chromatographed on silica gel with benzene–ethyl acetate (4:1) as eluent to give the acetamides of **4a** and **3n**. The acetamide of **3n**: mp 225–226 °C (from hexane–benzene); ^{1}H NMR ($CDCl_3$) δ 1.9 (s, 3 H), 3.4–3.5 (m, 2 H), 5.4–5.8 (m, 2 H), 5.9–6.0 (m, 2 H), 7.0–7.3 (m, 3 H); IR ($CHCl_3$) 3340, 1670 cm^{-1}; MS, *m/e* 221 (M^+), 186 (M^+ – Cl), 162 (M^+ – NH_2COMe), 143, 128. Anal. Calcd for $C_{12}H_{12}NOCl$: C, 65.01; H, 5.46; N, 6.32; Cl, 15.99. Found: C, 64.92; H, 5.44; N, 6.33; Cl, 15.69.

Photoamination of *m*-Dimethoxybenzene (1l). The aminated products were acetylated with Ac_2O–pyridine and then chromatographed on silica gel with hexane–benzene (1:1) to give the acetamides of **4d** and **4e**. The acetamide of **4d**: mp 118–120 °C (from benzene); ^{1}H NMR ($CDCl_3$) δ 2.15 (s, 3 H), 3.75 (s, 3 H), 3.80 (s, 3 H), 6.25–6.6 (m, 2 H), 7.55 (br s, 1 H), 8.0–8.3 (m, 1 H); IR ($CHCl_3$) 3450, 1680 cm^{-1}; MS, *m/e* 195 (M^+), 137 (M^+ – NHCOMe). Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.52; H, 6.71; N, 7.18. Found: C, 61.43; H, 7.00; N, 7.13. The acetamide of **4e**: ^{1}H NMR (CCl_4) δ 2.05 (s, 3 H), 3.75 (s, 3 H), 6.5–7.0 (m, 3 H), 7.65 (br s, 1 H), 8.1–8.4 (m, 1 H). The structure of the acetamide of **4e** was determined by direct comparison with an authentic sample.

Photoamination of Biphenyl (1m). The aminated products were separated by chromatography on silica gel with hexane–benzene (1:1) as eluent. The structures of **4f** and **4g** were determined by direct comparison with authentic samples. Compound **4f**: mp 176–177 °C (for the acetamide; from benzene); ^{1}H NMR (CCl_4) δ 3.40 (br s, 2 H), 6.25–6.70 (m, 2 H), 6.9–7.7 (m, 7 H); IR 3480, 3400 cm^{-1}. Compound **4g**: ^{1}H NMR (CCl_4) δ 3.56 (br s, 2 H), 6.4–7.5 (m, 9 H); IR ($CHCl_3$) 3480, 3400 cm^{-1}.

1-Methyl-2,4-dicyanobenzene (9a): mp 142–143 °C (from methanol); ^{1}H NMR (CCl_4) δ 2.56 (s, 3 H), 7.36 (d, *J* = 8 Hz, 1 H), 7.66 (dd, *J* = 8, 2 Hz, 1 H), 7.76 (m, 1 H); IR ($CHCl_3$) 2250 cm^{-1}; MS, *m/e* 142 (M^+), 115. Anal. Calcd for $C_9H_6N_2$: C, 76.04; H, 4.25; N, 19.71. Found: C, 75.84; H, 4.19; N, 19.61.

1-Ethyl-2,4-dicyanobenzene (9b): ^{1}H NMR (CCl_4) δ 1.33 (t, *J* = 8 Hz, 3 H), 2.96 (q, *J* = 8 Hz, 2 H), 7.30 (d, *J* = 8 Hz, 1 H), 7.63 (dd, *J* = 8, 2 Hz, 1 H), 7.76 (m, 1 H); IR ($CHCl_3$) 2250 cm^{-1}; MS, *m/e* 156 (M^+), 141 (M^+ – Me), 127 (M^+ – Et), 114.

BF_3-Catalyzed Cycloadditions of Naturally Occurring Sesquiterpene *p*-Benzoquinones

Pedro Joseph-Nathan,* María E. Garibay, and Rosa L. Santillan

Departamento de Química del Centro de Investigación y de Estudios Avanzados, Instituto Politécnico Nacional, Apartado 14-740, México, D.F., 07000 México

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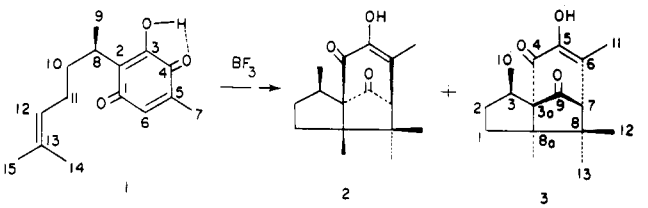
Lewis acid catalyzed reactions of all known naturally occurring perezone analogues and two allylic alcohols prepared from perezone and hydroxyperezone show that these *p*-benzoquinones exhibit a complex behavior upon acid treatment. As in the case of perezone, *O*-angeloylperezone and 6-angeloxyperezone afforded pipitzol analogues. Hydroxyperezone and *O*-angeloyl-6-hydroxyperezone yielded a stable boron adduct of perezinone. Curcuquinone, the simplest sesquiterpene quinone, afforded mainly polymeric material, while 15-hydroxyperezone and hydroxyperezone derivatives gave a dibenzofurandione and a tricyclic molecule containing a new skeleton, respectively. The results for *O*-angeloylperezone, compared with those of perezone, show that steric effects play an important role in these transformation allowing at present complete stereocontrol of the reaction outcome.

