# Synthesis and Monoamine Transporter Binding Properties of 2,3-Diaryltropanes

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Synthetic procedures were developed for the synthesis of  $2\beta$ ,  $3\beta$ - and  $2\alpha$ ,  $3\alpha$ -diaryltropanes. These compounds are analogues of the 3-aryltropane- $2\beta$ -carboxylic acid methyl ester class of monoamine uptake inhibitors, where the  $2\beta$ -carbomethoxy group has been replaced by an aryl group. The compounds were evaluated for inhibition of radioligand binding at the dopamine, norepinephrine, and serotonin transporters (DAT, NET, and 5-HTT, respectively). The results showed that the replacement of the  $2\beta$ -carbomethoxy group in the 3-aryltropane class with a  $2\beta$ -aryl group led to compounds possessing very similar monoamine transporter binding properties. However, the  $2\beta$ ,  $3\beta$ -diaryltropanes tended to be more potent at the DAT and more selective for the DAT relative to the NET and 5-HTT. One of the most interesting compounds was  $3\beta$ -(4-methylphenyl)- $2\beta$ -(4-methylphenyl)tropane (**3d**), which showed an IC<sub>50</sub> of 1.23 nM at the DAT with 289- and 185-fold selectivity for the DAT relative to the NET and 5-HTT. The  $2\alpha$ ,  $3\alpha$ -diaryltropanes were much less potent at all three transporters than  $2\beta$ ,  $3\beta$ -diaryltropanes.

Cocaine (1) addiction is a significant socioeconomic problem of our times. Evidence of cocaine addiction being a disease of the brain with specific neurobiological characteristics<sup>1,2</sup> necessitates development of effective therapies to treat cocaine addiction. Cocaine has been shown to block the reuptake of dopamine (DA), serotonin (5-HT), and norepinephrine (NE) as well as to exert effects on the cholinergic, muscarinic, and  $\sigma$  receptors and sodium channels.<sup>3,4</sup> Results from animal studies suggest that the dopamine transporter (DAT) is a key target (receptor) for cocaine regarding the reinforcing effects of the drug.<sup>3,4</sup> Thus, compounds selective for the DAT relative to the norepinephrine transporter (NET) and serotonin transporter (5-HTT) are of particular interest as potential pharmacotherapies to treat cocaine addiction. A number of studies have been directed toward the characterization of the binding site on the DAT with the hope that the information would aid in the discovery of potential pharmacotherapies for treating cocaine addiction.<sup>3,5-8</sup> Many of these studies have been directed toward the 3-phenyltropane class of compounds where  $3\beta$ -phenyltropane- $2\beta$ -carboxylic acid methyl ester (2a, WIN 35,065-2) served as the lead compound. In this study, we describe the syntheses of  $2\beta$ ,  $3\beta$ - and  $2\alpha$ ,  $3\alpha$ -diaryltropanes (**3a**-**g** and **4a**-**f**, respectively) and report that some analogues show high potency for the DAT combined with high selectivity relative to the NET and 5-HTT. These compounds can be viewed as structures where the  $2\beta$ -carbomethoxy group present in 2a has been replaced by a phenyl or substituted phenyl ring. Preliminary results from some of these studies have been reported.<sup>9</sup>



CH3~

CO<sub>2</sub>CH<sub>3</sub>

CO<sub>2</sub>R

with the appropriate 2,3-diaryltrop-2-enes (**5a**-**g**), are shown in Scheme 1. Catalytic reduction of **5a** or **5b** in methanol using 5% palladium on carbon gave exclusively the  $2\alpha$ , $3\alpha$ -diaryltropanes **4a** and **4b**, respectively. No reduction conditions were found that would directly convert **5a** or **5b** to the  $2\beta$ , $3\beta$ -diaryltropanes **3a** and **3b**, respectively. Fortunately, we found that catalytic reduc-

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Scheme  $1^a$ 



<sup>a</sup> Reagents: (a) C<sub>6</sub>H<sub>5</sub>OCOCl, CH<sub>2</sub>Cl<sub>2</sub>, NaHCO<sub>3</sub>; (b) H<sub>2</sub>, Pd/C, CH<sub>3</sub>OH; (c) LiAlH<sub>4</sub>, (C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>O; (d) chromatography separation.

#### Scheme $2^a$



<sup>*a*</sup> Reagents: (a)  $(CF_3SO_2)_2NC_6H_4$ ,  $NaN[Si(CH_3)_3]_2$ , THF; (b) *p*-XC<sub>6</sub>H<sub>4</sub>B(OH)<sub>2</sub>, Pd[P(C<sub>6</sub>H<sub>5</sub>)\_3]\_4, CsF, DEM; (c) (i) 0.5 N KOH followed by 1 N HCl, (ii)  $(C_6H_5O_2PON_3, (C_2H_5)_3N$ , toluene; (d)  $C_2H_5OH$ , reflux 8 h; (e) reflux with 19% HCl for 1 h; (f) aryl MgBr,  $(C_2H_5)_2O$ ; (g) concentrated HBr, reflux, 15 min; (h)  $(CF_3SO_2)_2NC_6H_4$ ,  $NaN[Si(CH_3)_3]_2$ , THF.

tion of the *N*-phenoxycarbonyl-protected analogues **6a**–**g**, followed by lithium aluminum hydride reduction to convert the urethane to the *N*-methyl group, gave a mixture of the  $2\beta$ , $3\beta$ - and  $2\alpha$ , $3\alpha$ -isomers **3** and **4**, which could be readily separated by chromatography. The urethanes **6a**–**g** were obtained by N-demethylation of **5a**–**g** with phenyl chloroformate. The relative stereo-chemistry of each compound was determined by analyses of the <sup>1</sup>H NMR spectra.

The 2,3-diaryltrop-2-enes  $(5\mathbf{a}-\mathbf{g})$  needed to prepare  $3\mathbf{a}-\mathbf{h}$  and  $4\mathbf{a}-\mathbf{g}$  were synthesized starting with 2-carbomethoxy-3-tropinone (7) as outlined in Scheme 2.<sup>10,11</sup> The addition of *N*-phenyltrifluoromethanesulfonamide to a tetrahydrofuran solution of 7 containing sodium bis-

(trimethylsilyl)amide afforded the triflate 8. Reaction of 8 with phenyl- or 4-methylphenylboronic acid in refluxing diethoxymethane (DEM) using tetrakis(triphenylphosphine)palladium(0) as catalyst followed by chromatographic purification gave 3-phenyl- or 3-(4methylphenyl)-2-tropenes 9a or 9b in 88% and 89% yields, respectively. Hydrolysis of 9a and 9b with 0.5 N potassium hydroxide solution followed by acidification to pH 6 gave the corresponding carboxylic acid, which was treated with diphenylphosphoryl azide in toluene containing triethylamine. The resulting intermediate isocyanate 10a or 10b was refluxed in ethanol to afford the corresponding urethane, which was hydrolyzed with 19% hydrochloride acid to give the desired (*R*)-2Table 1. Monoamine Transporter Binding Properties of 2,3-Diaryltropanes



						IC <sub>50</sub> , nM (K <sub>i</sub> , nM)			
,	37	37	7			DAT	NET	5-HTT	
compd	X	Ŷ	Z	isomer	structure	[ <sup>9</sup> H]WIN 35,428	[ <sup>9</sup> H]Nisoxetine	[ <sup>3</sup> H]paroxetine	
cocaine						89.1	3300 (1990)	1050 (45)	
$2a^a$	Н			$2\beta, 3\beta$	Α	$23\pm5$	$920 \pm 70~(550 \pm 44)$	$1960 \pm 61(178 \pm 6)$	
$2\mathbf{b}^a$	$CH_3$			$2\beta, 3\beta$	Α	$1.7\pm0.3$	$60 \pm 1  (36 \pm 1)$	$240 \pm 27~(23 \pm 3)$	
$14^{a}$	$CH_3$	Η	Η	2α,3α	Α	$23.4 \pm 4.2$	$3850 \pm 1270~(1930 \pm 63)$	>2000	
3a	Н	Η	Η	$2\beta, 3\beta$	В	$12.6\pm1.9$	$920 \pm 150~(550 \pm 89)$	$21000 \pm 3300 \ (1900 \pm 300)$	
4a	Η	Н	Η	2α,3α	В	$690\pm37$	$1040 \pm 41~(626 \pm 24)$	$41000 \pm 5300  (3700 \pm 481)$	
3b	$CH_3$	Η	Η	$2\beta, 3\beta$	В	$1.96\pm0.08$	$480 \pm 86 \ (280 \pm 51)$	$1100\pm83(100\pm7)$	
<b>4b</b>	$CH_3$	Η	Η	2α,3α	В	$430\pm59$	$4850 \pm 72 \ (2920 \pm 43)$	$16000 \pm 3700  (1500 \pm 340)$	
3c	н	$CH_3$	Η	$2\beta, 3\beta$	В	$22.4\pm5.5$	$6100 \pm 1100~(3700 \pm 640)$	$45000 \pm 9500~(4100 \pm 860)$	
<b>4c</b>	н	$CH_3$	Η	2α,3α	В	$540\pm57$	$4700 \pm 200~(2800 \pm 120)$	$11000 \pm 2600~(1000 \pm 240)$	
3d	$CH_3$	$CH_3$	Η	$2\beta, 3\beta$	В	$1.35\pm0.34$	$780 \pm 84~(390 \pm 42)$	$1010 \pm 20~(250 \pm 5)$	
<b>4d</b>	$CH_3$	$CH_3$	Η	2α,3α	В	$340\pm9$	$13000 \pm (7800 \pm$	$10000 \pm 1100~(910 \pm 100)$	
3e	$CH_3$	$CH_3O$	Η	$2\beta, 3\beta$	В	$1.23\pm0.13$	$282 \pm 44~(191 \pm 22)$	$1669 \pm 167~(410 \pm 41)$	
<b>4e</b>	$CH_3$	$CH_3O$	Η	2α,3α	В	$238\pm32$	NT	$1530 \pm 255~(376 \pm 63)$	
3f	$CH_3$	$CH_3O$	$CH_3O$	$2\beta, 3\beta$	В	$23.3\pm0.8$	$10000 \pm 1400~(6000 \pm 840)$	$13700\pm7100~(1250\pm646)$	
<b>4f</b>	$CH_3$	$CH_3O$	$CH_3O$	2α,3α	В	$980\pm48$	$78000 \pm 2800 \ (46000 \pm 16000)$	$16200 \pm 1700 \ (1470 \pm 154)$	
3g	$CH_3$	F	Η	$2\beta, 3\beta$	В	$0.90\pm0.12$	$132 \pm 25  (61 \pm 13)$	$100 \pm 6.0 \; (25 \pm 2)$	

