Further BF-EtO-catalyzed Cycloadditions of Sesquiterpenic p-Benzoquinones

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FURTHER BF_3·ET_2O-CATALYZED CYCLOADDITIONS OF SESQUITERPENIC *p*-BENZOQUINONES

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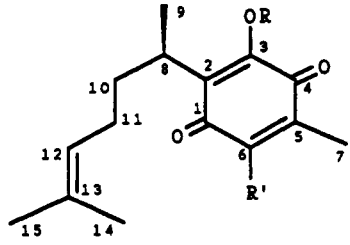
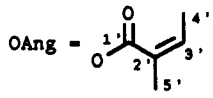
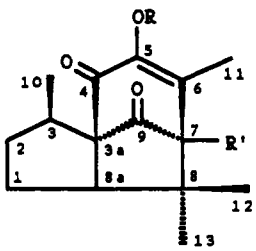
ABSTRACT.—Cycloaddition reactions of *O*-methylperezone [**4**], *O*-methyl-6-methoxyperezone [**13**], the mixture of *O*-angeloyl-6-methoxyperezone [**14**] and *O*-methyl-6-angeloxyperezone [**15**], 6-methoxyperezone [**16**], and *O*-methyl-6-hydroxyperezone [**17**] are described. The results obtained from **16** and **17** allow confirmation of previous suggestions indicating that BF_3·Et_2O-catalyzed reactions of these quinones afford pipitzols or pipitzol derivatives when position 6 is either free or has a protected alcohol, while they afford perezinone: BF_2 [**10**] and/or perezinone [**21**] when a free hydroxyl group is present at C-6. The structures of 7-methoxy-α-pipitzol [**18**] and 7-methoxy-β-pipitzol [**19**], obtained from **13**, were independently confirmed by single crystal X-ray diffraction analyses.

The thermal transformation of perezone [**1**] into α-pipitzol [**2**] and β-pipitzol [**3**] has been known for more than a century (1). The reaction was postulated (2,3) and then shown (4) to proceed by a concerted [π4s+π2s] cycloaddition (5). However, in the thermal transformation (2,4,6) there is a lack of stereochemical induction by the chiral center of perezone [**1**], since equal amounts of α-pipitzol [**2**] and β-pipitzol [**3**] are obtained. Later, it 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 **2** and **3** in 98% yield (7). Subsequent studies demonstrated that the course of the perezone-to-pipitzols transformation may be altered in favor of the β-isomer when *O*-methylperezone [**4**] is treated with $AlCl_3/Et_2S$ (8), since there is a steric crowding of the secondary methyl and methoxy group in the transition state. In 1987 the same intramolecular BF_3·Et_2O-

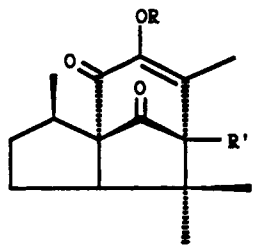




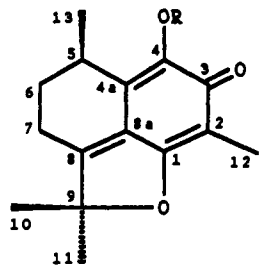
1 R=R′=H
4 R=Me, R′=H
5 R=Ang, R′=H
6 R=H, R′=OH
7 R=Ang, R′=OH
8 R=H, R′=OAng
13 R=Me, R′=OMe
14 R=Ang, R′=OMe
15 R=Me, R′=OAng
16 R=H, R′=OMe
17 R=Me, R′=OH



2 R=R'=H
11 R=H, R'=OAng
18 R=H, R'=OMe
20 R=H, R'=OH



3 R=R'=H
9 R=Ang, R'=H
12 R=H, R'=OAng
19 R=H, R'=OMe



10 R=BF_2
21 R=H

catalyzed cycloaddition reactions of all known natural perezone analogues (9), which include *O*-angeloylperezone [**5**], 6-hydroxyperezone [**6**], and the equimolecular mixture of hydroxyperezone monoangelates **7** and **8**, showed that reaction of **5** provides a 9:1 mixture of β-pipitzol [**3**] and *O*-angeloyl-β-pipitzol [**9**], in 90% yield. In contrast to perezone, which yields pipitzols, cycloaddition of **6** only affords a stable boron adduct of perezinone [**10**], while the natural mixture of **7** and **8** reacts with BF_3·Et_2O to afford **10** and a mixture of α-perezol [**11**] and β-perezol [**12**].