Cycloaddition reactions have been a subject of increased interest and continue to attract attention largely due to their synthetic versatility.[1-4] However, little attention has been paid to intramolecular cycloadditions of the type represented by the perezone (**1**) to pipitzol (**2** and **3**) transformation.[5] Previous investigations of the thermally allowed reaction of perezone (**1**) have shown that it involves the coexistence of a sigmatropic change of order [1, 9] and a type B, ionic [$_\pi4_s + _\pi2_s$] cycloaddition.[6,7] Classically, the thermal transformation has been performed by refluxing perezone (**1**) in tetralin[8,9] or cumene,[10] affording an equimolecular mixture of α- (**2**) and β-pipitzol (**3**). Later, it



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was revealed that perezone (**1**) undergoes a mild highly stereoselective cycloaddition in the presence of boron trifluoride etherate to yield a 9:1 mixture of α- (**1**) and β-pipitzol (**2**) in 98% yield.[11] Subsequent studies also demonstrated that the stereoselectivity may be reversed in favor of the β isomer (**3**) by $AlCl_3$–Et_2S treatment of *O*-methylperezone, presumably due to steric crowding between the secondary methyl and methoxyl groups in the transition state.[12] The data provided so far seem to in-

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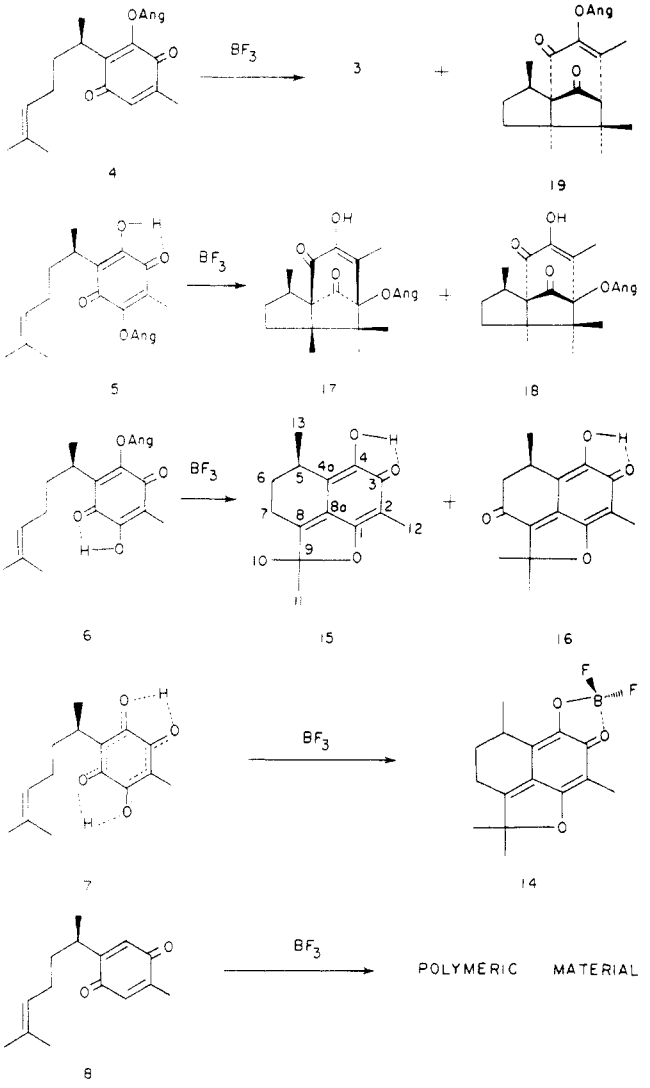
dicate that substituents in the parent ring play an important role in determining reaction outcome and in some cases stereoselectivity.

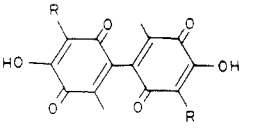
The investigation described herein was designed to address the issue of substituent effects in the intramolecular Lewis acid catalyzed cycloaddition reactions of all known naturally occurring perezone analogues. For this purpose we have explored the boron trifluoride catalyzed reactions of *O*-angeloylperezone[13] (**4**), the equimolecular mixture of hydroxyperezone monoangelates[14] (**5** and **6**), hydroxyperezone[15] (**7**), and curcuquinone[16,17] (**8**).



The results revealed that the stereochemical and regiochemical outcome of the reactions is very sensitive to electronic and steric factors. No attempt has been made in this initial effort to prove the scope of this process by varying the nature of the Lewis acid, although the effect of substitution at C-15 in perezone and hydroxyperezone was analyzed. The results indicate that hydroxyquinones exhibit a complex, as yet unpredictable behavior upon acid treatment, showing also that the boron trifluoride catalyzed intramolecular reaction is a viable process for the synthesis of pipitzol analogues in those cases where position 6 of the quinone is either free or has a protected hydroxyl group. In those cases only the transformation may provide a general route to these highly functionalized structures, heterocycles included.[18]

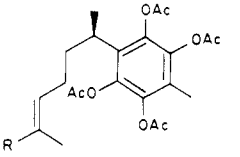
Results and Discussion

Syntheses of Allylic Alcohols. Preparation of 15-hydroxyperezone (**9**) was achieved by reductive acetylation of the quinone ring of perezone followed by selenium dioxide oxidation at C-15. Subsequent $NaBH_4$ reduction of the derived aldehyde yielded 15-hydroxyleucotriacetylperezone,[10] which was transformed into the desired 15-hydroxyperezone (**9**) by means of lithium aluminum hydride followed by air oxidation. This is confirmed by the presence of the quinonoid quartet at 6.48 (J = 1.8 Hz) ppm in the ^1H NMR spectrum. A major byproduct of the reduction was characterized as 15-hydroxydiperezone (**10**) as evidenced by the absence of the quinonoid proton. The same compounds (**9** and **10**) were obtained by direct selenium dioxide oxidation of perezone (**1**), although the yields were considerably lower.



