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CONDENSED CYCLIC AND BRIDGED-RING SYSTEMS : PART 12[1]. A NOVEL SYNTHETIC ROUTE TO 4-p-METHOXYPHENYL-BICYCLO[2.2.2]OCTAN-2-ONES AND SOME BICYCLO[3.2.1]OCTANE DERIVATIVES BY ACID-CATALYZED INTRAMOLECULAR C-ALKYLATION AND REARRANGEMENT REACTIONS.

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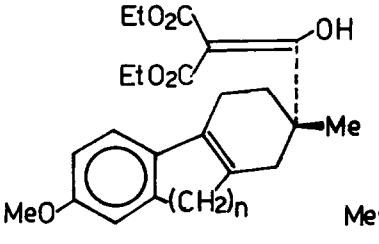
Abstract - The efficacy of a new acid-catalyzed intramolecular C-alkylation has been demonstrated by the synthesis of 1-methyl-4-p-methoxyphenylbicyclo[2.2.2]octan-2-one (5) and 4-p-methoxyphenylbicyclo[2.2.2]octan-2-one (6) from easily accessible starting materials. The carbinol 20, derived from 5, undergoes facile rearrangement leading to 1-p-methoxyphenyl-4-methyl bicyclo[3.2.1]oct-3-ene (22), which has been transformed to endo-1-p-methoxyphenyl-4-methylbicyclo[3.2.1]octan-3-one (25).

Although there are numerous examples[2] where intermolecular alkylations of β-ketoesters and β-diketones have been realized through the corresponding enols in the presence of Lewis acids with tertiary and secondary carbocations generated from the corresponding alcohols, halides or the olefins, the intramolecular version of this reaction has only been reported recently[3,4]. As a part of our synthetic studies towards the carbocyclic ring systems of stemodin, stemarin and the antheridium inducing factor A_{An} we have reported[5] a remarkably simple and potentially useful method of carbon-carbon bond formation involving a prototype of acid-catalyzed intramolecular Michael reaction of the enolized keto-diesters 1 and 2 to the respective tetracyclic ketones 3 and 4 in excellent yields. We now describe in detail an extension of this method leading to a simple synthetic route to 4-p-methoxyphenyl-1-methyl disubstituted and 4-p-methoxyphenyl substituted bicyclo[2.2.2]octan-2-ones (5)[6] and (6) along with further transformations of 5 to a few substituted bicyclo[3.2.1]octane derivatives involving an interesting rearrangement.



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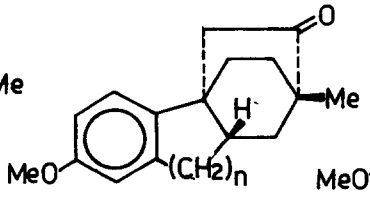

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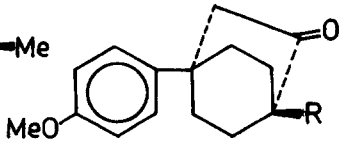
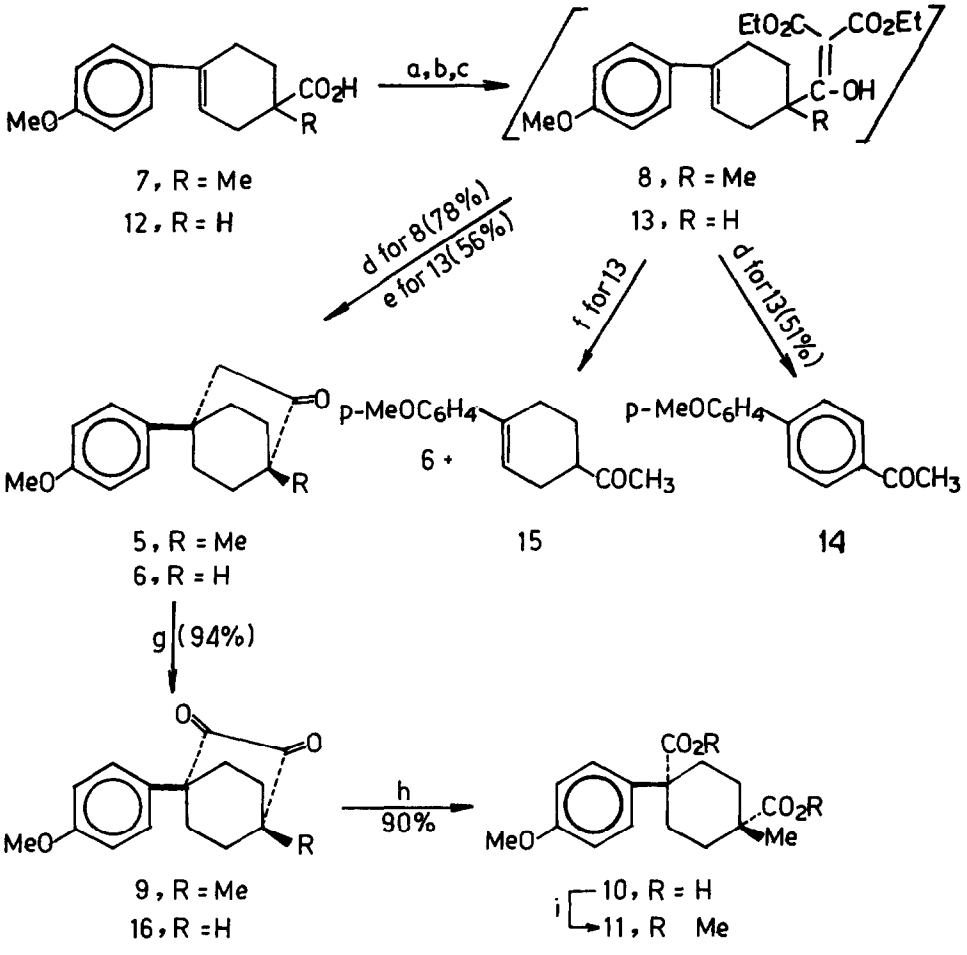