The diversity of products obtained during these cycloadditions indicates that there is a marked influence of the substitutents on the reaction outcome. In continuation of our studies of BF_3-catalyzed cycloaddition reactions, we now report the results for *O*-methylperezone [**4**], *O*-methyl-6-methoxyperezone [**13**], the mixture of *O*-angeloyl-6-methoxyperezone [**14**] and *O*-methyl-6-angeloxyperezone [**15**], 6-methoxyperezone [**16**], and *O*-methyl-6-hydroxyperezone [**17**].

RESULTS AND DISCUSSION

Perezone [**1**], 6-hydroxyperezone [**6**], and the mixture of hydroxyperezone monoangelates **7** and **8** were obtained from dried roots of *Perezia hebeclada*, A. Gray (Compositae) as reported previously (10,11). *O*-Methylperezone [**4**], *O*-methyl-6-methoxyperezone [**13**], and the mixture of *O*-angeloyl-6-methoxyperezone [**14**] and *O*-methyl-6-angeloxyperezone [**15**] were obtained by reaction of the corresponding natural products, **1**, **6**, **7**, and **8** with Me_2SO_4/K_2CO_3 under reflux in anhydrous Me_2CO. Compounds **4** and **13** were identified by comparison of their spectroscopic data with those of authentic samples (2,12). The mixture of **14** and **15** was identified based on its ^{1}H-nmr spectrum which shows characteristic signals for the OMe groups at 4.00 and 3.97 ppm.

6-Methoxyperezone [**16**] and *O*-methyl-6-hydroxyperezone [**17**] were prepared by treating THF solutions of the mixture of **14** and **15** with 1% aqueous KOH, followed by cc separation and identification based on spectral characteristics. As expected, the ^{1}H-nmr spectra of these compounds were very similar; therefore the assignment was based on their ^{13}C-nmr spectra which show notable differences in the sp^2 region. The most significant differences were found for the C-2 and C-5 signals, which in the case of 6-methoxyperezone [**16**] appear at 121.9 (C-2) and 122.4 (C-5) ppm, while for *O*-methyl-6-hydroxyperezone [**17**] they appear at 131.2 (C-2) and 114.2 (C-5) ppm. The assignment of the ^{13}C-nmr signals corresponding to the quinonoid ring in these compounds (Table 1) is based on substituent effects in quinones (13) and was confirmed by measurement of ^{1}H-coupled ^{13}C-nmr spectra. Assignment of the side chain signals is trivial based on comparison with related compounds (12,13).

TABLE 1. ^{13}C-nmr Data of Perezone Derivatives **16** and **17** and Pipitzol Derivatives **18** and **19**.

Carbon	Compound		Carbon	Compound	
	16	**17**		**18**	**19**
C-1	183.5	183.7	C-1	26.4	25.2
C-2	121.9	131.2	C-2	36.6	35.1
C-3	150.9	157.8	C-3	35.4	34.9
C-4	184.4	184.1	C-3a	72.6	71.0
C-5	122.4	114.2	C-4	193.2	193.0
C-6	157.4	150.9	C-5	146.0	146.0
C-7	8.0	7.7	C-6	129.0	131.1
C-8	29.4	29.6	C-7	93.4	92.3
C-9	18.4	18.9	C-8	40.6	40.5
C-10	34.2	34.6	C-8a	56.4	58.3
C-11	26.7	26.8	C-9	204.9	204.7
C-12	124.5	124.4	C-10	14.7	13.6
C-13	131.4	131.7	C-11	12.7	12.9
C-14	17.7	17.7	C-12	24.9	25.1
C-15	25.7	25.7	C-13	20.3	18.0
OMe	61.5	61.7	OMe	55.0	55.1

CYCLOADDITION REACTIONS.—Reactions of *O*-methylperezone [**4**] in anhydrous CH_2Cl_2 at 0° and at −20° in the presence of $BF_3{\cdot}Et_2O$ yield mixtures of α-pipitzol [**2**] and β-pipitzol [**3**]. Integration of the signals at 2.83 and 2.76 ppm in the ^{1}H-nmr spectra, corresponding to the H-7 of **2** and **3**, respectively, indicated that in all cases the major product was the β-isomer. Overall yields (71–94%) and stereoselectivities (1:5 to 1:8 in favor of the β-isomer) obtained from the $BF_3{\cdot}Et_2O$ cyclization reactions of **4** are higher than those obtained using $AlCl_3$ (1:3 in favor of the β-isomer and 36% overall yield) (8).

