-1,3-oxathiolane *t*-3-Oxide ((-)-3). To a sample of 1 g of (+)-7, obtained as described before,<sup>4</sup> in 5 mL of CH<sub>3</sub>COOH was added 2.5 mL of cold 30% H<sub>2</sub>O<sub>2</sub>. After 0.5 h at room temperature, the reaction mixture was made alkaline with 10% NaOH and extracted with CHCl<sub>3</sub> to give 1.1 g of a mixture (oil), which was chromatographed on a silica gel column with CHCl<sub>3</sub>-petroleum ether-absolute ethanol-concentrated NH<sub>4</sub>OH (340:60:65:8) as eluent.

The first fraction (*R<sub>f</sub>* 0.60) was (2*R*,3*R*,5*R*)-*c*-2-methyl-*r*-5-[(dimethylamino)methyl]-1,3-oxathiolane *t*-3-oxide ((-)-3): yield 0.7 g;  $[\alpha]^{20}_D$  -108.0° (EtOH); CD (EtOH)  $\lambda$  243 nm,  $\Delta\epsilon$  = -0.110.

The compound is in every respect identical with that obtained by resolution of the racemate; treated with CH<sub>3</sub>I, as described above, it gave (2*R*,3*R*,5*R*)-*c*-2-methyl-*r*-5-[(dimethylamino)methyl]-1,3-oxathiolane *t*-3-oxide methiodide ((-)-1):  $[\alpha]^{20}_D$  -48.0° (EtOH).

The second fraction (*R<sub>f</sub>* 0.26) was (2*R*,3*S*,5*R*)-*c*-2-methyl-*r*-5-[(dimethylamino)methyl]-1,3-oxathiolane *c*-3-oxide ((+)-8): yield 0.25 g;  $[\alpha]^{20}_D$  +8.0° (EtOH); CD (EtOH)  $\lambda$  236 nm,  $\Delta\epsilon$  = -0.191. It shows the same IR and <sup>1</sup>H NMR spectra as the racemate.<sup>5</sup>

(2*S*,3*S*,5*S*)-*c*-2-Methyl-*r*-5-[(dimethylamino)methyl]-1,3-oxathiolane *t*-3-Oxide ((+)-3). With the same procedure described for (-)-3 and starting from (-)-7, we obtained (+)-3, (+)-1, and (-)-8. (2*S*,3*S*,5*S*)-*c*-2-Methyl-*r*-5-[(dimethylamino)methyl]-1,3-oxathiolane *t*-3-oxide ((+)-3):  $[\alpha]^{20}_D$  +108.3° (EtOH); CD (EtOH)  $\lambda$  243 nm,  $\Delta\epsilon$  = +0.118.

The compound is in every respect identical with that obtained by resolution of the racemate; treated with CH<sub>3</sub>I as described above, it gave (2*S*,3*S*,5*S*)-*c*-2-methyl-*r*-5-[(dimethylamino)methyl]-1,3-oxathiolane *t*-3-oxide ((+)-1):  $[\alpha]^{20}_D$  +47.7° (EtOH).

(2*S*,3*R*,5*S*)-*c*-2-Methyl-*r*-5-[(dimethylamino)methyl]-1,3-oxathiolane *c*-3-oxide ((-)-8):  $[\alpha]^{20}_D$  -7.6° (EtOH); CD (EtOH)  $\lambda$  236 nm,  $\Delta\epsilon$  = +0.164. The compound shows IR and

<sup>1</sup>H NMR spectra identical with those of the enantiomer.

(2*R*,3*S*,5*R*)-*c*-2-Methyl-*r*-5-[(dimethylamino)methyl]-1,3-oxathiolane *c*-3-Oxide Methiodide ((+)-9). Using the same procedure described for (-)-1 and starting from (+)-8, we obtained compound (+)-9 in 90% yield: mp 152–154 °C (lit.<sup>5</sup> mp 165–168 °C for the racemate);  $[\alpha]^{20}_D$  +29.6° (EtOH); CD (EtOH)  $\lambda$  243 nm;  $\Delta\epsilon$  = -0.127. The IR and <sup>1</sup>H NMR spectra are identical with those of the racemate.