10: R = CH(Me)CH_2CH_2CH=C(Me)CH_2OH

6,15-Dihydroxyperezone (**13**) was prepared from 6-hydroxyperezone[15] (**7**) by using a similar sequence of reactions. Treatment of 6-acetoxyleucotriacetylperezone[14] with selenium dioxide in a mixture of acetone, dioxane, and acetic acid yielded exclusively the corresponding 15-aldehyde (**11**) which showed the expected ^1H NMR resonance at 9.44 ppm. Sodium borohydride reduction of **11** yielded the corresponding alcohol **13**, showing a signal at 3.93 ppm for the C-15 methylene. Final treatment of 6-acetoxy-15-hydroxyleucotriacetylperezone (**12**) with lithium aluminum hydride followed by air oxidation afforded the desired 6,15-dihydroxyperezone (**13**) as shown by the spectral data given in the Experimental Section.



11: R = CHO
12: R = CH_2OH

Cycloaddition Reactions. Cyclization of hydroxyperezone (**7**) at 4 °C in the presence of BF_3 and in methylene chloride solutions affords exclusively the surprisingly stable boron adduct **14** if the reaction is carried out under a nitrogen atmosphere and extraction does not include neutralization with a dilute sodium bicarbonate solution. Although, in general, the ^1H NMR resonances of perezinone·BF_2 (**14**) bore some resemblance to perezinone[9] (**15**), which constitutes the product from the H_2SO_4-catalyzed reaction[19] of **7**, the H-7, CH_3-13, and CH_3-10,11 singlets proved to be indicative of coordination, since they appeared at lower field in the complex (**14**). Additional spectroscopic evidence was obtained by ^{11}B and ^{19}F NMR,

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spectrometry, which showed signals in agreement with those reported for 1,3-diketonate adducts.[20] To verify the structure of **14**, the boron complex was extracted by using ethyl acetate–water and successive washings with a sodium bicarbonate solution and water to give perezinone (**15**) as determined by direct comparison with an authentic sample.[9]

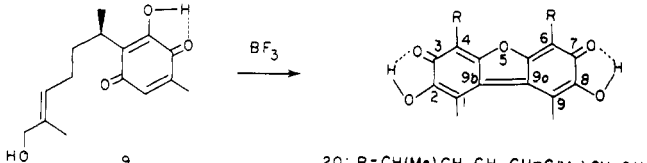
In contrast to perezinone·BF_2 (**14**), perezinone (**15**) was oxidized readily in acetone solutions to give the known oxoperezinone[19] (**16**). Moreover, if the reaction is carried out in the absence of a nitrogen atmosphere, a mixture containing perezinone (**15**) and oxoperezinone (**16**) is obtained.

We next investigated the natural mixture of hydroxyperezone monoangelates (**5** and **6**). Cyclization of this mixture afforded essentially three products identified as perezinone·BF_2 (**14**) and α- (**17**) and β-perezol (**18**). Structure **14** (major) separated readily by crystallization from the perezol mixture. The remaining compounds (**17** and **18**) were purified by chromatography and identified by direct comparison.[15] The products isolated in this reaction evidence that there is a marked difference in chemical behavior between the isomeric esters which is in severe contrast with their physical properties, since neither extensive chromatographic procedures including HPLC nor fractional distillation have provided even slight enrichment of one of the esters (**5** and **6**). Mechanistic considerations permit the conclusion that 6-angeloxyperezone (**5**) yields α- (**17**) and β-perezol (**18**) while *O*-angeloyl-6-hydroxyperezone (**6**) undergoes hydrolysis of the ester to yield perezinone·BF_2 (**14**) and angelic acid.[21]

On the basis of product selectivity observed in the cyclization of *O*-methylperezone,[12] *O*-angeloylperezone (**4**) was expected to yield predominantly β-pipitzol (**3**). In fact, cyclization of *O*-angeloylperezone (**4**) afforded two products in a 9:1 ratio of 90% combined yield, which were identified as β-pipitzol (**3**) and *O*-angeloyl-β-pipitzol (**19**). The latter displayed similar resonances to **3** as well as the characteristic[21] angeloyl ester signals in the ^1H NMR spectrum.

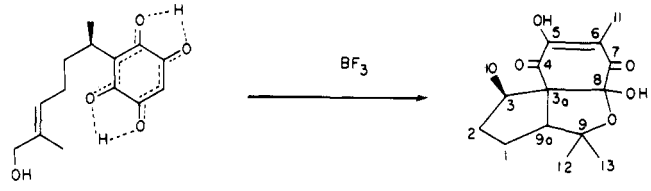
Dreiding model analysis of **1** suggests that a 3-*O*-substituent larger than hydrogen forces a severe interaction with the secondary methyl group in the array leading to α-pipitzol (**2**). Since this interaction is relieved by approach from the opposite side of the ring,[12] the reaction should lead predominantly to β-pipitzol (**3**), which is indeed obtained.