Reaction of *O*-methyl-6-methoxyperezone [**13**] with $BF_3{\cdot}Et_2O$ similarly gave a mixture of 7-methoxy-α-pipitzol [**18**] and 7-methoxy-β-pipitzol [**19**], which were purified by cc. Both compounds gave a positive $FeCl_3$ test (14), providing evidence for a methoxy group at position 7. Integration of the signals at 3.58 and 3.55 ppm, corresponding to the methoxyl groups of **18** and **19**, respectively, indicated that the major product was also the β-isomer. The stereochemistry of **18** and **19** was determined by comparison of their ORD data in the 589–365 nm region with those described for α-pipitzol [**2**] and β-pipitzol [**3**] (15), and for **20** (11). Additional evidence was obtained from ^{1}H-nmr data, since the *gem*-dimethyl group signals in **18** show a chemical shift difference (Δδ) of 0.06 ppm, in contrast to a Δδ=0.02 ppm observed for **19**, which is in accordance with the differences observed for the same signals in **2** and **3** (16) as well as for **11** and **12** (11). These results were independently confirmed by single crystal X-ray studies.

The monomethylether-monoangelate mixture of hydroxyperezones **14** and **15** was treated with 8 equiv of $BF_3{\cdot}Et_2O$ at 0°, yielding three products identified as perezinone: BF_2 [**10**] (9), **12**, and **19**, the latter being identical with the product obtained by reaction of **13**.

Although in 1987 it was suggested (9) that the $BF_3{\cdot}Et_2O$-catalyzed reactions of these quinones afford pipitzol or pipitzol derivatives only in those cases when position 6 is either free or has a protected alcohol and that substitution at C-6 by a free hydroxyl group leads to perezinone:BF_2 [**10**] and/or perezinone [**21**], these propositions could not be confirmed at that time, because we were unable to separate the starting quinones (monoangelates of hydroxyperezone **7** and **8**) even after careful liquid cc. In order to

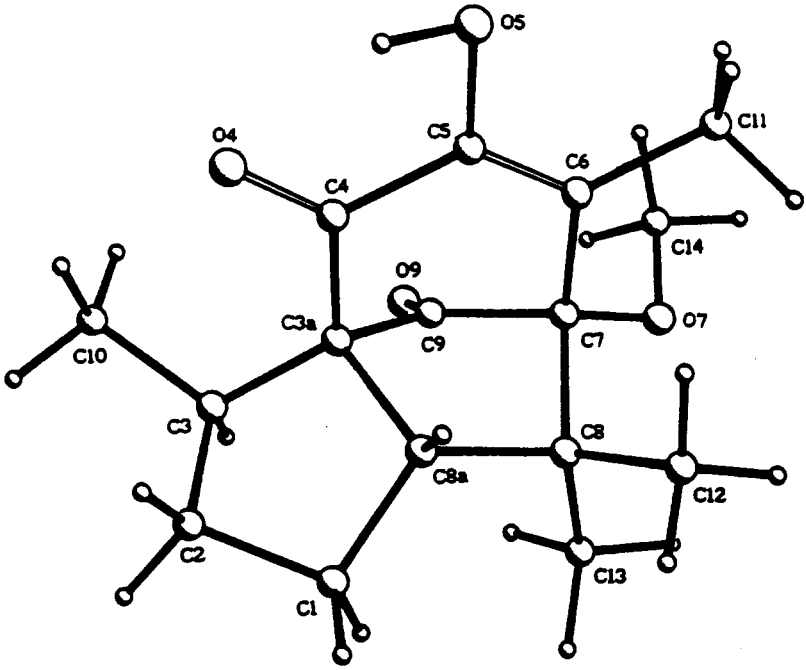


FIGURE 1. Perspective view of the molecular structure of **18**.

afford further evidence for these propositions, **16** and **17** were independently reacted with 8 equiv of $BF_3 \cdot Et_2O$ at 0° and −20°. Thus, the $BF_3 \cdot Et_2O$-catalyzed cyclization of **16** yields **18** and **19** in a 2.5 to 1.0 ratio in favor of the α-isomer. Both products were