5, R = Me
6, R = H

RESULTS AND DISCUSSION

The sodium salt of the known acid 7, prepared by Diels-Alder reaction[7], on consecutive treatments with oxalyl chloride[7], and diethyl ethoxymagnesium malonate[8] (Scheme-1) gave 8, which was used directly without further purification. After a systematic study an optimal condition for the intramolecular cyclization of 8 was established. Thus, treatment of 8 with a mixture of CH_3CO_2H, H_2SO_4 and H_2O (40:7:10 v/v) at room temperature (25-35°C) followed by refluxing gave the bridged-ketone 5, mp 87-88°C in 78% yield. The spectral and analytical data of this ketone are in complete agreement with the assigned structure. The structure of 5 was further proved by it's oxidation[9] with SeO_2 in acetic anhydride to the respective diketone 9, mp 160°C, in excellent yield. This on oxidative cleavage[10] afforded the diacid 10, mp 196-197°C in 90% yield; the corresponding dimethyl ester 11 was characterized by spectral data.

Scheme - 1

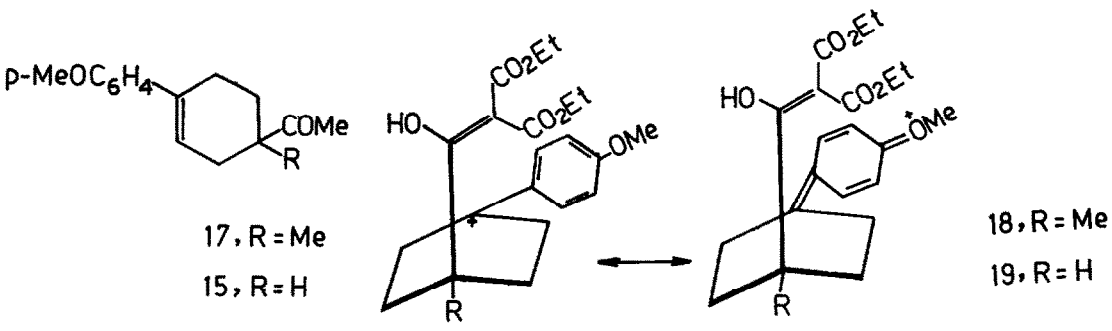


Reagents: a, NaOMe-MeOH; b, $(COCl)_2$-Py.-C_6H_6; c, $EtOMgCH(CO_2Et)_2$ Et_2O, -5°C-0°C; d, CH_3CO_2H-H_2SO_4-H_2O (40:7:10) at 25°-35°C 16h and reflux 7h; e, CH_3CO_2H-H_2SO_4-H_2O (40:7:10) at 10°-15°C for 16h and reflux 7h; f, CH_3CO_2H-H_2SO_4-H_2O (40:7:10) at 15°-30°C, 16h and reflux 7h; g, SeO_2, Ac_2O, 160°C; h, H_2O_2 (30%), NaOH(10%), t-BuOH; i, CH_2N_2-Et_2O.