When 15-hydroxyperezone (**9**) was treated with boron trifluoride etherate, a single compound could be identified.



This compound, which was characterized as the dibenzofurandione **20** by NMR, was quite labile and decomposed upon purification by column chromatography and/or standing in chloroform solution. The appearance of characteristic signals in the ^1H NMR spectrum of **20** at 5.30 (m, H-4'), 3.94 (H_2-6'), 2.31 (s, 1,9-CH_3), 1.58 (s, 5'-CH_3), and 1.25 (d, J = 6 Hz, 1'-CH_3) ppm was compatible with the dibenzofurandione derivative obtained by reaction by dihydroperezone with F_3B·OEt_2.[22]

The reaction of 6,15-dihydroxyperezone (**13**) with the Lewis acid gave a complex mixture of products among which small amounts of the tricyclic derivative **21** were isolated. The structural assignment of this compound



containing a new skeleton and a newly formed methyl group when compared with starting material was made on the basis of its spectral characteristics. Compound **21** exhibits carbonyl absorptions at 1641 cm^{-1} in the infrared spectra, as well as UV absorptions at 244 (log ϵ 3.30) and 2.93 nm (3.37). The ^1H NMR spectrum showed signals at 7.58 and 4.87 ppm which disappeared upon equilibration with D_2O, three methyl singlets at 2.03, 1.38, and 1.13, and a doublet at 0.72 ppm (J = 5 Hz). Further evidence was obtained from ^{13}C chemical shifts since the signals corresponding to C-1 (28.0), C-2 (39.5), C-3 (39.1), C-3a (73.1), and C-9a (61.9) show chemical shifts similar to cedranolides[23] while the signals corresponding to C-4 (197.2), C-5 (154.9), C-6 (119.3), and C-7 (193.0) show shifts in agreement with quinones.[24]

The reaction with curcuquinone (**8**) resulted in the formation of an intractable complex mixture of polymeric material from which no product could be characterized, even when the temperature of the reaction was lowered to −22 °C.

Assignments of ^{13}C spectra of perezinone·BF_2 (**14**), perezinone (**15**), and oxoperezinone (**16**) are based on heteronuclear long-range spin–spin coupling constants and comparison within the three samples. In all compounds, the α,β-unsaturated carbonyl carbon exhibited a characteristic low-field chemical shift ranging from 181.9 to 192.5 ppm while the unsaturated carbons C-2 and C-1 displayed low-field quartets. The largest induced shifts were observed for C-4 and C-1 evidencing the increased electron delocalization upon complexation in **14**. As far as the methyl signals are concerned, C-12 shows shifts in agreement with carbons in similar environments[24] while in **15** and **16** the *gem*-dimethyl methyl groups were tentatively assigned.

The ^{13}C spectra of the perezone and 6-hydroxyperezone analogues (**9**, **10**, and **13**) can easily be assigned on the basis of one-bond and long-range coupling constants as well as by comparison with model compounds.[24]

In summary, the results show that even slight changes in the structure of the quinones may exert a considerable effect on the course of the reaction. In *O*-angeloylperezone (**4**) and 6-angeloxyperezone (**5**), the cycloadducts (**3** and **17**–**19**) were formed to the practical exclusion of other compounds, in analogy with perezone (**1**). However, hydroxyperezone (**7**) which has been shown to have an electron-delocalized structure in solution,[24] and *O*-angeloyl-6-hydroxyperezone (**6**) are forced to seek an alternative more favorable path. In the case of curcuquinone (**8**), the amount of polymer increased to such a degree that isolation of products was not possible.

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The results suggest that the $F_3B{\cdot}OEt_2$-catalyzed reaction of these quinones involves initial coordination of the catalyst, which in turn induces polarization of the conjugated enone system promoting 1,4-additions only in those cases where position 6 is either free or has a protected alcohol. Substitution of a hydroxyl group at position 15 induces perturbation of the ethylene molecular orbital, probably by increasing the HOMO–LUMO energy gap, thus favoring an alternative path. Moreover, there seems to be a significant influence of steric factors in these cycloaddition reactions, as seen by the stereochemical outcome of products derived from 1 vs. those from *O*-angeloylperezone (4).