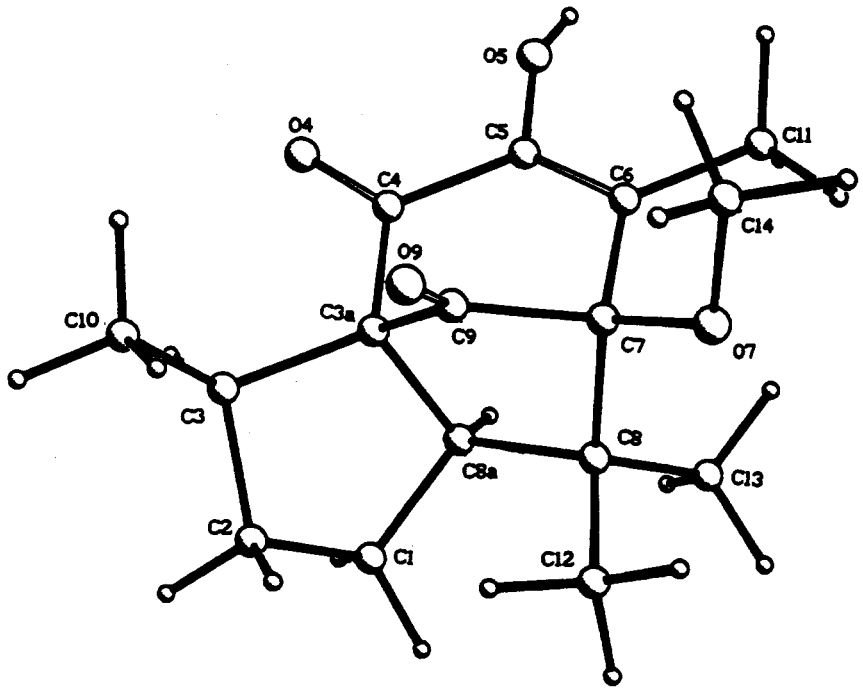


FIGURE 2. Perspective view of the molecular structure of **19**.

TABLE 2. Experimentally Refined Fractional Atomic Coordinates (10^4) of **18**[a].

Atom	*x*	*y*	*z*
O-4	7109 (7)	6348 (5)	10066 (2)
O-5	6856 (7)	8762 (6)	10793 (3)
O-7	5184 (5)	11008 (4)	8576 (3)
O-9	4063 (6)	8148 (5)	8404 (3)
C-1	8917 (10)	7294 (8)	7994 (4)
C-2	8395 (9)	5822 (8)	8221 (4)
C-3	6644 (9)	6916 (7)	8447 (4)
C-3a	6669 (8)	7379 (7)	8881 (4)
C-4	6774 (9)	7368 (8)	9691 (4)
C-5	6590 (8)	8757 (7)	10036 (4)
C-6	6248 (8)	9904 (7)	9680 (4)
C-7	6029 (8)	9845 (7)	8852 (3)
C-8	7654 (8)	9755 (7)	8420 (3)
C-8a	8177 (9)	8220 (7)	8612 (4)
C-9	5353 (8)	8408 (7)	8683 (4)
C-10	5910 (11)	4737 (8)	8823 (4)
C-11	6163 (11)	11308 (7)	10070 (4)
C-12	8865 (10)	10810 (7)	8702 (4)
C-13	7330 (10)	9996 (9)	7610 (3)
C-14	3536 (9)	11123 (8)	8807 (4)

[a]ESDs in the last significant digits are shown in parentheses.

identical to those obtained by reaction of **13**. In contrast, reaction of **17** with the same Lewis acid, under the same reaction conditions, gave perezinone:BF_2 [**10**] and perezinone [**21**] in 1.7 to 1.0 and in 2.0 to 1.0 ratios, in favor of **10**, for the reactions performed at 0° and −20°, respectively. Thus, the results obtained from the reactions of **16** and **17** confirm the previous suggestions.

TABLE 3. Experimentally Refined Fractional Atomic Coordinates (10^4) of **19**[a].