<sup>a</sup> Taken from ref 12.

tropinone **11a** or **11b** in 62% and 55% yields, respectively, from **7**. Addition of the appropriate arylmagnesium bromide to **11a** or **11b** gives the addition products **12a-c**, which were dehydrated with concentrated hydrobromic acid to yield the 2,3-diaryltropenes **5a-c**. Tropenes **5d-g** as well as **5a** were prepared by converting **11a** and **11b** to triflates **13a** and **13b** using *N*phenyltrifluoromethanesulfonamide and sodium bis-(trimethylsilyl)amide. Reaction of **13a** or **13b** with the appropriate boronic acid in diethoxymethane using tetrakis(triphenylphosphine)palladium(0) gave the desired tropenes **5a** and **5d-g**.

#### Biology

The IC<sub>50</sub> values for the inhibition of radioligand binding at the dopamine, serotonin, and norepinephrine transporters for  $3\mathbf{a}-\mathbf{g}$  and  $4\mathbf{a}-\mathbf{f}$  are listed in Table 1. For comparison, the previously reported IC<sub>50</sub> values for cocaine (1), **2a**, **2b** (RTI-32), and  $3\alpha$ -(4-methylphenyl)tropane-2 $\alpha$ -carboxylic acid methyl ester (14) are also listed.<sup>12</sup> The binding affinities at the dopamine, sero-



tonin, and norepinephrine transporters were determined via competitive binding assays using previously reported procedures.<sup>13,14</sup>

## **Results and Discussion**

Studies from our laboratory as well as from others have shown that replacing the  $2\beta$ -carbomethoxy group present in **2a** and other  $3\beta$ -aryl substituted analogues with a carboxamido, heterocyclic, olefinic, keto, or alkyl group has very little effect on binding affinity at the DAT.<sup>5</sup> In the present study, we report the effect of replacing the  $2\beta$ -carbomethoxy group with various aryl groups. Replacement of the  $2\beta$ -carbomethoxy group of **2a** with a  $3\beta$ -phenyl group to give **3a** results in an essential 2-fold increase in binding affinity (12.6 vs 23 nM IC\_{50}). In the case of the  $3\beta$ -(4'-methylphenyl) analogue **2b**, replacing the  $2\beta$ -carbomethoxy group with a  $2\beta$ -phenyl ring had almost no effect on binding affinity  $(1.96 \text{ vs } 1.7 \text{ nM IC}_{50})$ . The addition of a 4-methyl group to 2a to give 3c or the addition of 4-methyl, 4-methoxy, or 4-fluoro group to 3b to give 3d, 3e, and 3g, respectively, had very little effect on binding affinity to the DAT. The most potent compound was the 4-fluoro analogue 3g, which possessed a 0.9 nM IC<sub>50</sub> value at the DAT. Results for the  $2\alpha$ ,  $3\alpha$  analogues were quite different from those of the  $2\beta$ ,  $3\beta$  analogues. For example, replacement of the  $2\alpha$ -carbomethoxy group in the  $2\alpha$ ,  $3\alpha$  compound **14** with a  $3\alpha$ -phenyl group to give **4b** results in an 18-fold loss in binding affinity at the DAT (430 vs 23.4 nM IC<sub>50</sub>). The IC<sub>50</sub> values for the  $2\alpha$ ,  $3\alpha$ -(4-methylphenyl)tropanes (4b-f) ranged from 340 to 980 nM. The  $2\alpha$ ,  $3\alpha$ -diphenyl analogue **4a** possessed an IC<sub>50</sub> of 690 nM. None of the compounds evaluated have appreciable affinity at the 5-HTT and NET. In fact, compounds **3b**, **3d**, and **3e** with  $IC_{50}$  values of 1.96, 1.35, and 1.23 nM, respectively, at the DAT, with  $K_i$  values of 280, 390, and 191 nM at the NET and 100, 250, and 410 nM at the 5-HTT, respectively, are selective for the DAT relative to the NET and 5-HTT. Thus, even though the replacement of the carbomethoxy group of the 3-phenyltropanes **2a**,**b** with a  $2\beta$ -aryl group to give 3a-g had only a small effect on binding to the DAT. the overall effects of binding at the DAT, NET, and 5-HTT resulted in compounds with increased potency at the DAT and selectivity at the DAT relative to the NET and 5-HTT. The high potency and DAT selectivity of the  $2\beta$ ,  $3\beta$ -aryltropanes increase interest in this class of compounds as potential pharmacotherapies for co-caine addiction.

In summary, we developed procedures for the synthesis of  $2\beta$ ,  $3\beta$ -diaryltropanes. The compounds can be viewed as analogues of **2a** and **2b** where the  $2\beta$ -carbomethoxy group has been replaced by a substituted phenyl ring. The compounds having the  $2\beta$ -aryl group tended to be more potent at the DAT than the corresponding  $2\beta$ -carbomethoxy analogues and more selective relative to binding at the NET and 5-HTT. The  $2\beta$ -(4-methylphenyl)tropane (**3d**) was the most potent and selective analogue.

### **Experimental Section**

Commercial reagents and solvents were used as received. All reactions were run under dry N<sub>2</sub> in oven-dried glassware. The HCl (1 M), NaOH (6 M), Na<sub>2</sub>CO<sub>3</sub> (saturated), NH<sub>4</sub>Cl (saturated), and NaCl (saturated) used in various procedures refer to aqueous solutions. All organic solvents used, unless otherwise mentioned, were either distilled before use or were purchased anhydrous and used directly. Reactions were monitored by TLC on silica gel GF plates ( $0.25 \,\mu m$  film thickness). Preparative separations were performed using flash column chromatography on silica gel (grade 62, 60-200 mesh) and PTLC on 20 cm  $\times$  20 cm silica gel GF plates; band elution was monitored using a hand-held UV lamp. Optical rotations were measured on an AutoPol III polarimeter, purchased from Rudolf Research. Elemental analyses were performed by Atlantic Microlab, Norcross, GA. Melting points were uncorrected. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were measured in CDCl<sub>3</sub> at 300, 250, 62.5, and 75 MHz, respectively, and were referenced to internal (CH<sub>3</sub>)<sub>4</sub>Si, as the free bases.

(R)-2-Carbomethoxy-3-tropinone 3-Triflate (8). To a solution of (R)-(+)-2-carbomethoxy-3-tropinone (7, 7.08 g, 36 mmol) in dry THF (200 mL) at -78 °C was added dropwise NaN(TMS)2 (1 M solution in THF, 43 mL) in 10 min. The mixture was stirred for 30 min, the mixture was allowed to warm to 0 °C, and N-phenyltrifluoromethanesulfonamide (15.4 g, 43 mmol) was added portionwise in 10 min. The reaction mixture was stirred at 0 °C for 1 h and then at room temperature for 4 h. After removal of the solvents, the residue was taken up with water (50 mL) and extracted with EtOAc  $(4 \times 100 \text{ mL})$ . The EtOAc extracts were washed with brine (20 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated. The crude product was purified by flash column chromatography on SiO<sub>2</sub>, using EtOAc followed by 5% Et<sub>3</sub>N in EtOAc as eluent to afford 8 as an amber oil (10.94 g, 92%):  $[\alpha]^{23}_{D}$  +9.86° (c 7.25, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  3.94 (d, J = 4.9 Hz, 1H), 3.82 (s, 3H), 3.43 (m, 1H), 2.85 (dd, J = 4.6, 18.7 Hz, 1H), 2.40 (s, 3H), 2.25–2.10 (m, 2H), 2.05–1.93 (m, 2H), 1.61 (m, 1H);  $^{13}$ C NMR (CDCl<sub>3</sub>)  $\delta$ 163.7, 149.0, 125.2, 118.2 (q, J = 317.8 Hz), 60.0, 57.4, 52.0, 34.8, 34.6, 33.0, 30.0. Anal. (C<sub>11</sub>H<sub>14</sub>F<sub>3</sub>NO<sub>5</sub>S) C, H, N.

