acetone (7.6 mL) and 2 N aqueous HCl (0.4 mL), stirred, and refluxed under N_2 for 3 h. The mixture was evaporated in vacuo and the residue dissolved in CH_2Cl_2. The solution was washed with saturated brine containing a few drops of $NaHCO_3/H_2O$ to make it basic and then with brine, dried (Na_2SO_4), filtered, and evaporated in vacuo to give 44 mg (90%) of crude acetoxy ketone, which was further purified by chromatography on silica (10% Et_2O/CH_2Cl_2) to give a mixture of epimers **3c** and **3d** (25 mg, 3:2, 73%). NMR ($CDCl_3$) 4.9 (m, 1 H, 3-H), 4.08 (br s, 2 H, 7-CH_2), 2.07 and 2.10 (2 s, 3 H, $OCOCH_3$), 1.17 and 1.25 (2 s, 3 H, 2-CH_3), 0.9 (t, 3 H, CH_2CH_3).

(2*RS*,3*SR*)-3-Acetoxy-6-(carbethoxymethylidene)-2-methyl-2-propyloxepane (14). Ethyl (diethoxyphosphinyl)-acetate (728 mg) was added dropwise to a suspension of NaH (99%, 68 mg) in anhydrous benzene (25 mL). The suspension was heated to 70 °C and stirred vigorously until the evolution of hydrogen ceased. A solution of **3a** (260 mg) in anhydrous benzene (3 mL) was added slowly to the above solution and heated at 70–75 °C for 1 h. The resulting solution was cooled, Et_2O (150 mL) and 10% HCl (35 mL) were added, and the organic layer was separated. The aqueous layer was reextracted with Et_2O (3×), and the combined organic extracts were washed with brine (3×), filtered through phase-separating paper, and dried (Na_2SO_4). The solvent was removed in vacuo to give a residue (1.01 g) which contained **14** as the major component and a large quantity of excess ethyl (diethoxyphosphinyl)acetate. The residue was purified via silica gel chromatography (1% EtOAc/hexane) to give **14** (265 mg, 78%). IR (neat) 5.78, 5.86 μm (C=O), 5.1 (C=C); NMR ($CDCl_3$) 5.65 (br s, 1 H, C=CH), 4.8 (overlapping m, 3β-H and cis 7-CH_2), 3.9–4.3 (overlapping q and s, CH_3CH_2 and trans 7-CH_2), 2.04 (s, 3 H, $OCOCH_3$), 1.17 (s, 3 H, 2-CH_3) (integration indicates a 3:2 ratio of trans:cis isomers for the carbethoxymethylidene at C-6); GC/MS, m/z 298 (M^+) for each of the trans/cis isomers.

Anal. Calcd for $C_{16}H_{26}O_5$: C, 64.41; H, 8.78. Found: C, 64.78; H, 8.70.

(1*RS*,4*RS*,5*RS*)-4-Methyl-4-pentyl-3,8-dioxabicyclo-[3.2.1]octane-1-acetic Acid (15). A mixture of **4d** (350 mg) and (carbethoxymethylidene)triphenylphosphorane (1.8 g) was refluxed in xylene (10 mL) for 2 days under N_2. After the mixture was cooled, petroleum ether (30 mL) was added, refluxed for 30 min, and filtered. The petroleum ether filtrate was evaporated in vacuo and the crude residue chromatographed on SilicAR CC-7 with 10% Et_2O/CH_2Cl_2 to give the ethyl ester of **15** as a light yellow oil (470 mg, 96%). $NaOH/H_2O$ (2 N, 5 mL) was added, while stirring at 0 °C under N_2, to the ester in MeOH (5 mL). The mixture was then stirred at 20 °C for 3 days under N_2. The solvent was evaporated in vacuo and the residue extracted with CH_2Cl_2. The basic, aqueous solution was carefully acidified to pH 5 with 2 N HCl, extracted with CH_2Cl_2, washed with water and brine, dried (Na_2SO_4), filtered, and evaporated to give **15** as a yellow oil (210 mg, 50%). IR (neat) 5.72, 5.83 μm (C=O); NMR ($CDCl_3$) 3.90 (t, 1 H, 5-H), 3.56 (d of d, 2 H, 2-CH_2), 2.63 (s, 2 H, CH_2CO_2H), 1.03 (s, 3 H, 4-CH_3), 0.9 (t, 3 H, CH_2CH_3); GC/MS, Me_3Si derivative, m/z 328 (M^+).

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Metabolites of Cibenzoline: Synthesis of Hydroxylated 1,1-Diphenyl-2-imidazolylcyclopropanes and 5,5-Diphenyl-2*H*-pyrrolo[1,2-*a*]imidazolines

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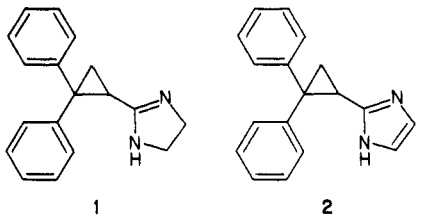
The (hydroxyphenyl)pyrrolo[1,2-*a*]imidazolines **7a** and **7b**, which are of interest as oxidative metabolites of the antiarrhythmic agent cibenzoline (1), were synthesized by the base-catalyzed rearrangement of the cyclopropylphenols derived from benzyl ethers **6a** and **6b**, respectively. The unsubstituted diphenylpyrrolo[1,2-*a*]-imidazoline **18** was prepared by treatment of the pyrrolidone imidate **17** with bromoethylamine.