Atom	*x*	*y*	*z*
O-4	3664 (8)	5791 (6)	8349 (5)
O-5	6536 (12)	5178 (9)	7693 (7)
O-7	8643 (6)	8465 (5)	8941 (4)
O-9	5581 (8)	8998 (5)	8544 (5)
C-1	4785 (11)	7149 (8)	11147 (7)
C-2	3628 (14)	7923 (13)	10745 (8)
C-3	3299 (11)	7541 (8)	9708 (7)
C-3a	4922 (11)	7249 (7)	9342 (6)
C-4	4959 (10)	6324 (7)	8629 (6)
C-5	6501 (11)	6088 (6)	8268 (6)
C-6	7674 (11)	6680 (7)	8483 (6)
C-7	7485 (10)	7722 (7)	9110 (6)
C-8	7373 (10)	7447 (7)	10233 (7)
C-8a	5806 (10)	6880 (7)	10287 (5)
C-9	5923 (10)	8139 (7)	8911 (6)
C-10	2460 (11)	8341 (11)	9094 (10)
C-11	9188 (10)	6333 (8)	8139 (8)
C-12	8630 (12)	6705 (8)	10599 (7)
C-13	7422 (12)	8561 (7)	10776 (7)
C-14	8752 (12)	8901 (8)	7974 (7)

[a]ESDs in the last significant digits are shown in parentheses.

In conclusion, higher stereoselectivities and overall yields were obtained by lowering reaction temperatures. At lower temperature, the ratio of Lewis acid to quinone had a considerable effect on the overall yields, and the best yields were obtained at −20° using a 1:16 ratio of quinone to BF_3·Et_2O.

The molecular structures of **18** and **19** are illustrated in Figures 1 and 2, respectively, and the corresponding atomic coordinates are listed in Tables 2 and 3, respectively. The stereochemistry evidenced from the X-ray analyses of **18** and **19** is in agreement with that deduced from ORD and ^{1}H-nmr data. The hydrogen-hydrogen dihedral angles for the five-membered rings (C-1–C-2–C-3–C-3a–C-8a) were compared with those deduced from ^{1}H-nmr measurements (17). The good agreement indicates that in both cases the conformation of the five-membered ring is similar in the solid state and in solution.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—^{1}H- and ^{13}C-nmr spectra were measured on a Varian XL-300GS spectrometer in $CDCl_3$ solutions containing TMS as the internal standard. Ir spectra were recorded as $CHCl_3$ solutions on a Nicolet MX-1-FT instrument, and uv spectra were determined on a Pye Unicam SP-800 spectrophotometer using 95% EtOH. Mass spectra were obtained with a Hewlett Packard 5989-A spectrometer at 70 eV. Optical rotations were performed at room temperature on a Perkin-Elmer 241 polarimeter in $CHCl_3$. Melting points were obtained on a Fisher-Johns melting point apparatus and are uncorrected. For gravity cc, Merck Si gel 60 (230–400 mesh ASTM) was used.

X-RAY DATA.[1]—Data collection for 7-methoxy-α-pipitzol [**18**] and 7-methoxy-β-pipitzol [**19**] was done in the θ:2θ scanning mode on a Nicolet R3m four circle diffractometer using CuKα radiation (λ=1.54178 Å). The collected reflections were corrected for background, Lorentz, and polarization effects; crystal decay was negligible and no absorption corrections were applied. The structures were solved by direct methods using the software provided by the diffractometer manufacturer. For structural refinements the non-hydrogen atoms were treated anisotropically, and the hydrogen atoms bonded to carbons, included in the structure factor calculation, were refined isotropically.

NATURAL PRODUCTS.—Perezone [**1**] and 6-hydroxyperezone [**6**] were obtained from air-dried roots of *P. hebeclada* as reported (10,11). Voucher specimens are deposited at the herbarium of Escuela Nacional de Ciencias Biológicas, Instituto Politécnico Nacional, Mexico City, México. The equimolecular mixture of hydroxyperezone monoangelates **7** and **8** was available from previous studies (9).

METHYL ETHERS.—*O-Methylperezone* [**4**].—A solution of perezone [**1**] (0.5 g) in 100 ml anhydrous Me_2CO was refluxed 3 h in the presence of 0.34 g K_2CO_3 and 0.21 ml Me_2SO_4. The solvent was evaporated, and the organic material was extracted with EtOAc. The organic layer was washed with H_2O, dried over Na_2SO_4, filtered, and evaporated to dryness. The residue was chromatographed over SiO_2, eluting with hexane-EtOAc (95:5), to yield 0.48 g (91.0%) of **4** (2,12).