Having satisfactorily attained a simple synthetic route to the 1,4-disubstituted bicyclo[2.2.2]octanone (5), attention was next turned to the 4-aryl-substituted ketone (6). The required acid 12[7] was converted to the enolized keto-diester 13 in the usual manner (Scheme-1) and the crude product on treatment with a mixture of CH_3CO_2H, H_2SO_4 and H_2O (40:7:10 v/v) exactly under the conditions described for 8 gave mostly the biphenyl methyl ketone 14. However, when the reaction mixture was left for 16 h at 10-15°C followed by 7 h reflux, the desired bridged ketone 6, mp 97-98°C was obtained in 56% yield. Attempted cyclization of 13 with the aforementioned mixture of CH_3CO_2H, H_2SO_4 and H_2O at various temperatures between 15 to 30°C gave mixtures of 6 and the methyl ketone 15[11] in various proportions. The structure of 6 was assigned from it's spectral and analytical data and it's transformation to the diketone 16, mp 130-132°C in 92% yield, by oxidation with SeO_2 in acetic anhydride.

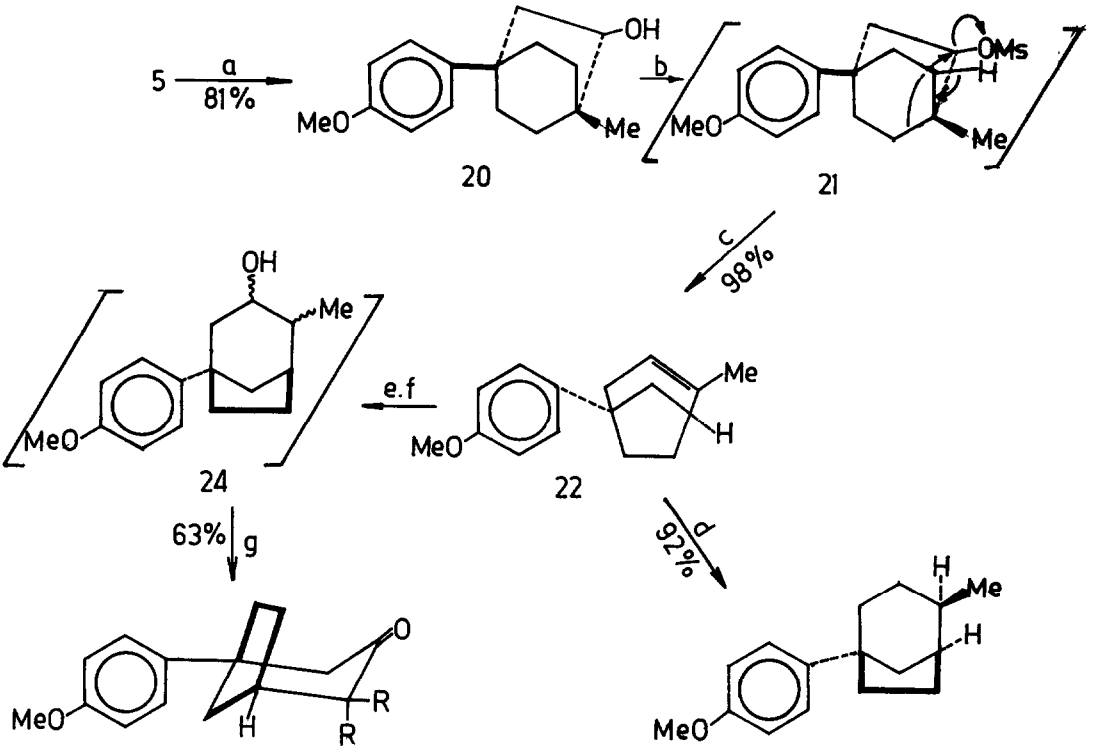
As observed[5] with the tricyclic systems (1 and 2), the cyclization reactions of the enolized β- keto-diesters 8 and 13 are highly sensitive on the reaction conditions and by changing the concentration of the acidic mixture or reaction temperature the competitive direct hydrolytic decarboxylation process becomes the major path leading to the respective methyl ketones 17[11] and 15. It seems that the first step in the cyclizations of 8 and 13 is the formation of the respective stabilized cations 18 and 19 (Scheme-2). In the absence of a p-methoxy stabilizing group[12], such cations are not generated as evidenced by persistent failures in attempted cyclization of the des-methoxy β-keto diesters related to 8 and 13. In each case, the corresponding methyl ketones was the only product.