(*R*)-2-Carbomethoxy-3-phenyl-2-tropene (9a). A mixture of compound 8 (3.29 g, 10 mmol), phenylboronic acid (1.46 g, 12 mmol), Pd(PPh<sub>3</sub>)<sub>4</sub> (0.035 g, 0.30 mmol), and cesium fluoride (3.34 g, 22 mmol) in DEM (20 mL) was stirred at 60 °C for 2 h. The reaction mixture was diluted with ether (200 mL), and the resulting solid was separated by filtration. The ether extracts were washed with H<sub>2</sub>O (10 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated. The resulting dark oil was purified by flash column chromatography (SiO<sub>2</sub>, 5% Et<sub>3</sub>N in EtOAc) to give **9a** as a light-yellow oil (2.27 g, 88%): [ $\alpha$ ]<sup>26</sup>D -61.4° (*c* 2.87, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.36 -7.24 (m, 3H), 7.15 -7.11 (m, 2H), 3.87 (d, *J* = 5.3 Hz, 1H), 3.47 (s, 3H), 3.36 (m, 1H), 2.77 (dd, *J* = 4.8, 18.9 Hz, 1H), 2.46 (s, 3H), 2.30 - 2.10 (m, 2H), 2.10 - 1.94 (m, 2H), 1.66 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  143.6, 141.1, 130.4, 127.9, 127.3, 126.6, 60.2, 57.4, 51.2, 37.4, 35.9, 34.2, 30.1. Anal. (C<sub>16</sub>H<sub>19</sub>NO) C, H, N.

(*R*)-2-Carbomethoxy-3-(4-methylphenyl)-2-tropene (9b). A mixture of compound 8 (4.95 g, 15 mmol), 4-methylphenylboronic acid (2.30 g, 11 mmol), Pd(PPh<sub>3</sub>)<sub>4</sub> (0.52 g, 0.045 mmol), and cesium fluoride (3.0 g, 33.0 mmol) in DEM (30 mL) was stirred at 60 °C for 2 h. The solvent was evaporated, and the reaction mixture was diluted with ether (200 mL). The resulting solid was separated by filtration, and the solvent was evaporated. The dark oil was purified by flash column chromatography (SiO<sub>2</sub>, 5% Et<sub>3</sub>N in EtOAc) to give **9b** as a light-yellow oil (3.61 g, 89%):  $[\alpha]^{23}{}_{D}$  –72.5° (*c* 3.68, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.13–7.09 (m, 2H), 7.03–7.00 (m, 2H), 3.83 (m, 1H), 3.48 (s, 3H), 3.33 (m, 1H), 2.73 (dd, J = 4.7, 18.8 Hz, 1H), 2.43 (s, 3H), 2.33 (s, 3H), 2.23–2.10 (m, 2H), 2.09–1.90 (m, 2H), 1.63 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  168.4, 143.3, 138.0, 136.9, 130.0, 128.5, 126.5, 60.2, 57.2, 57.1, 37.2, 35.7, 34.1, 30.0, 21.0. Anal. (C<sub>17</sub>H<sub>21</sub>NO<sub>2</sub>) C, H, N.

(R)-3-Phenyl-2-tropinone (11a). Methyl ester 9a (2.06 g, 8.01 mmol) was heated to reflux in KOH solution (0.5 N, 32 mL). After 30 min, the mixture was acidified to pH 6 using HCl solution (1 N). After removal of solvents, the resulting residue was extracted with absolute EtOH (3  $\times$  40 mL). Evaporation of EtOH gave the acid as a white solid. The acid was stirred with diphenylphosphoryl azide (2.64 g, 9.61 mmol) and  $Et_3N$  (3.35 mL, 24.03 mmol) in toluene (25 mL) at room temperature. After 30 min, the reaction mixture was maintained at 90 °C for another 30 min and then heated to reflux briefly. Absolute EtOH (10 mL) was added, and the reaction mixture was refluxed for 8 h. The residue obtained after removal of solvents was refluxed in 19% HCl solution (10 mL) for 1 h, basified to pH >9 with 6 N NaOH solution, and extracted with  $CH_2Cl_2$  (4 × 50 mL). The  $CH_2Cl_2$  extracts were washed with H<sub>2</sub>O (10 mL) and brine (10 mL) and dried (Na<sub>2</sub>- $SO_4$ ), and the solvents were removed. The resulting dark oil was purified by flash column chromatography (SiO<sub>2</sub>, 5-10%MeOH in EtOAc/Et<sub>3</sub>N, 90:0.5) to give 11a as a white solid (1.06 g, 62%): mp 104.0–105.5 °C;  $[\alpha]^{\bar{2}4}_{D}$  +29.8° (c 0.63, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 7.36-7.22 (m, 3H), 7.17-7.13 (m, 2H), 3.59 (dd, J = 8.1, 11.8 Hz, 1H), 3.46 (m, 2H), 2.46 (s, 3H), 2.44– 2.20 (m, 3H), 2.12 (m, 1H), 2.00–1.80 (m, 2H);  $^{13}\mathrm{C}$  NMR  $(CDCl_3) \delta 208.4, 138.3, 129.0, 128.5, 127.0, 71.8, 50.2, 49.3,$ 40.2, 37.9, 26.6. Anal. (C<sub>14</sub>H<sub>17</sub>NO) C, H, N.

(R)-3-(4-Methylphenyl)-2-tropanone (11b). Methyl ester 9b (1.42 g, 5.24 mmol) was heated to reflux in KOH solution (0.5 N, 21 mL). After 30 min, the mixture was acidified to pH 6 using HCl solution (1 N). After removal of solvents, the resulting residue was extracted with absolute EtOH  $(3 \times 40)$ mL). The solvent was evaporated to produce the acid as a white solid. The acid was stirred with diphenylphosphoryl azide (1.73 g, 6.29 mmol) and Et<sub>3</sub>N (2.2 mL, 15.7 mmol) in toluene (20 mL) at room temperature. After 30 min, the reaction mixture was maintained at 90 °C for another 30 min and then heated to reflux briefly. Absolute EtOH (10 mL) was added, and the reaction mixture was refluxed for 10 h. The residue obtained after removal of solvents was refluxed in 19% HCl solution (10 mL) for 1 h, basified to pH  $>\!9$  with 6 N NaOH solution, and extracted with  $CH_2Cl_2$  (4 × 50 mL). The  $CH_2Cl_2$  extracts were washed with H<sub>2</sub>O (10 mL) and brine (10 mL) and dried (Na<sub>2</sub>SO<sub>4</sub>), and the solvents were removed. The resulting dark oil was purified by flash column chromatography (SiO<sub>2</sub>, 5-10%MeOH in EtOAc/Et\_3N, 90:0.5) to give 11b as a white solid (0.65 g, 55%): mp 100–101.5 °C; [ $\alpha$ ]<sup>24</sup><sub>D</sub> +20.2° (*c* 0.59, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.12 (m, 2H), 7.02 (m, 2H), 3.53 (dd, J = 8.1, 11.8 Hz, 1H), 3.42 (m, 2H), 2.47 (s, 3H), 2.40-2.15 (m, 3H), 2.30 (s, 3H), 2.07 (m, 1H), 1.85 (2H);  $^{13}\mathrm{C}$  NMR (CDCl\_3)  $\delta$  208.3, 136.3, 135.2, 129.0, 128.7, 71.7, 60.0, 48.7, 40.0, 37.8, 26.4, 20.9. Anal. (C<sub>15</sub>H<sub>19</sub>NO) C, H, N.

(*R*)-2,3-Diphenyl-2-tropinol (12a). To a solution of ketone 11a (1.45 g, 6.75 mmol) in ethyl ether (35 mL) was added phenylmagnesium bromide solution (3 M in ether, 6.75 mL) at room temperature. The reaction mixture was stirred at room temperature for 11 h and diluted with ether (100 mL), and the reaction was quenched with H<sub>2</sub>O (50 mL). The aqueous layer was extracted with ether ( $3 \times 50$  mL). The ether extracts were washed with H<sub>2</sub>O (10 mL) and dried (Na<sub>2</sub>SO<sub>4</sub>), and the solvents were removed. The resulting residue was purified by flash column chromatography (SiO<sub>2</sub>, hexane/EtOAc followed

by EtOAc, then 5% MeOH in EtOAc/Et<sub>3</sub>N, 99.5:0.5) to give the desired alcohol **12a** as a white solid (0.67 g, 34%) (92% based on recovered ketone) (0.908 g, 63%): mp 92.5–94.0 °C;  $[\alpha]^{23}_{D}$ –137.3° (*c* 0.555, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.75–7.64 (m, 2H), 7.20–7.10 (m, 6H), 6.95–6.90 (m, 2H), 3.43 (m, 1H), 3.27 (m, 1H), 3.15 (dd, *J* = 5.3, 13.7 Hz, 1H), 2.50 (m, 1H), 2.41 (s, 3H), 2.35–2.00 (m, 3H), 1.89 (s, 1H), 1.82 (m, 1H), 1.67 (ddd, *J* = 3.1, 5.3, 13.0 Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  144.8, 139.9, 129.6, 128.4, 127.2, 126.7, 126.3, 126.2, 76.2, 72.9, 61.4, 46.2, 41.5, 36.6, 25.2, 22.1.