O-Methyl-6-methoxyperezone [**13**].—A solution of 0.7 g of **6**, 0.81 g of K_2CO_3, and 0.3 ml of Me_2SO_4 in 125 ml anhydrous Me_2CO was refluxed 3 h. Workup as in the case of **4** yielded 0.61 g (87.0%) of **13** (2,12).

O-Angeloyl-6-methoxyperezone [**14**] *and O-methyl-6-angeloxyperezone* [**15**].—The natural mixture of hydroxyperezone monoangelates **7** and **8** (0.15 g) was methylated using the conditions described for the obtention of **4**. The residue was chromatographed over Si gel, yielding, in the fractions eluted with hexane-EtOAc (95:5), 0.12 g (77.0%) of the mixture of **14** and **15**. ^{1}H nmr 6.33 (m, 2H, H-3′), 5.04 (m, 2H, H-12), 4.0 and 3.97 (s, 3H each, OMe), 3.12 and 3.03 (m, 1H each, H-8), 1.95 and 1.93 (s, 3H each, Me-7), 1.2 (d, 6H, Me-9).

Hydroxyperezone monomethylethers **16** *and* **17**.—A solution containing a mixture of **14** and **15** (0.40 g) in 100 ml of THF was treated with 20 ml of a 1% aqueous KOH solution. The mixture was stirred at room temperature 15 min and neutralized with 10% HCl. The organic layer was extracted with EtOAc, washed

[1]Atomic coordinates for these structures have been deposited with the Cambridge Crystallographic Data Centre and can be obtained on request from Dr. Olga Kennard, University Chemical Laboratory, 12 Union Road, Cambridge, CB2 1EZ, UK.

with H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness. The residue was chromatographed over Si gel. Those fractions eluted with hexane-EtOAc (90:10) gave 0.154 g of 6-methoxyperezone [**16**] as a red oil: uv λ max 288 (log ε 4.0), 214 (3.9); ir 3683 (free OH), 3619 (associated OH), 1517, 1474, 1421 cm^{-1} (quinonoid system and C=C); ^1H nmr δ 7.26 (s, 1H, OH), 5.08 (t heptet, J=7.0, 1.4, 1H, H-12), 4.08 (s, 3H, OMe), 3.09 (tq, J=8.0, 7.0, 1H, H-8), 1.93 (s, 3H, Me-7), 1.64 (s, 3H, Me-15), 1.53 (s, 3H, Me-14), 1.20 (d, J=7, 3H, Me-9); ms (70 eV) *m/z* (rel. int) $[M]^+$ 278 (42), 196 (100), 181 (91), 163 (55), 41 (36); ^{13}C nmr see Table 1. Those fractions eluted with hexane-EtOAc (7:3) afforded *O*-methyl-6-hydroxyperezone [**17**] (0.127 g) as a red oil: uv λ max 287 (log ε 4.01), 213 nm (log ε 3.77); ir 3682 (free OH), 3616 (associated OH), 1523, 1486, 1424, 1381 cm^{-1} (quinonoid system and C=C); ^1H nmr δ 7.24 (s, 1H, OH), 5.04 (t heptet, J=7.0, 1.4, 1H, H-12), 4.03 (s, 3H, OMe), 3.09 (tq, J=8.0, 7.0, 1H, H-8), 1.9 (s, 3H, Me-7), 1.64 (s, 3H, Me-15), 1.53 (s, 3H, Me-14), 1.18 (d, J=7, 3H, Me-9); ms (70 eV) *m/z* (rel. int.) $[M]^+$ 278 (59), 196 (100), 181 (54), 163 (46), 41 (22); ^{13}C nmr see Table 1. The overall yield for this reaction was 91%.

CYCLIZATION REACTIONS.—*General method.*—Cooled solutions of 0.1 g of the appropriate benzoquinone in 7 ml of anhydrous CH_2Cl_2 were treated with $BF_3{\cdot}Et_2O$ under N_2. After the time indicated for each procedure, the solution was quenched with H_2O, and the product was extracted with CH_2Cl_2. The organic layer was washed with H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness. The residue was chromatographed over Si gel.