Experimental Section

Melting points were obtained on a Fisher-Johns melting point apparatus and are uncorrected. ^1H NMR spectra were measured in $CDCl_3$ with Me_4Si as internal standard on a Varian Model EM-390 spectrometer at 90 MHz. ^{13}C NMR spectra were determined in $CDCl_3$ on either a Varian Model XL-100A-12FT-16K or a Varian Model XL-300GS spectrometer at 25.2 and 75.4 MHz, respectively. The ^{19}F NMR spectrum was recorded on a Varian Model EM-390 spectrometer in $CDCl_3$ solution with CF_3COOH as external reference. The ^{11}B NMR spectrum was determined on a Varian Model XL-100A-12FT spectrometer in $CDCl_3$ solution with $F_3B{\cdot}OEt_2$ as external reference. Infrared spectra were obtained on a Perkin-Elmer Model 421 or a Nicolet Model MX-1 spectrophotometer. The mass spectrum was obtained with a Hewlett Packard Model 5985-A mass spectrometer at an ionization potential of 70 eV. Gravity column chromatography was done by using Merck silica gel 60 (70–230-mesh ASTM). Preparative thin layer chromatography was done on Merck PLC plates silica gel 60 F_{254} (2-mm-layer thickness). All cycloaddition reactions were quenched by using water which was previously deoxigenated by passing a flow of argon during 1 h. 6-Hydroxyperezone (7) was obtained from the roots of *P. hebeclada*[15] and *O*-angeloylperezone (4) was extracted from *P. thurberi*[13] (oil): IR ($CHCl_3$) 1736 (Ang), 1659 (C=O) cm^{-1}; UV (ethanol) λ_{max} 223 (log ϵ 3.09), 253 nm (3.10); ^1H NMR (90 MHz, $CDCl_3$) δ 6.60 (q, 1 H, J = 1.6 Hz, H-6), 6.33 (m, 1 H, H-3′), 5.05 (t, with additional long-range couplings, 1 H, H-12), 2.09 (m, 9 H, CH_3-4′, CH_3-5′, CH_3-7), 1.65 (s, 3 H, CH_3-15), 1.53 (s, 3 H, CH_3-14), 1.20 (d, 3 H, J = 6 Hz, CH_3-9); ^{13}C NMR ($CDCl_3$) δ 186.6 (s, C-1), 180.5 (s, C-4), 164.3 (s, C-1′), 149.4 (s, C-3), 143.6 (s, C-5), 142.1 (d, C-3′), 139.7 (s, C-2), 133.9 (d, C-6), 131.7 (s, C-13), 126.0 (s, C-2′), 124.0 (d, C-12), 34.8 (t, C-10), 30.5 (d, C-8), 26.5 (t, C-11), 25.6 (q, C-15), 20.4 (q, C-5′), 18.6 (q, C-9), 17.6 (q, C-14), 15.9 (q, C-4′), 15.2 (q, C-7).

15-Hydroxyperezone (9). Method A. A solution of 100 mg (0.25 mmol) of 15-hydroxyleucotriacetylperezone[10] in 5 mL of anhydrous tetrahydrofuran was treated portion-wise with 80 mg (2.11 mmol) of lithium aluminum hydride at 0 °C. The reaction mixture was stirred at room temperature during 30 min and cooled to 0 °C, and the excess hydride was destroyed by slow addition of ethyl acetate and water. The mixture was stirred at room temperature during 30 min, filtered, concentrated under vacuum, and extracted with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was chromatographed on a silica gel plate, developing with a hexane/ethyl acetate mixture (1:1). This yielded 32 mg (0.12 mmol, 48%) of **9** as an orange solid: mp 47–50 °C; IR (film) 3425 (OH), 1657 and 1635 cm^{-1} (C=O); UV (ethanol) λ_{max} 223 (log ϵ 2.74), 265 nm (2.85); ^1H NMR δ (90 MHz, $CDCl_3$) 6.48 (q, 1 H, J = 1.8 Hz, H-6), 5.37 (t, 1 H, J = 6 Hz with additional long-range couplings, H-12), 3.97 (br s, 2 H, H-15), 3.08 (septet, 1 H, H-8), 2.08 (d, 3 H, J = 1.8 Hz, CH_3-7), 1.60 (br s, 3 H, CH_3-14), 1.22 (d, 3 H, J = 7 Hz, CH_3-9); ^{13}C NMR ($CDCl_3$) δ 187.2 (s, C-1), 184.0 (s, C-4), 151.1 (s, C-3), 140.5 (s, C-5), 135.6 (d, C-6), 134.6 (s, C-13), 126.1 (d, C-12), 124.2 (s, C-2), 68.9 (t, C-15), 33.6 (t, C-10), 29.1 (d, C-8), 26.1 (t, C-11), 18.2 (q, C-9), 14.7 (q, C-7), 13.6 (q, C-14).

Method B. Perezone[15] (1) (250 mg, 1.00 mmol) was dissolved in a mixture containing 10 mL of dioxane, 0.1 mL of acetic acid, and 0.5 mL of acetone and heated to 60 °C. The solution was treated with 250 mg (2.22 mmol) of selenium dioxide and stirred at 60 °C during 30 min. The reaction mixture was filtered hot over a Celite bed and the filtrate was placed directly in a solution of 1 g of thiourea in 100 mL 10% hydrochloric acid. The red precipitate that formed was removed over the same Celite filter and washed with small portions of ethyl acetate. The organic phase was diluted with additional ethyl acetate and washed successively with dilute hydrochloric acid, water, aqueous sodium bicarbonate, and water again, dried over anhydrous sodium sulfate, and evaporated to dryness. The residue was chromatographed over silica gel, eluting with hexane/benzene (1:1) to yield 5 mg (0.02 mmol 2%) of 15-hydroxyperezone, mp 47–50 °C, which was identical with the compound obtained in method A.