(R)-3-(4-Methylphenyl)-2-phenyl-2-tropinol (12b). To a solution of ketone 11b (0.84 g, 3.67 mmol) in ethyl ether (25 mL) was added phenylmagnesium bromide solution (3 M in ether, 3.67 mL) at room temperature. The reaction mixture was stirred at room temperature for 11 h and diluted with ether (100 mL), and the reaction was guenched with  $H_2O$  (50 mL). The aqueous layer was extracted with ether  $(3 \times 50 \text{ mL})$ . The ether extracts were washed with H<sub>2</sub>O (10 mL) and dried (Na<sub>2</sub>SO<sub>4</sub>), and the solvents were removed. The resulting residue was purified by flash column chromatography (SiO<sub>2</sub>, hexane/EtOAc followed by EtOAc, then 5% MeOH in EtOAc/ Et<sub>3</sub>N, 99.5:0.5) to give the desired alcohol 12b as a white solid (0.47 g, 42%, 89%) based on recovered ketone (0.448 g, 53%): mp 156.0–157.4 °C;  $[\alpha]^{23}$ <sub>D</sub> –163° (*c* 0.655, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.75–7.71 (m, 2H), 7.14–7.08 (m, 3H), 6.88 (d,  $J \simeq$ 8.0 Hz, 2H), 6.74 (d,  $J \cong$  8.0 Hz, 2H), 3.36 (m, 1H), 3.22 (m, 1H), 3.03 (dd, J = 5.4, 13.7 Hz, 1H), 2.41 (m, 1H), 2.33 (s, 3H), 2.26-2.00 (m, 3H), 2.22 (s, 3H), 1.77 (s, 1H), 1.74 (m, 1H), 1.58 (ddd, J = 3.1, 5.4, 13.0 Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  145.0, 136.8, 135.8, 129.5, 128.5, 128.1, 126.8, 126.3, 76.3, 73.0, 61.6, 46.1, 41.6, 37.0, 25.4, 22.1, 20.9. Anal. (C<sub>21</sub>H<sub>25</sub>NO) C, H, N.

(R)-3-Phenyl-2-(4'-methylphenyl)-2-tropinol (12c). To a solution of 11a (860 mg, 4 mmol) in ether (30 mL) at -30 °C was added dropwise a solution of 4-methylphenylmagnesium bromide (1 m, 8 mL) under N2 in 5 min. The mixture was stirred at -30 °C for 1 h, then warmed to 0 °C. The mixture was diluted with ether (100 mL), and the reaction was quenched with H<sub>2</sub>O (50 mL). The aqueous layer was extracted further with ether (50 mL  $\times$  3). Ether layers were combined, washed with H<sub>2</sub>O (10 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated. The crude residue was purified by flash column chromatography (SiO<sub>2</sub>, hexane/EtOAc, 2:1, then EtOAc, then 2% Et<sub>3</sub>N in EtOAc) to afford **12c** (0.78 g, 63%) and starting material (0.20 g, 23%): [α]<sup>25</sup><sub>D</sub> -140.5° (*c* 0.22, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.56 (d, J = 8.4 Hz, 2H), 7.08 (m, 3H), 6.89 (m, 4H), 3.35 (m, 1H), 3.21 (d, J = 6.4 Hz, 1H), 3.07 (dd, J = 5.3, 13.5 Hz, 1H), 2.43 (m, 1H), 2.33 (s, 3H), 2.24 (s, 3H), 2.20–2.00 (m, 2H), 1.79–1.67 (m, 2H), 1.55 (m, 2H);  $^{13}\mathrm{C}$  NMR (CDCl<sub>3</sub>)  $\delta$  153.7, 141.8, 140.0, 135.6, 129.6, 129.0, 128.3, 127.4, 127.2, 126.1, 115.1, 73.1, 61.4, 46.1, 41.5, 36.6, 25.2, 22.1, 20.8.

**2,3-Diphenyl-2-tropene (5a).** Alcohol **12a** (631 mg, 2.15 mmol) was refluxed in concentrated HBr (5 mL) for 15 min. The residue obtained after removal of solvents was taken up in saturated NaHCO<sub>3</sub> (10 mL) and extracted with EtOAc (4 × 15 mL). The EtOAc extracts were washed with brine (10 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated to give a yellow oil (580 mg, 98%), which was pure enough for the next step. Purification by flash column chromatography (5% Et<sub>3</sub>N in EtOAc) gave **5a** as a clear oil:  $[\alpha]^{23}_{D} - 277.6^{\circ}$  (c 0.75, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.17–7.05 (m, 6H), 7.02–6.96 (m, 4H), 3.75 (d, J = 5.8 Hz, 1H), 3.54 (m, 1H), 2.83 (dd, J = 4.4, 18.2 Hz, 1H), 2.64 (s, 3H), 2.40–2.11 (m, 3H), 2.05 (m, 1H), 1.80 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  140.7, 140.5, 137.7, 130.3, 129.2, 128.7, 128.0, 127.8, 126.4, 65.1, 58.3, 36.0, 35.8, 33.3, 30.0. Anal. (C<sub>20</sub>H<sub>21</sub>NO) C, H, N.

3-(4-Methylphenyl)-2-phenyl-2-tropene (5b). Alcohol 12b (331 mg, 1.07 mmol) was refluxed in concentrated HBr (3 mL) for 15 min. The reaction mixture was basified to pH >9 using 6 N NaOH and extracted with CH<sub>2</sub>Cl<sub>2</sub> (4 × 15 mL). The CH<sub>2</sub>-Cl<sub>2</sub> extracts were washed with brine (10 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated. The resulting solid was purified by flash column chromatography (SiO<sub>2</sub>, 20% MeOH in EtOAc/Et<sub>3</sub>N, 80: 0.5) to give **5b** as a colorless oil (251 mg, 81%):  $[\alpha]^{23}_{D}-254.1^{\circ}$  (*c* 13.84, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.17–7.05 (m, 3H), 7.05–

6.99 (m, 2H), 6.89 (m, 4H), 3.64 (d, J=5.7 Hz, 1H), 3.43 (m, 1H), 2.76 (dd, J=4.4, 18.0 Hz, 1H), 2.57 (s, 3H), 2.21 (s, 3H), 2.33–1.94 (m, 4H), 1.74 (m, 1H);  $^{13}\mathrm{C}$  NMR (CDCl<sub>3</sub>)  $\delta$  141.3, 138.0, 137.9, 135.7, 129.8, 129.2, 128.6; 128.4, 127.8, 126.0, 65.1, 58.1, 35.95, 35.97, 33.4, 30.2, 21.0.

**3-Phenyl-2-(4-methylphenyl)tropene (5c).** The **12c** (0.52 g, 1.67 mmol) was refluxed in concentrated HBr (4 mL) for 15 min. HBr was evaporated. The residue was taken up by saturated NaHCO<sub>3</sub> and extracted with EtOAc (15 mL × 4). EtOAc was washed with brine (10 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated to give a brownish oil. Purification of crude by flash column chromatography (SiO<sub>2</sub>, 5% Et<sub>3</sub>N in EtOAc) afforded **5c** as a clear oil:  $[\alpha]^{23}_{D} - 224.5^{\circ}$  (c 0.955, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.32–6.86 (m, 9H), 3.61 (d, J = 5.6 Hz, 1H), 3.41 (t, J = 6.3 Hz, 1H), 2.75 (dd, J = 17.3 Hz, 1H), 2.55 (s, 3H), 2.23 (s, 3H), 2.17–1.93 (m, 4H), 1.74 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  141.5, 138.5, 138.3, 135.7, 129.6, 129.1, 128.8, 128.6, 127.7, 126.1, 65.2, 58.2, 36.2, 33.6, 30.4, 21.1.

(R)-3-Phenyl-2-tropinone 2-Triflate (13a). A solution of  $NaN(TMS)_2$  was added slowly (5 min) to the ketone 11a in THF (20 mL) at -78 °C. The reaction mixture was stirred at room temperature for 30 min, then warmed to 0 °C. N-Phenyltrifluoromethanesulfonamide (0.826 g) was added in one portion. The reaction mixture was stirred for 1 h at 0 °C and then at room temperature for 22 h. The reaction was quenched with H<sub>2</sub>O (15 mL) and extracted with EtOAc (3  $\times$ 20 mL). The EtOAc extracts were washed with brine (10 mL) and dried (MgSO<sub>4</sub>). Removal of the solvents gave an amber oil, which was purified by column chromatography (SiO<sub>2</sub>, EtOAc then MeOH/EtOAc/Et<sub>3</sub>N, 5:94:1) to afford 13a as a light-yellow oil (250 mg, 34%):  $[\alpha]^{23}{}_{D}$  +16.7° (c 2.43, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.41–7.26 (m, 5H), 3.50 (d, J = 4.8 Hz, 1H), 3.47 (t, J = 5.5 Hz, 1H), 2.96 (dd, J = 4.5, 17.8 Hz, 1H), 2.55 (s, 3H), 2.27–2.17 (m, 3H), 2.10 (d, J = 17.6 Hz, 1H), 1.67 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 144.9, 135.0, 128.2, 128.0, 127.6, 125.8, 118.0 (q, J = 318.2 Hz), 61.4, 56.5, 35.2, 34.6, 33.9. 30.1.