Reaction of O-*methylperezone* [**4**].—Solutions containing *O*-methylperezone in anhydrous CH_2Cl_2 were cooled to 0° and −20°, treated with variable amounts of $BF_3{\cdot}Et_2O$, and worked up using the general procedure. After 6 h at 0° and 60 h at −20°, the products were chromatographed over Si gel, eluting with hexane-EtOAc (97:3) to yield a mixture of α-pipitzol [**2**] and β-pipitzol [**3**] identified by comparison with authentic samples (16).

Reaction of O-*methyl-6-methoxyperezone* [**13**].—Solutions of **13** in anhydrous CH_2Cl_2 were treated with 8 and 16 equiv of BF_3 at 0° and −20° and worked up using the general procedure. After 16 h at 0° and 160 h at −20°, the reaction products were chromatographed on Si gel, eluting with hexane-EtOAc (97:3). The first fractions yielded 7-methoxy-α-pipitzol [**18**] as colorless crystals: mp 118–120°; uv λ max 284 (log ε 3.76), 251 (log ε 3.46), 2.15 nm (log ε 3.24); ir 3447 (OH), 1766 (cyclopentanone C=O), 1674 and 1640 (O=C-COH=C) cm^{-1}; ^1H nmr δ 6.18 (s, 1H, OH), 3.58 (s, 3H, OMe), 2.26 (ddq, $J_{3\text{-}2\beta}$=11, $J_{3\text{-}2\alpha}$=5.6, $J_{3\text{-}10}$=7, 1H, H-3), 2.04 (s, 3H, Me-11), 2.01 (dd, $J_{8\alpha\text{-}1\beta}$=9, $J_{8\alpha\text{-}1\alpha}$=7, 1H, H-8a), 1.87 (m, 1H, H-2), 1.76 (m, 1H, H-1), 1.58 (m, 1H, H-2′), 1.49 (m, 1H, H-1′), 1.41 (d, J=7, 3H, Me-10), 0.98 (s, 3H, Me-13), 0.92 (s, 3H, Me-12); ms (70 eV) *m/z* (rel. int.) $[M]^+$ 278 (20.8), 55 (62), 53 (52), 43 (59), 41 (100); [α] λ (*c*=0.09) $^{589}/_{260}$, $^{578}/_{275}$, $^{546}/_{325}$, $^{436}/_{193}$, $^{465}/_{2754}$; ^{13}C nmr see Table 1.

The last fractions eluted with hexane/EtOAc yielded 7-methoxy-β-pipitzol [**19**] as colorless crystals: mp 116–118°; uv λ max 284 (log ε 3.84), 2.56 (log ε 3.56), 2.09 nm (log ε 3.48); ir 3466 (OH), 1767 (C=O cyclopentanone), 1669 and 1639 cm^{-1} (O=C-COH=C); ^1H nmr δ 6.14 (s, 1H, OH), 3.55 (s, 3H, OMe), 2.6 (ddq, $J_{3\text{-}10}$=7, $J_{3\text{-}2\beta}$=12, $J_{3\text{-}2\alpha}$=6, 1H, H-3), 2.04 (s, 3H, Me-11), 1.94 (dd, $J_{8\alpha\text{-}1\beta}$=10, $J_{8\alpha\text{-}1\alpha}$=3, 1H, H-8a), 1.85 (m, 1H, H-2), 1.79 (m, 1H, H-1), 1.58 (m, 1H, H-1′), 1.36 (m, 1H, H-2′), 1.34 (d, J=7, 3H, Me-10), 0.99 (s, 1H, Me-13), 0.97 (s, 3H, Me-12); ms (70 eV) *m/z* (rel. int.) $[M]^+$ 278 (13), 55 (77), 53 (61), 43 (73), 41 (100); ^{13}C nmr see Table 1; [α] λ (*c*=0.1) $^{589}/_{-239}$, $^{578}/_{-252}$, $^{546}/_{-300}$, $^{436}/_{-679}$, $^{365}/_{-2067}$.

Reaction of O-*angeloxyl-6-methoxyperezone* [**14**] *and* O-*methyl-6-angeloxy perezone* [**15**].—A solution containing a mixture of **14** and **15** was cooled to 0°, treated with 8 equiv of $BF_3{\cdot}Et_2O$, and stored at 0° for 16 h. After workup, the residue was crystallized from CH_2Cl_2/hexane to yield 7.0 mg (8.7%) of perezinone: BF_2 [**10**] as yellow needles, mp 170° (dec), identical with an authentic sample (9). The filtrate was evaporated and chromatographed over Si gel, eluting with hexane-EtOAc (97:3) to yield 6.0 mg (6.3%) of β-perezol [**12**] (9) and 20 mg (27.0%) of 7-methoxy-β-pipitzol [**19**]; the latter was identical to the product obtained by reaction of *O*-methyl-6-methoxyperezone [**13**].