Cibenzoline (1) is a class I antiarrhythmic agent which is currently undergoing clinical trials in the United States. The metabolism of ^{14}C-cibenzoline has been investigated in rats and dogs; after oral dosing, these animals excrete unchanged cibenzoline, the imidazole **2**,[1] and several hydroxylated metabolites in their conjugated form. Two of the conjugated metabolites were hydrolyzed, separated, and assigned structures **7a** and **7b** on the basis of NMR studies.[2] Since these compounds appear to represent rearranged products of primary metabolites, the corresponding (hydroxyphenyl)cyclopropanes, we have undertaken the work described in this paper to provide reference samples of these cyclopropanes as well as **7a** and **7b**. We also describe the synthesis of the "parent" 5,5-diphenyl-2*H*-pyrrolo[1,2-*a*]imidazoline (**18**), which was prepared for biological testing as an analogue of **1**.



1 2

The syntheses of **7a** and **7b** and the cyclopropyl derivatives **11** and **1i** are outlined in Scheme I. Thus the benzophenone **3a**[3] was converted to the hydrazone **4a** with excess hydrazine in ethanol. The crude hydrazone was oxidized with manganese dioxide in dichloromethane to the corresponding purple diphenyldiazomethane which was in turn reacted with acrylonitrile to give the nitriles **5a** in good yield as a mixture of diastereomers. While these

(1) Leinweber, F.-J.; Loh, A. C.; Szuna, A. J.; Carbone, J. J.; Williams, T. H.; Sasso, G. J.; Tilley, J. W.; Pace, D.; Dahlen, P.; Kovacs, J. L; Klevans, L. R. *Xenobiotics* **1983**, *13* 287.

(2) Loh, A. C.; Leinweber, F.-J.; et al., personal communication.

(3) Valette, M. *Bull. Soc. Chim. Fr.* **1930**, *47*, 289.

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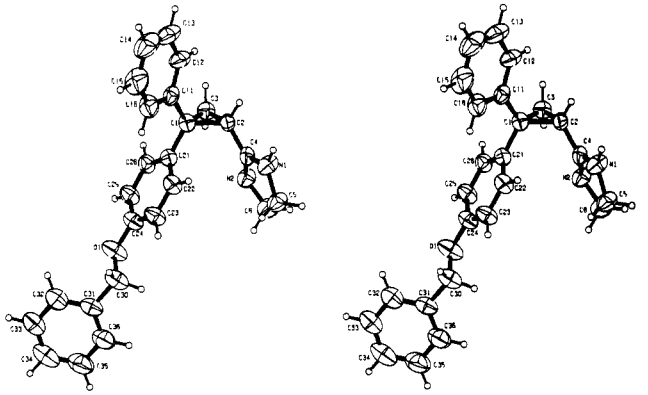
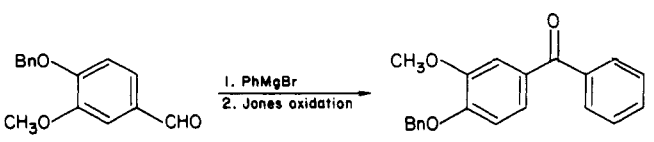


Figure 1. Stereodrawing of compound **9**.

nitriles were not separable by chromatography, the phenols obtained by debenzylation of **5a** could be separated and rebenzylated. However, the reaction of either the mixture or diastereomerically pure **5a** with ethylenediamine tosylate resulted in a similar mixture of isomeric cyclopropylimidazolines **6a**. The *Z* and *E* isomers could be purified by chromatography. The faster running isomer **9** was obtained from a thick layer plate and identified as the *Z* isomer by X-ray crystallographic analysis (see Figure 1). A quantity of the *E* isomer **10** was isolated from the tailing fractions of a silica gel column.

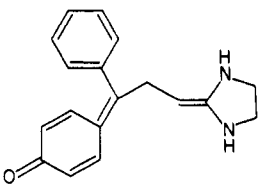
Since the pure isomers were difficult to obtain, the initial studies of the debenzylation of **6a** were performed on the crude mixture. Catalytic hydrogenation over palladium on carbon proceeded only slowly and led to a concomitant reductive opening of the cyclopropane ring to give the (diphenylpropyl)imidazoline **8a** in 76% yield. Catalytic transfer hydrogenation employing cyclohexene in ethanol over palladium hydroxide[4] afforded a mixture of **8a** and the rearranged product **7a** in 18% and 46% isolated yields, respectively. In the presence of hydrochloric acid, the catalytic transfer hydrogenation proceeded cleanly to an oily, inseparable mixture of cyclopropylphenols. Warming this mixture with 1 equiv of ptassium carbonate in ethanol led to a nearly quantitative conversion to **7a**. With use of the acidic transfer hydrogenation conditions without the base treatment, the diastereomerically pure benzyl ethers **9** and **10** were transformed into the hydrochloride salts of the corresponding phenols **11** and **12**, respectively. Analysis of blood samples after short hydrolysis periods by HPLC indicates that **11** and **12** are the metabolites formed in vivo and that **7a** arises as an artifact of the isolation procedure.[2]

In the 3-methoxy series the chemistry proceeded in a similar manner except that the base-mediated rearrangement of the phenol derived from **6b** into **7b** required slightly more forcing conditions, i.e., the use of sodium hydroxide rather than potassium carbonate. The starting benzophenone **3b** was obtained by treatment of vanillin *O*-benzyl ether (**13**)[5] with excess phenylmagnesium bromide followed by Jones oxidation.