**2,3-Diphenyl-2-tropene (5a) from 13a.** A mixture of triflate **13a** (95 mg, 0.27 mmol), phenylboronic acid (40 mg, 0.32 mmol), Pd(PPh<sub>3</sub>)<sub>4</sub> (9 mg), and cesium fluoride (90 mg, 0.59 mmol) in DEM (8 mL) was refluxed for 1 h. The solvent was removed, and the resulting residue was purified by flash column chromatography (SiO<sub>2</sub>, 2.5% Et<sub>3</sub>N in EtOAc) to give **5a** as a clear oil (55 mg, 74%). The <sup>1</sup>H NMR spectrum was identical to the compound prepared from **12a**.

(R)-3-(4-Methylphenyl)-2-tropinone 2-Triflate (13b). To a well-stirred hexane-washed suspension of 0.13 g (5.41 mmol) of NaH in THF at -78 °C was added 1.00 g (4.36 mmol) of 8b in 20 mL of THF over 10 min, and the mixture was stirred for 15 min. The mixture was then warmed to room temperature and stirred for 30 min, and 4.65 g (13.0 mmol) of N-phenyltrifluoromethanesulfonamide was added in one portion. The mixture was stirred at room temperature for 2 h. Concentration of the mixture, followed by extraction with ether, resulted in a heavy brown oil, which was purified by column chromatography using hexanes with increasing concentrations of EtOAc and Et<sub>3</sub>N to yield 0.93 g (59%) of 6 as a thick red oil that had the following properties:  $[\alpha]^{23}_{D} + 18.2^{\circ}$  (*c* 0.60, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.18 (s, 4H), 3.50 (d, J = 4.8 Hz, 1H), 3.33 (t, J = 5.5 Hz, 1H), 2.96 (dd, J = 17.8, 4.5 Hz, 1H), 2.54 (s,3H), 2.34 (s, 3H), 2.27–2.17 (m, 3H), 2.10 (d, J = 17.6 Hz, 1H), 1.67 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) & 144.0, 137.3, 131.4, 128.5, 128.3, 128.1, 126.9, 125.0, 119.5, 115.2, 60.8, 59.4, 56.0, 39.5, 37.2, 34.6, 34.1, 33.3, 29.5, 25.9, 20.4. Anal. (C<sub>16</sub>H<sub>18</sub>F<sub>3</sub>-NO<sub>3</sub>S) C, H, N.

**Synthesis of 5d–g.** Compounds **5d–g** were synthesized from triflate **13b** using conditions analogous to that described for the synthesis of **5a** from triflate **13a**.

**2,3-Di**(4-methylphenyl-2-tropene (5d). Yellow oil, 320 mg (84%);  $[\alpha]^{23}{}_{\rm D}$  –72.2° (c 3.75, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  6.90 (m, 8H), 3.60 (d, J = 5.7 Hz, 1H), 3.40 (t, J = 5.8 Hz, 1H), 2.73 (dd, J = 18.7, 4.6 Hz, 1H), 2.55 (s, 3H), 2.26 (s, 3H), 2.24 (s, 3H), 2.20–2.00 (m, 3H), 1.97 (dt, J = 11.6, 2.8 Hz, 1H),

1.74 (m, 1H);  $^{13}\mathrm{C}$  NMR (CDCl\_3)  $\delta$  138.5, 138.3, 138.0, 135.6, 129.3, 129.1, 128.6, 128.5, 128.4, 65.2, 58.1, 36.2, 33.5, 30.7, 21.1, 21.0.

**3-(4-Methylphenyl)-2-(4-methoxyphenyl)-2-tropene (5e).** White semisolid, 380 mg (96%);  $[\alpha]^{23}_{\rm D}-234.0^{\circ}$  (*c* 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  6.92 (m, 6H), 6.70 (d, J = 8.5 Hz, 2H), 3.74 (s, 3H), 3.60 (d, J = 6.0 Hz, 1H), 3.40 (t, J = 6.0 Hz, 1H), 2.73 (dd, J = 18.0, 4.5 Hz, 1H), 2.25 (s, 3H), 2.20–2.00 (m, 3H), 1.96 (dt, J = 9.5, 3.0 Hz, 1H), 1.73 (m, 1H); <sup>13</sup>C NMR  $\delta$  157.9, 139.0, 137.8, 135.6, 133.9, 130.3, 129.1, 128.7, 128.5, 113.3, 65.2, 58.2, 55.0, 36.6, 36.3, 33.5, 30.3, 21.0.

**3-(Methylphenyl)-2-(2,3-dimethoxyphenyl)-2-tropene** (**5f**). Light-yellow oil, 1.15 g (97%);  $[\alpha]^{23}{}_{\rm D}$  –189.1° (*c* 2.17, CHCl<sub>3</sub>); <sup>1</sup>H NMR  $\delta$  (CDCl<sub>3</sub>) 6.92 (m, 4H), 6.71 (d, J = 8.3 Hz, 1H), 6.65 (dd, J = 8.4, 1.7 Hz, 1H), 6.41 (d, J = 1.7 Hz, 1H), 3.82 (s, 3H), 3.65 (d, J = 5.7 Hz, 1H), 3.54 (s, 3H), 3.42 (t, J = 5.7 Hz, 1H), 2.76 (dd, J = 17.6, 4.3 Hz, 1H), 2.54 (s, 3H), 2.34 (s, 3H), 2.20–2.10 (m, 3H), 1.97 (dt, J = 8.7, 2.5 Hz, 1H), 1.75 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  147.9, 147.3, 138.7, 137.8, 135.6, 133.8, 129.4, 128.5, 128.4, 120.8, 113.4, 110.5, 64.9, 58.2, 55.6, 55.4, 36.5, 33.5, 30.1, 20.9.

**3-(4-Methylphenyl)-2-(4-fluorophenyl)-2-tropene (5g).** White semisolid, 365 mg (90%);  $[\alpha]^{23}_{D} - 125.2^{\circ}$  (*c* 2.35, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  6.97–6.92 (m, 4H), 6.88–6.82 (m, 4H), 3.57 (d, *J* = 6.0 Hz, 1H), 3.41 (t, *J* = 5.5 Hz, 1H), 2.74 (dd, *J* = 18.0, 4.0 Hz, 1H), 2.55 (s, 3H), 2.24 (s, 3H), 2.24 (s, 3H), 2.23 (m, 1H), 2.18–2.08 (m, 2H), 1.97 (dt, *J* = 9.5, 3.0 Hz, 1H), 1.74 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  163.1, 159.2, 137.9, 137.3, 137.2, 137.1, 135.7, 130.6, 130.5, 130.1, 128.5, 128.4, 114.8, 114.5, 65.1, 58.0, 36.1, 33.3, 30.1, 20.9.

(R)-N-Phenoxycarbonyl-2,3-diphenyl-2-tropene (6a). A mixture of diphenyltropene 5a (220 mg, 0.80 mmol), phenyl chloroformate (0.40 mL, 0.32 mmol), and NaHCO3 (402 mg, 4.8 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> was stirred at room temperature. After 16 h, the reaction was quenched with saturated NaHCO<sub>3</sub> (10 mL). The aqueous layer was separated and extracted further with EtOAc (3  $\times$  20 mL). The EtOAc extracts were washed with H<sub>2</sub>O (10 mL) and dried (Na<sub>2</sub>SO<sub>4</sub>). The residue obtained after removal of solvents was purified by flash column chromatography (SiO<sub>2</sub>, 20% ether in hexane) to give 6a as a white solid (286 mg, 94%):  $[\alpha]^{23}D - 337.8^{\circ}$  (c 0.97, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 250 MHz)  $\delta$  7.39–6.97 (m, 15H), 4.89 (d, J = 13.1 Hz, 1H), 4.62 (m, 1H), 3.13 (t, J = 13.6 Hz, 1H), 2.55-2.37 (m, 2H), 2.17-1.97 (m, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 152.8, 151.3, 141.6, 141.1, 140.6, 139.6, 139.4, 131.4, 130.3, 129.7, 129.34, 129.26, 128.9, 128.1, 128.0, 127.8, 126.7, 126.5, 125.2, 121.7, 121.6, 119.9, 115.3, 59.2, 59.0, 53.6, 53.4, 39.9, 38.8, 34.3, 30.6, 29.8.

(*R*)-*N*-Phenoxycarbonyl-2-phenyl-3-(4-methylphenyl)-2-tropene (6b). Compound 6b was prepared using a procedure similar to that described for 6a. The compound was obtained as a white semisolid: 296 mg (95%);  $[\alpha]^{23}_{D} - 279.0^{\circ}$ (*c* 0.935, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.40–7.30 (m, 2H), 7.32– 7.10 (m, 7H), 7.00–6.70 (m, 5H), 4.90 (m, 1H), 4.70 (m, 1H), 3.09 (m, 1H), 2.50–2.30 (m, 2H), 2.23 (s, 3H), 2.10–1.90 (m, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  152.7, 151.2, 141.2, 140.6, 139.8, 139.6, 137.5, 136.0, 131.1, 130.0, 129.7, 129.3, 129.2, 128.7, 128.5, 128.0, 127.9, 126.6, 125.2, 121.7, 121.6, 59.2, 58.9, 53.6, 53.3, 39.9, 38.7, 34.2, 33.3, 30.6, 29.7, 20.6.