Those fractions eluted with benzene afforded **15-hydroxydiperezone (10)**, which was further purified by thin layer chromatography developing with benzene/ethyl acetate (1:1) to yield 100 mg (0.19 mmol, 19%) of oily 15-hydroxydiperezone (**10**): IR ($CDCl_3$) 3388 (OH), 1669 (C=O), and 1635 (C=C) cm^{-1}; UV (ethanol) λ_{max} 209 (log ϵ 4.18), 274 (4.00) nm; ^1H NMR (90 MHz, $CDCl_3$) 7.30 (s, 2 H, 2 OH), 5.38 (t with additional long-range couplings, 2 H, J = 6 Hz, H-12), 3.98 (s, 4 H, H-15), 3.08 (m, 2 H, H-8), 1.92 (s, 6 H, CH_3-7), 1.63 (br s, 6 H, CH_3-14), 1.24 and 1.23 (2 d, 3 H each, J = 6 Hz, CH_3-9); ^{13}C NMR ($CDCl_3$) δ 185.1 and 184.9 (2 s, C-1 and C-1′), 183.0 and 182.9 (2 s, C-4 and C-4′), 151.4 (s, C-3 and C-3′), 140.0 and 139.9 (2 s, C-5 and C-5′), 138.4 and 138.3 (2 s, C-6 and C-6′), 134.6 (s, C-13 and C-13′), 125.8 (d, C-12 and C-12′), 124.5 (s, C-2 and C-2′), 68.6 (t, C-15 and C-15′), 33.7 (t, C-10 and C-10′), 29.6 (d, C-8 and C-8′), 26.2 (t, C-11 and C-11′), 18.4 and 18.2 (2 q, C-9 and C-9′), 13.6 (q, C-14 and C-14′), 13.0 (q, C-7 and C-7′).

Selenium Dioxide Oxidation of 6-Acetoxyleucotriacetylperezone. Method A. A vigorously stirred solution of 250 mg (0.57 mmol) of 6-acetoxyleucotriacetylperezone[14] in 10 mL of ethanol was treated at 60 °C with 125 mg (1.13 mmol) of selenium dioxide. The mixture was refluxed during 1 h and filtered hot over a Celite bed. The filtrate was placed directly in a solution of 1 g of thiourea in 50 mL of 10% hydrochloric acid. The red precipitate that formed was removed over the same Celite filter, which was then washed with ethyl acetate. The organic solution was diluted with additional ethyl acetate and washed with dilute hydrochloric acid, water, aqueous sodium bicarbonate, and water again, dried over anhydrous sodium sulfate, and evaporated to dryness. The residue was chromatographed over silica gel. The fractions eluted with benzene/chloroform (1:1) gave 40 mg (0.09 mmol, 16%) of aldehyde **11** as an oil: IR (film) 1781 (Ac) 1695 cm^{-1} (α,β-unsaturated ester); UV (ethanol) λ_{max} 223 nm (log ϵ 2.8); ^1H NMR (90 MHz, $CDCl_3$) δ 9.44 (s, 1 H, CHO), 6.41 (t, 1 H, J = 7 Hz with additional long-range couplings, H-12), 2.30 (s, 12 H, Ac), 1.68 (br s, 3 H, CH_3-14), 1.23 (d, 3 H, J = 7 Hz, CH_3-9).

Those fractions eluted with chloroform gave 10 mg (0.02 mmol, 4%) of alcohol **12** as an oil: IR (film) 3505 (OH) 1780 cm^{-1} (Ac); UV λ_{max} 220 nm (log ϵ 3.1); ^1H NMR (90 MHz, $CDCl_3$) δ 3.93 (s, 2 H, H-15), 2.32 and 2.30 (2 s, 6 H each, 4 Ac), 1.95 (s, 3 H, CH_3-7), 1.54 (br s, 3 H, CH_3-14), 1.18 (d, 3 H, J = 7 Hz, CH_3-9).

Method B. 6-Acetoxyleucotriacetylperezone (500 mg, 1.15 mmol) was dissolved in 4 mL of a mixture of dioxane, acetone, and acetic acid (1:2:1). The solution was heated to 60 °C, treated with 280 mg (2.52 mmol) of selenium dioxide, and refluxed during 1 h. Workup as in the case of method A yielded an oily residue which was chromatographed over silica gel. The fractions eluted with benzene/chloroform (1:1) yielded 200 mg (0.45 mmol, 39%) of aldehyde **11** which was identical with the compound obtained in method A.

Reduction of Aldehyde 11. A solution of 100 mg (0.22 mmol) of aldehyde **11** in 10 mL of methanol was cooled to 0 °C and treated with 20 mg (0.53 mmol) of sodium borohydride. The reaction mixture was stirred in the cold for 3 h and quenched with 10% hydrochloric acid. The organic layer was extracted with ethyl acetate, washed three times with water, dried over anhydrous sodium sulfate, filtered, and evaporated under vacuum. The residue was chromatographed over silica gel, yielding in the fractions eluted with chloroform 70 mg (0.15 mmol, 70%) of alcohol **12** which was identical with the compound obtained in method A.