13 3b

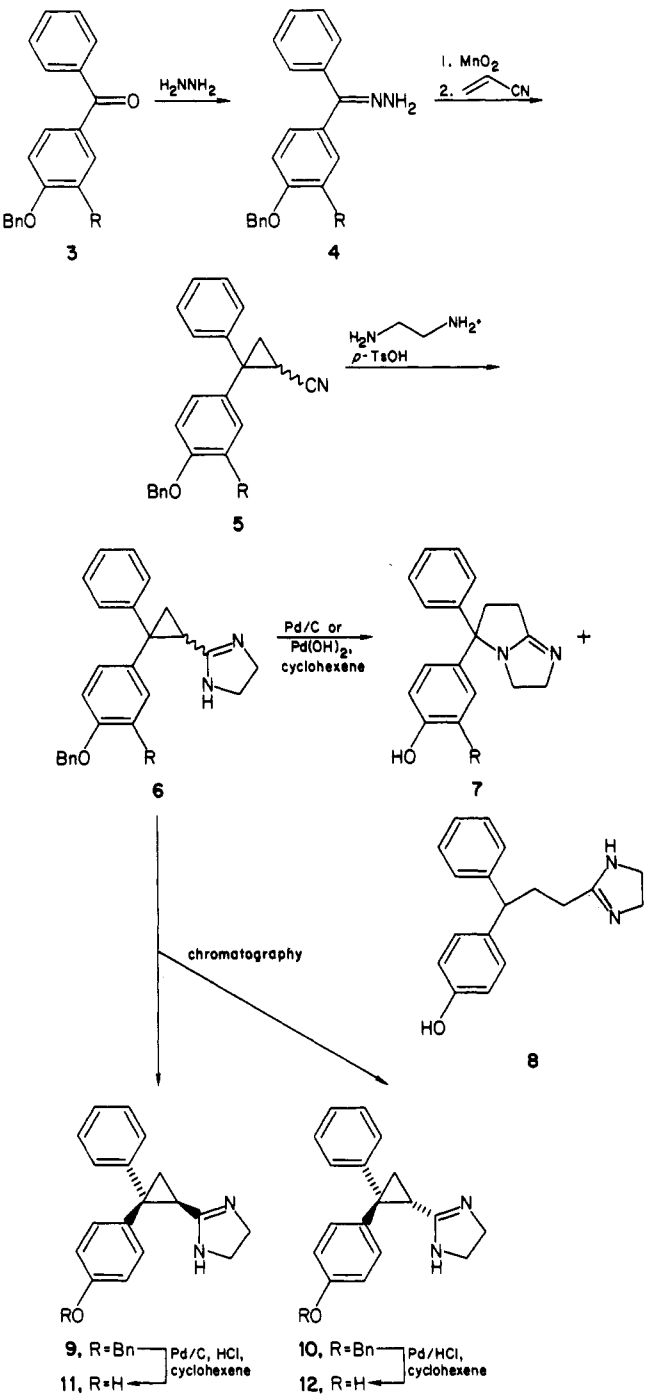
Although we have not studied the mechanism of the rearrangement of the cyclopropylphenols derived from **6** into **7**, a probable reaction course proceeds via a base-catalyzed ring opening to a quinone methide such as **14**



14

or similar intermediate which would be inaccessible to the nonhydroxylated compound **1**. As expected, **1** did not undergo rearrangement to **18** under either acidic or basic conditions and consequently the sequence described in

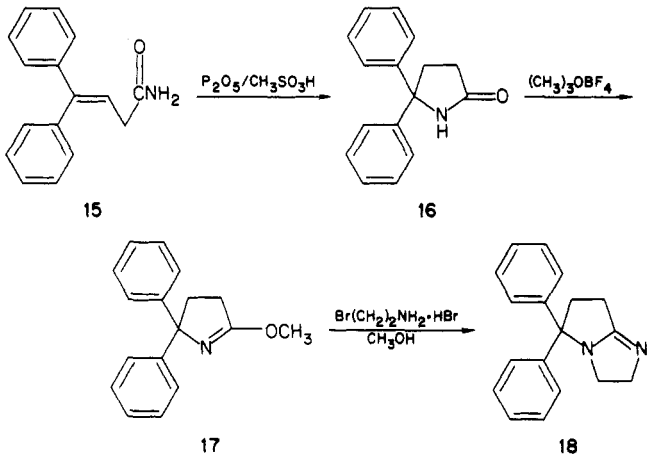
Scheme I[a]



[a] **3–7**: a, R = H; b, R = OCH_3.

(4) Hanessian, S.; Liak, T. J.; Vanasse, B. *Synthesis* **1981**, 396.
(5) Lovecy, A.; Robinson, R.; Sugasawa, S. *J. Chem. Soc.* **1930**, 817.

Scheme II



Scheme II was developed for the synthesis of this compound.

Although attempted cyclization of the known amide **15**[6] using polyphosphoric acid gave poor results in our hands, cyclization medicated by a mixture of phosphorus pentoxide and methanesulfonic acid[7] proceeded smoothly to give the lactam **16** in 60% yield. Conversion of **16** to the desired pyrroloimidazoline **18** proved to be problematic due to the steric hindrance provided the amide carbonyl moiety by the geminal phenyl groups. After examination of several unsuccessful approaches, lactam **16** was converted nearly quantitatively to imidate **17** by reaction with freshly prepared trimethyloxonium tetrafluoroborate[8] for 3 days at room temperature. It is interesting to note that reaction with triethyloxonium tetrafluoroborate failed to give any detectable quantity of the corresponding ethyl imidate. For completion of the synthesis, the imidate **17** was treated with 1 equiv of bromoethylamine hydrobromide in refluxing methanol to give after chromatography a 58% yield of **18**.

Experimental Section

General Methods. Melting points were taken on a Buchi 510 melting point apparatus and are uncorrected. Proton magnetic resonance spectra were taken on a Varian XL-100 spectrometer with Me_4Si internal reference. Infrared spectra were obtained on a Beckman IR-9 or IR-12 spectrometer. Mass spectra were taken on a CEC 21-110 mass spectrometer at 70 eV. Preparative high-pressure liquid chromatography was performed on silica Prep-Pak 500 cartridges using a Waters Associates Prep LC 500A. Tetrahydrofuran was distilled from sodium and benzophenone. Dichloromethane was distilled from P_2O_5. Triethylamine was distilled from CaH_2. Methanol and DMF were stored over Linde 3-A sieves.