(*R*)-*N*-Phenoxycarbonyl-2-(4-methylphenyl)-3-phenyl-2-tropene (6c). Compound 6c was prepared using a procedure similar to that described for 6a. The compound was obtained as a white semisolid: 495 mg (75%); [α]<sup>23</sup><sub>D</sub> -327.9° (*c* 1.06, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.40-7.30 (m, 2H), 7.25-7.00 (m, 6H), 7.04-6.90 (m, 6H), 4.90 (m, 1H), 4.70 (m, 1H), 3.10 (m, 1H), 2.53-2.30 (m, 2H), 2.23 (s, 3H), 2.15-1.80 (m, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 152.8, 151.3, 141.5, 141.0, 140.8, 136.4, 130.9, 129.3, 128.9, 127.8, 126.4, 125.2, 121.8, 59.3, 58.9, 53.7, 53.4, 40.0, 38.8, 34.3, 33.4, 30.7, 29.8, 21.1.

(*R*)-*N*-Phenoxycarbonyl-2,3-di-(4-methylphenyl)-2-tropene (6d). Compound 6d was prepared using a procedure similar to that described for 6a. The compound was obtained as a colorless heavy oil;  $[\alpha]^{23}_{D} - 310.0^{\circ}$  (*c* 2.55, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.35 (m, 2H), 7.17 (m, 3H), 6.92 (m, 8H), 4.87 (d, *J* 

= 14.7 Hz, 1H), 4.64 (d, J = 18.5 Hz, 1H), 3.08 (t, J = 17.2, 1H), 2.50–2.30 (m, 2H), 2.25 (s, 3H), 2.24 (s, 3H), 2.20–1.80 (m, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  152.7, 151.3, 141.0, 140.5, 137.8, 136.8, 136.6, 136.2, 136.0, 129.6, 129.2, 128.7, 128.5, 125.2, 121.8, 121.7, 59.3, 58.9, 53.7, 53.4, 40.0, 38.8, 34.2, 33.3, 30.5, 29.8, 21.1, 21.0.

(*R*)-*N*-Phenoxycarbonyl-2-(4-methoxyphenyl)-3-(4-methylphenyl)-2-tropene (6e). Compound 6e was prepared using a procedure similar to that described for 6a. The compound was obtained as a white semisolid: 380 mg (85%);  $[\alpha]^{23}_{D} - 330.0^{\circ}$  (c 0.25, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.40 (m, 2H), 7.30–7.15 (m, 4H), 7.09 (m, 2H), 6.96 (m, 4H), 6.80–6.70 (m, 3H), 4.92 (dd, J = 16.0, 4.3 Hz, 1H), 4.70 (m, 1H), 3.75 (s, 3H), 3.12 (dt, J = 16.5, 3.5 Hz, 1H), 2.60–2.40 (m, 2H), 2.29 (s, 3H), 2.20–1.90 (m, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  158.2, 156.2, 152.7, 151.3, 140.5, 140.0, 137.7, 136.0, 132.0, 131.8, 130.8, 130.5, 130.3, 129.3, 129.2, 128.7, 128.6, 125.2, 121.8, 121.6, 119.8, 115.5, 113.4, 59.3, 58.9, 55.0, 53.6, 53.4, 39.9, 38.8, 34.2, 33.3, 30.5, 29.8, 21.0.

(*R*)-*N*-Phenoxycarbonyl-2-(2,3-dimethoxyphenyl-3)-4methylphenyl-2-tropene (6f). Compound 6f was prepared using a procedure similar to that described for 6a. The compound was obtained as a white semisolid: 1.34 g (90%);  $[\alpha]^{23}_{D} - 270.7^{\circ}$  (c 1.10, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.34 (m, 2H), 7.16 (m, 3H), 6.92 (m, 4H), 6.72 (m, 2H), 6.54 (d, J = 19.3 Hz, 1H), 4.91 (dd, J = 17.2, 4.2 Hz, 1H), 4.65 (m, 1H), 3.80 (s, 3H), 3.58 (s, 3H), 3.49 (s, 3H), 3.09 (t, J = 17.2 Hz, 1H), 2.53–2.30 (m, 2H), 2.24 (s, 3H), 2.20–1.90 (m, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$ 152.7, 151.2, 148.1, 147.7, 140.6, 140.3, 137.9, 136.0, 132.1, 131.9, 130.5, 129.4, 129.2, 128.5, 125.1, 121.7, 121.6, 121.0, 113.2, 110.5, 59.0, 58.6, 55.6, 55.4, 53.5, 53.4, 39.9, 38.8, 34.3, 33.4, 30.5, 29.8, 20.9.

(*R*)-*N*-Phenoxycarbonyl-2-(4-fluorophenyl)-3-(4-methylphenyl)-2-tropene (6g). Compound 6g was prepared using a procedure similar to that described for 6a. The compound was obtained as a thick colorless oil: 320 mg (95%);  $[\alpha]^{23}_{\rm D}$  -298° (*c* 0.20, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 7.38 (m, 2H), 7.20–7.10 (m, 3H), 7.08 (m, 2 H), 6.98–6.70 (m, 6 H), 4.90 (dd, *J* = 16.0, 4.3 Hz, 1 H), 4.70 (m, 1 H), 3.20 (dt, *J* = 16.0, 4.0 Hz, 1 H), 2.20 (s, 3 H), 2.19–1.90 (m, 3 H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$ : 163.1, 159.2, 152.8, 152.0, 147.9, 147.3, 140.5, 140.0, 138.5, 137.7, 136.0, 132.0, 131.8, 129.4, 128.7, 128.2, 120.9, 114.8, 114.0, 113.5, 113.0, 65.0, 57.5, 35.5, 33.3, 30.0, 20.9.

 $2β_3β_-$  and  $2α_3α_-$ Diphenyltropanes (3a and 4a). A mixture of carbamate alkene **6a** (216 mg, 0.56 mmol) and 5% Pd/C (215 mg) in MeOH (5 mL) was hydrogenated at room temperature under 50 psi. After 4 days, the solvent was evaporated to give the reduced carbamate as a clear oil (221 mg). The carbamate (156 mg, 0.407 mmol) and LAH (77 mg, 2.03 mmol) were refluxed in ether (15 mL) under N<sub>2</sub> for 3 h, and the reaction mixture was diluted with ether (50 mL). The reaction was quenched with H<sub>2</sub>O (0.5 mL). The reaction mixture was stirred with Celite (1 g) and Na<sub>2</sub>SO<sub>4</sub> (2.0 g) and filtered. Removal of the solvent produced a clear oil (130 mg). Purification by flash column chromatography (SiO<sub>2</sub>, MeOH/CH<sub>2</sub>Cl<sub>2</sub>/Et<sub>3</sub>N, 5:95:0.5) afforded **3a** as a white solid (39 mg, 35%) and **4a** (46 mg, 41%) as a clear oil. The free bases were converted to the HCl salt using HCl/ether (1 M).

**2**β,3β-3a·HCl: mp 240 °C (dec);  $[\alpha]^{24}{}_{\rm D}$  –21.8° (c 0.17, CH<sub>3</sub>-OH); <sup>1</sup>H NMR (free base, CDCl<sub>3</sub>)  $\delta$  7.26–6.95 (m, 9H), 3.99 (m, 1H), 3.82 (m, 1H), 3.54 (m, 1H), 3.31 (m, 1H), 2.64 (m, 1H), 2.37 (s, 3H), 2.14–1.91 (m, 2H), 1.90–1.78 (m, 2H), 1.46 (m, 1H); <sup>13</sup>C NMR (free base, CDCl<sub>3</sub>)  $\delta$  144.0, 142.7, 128.4, 128.3, 127.9, 127.2, 125.5, 124.8, 64.3, 60.4, 49.4, 40.7, 37.1, 36.9, 27.3, 22.6. Anal. (C<sub>20</sub>H<sub>24</sub>ClN·0.25H<sub>2</sub>O) C, H, N.

**2**α,3α-4a·HCl: mp 233.4–235 °C;  $[\alpha]^{23}_{D}$  +8.33° (*c* 0.12, CH<sub>3</sub>-OH); <sup>1</sup>H NMR (free base, CDCl<sub>3</sub>)  $\delta$  7.40–7.36 (m, 2H), 7.08–6.98 (m, 6H), 6.89–6.86 (m, 2H), 3.45–3.29 (m, 3H), 2.92 (m, 1H), 2.45 (t, *J* = 12.7 Hz, 1H), 2.27 (s, 3H), 2.27–2.21 (m, 2H), 1.82 (m, 2H), 1.69 (m, 1H); <sup>13</sup>C NMR (free base, CDCl<sub>3</sub>)  $\delta$  142.9, 142.4, 130.6, 127.9, 127.6, 127.1, 125.5, 125.4, 67.8, 62.0, 53.1, 41.9, 37.2, 35.0, 27.3, 25.0. Anal. (C<sub>20</sub>H<sub>24</sub>ClN·0.5H<sub>2</sub>O) C, H, N.

(*R*)-3 $\beta$ -(Methylphenyl)-2 $\beta$ -phenyltropane (3b) and (*R*)-3 $\alpha$ -(Methylphenyl)-2 $\alpha$ -phenyltropane (4b). A mixture of carbamate alkene 6b (296 mg, 0.75 mmol) and 10% Pd/C (150 mg) in MeOH (10 mL) was hydrogenated at room temperature under 50 psi. After 3 days, more catalyst (500 mg) was added, and the reduction was continued for an additional 4 days. The catalyst was separated by filtration and washed with ether (100 mL). The solvent was evaporated to give the carbamates, which were separated by flash column chromatography (SiO<sub>2</sub>, 30% EtOAc in hexane) to give the  $2\alpha$ ,3 $\alpha$ -isomer 4b (86 mg, 30%) and the  $2\beta$ ,3 $\beta$ -isomer 3b (88 mg, 30%).