6,15-Dihydroxyperezone (13). A solution of 100 mg (0.22 mmol) of alcohol **12** in 5 mL of anhydrous tetrahydrofuran was

treated with 67 mg (1.76 mmol) of lithium aluminum hydride at 0 °C. The reaction mixture was stirred during 30 min and quenched with ethyl acetate and water. Workup as in the case of **9** gave 21 mg (0.07 mmol, 34%) of **13** as a red powder; mp 93–95 °C; IR ($CHCl_3$) 3370 (OH), 1650 cm^{-1} (C=O); UV (ethanol) λ_{max} 220 (log ϵ 3.1), 294 nm (3.3); ^1H NMR (90 MHz, $CDCl_3$) δ 7.78 (br, 2 OH), 5.35 (t, 1 H, J = 6 Hz, with additional long-range couplings, H-12), 3.93 (s, 2 H, H-15), 1.95 (s, 3 H, CH_3-7), 1.58 (br s, 3 H, CH_3-14), 1.18 (d, 3 H, J = 7 Hz, CH_3-9); ^{13}C NMR ($CDCl_3$) δ 167.4 (br, C-1, 3,4,6), 134.7 (s, C-13), 126.1 (d, C-12), 118.9 (s, C-2), 111.4 (s, C-5), 68.9 (t, C-15), 33.7 (t, C-10), 29.0 (d, C-8), 26.0 (t, C-11), 18.3 (q, C-9), 13.6 (q, C-14), 7.4 (q, C-7).

Reaction of *O*-Angeloylperezone (4). A stirred, ice-cooled solution of *O*-angeloylperezone (**4**) (100 mg, 0.29 mmol) in 3 mL of dichloromethane was treated with $F_3B{\cdot}OEt_2$ (0.8 mL, 6.5 mmol) under a nitrogen atmosphere, and the reaction was allowed to proceed for 30 min at 0 °C. After the reaction was quenched with water, the product was extracted with dichloromethane. The organic layer was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated under vacuum. The residue was chromatographed on a silica gel plate, developing with a benzene/acetone mixture (95:5). β-Pipitzol (**3**) (64 mg, 0.25 mmol, 85%) was isolated as white crystals and recrystallized from benzene: mp 131–132 °C (lit.[9] mp 131–132 °C). *O*-Angeloyl-β-pipitzol was a colorless oil (5 mg, 0.02 mmol, 5%): IR (film) 1761 (C=O), 1733 (Ang), and 1687 cm^{-1}; UV (ethanol) λ_{max} 218 (log ϵ 4.20), 281 nm (3.73); ^1H NMR (90 MHz, $CDCl_3$) δ 6.22 (m, 1 H, H-3′) 2.03 (m, 9 H, CH_3-4′,5′,11), 1.30 (d, J = 6 Hz, 3 H, CH_3-10), 1.20 (s, 3 H, CH_3-12), 1.12 (s, 3 H, CH_3-13); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 203.85 (s, C-9), 190.17 (s, C-4), 165.24 (s, C-1′), 145.50 (s, C-5), 142.7 (s, C-6), 140.86 (d, C-3′), 126.59 (s, C-2′), 69.00 (d, C-7), 54.57 (d, C-8a), 38.6 (s, C-8), 35.26 (t, C-2), 35.0 (d, C-3), 26.65 (q, C-12), 25.57 (t, C-1), 24.02 (q, C-13), 20.54 (q, C-5′), 18.98 (q, C-11), 15.98 (q, C-4′), 13.44 (q, C-10).

Perezinone·BF_2 (14). A stirred, ice-cooled solution of hydroxyperezone (**7**) (50 mg, 0.19 mmol) in 2 mL of dichloromethane was treated with $F_3B{\cdot}OEt_2$ (0.2 mL, 1.6 mmol) under a nitrogen atmosphere, and the reaction was allowed to proceed overnight at 4 °C. After workup, the residue was crystallized from acetone/water to yield 52 mg (0.18 mmol, 95%) of **14** as yellow needles: mp 170 °C dec; IR (KBr) 1646, 1512 (C=O), 1367 (B—O), 1137–1066 (B—O, B—F) cm^{-1}; MS, m/e (relative intensity) 294 (M^+, 38), 278 (24), 279 (100), 43 (20); ^1H NMR (90 MHz, $CDCl_3$) δ 3.10 (sext, 1 H, J = 6 Hz, H-5), 2.73 (t, 2 H, J = 6 Hz, H-7), 2.07 (s, 3 H, CH_3-12), 1.68 (s, 6 H, CH_3-10,11), 1.37 (d, 3 H, J = 7 Hz, CH_3-13); ^{11}B NMR (32.1 MHz, $CDCl_3$) δ 7.3; ^{19}F NMR (84.7 MHz, $CDCl_3$) δ 141.2; ^{13}C NMR ($CDCl_3$) δ 181.9 (s, C-3), 178.9 (s, C-4), 174.6 (s, C-1), 147.7 (s, C-4a), 127.5 (s, C-8a), 111.8 (s, C-8), 101.9 (s, C-2), 100.9 (s, C-9), 31.2 (t, C-6), 27.2 (d, C-5), 23.3 (q, C-10 and C-11), 22.2 (t, C-7), 18.1 (q, C-13), 7.1 (q, C-12).

Perezinone (15). The title compound was prepared from 100 mg of hydroxyperezone (**7**) (0.37 mmol) by using the procedure described for perezinone·BF_2 (**14**). The reaction was quenched with water and the solvent was evaporated under vacuum. The residue was diluted with ethyl acetate, washed successively with sodium bicarbonate and water, dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. The residue afforded 61 mg (0.25 mmol, 66%) of yellow plates of perezinone (**15**) which were recrystallized from acetone/water: mp 145–146 °C (lit.[9,19] mp 146–147 °C); ^{13}C NMR ($CDCl_3$) δ 182.4 (s, C-3), 166.8 (s, C-1), 160.0 (s, C-4), 143.0 (s, C-4a), 124.9 (s, C-8a), 110.8 (s, C-8), 103.6 (s, C-2), 95.8 (s, C-9), 30.5 (t, C-6), 26.3 (d, C-5), 24.4 and 24.1 (2 q, CH_3-10 and CH_3-11), 19.6 (t, C-7), 18.0 (q, C-13), 7.7 (q, C-12).