[3-Methoxy-4-(phenylmethoxy)phenyl]phenylmethanone (3b). A solution of phenylmagnesium bromide in 50 mL of dry THF was prepared from 16.9 g (0.108 mol) of bromobenzene and 2.62 g (0.108 mol) of magnesium turnings. The solution of Grignard reagent was cooled in an ice bath, and 18.6 g (0.077 mol) of vanillin *O*-benzyl ether (**13**) in 30 mL of dry THF was added dropwise. After being stirred an additional 15 min, the reaction was quenched with 30 mL of 6 N HCl. The mixture was filtered, and the filtrate was extracted with three 100-mL portions of ethyl acetate. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under vacuum to yield 21.4 g (86%) of crude alcohol which was used without purification.

A solution of the above alcohol in 250 mL of acetone as 0 °C was treated with 118.6 mL (0.95 mol) of 8 N Jones reagent added dropwise over 1.5 h. The resulting mixture was stirred an additional 25 h at room temperature. After being quenched with 2-propanol, the reaction mixture was filtered through Celite and then concentrated on a rotary evaporator. The residue was partitioned between 200 mL of ethyl acetate and 200 mL of water. The aqueous layer was extracted once with 100 mL of ethyl acetate. The combined organic layers were washed with 250 mL of 5% sodium bicarbonate, dried ($MgSO_4$), and evaporated to an oil. This was filtered through a short silica gel column, eluting with 3:1 hexane–ethyl acetate, to give 12.0 (56%) of crystalline **3b**: mp 88–89 °C; ^1H NMR ($CDCl_3$) δ 3.92 (s, 3 H), 5.21 (s, 2 H), 6.89 (d, 1 H, J = 8 Hz), 7.2–7.6 (m, 11 H), 7.75 (m, 1 H); IR ($CHCl_3$) 1650 cm^{-1}; MS, m/e (relative intensity) 318 (12), 91 (100).

Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.22; H, 5.70. Found: C, 78.98; H, 5.68.

Phenyl[4-(phenylmethoxy)phenyl]methanone Hydrazone (4a). A solution of 62.63 g (0.217 mol) of 4-(benzyloxy)benzophenone[9] in 60 mL of hydrazine hydrate and 250 mL of absolute ethanol was heated to reflux for 18 h, filtered, and diluted with water to give a gummy solid which was recrystallized from ether–hexane to give 26.22 g (40%) of **4a**, mp 97–100 °C. Recrystallization of a portion from ether–hexane gave the analytical sample: mp 102–104 °C; ^1H NMR ($CDCl_3$) δ 5.05 (s, 2 H), 5.28 (br, s, 2 H), 6.90 (d, 2 H, J = 9 Hz), 7.22–7.55 (m, 12 H); MS, m/e (relative intensity) 302 (38), 91 (100).

Anal. Calcd for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.66; H, 6.10; N, 9.31.

[3-Methoxy-4-(phenylmethoxy)phenyl]phenylmethanone hydrazone (4b) was obtained similarly from 38.0 g (0.119 mol) of **3b** and 30 mL of hydrazine hydrate in 150 mL of ethanol to give 40 g (81%) of **4b** as an oil consisting of a 55:45 mixture of isomers by NMR analysis and suitable for use in the next step. The crude product from a separate run was purified by chromatography on silica gel, eluting with 3:1 hexane–ethyl acetate and was crystallized from ether–hexane to give a pure sample of one isomer: mp 97–98 °C; ^1H NMR ($CDCl_3$) δ 3.88 (s, 3 H), 5.11 (s, 2 H), 5.29 (br, s, 2 H) 6.57 (m, 1 H), 6.72 (m, 1 H), 7.1–7.6 (m, 11 H); IR ($CHCl_3$) 1605, 1515 cm^{-1}; MS, m/e (relative intensity) 332 (12), 241 (65), 91 (100).

Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.22, H, 606; N, 8.43. Found: C, 75.74; H, 6.24; N, 8.47.

(*E*/*Z*)-2-Phenyl-2-[4-(phenylmethoxy)phenyl]cyclopropanecarbonitrile (5a). A suspension of 26.22 g (0.0867 mol) of **4a** in 250 mL of dichloromethane was stirred over 52.4 g (0.50 mol) of manganese dioxide for 3 h and was filtered, washing with 100 mL of dichloromethane. The filtrate was added over 30 min to a refluxing solution of 6.6 mL (0.10 mol) of acrylonitrile in 200 mL of heptane. After completion of the addition, the reaction mixture was held at reflux for 3 h until the purple color of the diazo compound was discharged. The dichloromethane was removed by distillation until the internal temperature of the reaction mixture had reached 80 °C. The mixture was held at this temperature for 3 h and was diluted with ethyl acetate to obtain a homogeneous solution. After cooling, 21.97 g (78%) of **5a** separated, mp 105–115 °C. Concentration of the mother liquors afforded an additional 2.20 g (8%), mp 101–109 °C. An analytical sample consisting of a 4:1 mixture of diastereomers by NMR was obtained from ether–hexane: mp 115–121 °C; ^1H NMR ($CDCl_3$) δ 1.68–1.81 (m, 1 H), 1.90–2.01 (m, 1 H), 2.10–2.26 (m, 1 H), 5.02 (s, 2 H), 6.95 (d, 2 H, J = 8 Hz), 7.20–7.4 (m, 12); IR ($CHCl_3$) 2240 cm^{-1}; MS, m/e (relative intensity) 325 (4), 234 (40), 91 (100).

Anal. Calcd for $C_{23}H_{19}NO$: C, 84.89; H, 5.98; N, 4.30. Found: C, 85.00; H, 5.88; N, 4.38.