**2** $\alpha$ ,3 $\alpha$ -Isomer: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.40–6.76 (m, 14H), 4.84–4.50 (m, 2H), 4.20 (m, 1H'), 3.64 (m, 1H), 2.80 (m, 1H), 2.19 (s, 3H), 2.20–1.50 (m, 5H).

**2\beta,3\beta-Isomer:** <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.30–7.00 (m, 8H), 6.95–6.85 (m, 4H), 6.65 (m, 2H), 4.82 (m, 1H), 4.70 (m, 1H), 3.64 (m, 1H), 3.26 (m, 1H), 2.70 (m, 1H), 2.11 (s, 3H), 2.26–2.00 (m, 3H), 1.93 (m, 2H).

The 2α,3α-carbamate (86 mg, 0.22 mmol) and LAH (42 mg, 1.10 mmol) were refluxed in ether (20 mL) under N<sub>2</sub> for 3 h, the reaction mixture was diluted with ether (50 mL), and the reaction was quenched with  $H_2O$  (0.5 mL). The reaction mixture was stirred with Celite (1 g) and Na<sub>2</sub>SO<sub>4</sub> (2.0 g), filtered, and washed with ether. Removal of the solvent and purification of the residue by flash column chromatography (SiO<sub>2</sub>, 5% Et<sub>3</sub>N in EtOAc) afforded **4b** (50 mg, 79%) as a clear oil. The amine was converted to the HCl salt as a white solid using HCl/ether: mp 226.0–227.5 °C;  $[\alpha]^{24}_{D}$  +5.24° (c 0.21, CH<sub>3</sub>OH); <sup>1</sup>H NMR (free base, CDCl<sub>3</sub>) & 7.20-7.06 (m, 5H), 6.86 (dd, J = 8.2, 19.9 Hz, 4H), 3.93 (m, 1H), 3.79 (m, 1H), 3.54 (m, 1H),1H), 3.29 (m, 1H), 2.61 (m, 1H), 2.36 (m, 3H), 2.17 (s, 3H), 2.10 (m, 1H), 2.05–1.75 (m, 3H), 1.44 (m, 1H);  $^{13}\mathrm{C}$  NMR (free base, CDCl<sub>3</sub>) & 142.9, 140.9, 134.0, 128.3, 128.1, 127.9, 125.4, 64.2, 60.5, 49.2, 40.7, 37.3, 36.6, 26.9, 22.7, 20.7. Anal. (C<sub>21</sub>H<sub>26</sub>- $ClN \cdot 0.25H_2O) C, H, N.$ 

The  $2\beta$ ,  $3\beta$ -carbamate (88 mg, 0.221 mmol) and LAH (42 mg, 1.10 mmol) were refluxed in ether (20 mL) under N<sub>2</sub> for 3 h, the reaction mixture was diluted with ether (50 mL), and the reaction was quenched with H<sub>2</sub>O (0.5 mL). The reaction mixture was stirred with Celite (1 g) and Na<sub>2</sub>SO<sub>4</sub> (2.0 g) and filtered. Removal of the solvent and purification of the residue by flash column chromatography (SiO<sub>2</sub>, MeOH:CH<sub>2</sub>Cl<sub>2</sub>/Et<sub>3</sub>N, 3:97:0.5) afforded **3b** as a white solid (39 mg, 35%). The amine was converted to the HCl salt as a white solid using HCl/ether (1 M): mp 228 °C (dec);  $[\alpha]^{23}$ <sub>D</sub> -17.1° (*c* 0.21, CH<sub>3</sub>OH); <sup>1</sup>H NMR (free base, CDCl<sub>3</sub>) & 7.41-7.37 (m, 2H), 7.10-7.00 (m, 3H), 6.80 (dd, J = 8.0, 17.9 Hz, 4H), 3.41 - 3.24 (m, 3H), 2.90 (m,1H), 2.38 (m, 1H), 2.24 (s, 3H), 2.18 (s, 3H), 2.30-2.00 (m, 2H), 1.80 (m, 2H), 1.64 (m, 2H);  $^{13}$ C NMR (free base, CDCl<sub>3</sub>)  $\delta$  143.0, 140.0, 134.8, 130.7, 128.3, 127.8, 127.0, 125.4, 67.8, 62.0, 53.2, 42.0, 37.0, 35.5, 27.3, 25.1, 20.9. Anal. (C<sub>21</sub>H<sub>26</sub>ClN·1.5H<sub>2</sub>O) C, H. N.

3β-Phenyl-2β-(4-methylphenyl)tropane (3c) and 3α-Phenyl-2α-(4-methylphenyl)tropane (4c). Compounds 3c and 4c were prepared using a procedure similar to that described for 3a and 4a. From 305 mg (0.77 mmol) of 6c, 76 (34%) and 82 mg (36%) of the 2α,3α- and 2β,3β-isomers were obtained.

**2β,3β-3c·HCl:** mp 230–232 °C (dec);  $[α]^{24}{}_D$  –25.0° (c 0.28, CH<sub>3</sub>OH); <sup>1</sup>H NMR (free base CDCl<sub>3</sub>) δ 7.26 (m, 2H), 7.08–6.95 (m, 3H), 6.90–6.80 (m, 4H), 3.40–3.24 (m, 3H), 2.86 (dd, J = 2.2, 6.6, Hz, 1H), 2.36 (dt, J = 2.7, 1.29 Hz, 1H), 2.23 (s, 3H), 2.19 (s, 3H), 2.10–2.00 (m, 2H), 1.84–1.70 (m, 2H), 1.64 (dt, J = 4.1, 12.6 Hz, 1H); <sup>13</sup>C NMR (free base, CDCl<sub>3</sub>) δ 143.3, 139.8, 134.7, 130.4, 128.0, 127.8, 127.5, 125.4, 67.9, 61.93, 52.9, 42.0, 37.4, 35.2, 27.3, 25.1, 20.9. Anal. (C<sub>21</sub>H<sub>26</sub>ClN·1.25H<sub>2</sub>O): C, H, N.

**2** $\alpha$ ,**3** $\alpha$ -**4c**·**HCl:** mp 224–225 °C (dec);  $[\alpha]^{24}_{D}$  –6.84° (c 0.19, CH<sub>3</sub>OH); <sup>1</sup>H NMR (free base CDCl<sub>3</sub>)  $\delta$  7.03–6.85 (m, 9H), 3.96 (dd, J = 8.0, 5.1 Hz, 1H), 3.79 (dd, J = 7.7, 14.0 Hz, 1H), 3.50 (m, 1H), 3.28 (m, 1H), 2.62 (m, 1H), 2.35 (s, 3H), 2.22 (s, 3H), 2.21–1.90 (m, 2H), 1.89–1.77 (m, 2H), 1.43 (m, 1H); <sup>13</sup>C NMR (free base, CDCl<sub>3</sub>)  $\delta$  144.1, 139.5, 134.7, 128.6, 128.4, 128.1,

127.2, 124.7, 64.4, 60.4, 49.0, 40.7, 37.1, 36.8, 27.3, 22.5, 20.9. Anal.  $(C_{21}H_{26}ClN\cdot 1.0H_2O)$  C, H, N.

 $2\beta$ , $3\beta$ - and  $2\alpha$ , $3\alpha$ -Di(4-methylphenyl)tropane (3d and 4d). Compounds 3d and 4d were prepared by a procedure similar to that described for 3a and 4a. From 158 mg (0.39 mmol) of 6d, 33 mg (28%) and 44 mg (38%) of 3d and 4d were obtained.

 $2\beta,3\beta\cdot 4d\cdot HCl:$  mp 233–244 °C (dec);  $[\alpha]^{24}{}_{\rm D}$ -9.3° (c, 0.22, CH<sub>3</sub>OH); <sup>1</sup>H NMR (free base CDCl<sub>3</sub>)  $\delta$  7.26 (d, J = 8.1 Hz, 2H), 6.86 (m, 4H), 6.75 (d, J = 8.1 Hz, 2H), 3.38 (m, 1H), 3.25 (m, 2H), 2.85 (dd, J = 2.5, 6.5 Hz, 1H), 2.31 (m 3H), 2.22 (s, 3H), 2.21 (s, 3H), 2.19 (s, 3H), 1.76 (m, 2H), 1.62 (m, 1H); ^{13}C NMR (free base, CDCl<sub>3</sub>)  $\delta$  141.1, 139.8, 134.8, 134.0, 128.7, 128.4, 128.3, 64.4, 60.6, 49.9, 40.7, 37.3, 36.6, 27.0, 22.7, 20.9, 20.8. Anal. (C<sub>22</sub>H<sub>28</sub>ClN·0.5H<sub>2</sub>O) C, H, N.