In the same way, starting from (-)-8, we obtained (2*S*,3*R*,5*S*)-*c*-2-methyl-*r*-5-[(dimethylamino)methyl]-1,3-oxathiolane *c*-3-oxide methiodide ((-)-9) in 90% yield: mp 153–154 °C;  $[\alpha]^{20}_D$  -29.0° (EtOH); CD (EtOH)  $\lambda$  243 nm;  $\Delta\epsilon$  = +0.144. IR and <sup>1</sup>H NMR spectra are identical with those of the enantiomer.

(2*R*,5*R*)-*cis*-2-Methyl-5-[(dimethylamino)methyl]-1,3-oxathiolane 3,3-Dioxide ((-)-4). To a sample of 1.0 g of (-)-3 (or (+)-8) in CH<sub>3</sub>COOH (5 mL) was added 2.5 mL of 30% H<sub>2</sub>O<sub>2</sub>, and the solution was left at room temperature for 24 h. The reaction mixture was made alkaline with NaHCO<sub>3</sub> and extracted with CHCl<sub>3</sub> to give 0.8 g of an oil, which was purified from some starting material through column chromatography, with the same eluent as used for (-)-3: yield 0.65 g;  $[\alpha]^{20}_D$  -42.0° (EtOH). The IR and <sup>1</sup>H NMR spectra are identical with those of the racemate.

In the same way, starting from (+)-3 (or (-)-8), we obtained (2*S*,5*S*)-*cis*-2-methyl-5-[(dimethylamino)methyl]-1,3-oxathiolane 3,3-dioxide ((+)-4):  $[\alpha]^{20}_D$  +41.2° (EtOH). IR and <sup>1</sup>H NMR spectra are identical with those of the enantiomer.

(2*R*,5*R*)-*cis*-2-Methyl-5-[(dimethylamino)methyl]-1,3-oxathiolane 3,3-Dioxide Methiodide ((-)-2). Using the same procedure as described for (-)-1, and starting from (-)-4, we obtained compound (-)-2 in 90% yield: mp 201–202 °C (lit.<sup>5</sup> mp 178–180 °C for the racemate);  $[\alpha]^{20}_D$  -12.5° (EtOH). IR and <sup>1</sup>H NMR spectra are identical with those of the racemate.

In the same way, starting from (+)-4, we obtained (2*S*,5*S*)-*cis*-2-methyl-5-[(dimethylamino)methyl]-1,3-oxathiolane 3,3-dioxide methiodide ((+)-2) in 90% yield: mp 200–202 °C;  $[\alpha]^{20}_D$  +11.9° (EtOH). IR and <sup>1</sup>H NMR spectra are identical with those of the enantiomer.

**Pharmacology.** The protocols used to obtain the results shown in Table I on guinea pig ileum and frog rectus abdominis have been previously reported.<sup>4</sup>

**Acknowledgment.** We thank Cristina Bellucci for her excellent technical assistance.

**Registry No.** (±)-1, 109280-12-8; (+)-1, 109280-06-0; (-)-1, 109280-05-9; (±)-2, 98311-68-3; (+)-2, 109280-11-7; (-)-2, 109280-10-6; (±)-3, 109280-01-5; (+)-3, 109280-03-7; (-)-3, 109280-02-6; (+)-4, 109280-09-3; (-)-4, 109280-14-0; (+)-5, 109361-01-5; (-)-5, 109361-02-6; (+)-6, 109361-03-7; (+)-7, 103066-62-2; (-)-7, 103066-64-4; (+)-8, 109280-04-8; (-)-8, 109280-07-1; (±)-9, 109280-13-9; (+)-9, 109361-04-8; (-)-9, 109280-08-2.

## Additions and Corrections

1987, Volume 30

**P. W. Erhardt:** In Search of the Digitalis Replacement.

Page 233. Drug 4 (dopexamine) should not be included in Table I since it is predominantly a  $\beta_2$ -adrenergic receptor agonist and DA<sub>1</sub>-dopaminergic receptor agonist with only very weak activity at  $\beta_1$ -adrenergic receptors.