(*E*/*Z*)-2-[3-Methoxy-4-(phenylmethoxy)phenyl]-2-phenylcyclopropanecarbonitrile (5b) was obtained by using the above procedure. Starting with 2.4 g (7.2 mmol) of **4b**, there was obtained 2.2 g (85%) of **5b** as an oily mixture of diastereomers after HPLC, eluting with 5:1 hexane–ethyl acetate. Crystallization of a portion from ethyl acetate–hexane gave a sample, mp 105–107 °C, consisting of a 3:1 mixture of diastereomers by NMR analysis: ^1H NMR ($CDCl_3$) δ 1.5–2.3 (m, 3 H), 3.81 and 3.86 (s, 3 H), 5.10 (s, 2 H), 6.7–7.0 (m, 3 H), 7.1–7.5 (m, 10 H); IR ($CHCl_3$) 2235, 697 cm^{-1}; MS, m/e (relative intensity) 355 (15), 264 (100), 91 (74).

Anal. Calcd for $C_{24}H_{21}NO_2$: C, 81.10; H, 5.96; N, 3.94. Found: C, 81.18; H, 6.18; N, 3.97.

4,5-Dihydro-2-[2-phenyl-2-[4-(phenylmethoxy)phenyl]-cyclopropyl]-1*H*-imidazole (6a) and (*E*)-*rac*-4,5-Dihydro-

(6) Yamawaki, Y.; Wantanabe, M.; Yamamura, S.; Saito, *J. Pharm. Soc. Jpn.* **1977**, *97*, 127.
(7) Eaton, P. E.; Carlson, G. R.; Lee, J. T. *J. Org. Chem.* **1973**, *38*, 4071.
(8) Gurphey, T. J. *Org. Synth.* (*N.Y.*) **1971**, *51*, 142.

2-[2-phenyl-2-[4-(phenylmethoxy)phenyl]cyclopropyl]-1*H*-imidazole (10). An intimate mixture of 24.17 g (0.0743 mol) of **5a** and 24.0 g (0.10 mol) of ethylenediamine tosylate was heated to a bath temperature of 190 °C for 8 h. The product was dissolved in ethanol and partitioned between water and dichloromethane. The combined organic layers were dried (K_2CO_3) and evaporated. The residue was recrystallized from ethyl acetate–hexane to give 16.41 g (60%) of **6a** as a mixture of diastereomers, mp 112–133 °C. The mother liquor was evaporated to give 11.20 g of a red oil which was chromatographed by preparative HPLC (2:5:93 $N(C_2H_5)_3/CH_3OH/CH_2Cl_2$). The middle fractions were combined, evaporated, diluted with dichloromethane, washed with water and saturated sodium chloride solution, and dried (K_2CO_3). Crystallization of the residue from ethyl acetate–hexane gave 2.66 g (10%) of the diastereomeric mixture, mp 113–119 °C.

Anal. Calcd for $C_{25}H_{24}N_2O$: C, 81.49; H, 6.57; N, 7.60. Found: C, 81.32; H, 6.78; N, 7.51.

The later fractions contained mainly the lower running *E* isomer **10**. The material was isolated as above and was recrystallized from ethyl acetate–hexane and finally from ethyl acetate to give 0.60 g (4%) of **10**: mp 134–137 °C; ^1H NMR ($CDCl_3$) δ 1.61 (dd, 1 H, J = 6 Hz, J = 9 Hz), 1.92 (t, 1 H, J = 6Hz), 2.54 (dd, 1 H, J = 6 Hz, J = 9 Hz), 5.00 (s, 2 H), 6.86 (d, 2 H, J = 8 Hz), 7.15–7.50 (m, 12 H); MS, m/e (relative intensity) 368 (15), 277 (100).

Anal. Calcd for $C_{25}H_{24}N_2O$: C, 81.49; H, 6.57; N, 7.60. Found: C, 81.10; H, 6.45; N, 7.66.

4,5-Dihydro-2-[[3-methoxy-4-(phenylmethoxy)phenyl]-2-phenylcyclopropyl]-1*H*-imidazole (6b). An intimate mixture of 1.0 g (2.8 mmol) of **5b** and 0.9 g (3.7 mmol) of ethylenediamine monotosylate was stirred under argon for 18 h at 120 °C and 12 h at 150 °C. After cooling slightly, 30 mL of absolute ethanol was added to dissolve the residue, and the solution was partitioned between 150 mL of methylene chloride and 150 mL of water. The aqueous layer was extracted with two 50-mL portions of methylene chloride. The combined organic layers were dried (K_2CO_3) and evaporated to an oil. Chromatography through a short silica gel column, eluting with 95:5 methanol/triethylamine, afforded 0.5 g (45%) of **6b**, mp 127.5–129 °C.

Anal. Calcd for $C_{26}H_{26}N_2O_2$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.14; H, 6.65; N, 7.13.

In a separate experiment, a sample of **6b** was chromatographed by HPLC, eluting with 10% triethylamine in methylene chloride, to afford, after recrystallization from hexane–ethyl acetate, pure samples of each of the diastereomeric cyclopropylimidazolines. Stereochemistry was assigned by analogy with the relative polarities of **9** and **10**.

***Z* isomer (less polar)**: mp 150–152 °C; NMR ($CDCl_3$) δ 1.61 (dd, 1 H, J = 6 Hz, 9.5 Hz), 1.89 (t, 1 H, J = 6 Hz), 2.54 (dd, 1 H, J = 6 Hz, 9.5 Hz), 2.8–3.6 (m, 5 H), 3.82 (s, 3 H), 5.10 (s, 2 H), 6.7–7.0 (m, 3 H), 7.0–7.5 (m, 10 H).