**2** $\alpha$ ,**3** $\alpha$ ·**4d**·**HCl:** mp 218 °C (dec);  $[\alpha]^{23}_{D} - 10.5^{\circ}$  (*c*, 0.19, CH<sub>3</sub>-OH); <sup>1</sup>H NMR (free base CDCl<sub>3</sub>)  $\delta$  6.96 (m, 4H), 6.94–6.82 (m, 4H), 3.90 (dd, J = 5.0, 7.9 Hz, 1H), 3.76 (dd, J = 7.2, 13.5 Hz, 1H), 3.51 (m, 1H), 3.27 (m, 1H), 2.59 (pent. J = 6.8 Hz, 1H), 2.35 (s, 3H), 2.25 (s, 3H), 2.18 (s, 3H), 2.10 (m, 1H), 1.97 (m, 1H), 1.84 (m, 2H), 1.43 (m, 1H); <sup>13</sup>C NMR (free base, CDCl<sub>3</sub>)  $\delta$  140.3, 140.0, 134.7, 134.6, 130.5, 128.3, 127.9, 127.8, 68.1, 62.0, 52.8, 42.0, 37.0, 36.0, 27.3, 25.1, 21.0, 20.8. Anal. (C<sub>22</sub>H<sub>28</sub>ClN·0.75H<sub>2</sub>O) C, H, N.

 $3\beta$ -(4-Methoxyphenyl)- $2\beta$ -(4-methylphenyl)tropane (3e) and  $3\alpha$ -(4-Methoxyphenyl)- $2\alpha$ -(4-methylphenyl)tropane (4e). Compounds 3e and 4e were prepared using a procedure similar to that described for 3a and 4a. From 239 mg (0.56 mmol) of 6e, 32 mg (18%) and 35 mg (19%) of the  $3\alpha$  and 4ewere obtained.

 $2\beta,3\beta\cdot 3e\cdot HCl:$  mp 218–220 °C;  $[\alpha]^{23}{}_{\rm D}$ –20.6° (c 1.00, CH<sub>3</sub>-OH);  $^{1}{\rm H}$  NMR (free base, CDCl<sub>3</sub>)  $\delta$  7.32 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.0 Hz, 2H), 6.73 (d, J = 8.0 Hz, 2H), 6.60 (d, J = 8.0 Hz, 2H), 3.71 (s, 3H), 3.37–3.19 (m, 3H), 2.83 (m, 1H), 2.27 (s, 3H), 2.19 (s, 3H), 2.18–2.10 (m, 3H), 1.74 (m, 2H), 1.60 (m, 1H);  $^{13}{\rm C}$  NMR  $\delta$  157.4, 140.3, 135.3, 134.8, 131.6, 128.3, 127.9, 112.3, 68.0, 62.0, 55.0, 52.4, 42.0, 37.2, 35.5, 27.3, 25.0, 20.9. Anal. (C<sub>22</sub>H<sub>28</sub>ClN·0.25H<sub>2</sub>O) C, H, N.

**2**α,3α·4e·HCl: mp 151–153 °C;  $[\alpha]^{23}_{D}$ –13.0° (*c* 0.13, CH<sub>3</sub>-OH); <sup>1</sup>H NMR (free base, CDCl<sub>3</sub>)  $\delta$  6.97 (d, J = 8.3 Hz, 2H), 6.91 (m, 4H), 6.71 (d, J = 8.3 Hz, 2H), 3.89 (m, 1H), 3.73 (m, 4H), 3.48 (m, 1H), 3.28 (m, 1H), 2.59 (m, 1H), 2.35 (s, 3H), 2.19 (s, 3H), 2.11–1.96 (m, 2H), 1.82 (m, 2H), 1.46 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  157.3, 141.0, 135.0, 134.0, 129.1, 128.3, 128.0, 113.3, 64.5, 60.5, 55.0, 48.6, 40.7, 37.0, 36.6, 27.1, 22.5, 20.7. Anal. (C<sub>22</sub>H<sub>28</sub>ClNO·0.2H<sub>2</sub>O) C, H, N.

 $3\beta$ -(4'-Methylphenyl)- $2\beta$ -(3,4-dimethoxyphenyl)tropane (3f) and  $3\alpha$ -(4-Methylphenyl)- $2\beta$ -(3,4-dimethoxyphenyl)tropane (4f). Compounds 3f and 4f were prepared using a procedure similar to that described for 3a and 4a. From 312 mg (0.69 mmol) of 6f, 73 mg (31%) and 83 mg (35%) of 3f and 4f were obtained.

 $2\beta,3\beta-3f\text{-}HCl:$  mp 144–146 °C (dec);  $[\alpha]^{23}{}_{\mathrm{D}}$ –1.6 ° (c 0.19, CH<sub>3</sub>OH); <sup>1</sup>H NMR (free base, CDCl<sub>3</sub>)  $\delta$  7.06 (dd, J = 1.9, 83 Hz, 1H), 6.97 (d, J = 1.9 Hz, 1H), 6.86 (d, J = 7.9 Hz, 2H), 6.71 (d, J = 7.9 Hz, 2H), 6.58 (d, J = 8.3 Hz, 1H), 3.79 (s, 3H), 3.63 (s, 3H), 3.37 (m, 2H), 3.25 (m, 1H), 2.76 (dd, J = 2.4, 6.6 Hz, 1H), 2.35–2.05 (m, 3H), 2.27 (s, 3H), 2.19 (s, 3H), 1.77 (m, 2H), 1.57 (m, 1H); ^{13}C NMR (free base, CDCl<sub>3</sub>)  $\delta$  147.2, 146.6, 140.2, 135.6, 134.8, 128.2, 128.0, 122.5, 114.5, 109.7, 67.6, 61.9, 55.5, 55.4, 52.3, 41.8, 37.5, 35.4, 27.3, 24.9, 20.8. Anal. (C<sub>23</sub>H<sub>30</sub>ClNO·0.25H<sub>2</sub>O) C, H, N.

**2**α,3α-4f·HCl: mp 132–134 °C (dec);  $[\alpha]^{23}{}_{\rm D}$  –20.0° (c 0.13, CH<sub>3</sub>OH); <sup>1</sup>H NMR (free base, CDCl<sub>3</sub>)  $\delta$  6.94–6.84 (m, 4H), 6.69 (d, J = 8.3 Hz, 1H), 6.61 (dd, J = 1.7, 8.3 Hz, 1H), 6.48 (d, J = 1.7 Hz, 1H), 3.91 (m, 1H), 3.81 (s, 3H), 3.73 (m, 1H), 3.67 (s, 3H), 3.46 (t, J = 5.5 Hz, 1H), 3.30 (t, J = 6.0 Hz, 1H), 2.61 (m, 1H) 2.36 (s, 3H), 2.19 (s, 3H), 2.05 (dd, J = 5.8, 11.7 Hz, 2H), 1.08 (m, 2H), 1.53 (m, 1H); <sup>13</sup>C NMR (free base, CDCl<sub>3</sub>)  $\delta$  148.1, 146.7, 141.0, 135.4, 134.1, 128.6, 128.5, 128.2, 128.0, 120.4, 112.1, 110.6, 64.7, 60.4, 55.6, 55.4, 49.0, 40.7, 36.7, 36.5, 27.5, 22.3, 20.7. Anal. (C<sub>23</sub>H<sub>30</sub>ClNO<sub>2</sub>·H<sub>2</sub>O) C, H, N.

 $2\beta$ -(4-Fluorophenyl)- $3\beta$ -(4-methylphenyl)tropane (3g). Compound 3g was prepared by a procedure similar to that described for **3a**. In this case, it was necessary to prepare the tartarate salt  $2\beta$ , $3\beta$ -**4f**·CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>: mp 174–177 °C;  $[\alpha]^{23}_{\rm D}$  -17.0° (*c* 0.13, CH<sub>3</sub>OH); <sup>1</sup>H NMR (free base, CDCl<sub>3</sub>)  $\delta$  7.37 (dd, J = 5.8, 2.1 Hz, 2H), 6.85 (d, J = 7.9 Hz, 2H), 6.71 (d, J = 8.3 Hz, 6H), 6.85 (d, J = 7.9 Hz, 2H), 6.71 (d, J = 8.3 Hz, 4H), 3.38–3.23 (m, 3H), 2.83 (m, 2H), 2.23 (s, 3H), 2.19 (s, 3H), 2.35–2.06 (m, 4H), 1.79 (m, 3H), 1.60 (m, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  162.8, 159.5, 139.9, 138.6, 135.0, 132.0, 131.9, 128.4, 127.9, 120.9, 113.8, 113.5, 67.7, 62.0, 52.4, 42.0, 37.0, 35.2, 27.3, 25.0, 20.9. Anal. (C<sub>28</sub>H<sub>32</sub>FNO<sub>3</sub>S·1.75H<sub>2</sub>O) C, H, N.

(*R*)-2 $\alpha$ ,3 $\alpha$ -Diphenyltropane (4a). A mixture of alkene 6a (61 mg, 0.21 mmol) and Pd/C (5%) in CH<sub>3</sub>OH (3 mL) was hydrogenated under H<sub>2</sub> (50 psi). After 8 days, the catalyst was removed by filtration. The residue obtained after removal of solvent was purified by flash column chromatography (SiO<sub>2</sub>, 10% CH<sub>3</sub>OH in CH<sub>2</sub>Cl<sub>2</sub>/Et<sub>3</sub>N (99.5/0.5) to give the starting material (22 mg, 36%) and the 2 $\alpha$ ,3 $\alpha$ -isomer 4a as a clear oil (19 mg, 31%).

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**Supporting Information Available:** Results from elemental analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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