Oxoperezinone[19] (16). The title compound was obtained as a byproduct in the preparation of perezinone (**15**) when the reaction was carried out in the absence of a nitrogen atmosphere or by slow oxidation of perezinone (**15**) in acetone solution. Compound **16** was recrystallized from benzene and identified by direct comparison with an authentic sample: mp 164–166 °C (lit.[19] mp 167–168 °C); ^1H NMR (90 MHz, $CDCl_3$) δ 1.27 (d, 3 H, J = 7 Hz, H-13), 1.62 and 1.57 (2s, 3 H each, Me-10 and Me-11), 1.93 (s, 3 H, H-12), 2.45 and 2.85 (2 H, J_{AB} = 15 Hz, J_{BX} = 4.5 Hz, J_{AX} = 6 Hz, H-6), 3.47 (1 H, J_{AX} = 6 Hz, J_{BX} = 4.5 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 192.5 (s, C-3), 182.1 (s, C-7), 166.3 (s, C-1), 145.9 (s, C-4), 144.0 (s, C-4a), 139.2 (s, C-8a), 109.2 (s, C-8), 107.0 (s, C-2), 95.5 (s, C-9), 46.7 (t, C-6), 29.4 (d, C-5), 25.5 and 24.8 (2 q, CH_3-10 and CH_3-11), 20.6 (q, C-13), 7.9 (q, C-7).

Reaction of the Equimolecular Mixture of Hydroxyperezone Monoangelates (5 and 6). A solution containing 300 mg (0.87 mmol) of the natural mixture of hydroxyperezone monoangelates (**5** and **6**) in 15 mL of dichloromethane was cooled to 4 °C and treated with boron trifluoride etherate (1.6 mL, 13.0 mmol) with stirring under a nitrogen atmosphere. The reaction mixture was stored overnight at 4 °C, quenched, and worked up in the usual manner. The residue was dissolved in hexane, from which there crystallized 87 mg (0.29 mmol, 34%) of perezinone·BF_2 (**14**), mp 170 °C, identical with the product obtained by reaction of hydroxyperezone (**8**). The remaining oily fraction was chromatographed over silica gel, eluting with benzene to yield 90 mg (0.27 mmol, 31%) of α-perezol (**17**), mp 164–167 °C (lit.[15] mp 164–167 °C). Those fractions eluted with benzene/chloroform (1:1) gave 30 mg (0.09 mmol, 10%) of β-perezol (**18**): mp 108–109 °C (lit.[15] mp 108–109 °C).

Dibenzofurandione (20). A solution of 80 mg (0.30 mmol) of 15-hydroxyperezone (**9**) in 3 mL of dichloromethane was cooled to 0 °C and treated with 0.3 mL of boron trifluoride etherate (2.44 mmol) under a nitrogen atmosphere. The reaction was stirred at 0 °C during 30 min followed by addition of degassed water. The organic phase was extracted with dichloromethane and worked up in the usual manner to yield 14 mg (0.03 mmol, 9%) of furanone (**20**) as an oil which was purified by thin layer chromatography developing with a hexane/ethyl acetate mixture: ^1H NMR (90 MHz, $CDCl_3$) δ 7.57 (2 H, 2 OH), 5.30 (m, 2 H, H-4′), 3.94 (br s, 4 H, H-6′), 2.31 (s, 6 H, 1,9-CH_3), 1.58 (s, 6 H, 5′-CH_3), 1.25 (d, 6 H, J = 6 Hz, 1′-CH_3).

Tricyclic Hemiketal 21. A solution of 500 mg (2.0 mmol) of 6,15-dihdroxyperezone (**13**) in 30 mL of dichloromethane was cooled to 0 °C and treated with 2.0 mL (16 mmol) of boron trifluoride etherate under a nitrogen atmosphere. The reaction mixture was stirred at 0 °C during 30 min and quenched with water. After workup in the usual manner, the residue was chromatographed over silica gel to yield 30 mg (0.1 mmol, 6%) of **21**: IR (KBr) 3450 (OH), 1641 (CO) cm^{-1}; UV (ethanol) 2.44 (log ϵ 3.30), 2.93 nm (3.37); ^1H NMR (90 MHz, $CDCl_3$) δ 7.58 (s, 1 H, OH), 4.87 (s, 1 H, OH), 2.03 (s, 3 H, CH_3-11), 1.38 and 1.13 (s, 3 H, CH_3-12 and CH_3-13), 0.72 (d, 3 H, J = 5 Hz, CH_3-10); ^{13}C NMR ($CDCl_3$) δ 197.2 (s, C-4), 193.0 (s, C-7), 154.9 (s, C-5), 119.3 (s, C-6), 99.6 (s, C-8), 83.6 (s, C-9), 73.1 (s, C-3a), 61.9 (d, C-9a), 39.5 (t, C-2), 39.1 (d, C-3), 31.3 (q, C-13), 28.0 (t, C-1), 26.2 (q, C-12), 16.4 (q, C-10), 8.8 (q, C-11).

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