***E* isomer (more polar)**: mp 149.5–150.5 °C; NMR ($CDCl_3$) δ 1.59 (dd, 1 H, J = 6 Hz, 9 Hz), 1.91 (t, 1 H, J = 6 Hz), 2.54 (dd, 1 H, J = 6 Hz, 9 Hz), 2.7–3.6 (m, 5 H), 3.81 (s, 3 H), 5.07 (s, 2 H), 6.78 (m, 3 H), 7.2–7.6 (m, 10 H).

***rac*-4-(5-Phenyl-2,3,6,7-tetrahydro-5*H*-pyrrolo[1,2-*a*]-imidazol-5-yl)phenol (7a).** A solution of 6.00 g (0.0163 mol) of **6a** in 150 mL of absolute ethanol, 80 mL of cyclohexene, and 10 mL of 4 N ethanolic hydrochloric acid over 2.0 g of 10% palladium on charcoal was heated to reflux for 7 h. The mixture was filtered and evaporated to dryness. The residue was dissolved in 100 mL of ethanol containing 2.15 g (0.0163 mol) of potassium carbonate, and the bath temperature was raised to 75 °C for 4 h at which time TLC (2:13:85 $NH_4OH/CH_3OH/CH_2Cl_2$) indicated complete conversion of the intermediate cyclopropylimidazoline to **7a**. The mixture was filtered, the filtrate was evaporated, and the residue was triturated with hot 1:1 ethanol–water to give 4.13 g (90%) of **7a**, mp 216–218 °C. Recrystallization from ethanol–water gave 3.53 g: mp 218–220 °C; ^1H NMR ($CDCl_3$) δ 2.64–3.05 (m, 6 H), 3.86 (m, 2 H), 6.72 (d, 2 H, J = 8 Hz), 6.91 (d, 2 H, J = 8 Hz), 7.15 (m, 2 H), 7.33 (m, 3 H), 9.47 (s br, 1 H); MS, m/e (relative intensity) 278 (23), 201 (100).

Anal. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.06. Found: C, 77.40; H, 6.40; N, 10.01.

4-(2,3,6,7-Tetrahydro-5-phenyl-5*H*-pyrrolo[1,2-*a*]-imidazol-5-yl)-2-methoxyphenol (7b). A mixture of 0.85 g (2.13 mmol) of **6b**, 10 mL (99 mmol) of cyclohexene, and 250 mg of 10% palladium on carbon in 21 mL of 2.5 M ethanolic HCl was refluxed for 12 h. The mixture was filtered and evaporated to dryness. The residue was dissolved in 15 mL of ethanol containing 170 mg (4.25 mmol) of sodium hydroxide, and the solution was heated to reflux for 2 min. After cooling, the reaction mixture was neutralized with 1 M HCl and extracted with chloroform. The organic layer was dried ($MgSO_4$) and evaporated to give 0.53 g of **7b** as an amorphous hydrated solid whose spectral properties were in complete agreement with the assigned structure. Although a water-free sample could not be prepared, an analytical sample, mp 167–170 °C dec, whose NMR spectrum was identical with that of the crude sample, was prepared by chromatography on silica gel, eluting with 5% triethylamine in methylene chloride, followed by recrystallization from ethanol–ethyl acetate: ^1H NMR ($CDCl_3$) δ 2.55–2.75 (m, 2 H), 2.8–3.2 (m, 4 H), 3.74 (s, 3 H), 4.06 (br t, 2 H), 6.36 (br, 1 H), 6.58–6.84 (m, 3 H), 7.1–7.5 (m, 5 H); IR ($CHCl_3$) 3345, 1673, 1645 cm^{-1}; MS, m/e (relative intensity) 308 (37), 231 (100).

Anal. Calcd for $C_{19}H_{20}N_2O_2 \cdot 0.3H_2O$: C, 72.72; H, 6.62; N, 8.93; H_2O, 1.72. Found: C, 72.41; H, 6.60; N, 8.69; H_2O, 1.50.

***rac*-4-[3-(4,5-Dihydro-1*H*-imidazol-2-yl)-1-phenylpropyl]phenol (8).** A solution of 0.60 g (1.63 mmol) of **6a** in 50 mL of ethanol was hydrogenated over a total of 0.24 g of 10% palladium on carbon added in two portions over 6 h. The residue obtained after filtration and evaporation of the reaction mixture was crystallized from ethanol–hexane to give 0.35 g (76%) of **8**, mp 204–208 °C. The analytical sample was obtained from ethanol–DMF–hexane: mp 206–208 °C; ^1H NMR (Me_2SO-d_6) δ 1.84–2.24 (m, 3 H), 3.34 (s, 2 H), 3.81 (t, 1 H, J = 7 Hz), 6.64 (d, 2 H, J = 8 Hz), 7.04 (d, 2 H, J = 8 Hz), 7.22 (m, 5 H); MS, m/e (relative intensity) 280 (3), 176 (12), 84 (100); IR (KBr) 3335, 2460 (br).

Anal. Calcd for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.99. Found: C, 77.03; H, 7.14; N, 9.97.

Mixture of 7a and 8. A suspension of 0.60 g of **6a** and 0.15 g of 20% palladium hydroxide on carbon in 12 mL of ethanol and 6 mL of cyclohexene was stirred at reflux for 3 h. The residue obtained after filtration and evaporation was chromatographed on 60 g of silica gel, eluting with 2:13:85 $NH_4OH/CH_3OH/CH_2Cl_2$. The first product to elute was crystallized successively from ethanol–hexane and ethanol–water to give 0.106 g (23%) of **7a**, mp 218–220 °C. The mother liquors afforded a further 0.102 g (23%), mp 217–219 °C. The second compound to elute was recrystallized from ethanol–hexane to give 0.082 g (18%) of **8**, mp 204–205.5 °C.