Scheme - 2



With the successful development of an efficient intramolecular alkylation route to the 1,4-disubstituted bicyclo[2.2.2]octan-2-one (5), we have also examined the skeletal rearrangement[13] of the simple model alcohol 20, obtained in excellent yield by reduction of 5 with diborane in THF, pertaining to our synthetic studies[5] on stemodin and stemarin. Reduction of 5 with $LiAlH_4$ or $NaBH_4$ gave relatively poorer yield and less pure product. The alcohol 20 was converted to the unstable mesylate 21 with methanesulfonyl chloride in the presence of triethylamine, which underwent facile rearrangement to the bicyclo[3.2.1]octene 22 in situ (Scheme-3). The rearrangement was completed on chromatography of the crude product on a neutral alumina column. The hydrocarbon 22 (homogeneous in GLC) exhibited an olefinic methyl doublet at δ 1.68 (J=2 Hz) overlapped with methylene protons, along with an aromatic methoxy singlet at 3.70 and a broad olefinic proton signal at 5.01, in conformity with the assigned structure 22.. Catalytic hydrogenation of 22 in the presence of palladium on charcoal (10%) afforded practically a pure epimer 23 (mp 60°C) in excellent yield. The ^1H NMR spectral data are in complete agreement with the

Scheme - 3



Reagents: a, B_2H_6,THF, 2h; b, CH_3SO_2Cl, NEt_3 CH_2Cl_2; c, neutral alumina petroleum ether(b.p 60°-80°C); d, H_2, EtOH, 10% pd-C · e, B_2H_6,THF, 2h; f, H_2O_2(30%), H_2O, NaOH; g, Jones reagent.

assigned structure 23, and the stereochemistry of the endo-methyl group is based on the steric consideration of its formation through catalytic hydrogenation of 22 by analogy with similar cases[7]. An additional support for the assigned structure of the rearranged olefin 22 was obtained from the sequence of reactions shown in Scheme-3. Thus, interaction of 22 with an excess of diborane in THF followed by oxidation with alkaline H_2O_2 afforded a mixture of epimeric alcohols 24. This was directly oxidized with an excess of Jones reagent to an epimeric mixture of ketones (25 and 26) in a ratio ∿90:10 (by GLC) from which the major epimer 25 (mp 72-73°C), tentatively assigned by the endo-methyl stereochemistry, was separated by crystallization. The IR and ^1H NMR spectral data of this compound are in complete agreement with the assigned structure.

In conclusion, the present investigation clearly shows the potential of the new intramolecular alkylation reaction in the synthesis of substituted bicyclo[2.2.2]octan-2-ones[14] and the usefulness of such intermediates for the synthesis substituted bicyclo[3.2.1]octanones[7,15].

EXPERIMENTAL

The compounds described are all racemates. Melting points, taken in open capillary, are uncorrected. IR spectra were recorded on a Perkin-Elmer model 21 or a model 298 spectrometer. UV spectra were recorded on a Beckman DU or a Shimadzu UV-Vis 210A spectrameter for solutions in 95% ethanol. ^{1}H NMR spectra were taken in the indicated solvents on a Varian Associates Models T-60A and XL-200 FT spectrometers with TMS acting as internal standard (δ = 0 ppm). Analytical GLC was performed on a Hewlett-Packard Model 5730A chromatograph equipped with an FID and using a 20 x $^1/_8$ in. 10% UCW-982 column with N_2 as carrier gas. Elemental analyses were performed by Mrs. C. Dutta and Mr. P.P. Bhattacharyya of this laboratory. Column chromatography was performed on "Brockman" neutral alumina. (M/s. Sarabhai M. Chemicals). Petroleum and light petroleum refer to the fractions with boiling point of 60-80°C and 40-60°C respectively.