Reaction of 6-*methoxyperezone* [**16**].—Solutions of **16** in anhydrous CH_2Cl_2 were cooled to 0° and −20° under an N_2 atmosphere and treated with 8 and 16 equiv respectively, of $BF_3{\cdot}Et_2O$. The reaction mixtures were stored 16 h at 0° and 196 h at −20°. After workup as described in the general method, the residues were chromatographed over Si gel to yield 12.3 mg of **18** and 5.0 mg of **19** for the reactions at 0°, and 12.8 mg of **18** and 5.12 mg of **19** for reactions at −20°. The overall yields were 17.3% and 17.9% for the reactions performed at 0° and −20°, respectively.

Reaction of O-*methyl-6-hydroxyperezone* [**17**].—Solutions of **17** were treated with 8 equiv of $BF_3{\cdot}Et_2O$ at 0° and −20° under the conditions described for **4**. The reaction mixture was stored 6 h at 0°, quenched, and worked up in the usual manner. The residue was dissolved in CH_2Cl_2/hexane, yielding 33 mg of solid perezinone: BF_2 [**10**], identical with the product obtained by reaction of the mixture of **14** and **15**. The filtrate was evaporated and chromatographed over Si gel eluting with hexane/EtOAc mixtures of increasing

polarity. This provided 20 mg of perezinone [**21**] (11), mp 145–146°. In another experiment, the reaction mixture was stored 12 h at −20° and worked up as usual, to yield 33.0 of **10** and 17.0 mg of **21**. The overall yields were 53% at 0° and 50% at −20°.

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LITERATURE CITED

1. R. Anchütz and W. Leather, *Chem. Ber.*, **18**, 715 (1885).
2. F. Walls, M. Salmón, J. Padilla, P. Joseph-Nathan, and J. Romo, *Bol. Inst. Quím. Univ. Nal. Autón. Méx.*, **17**, 3 (1965).
3. R.B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, 1979, p. 87.
4. P. Joseph-Nathan, V. Mendoza, and E. García, *Tetrahedron*, **33**, 1573 (1977).
5. I. Fleming, "Frontier Orbitals and Organic Chemical Reactions," Wiley, New York, 1976, p. 92.
6. F. Walls, J. Padilla, P. Joseph-Nathan, F. Giral, M. Escobar, and J. Romo, *Tetrahedron*, **22**, 2387 (1966).
7. I.H. Sánchez, R. Yáñez, R. Enríquez, and P. Joseph-Nathan, *J. Org. Chem.*, **46**, 2818 (1981).
8. I.H. Sánchez, F. Basurto, and P. Joseph-Nathan, *J. Nat. Prod.*, **47**, 382 (1984).
9. P. Joseph-Nathan, M.E. Garibay, and R.L. Santillan, *J. Org. Chem.*, **52**, 759 (1987).
10. P. Joseph-Nathan, M.P. González, E. García G., H. Barrios, and F. Walls, *Tetrahedron*, **30**, 3461 (1974).
11. P. Joseph-Nathan, M.P. González, and V.M. Rodríguez, *Phytochemistry*, **11**, 1803 (1972).
12. P. Joseph-Nathan, M.P. González, L.F. Johnson, and J.N. Shoolery, *Org. Magn. Reson.*, **3**, 23 (1971).
13. P. Joseph-Nathan, D. Abramo-Brumo, and D.A. Ortega, *Org. Magn. Reson.*, **15**, 311 (1981).
14. R.L. Shriner, R.C. Fuson, and D.Y. Curtin, "Systematic Identification of Organic Compounds," Wiley & Son, New York, 1964.
15. G. Snatzke, Ed., "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Heyden Londres, 1967, pp. 13, 135.
16. F. Walls, J. Romo, P. Joseph-Nathan, F. Giral, and J. Romo, *Tetrahedron Lett.*, **21**, 1577 (1965).
17. C.M. Cerda-García-Rojas, L.G. Zepeda, and P. Joseph-Nathan, *Tetrahedron Comput. Methodol.*, **3**, 113 (1990).

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