(*Z*)-*rac*-4,5-Dihydro-2-[2-phenyl-2-[4-(phenylmethoxy)-phenyl]cyclopropyl]-1*H*-imidazole (9). A total of 0.160 g of **6a** was applied to two 20 × 20 cm silica gel thick layer plates and was developed 2× (15:15:70 $HOAc/n\text{-}C_4H_9OH/CH_2Cl_2$). The bands at R_f 0.4 and 0.6 were isolated and extracted with methanol. The methanol was evaporated, and the residues were dissolved in dichloromethane, washed with sodium carbonate and brine, dried (K_2CO_3), and evaporated. The band at R_f 0.4 yielded 20 mg of **10**, mp 133–134 °C. The band at R_f 0.6 contained 72 mg of a mixture which was crystallized from dichloromethane–hexane and then from ethyl acetate–hexane–ether to give 10.0 mg of **9**, mp 136–137 °C, which contained 0.15 mol of ether: ^1H NMR δ 1.54 (dd, 1 H, J = 6 Hz, 9 Hz), 1.92 (t, 1 H, J = 6 Hz), 2.55 (dd, 1 H, J = 6 Hz, 9 Hz); MS, m/e (relative intensity) 368 (12), 277 (100).

Anal. Calcd for $C_{25}H_{24}N_2O \cdot 0.15C_4H_{10}O$: C, 81.00, H, 6.77; N, 7.38. Found: C, 80.89; H, 6.63; N, 7.47.

Crystals of **9** are monoclinic, space group $P2_1/a$, with a = 10.203 (2) Å, b = 11.216 (1) Å, c = 17.950 (3) Å, β = 94.30 (1)°, and d_{calcd} = 1.195 g cm^{-3} for z = 4. The intensity data were measured on a Hilger-Watts diffractometer (Ni-filtered Cu Kα radiation, θ–2θ scans, pulse-height discrimination). The size of the crystal used for data collection was approximately 0.06 × 0.10 × 0.30 mm; the data were not corrected for absorption (μ = 5.8 cm^{-1}). Of the 1917 independent reflections for θ < 48°, 1201 were considered to be observed [$I > 2.5\sigma(I)$]. The structure was solved by a multiple-solution procedure[9] and was refined by full-matrix least squares. In the final refinement, anisotropic thermal parameters were used

(9) Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr.* **1971**, 368.

for the non-hydrogen atoms and isotropic temperatures factors were used for the hydrogen atoms. The hydrogen atoms were included in the structure factor calculations but their parameters were not refined. The final discrepancy indices are $R = 0.043$ and $R_w = 0.036$ for the 1201 observed reflections. The final differences map has no peaks greater than ± 0.2 e A^{-3}.

(*Z*)-*rac*-4-[2-(4,5-Dihydro-1*H*-imidazol-2-yl)-1-phenylcyclopropyl]phenol Hydrochloride (11). A suspension of 81 mg (0.22 mmol) of **9** and 43 mg of 10% palldium on carbon in 2 mL of ethanol, 0.3 mL of 3.9 M ethanolic hydrochloric acid, and 1.0 mL of cyclohexene was heated to reflux for 5 h. The residue obtained after filtration and evaporation was recrystallized from ethanol–ether to give 41 mg (59%) of **11**: mp 203–204 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.79 (dd, 1 H, J = 6 Hz, 10 Hz), 2.37 (t, 1 H, J = 6 Hz) 2.71 (dd, 1 H, J = 6 Hz, 10 Hz), 3.45–3.75 (m, 4), 6.73 (d, 2 H, J = 9 Hz), 7.15 (d, 2 H, J = 9 Hz), 7.21–7.46 (m, 5), 9.55 (s, 1 H), 9.88 (s br, 2 H).

Anal. Calcd for $C_{18}H_{18}N_2O$·HCl: C, 68.67; H, 6.08; N, 8.90; Cl, 11.26. Found: C, 68.62; H, 6.03; N, 8.82; Cl, 11.49.

(*E*)-*rac*-4-[2-(4,5-Dihydro-1*H*-imidazol-2-yl)-1-phenylcyclopropyl]phenol Hydrochloride Ethanolate (12). A suspension of 0.60 g (1.63 mmol) of **10** and 0.20 g of 10% palladium on carbon in 15 mL of ethanol, 2 mL of 3.9 M ethanolic hydrochloric acid, and 7.5 mL of cyclohexene was heated to reflux for 3 h. The residue obtained after filtration and evaporation was crystallized from ethanol–ether to give 0.48 g (94%) of **12**: mp 130–134 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.06 (t, 3 H, J = 7 Hz), 1.76 (dd, 1 H, J = 6 Hz, J = 9 Hz), 2.37 (t, 1 H, J = 6 Hz), 2.67 (dd, 1 H, J = 6 Hz, J = 9 Hz), 3.40–3.75 (m, 6 H), 6.68 (d, 2 H, J = 9 Hz), 7.24 (d, 2 H, J = 7 Hz), 7.34 (m, 5 H), 9.45 (s, 1 H), 9.87 (s br, 2 H); MS, m/e (relative intensity) 268 (38), 201 (100).

Anal. Calcd for $C_{18}H_{18}N_2O$·HCl·C_2H_5OH: C, 66.56; H, 6.98; N, 7.76; Cl, 9.83. Found: C, 66.57; H, 6.96; N, 7.76; Cl, 10.25.

5,5-Diphenyl-2-pyrrolidinone (16). A solution of phosphorus pentoxide in methanesulfonic acid was prepared by stirring a 1:10 (w/w) mixture of P_2O_5 and methanesulfonic acid at 100 °C under argon until the solution was homogeneous (45 min). To 260 g of this mixture was added 30 g (0.126 mol) of amide **15**, and the resulting mixture was stirred at 80–90 °C for 6 h. After cooling, the mixture was slowly poured into 600 mL of ice-cold water, and the resulting suspension was stirred at room temperature for 1 h. The crystals were filtered, washed with water, and dried overnight under suction in a Büchner funnel to give 30 g of crude lactam. This was recrystallized from 600 mL of 2:1 ethyl acetate–hexane to give 18.1 g (60%) of lactam **16**, mp 190–192 °C (lit.[6] mp 188–189 °C).

3,4-Dihydro-5-methoxy-2,2-diphenyl-2*H*-pyrrolium Tetrafluoroborate (17·HBF$_4$). A solution of 2.85 g (12 mmol) lactam **16** in 50 mL of methylene chloride was treated with 1.80 g (12.2 mmol) of trimethyloxonium tetrafluoroborate,[7] and the resulting suspension was stirred at room temperature under argon for 65 h. The mixture became homogeneous after a few hours but began to deposit crystals toward the end of the reaction period. The mixture was diluted with 25 mL of anhydrous ether, cooled briefly in an ice bath, and filtered. The crystals were washed with ether and dried under vacuum at 50 °C to give 4.05 g (99%) of the imidate, as the BF_4^- salt: mp 168–170.5 °C; ^{1}H NMR ($CDCl_3$) δ 3.10 (m, 4 H), 4.37 (s, 3 H), 7.2–7.6 (m, 11 H); IR (KBr) 3200, 1683, 1647 cm^{-1}; MS, m/e (relative intensity) 251 (47), 174 (100).

Anal. Calcd for $C_{17}H_{17}NO$·HBF_4: C, 60.21; H, 5.25; N, 4.13; F, 7.90. Found: C, 60.02; H, 5.38; N, 4.14; F, 7.77.

3,5,6,7-Tetrahydro-5,5-diphenyl-2*H*-pyrrolo[1,2-*a*]imidazole (18). Imidate **17** was converted to its free base by shaking a methylene chloride suspension of the tetrafluoroborate salt with excess aqueous 1 M sodium hydroxide until disolution was complete. The methylene chloride layer was dried (K_2CO_3) and evaporated to give the imino ether, which was generally used immediately.

A solution of 1.56 g (6.21 mmol) of the imino ether and 1.30 g (6.28 mmol) of 99% bromoethylamine hydrobromide in 30 mL of methanol was heated at reflux for 23 h. After cooling, the reaction mixture was diluted with 150 mL of chloroform, washed with 25 mL of 1 M sodium hydroxide, dried ($MgSO_4$), and evaporated to give 2.0 g of a foam. This was chromatographed on silica gel, eluting with 2.5% triethylamine in methylene chloride, to give 0.95 g (58%) of **18** mp 141–144 °C. An analytical sample, mp 143–146 °C, was prepared by recrystallization from DMF–water: ^{1}H NMR ($CDCl_3$) δ 2.5–2.8 (m, 2 H), 2.8–3.15 (m, 4 H), 4.08 (br t, 2 H), 7.0–7.6 (m, 10 H); IR ($CHCl_3$) 1646 cm^{-1}; MS, m/e (relative intensity) 262 (21), 185 (100).

Anal. Calcd for $C_{18}H_{18}N_2$: C, 82.41; H, 6.92; N, 10.68. Found: C, 82.34; H, 6.87; N, 10.68.

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Registry No. 1, 53267-01-9; **3a**, 54589-41-2; **3b**, 96306-54-6; **3b** (alcohol), 96306-72-8; **4a**, 96306-55-7; **4b**, 96306-56-8; (±)-*cis*-**5a**, 96306-57-9; (±)-*trans*-**5a**, 96306-58-0; (±)-*cis*-**5b**, 96306-59-1; (±)-*trans*-**5b**, 96306-60-4; (±)-*cis*-**6b**, 96306-62-6; (±)-*trans*-**6b**, 96306-63-7; (±)-**7a**, 96306-64-8; (±)-**7b**, 96306-65-9; (±)-**8**, 96306-66-0; (±)-**9**, 96306-61-5; (±)-**10**, 96326-01-1; (±)-**11**, 96306-67-1; (±)-**12**, 96306-68-2; **13**, 2426-87-1; **15**, 26004-45-5; **16**, 40052-79-7; **17**·HBF_4, 96306-70-6; **18**, 96306-71-7; BrPh, 108-86-1; *p*-$PhCH_2OC_6H_4CBPh$, 54589-41-2; $H_2NCH_2CH_2NH_2$·TsOH, 23571-07-5; $Br(CH_2)_2NH_2$·HBr, 2576-47-8; CH_2=CHCN, 107-13-1.

Supplementary Material Available: Tables listing the final atomic parameters, the final anisotropic thermal parameters, bond lengths, and bond angles for **9** (5 pages). Ordering information is given on any current masthead page.

Reactions of Ketenes with Sulfilimines. Synthetic Routes to Oxazolinones and Indolinones

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The reactions of diphenylketene and *tert*-butylcyanoketene with several sulfilimines were investigated. 5,5-Diphenyl-2-oxazolin-4-ones were produced from *N*-acylsulfilimines and diphenylketene while a 2-indolinone was obtained from *N*-arylsulfilimine and the same ketene. *tert*-Butylcyanoketene afforded either simple substituted or ortho-rearranged amides when *S*,*S*-dimethylsulfilimines were used as substrates. The structure of 2,5,5-triphenyloxazolidin-4-one (**7b**) was confirmed by single-crystal X-ray examination. Possible mechanistic pathways which account for all observed products are discussed.

Although the cycloaddition reactions of diphenylketene and *tert*-butylcyanoketene with allenes,[2a–c] alkynes,[3a–c] alkyl azides,[4] oxaziridines,[5a–c] olefins,[6a–c] diimides,[7a,b] ylids,[7a,8] enamines[7a–9] nitrones,[10a–c] imines,[11a–c] thiazoles,[12a,b] tertiary

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