1-Methyl-4-p-methoxyphenylbicyclo[2.2.2]octan-2-one (5). The acid 7 (1.0 g, 4mmol) was converted to the corresponding acid chloride with oxalyl chloride (1.5 g, 12.2 mmol) as described earlier[7]. To the crude acid chloride in Et_2O (25 ml) was added dropwise with stirring at 0°C to -5°C an Et_2O solution of $(EtO)MgCH(CO_2Et)_2$ [prepared[8] from Mg (1.0 g, 0.04 g atom), $CH_2(CO_2Et)_2$ (6 ml) and EtOH (4.2 ml) in presence of a catalytic amount of CCl_4]. The reaction mixture was stirred for 2 h at that temperature and allowed to stand overnight at room temperature following which it was decomposed with ice-cold H_2SO_4 aq. (2N, 100 ml). The Et_2O layer was separated and the aqueous layer was extracted with Et_2O (3 x 50 ml). The combined Et_2O layer was repeatedly washed with 5% $NaHCO_3$ aq. and finally with H_2O and dried (Na_2SO_4). Removal of the solvent afforded the β-ketodiester 8 mixture with $CH_2(CO_2Et)_2$ (pink colour with $FeCl_3$), which was dried under vacuo and added to a solution of CH_3CO_2H (40 ml), H_2SO_4 (7 ml) and H_2O (10 ml). The resulting solution was left under N_2 for 16 h at room temperature (25-35°C) and then refluxed for 7 h. The solution was diluted with cold H_2O (200 ml) and extracted with Et_2O (4 x 50 ml). The Et_2O layer was washed repeatedly with H_2O, 5% $NaHCO_3$ aq. and finally with H_2O. Subsequent drying (Na_2SO_4) and removal of the solvent yielded a gummy mass, which was chromatographed over a short column of neutral alumina (10 g). The petroleum eluates afforded ketone 5 (750 mg, 78%), mp 87-88°C; λ_{max} 225 nm (log ε 4.18), 276 nm (log ε 3.31); ν_{max} (KBr) 2920, 1700, 1600, 1580, 1505 cm^{-1}; ^{1}H NMR (200 MHz) δ $CDCl_3$ 1.05 (3H, s, CH_3), 1.71-2.17 (8H, m), 2.57 (2H, unresolved q, $COCH_2$); 3.83 (3H, s, $ArOCH_3$), 6.97 (2H, d, J = 8 Hz, ArH), 7.33 (2H, d, J = 8 Hz, ArH). Anal. Calcd. for $C_{16}H_{20}O_2$: C, 78.65, H, 8.25. Found: C, 78.6; H, 8.1%

Cyclisation studies of 13. (A) 4-p-Methoxyphenylbicyclo[2.2.2]octan-2-one (6). The acid 12 (500 mg, 2.1 mmol) was converted into the respective acid chloride with oxalyl chloride (0.75 g, 6.1 mmol) in the usual manner[7]. A solution of $(EtO)MgCH(CO_2Et)_2$ [prepared from Mg (500 mg, 0.02 g atom), $CH_2(CO_2Et)_2$ (3 ml) and EtOH (2.1 ml)] was condensed with the acid chloride in the usual manner. Work-up of the reaction mixture as described, afforded the crude enolized β-keto diester 13 (pink coloration with $FeCl_3$), which was dried under vacuo and treated with an ice-cold solution of CH_3CO_2H (40 ml), H_2SO_4 (7 ml) and H_2O (10 ml). The reaction mixture was kept at 10 - 15°C for 16 h and then refluxed for 7 h. Usual work-up followed by removal of solvent afforded a gummy mass which on purification by filtration through a short column of neutral alumina (5 g) afforded the pure ketone 6 (280 mg, 56%) mp 97 - 98°C (light petroleum) λ_{max} 225 nm (log ε 4.11); 278 nm (log ε 3.40); ν_{max} (KBr) 2940, 1700, 1600, 1580, 1510 cm^{-1}; ^{1}H NMR (200 MHz) δ $CDCl_3$ 1.72 - 2.12 (8H, m), 2.39 (1H, brs), 2.52 (2H, s, $COCH_2$), 3.80 (3H, s, $ArOCH_3$), 6.92 (2H, d, J = 8 Hz, ArH) 7.26 (2H, d, J = 8 Hz, ArH). Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.2; H, 7.9. Found: C, 78.5; H, 8.2%.

(B) 4-Acetyl-4'-methoxybiphenyl (14). The crude enolized β-ketodiester 13 prepared from the acid 12 (500 mg, 2.1 mmol) was treated with a solution of CH_3CO_2H (40 ml), H_2SO_4 (7 ml) and H_2O (10 ml) and kept at room temperature (25-35°C) under N_2 for 16 h. The solution was then refluxed for 7 h and worked-up as described above. The gummy product on chromatography over neutral alumina (5 g) and elution with petroleum afforded 14 (250 mg, 51%); mp 81-82°C (ether-petroleum, 1:3); λ_{max} 203 nm (log ε 4.296), 225 nm (log ε 4.004), 305 nm (log ε 3.97); ν_{max} (KBr) 1670 cm^{-1}; ^{1}H NMR (200 MHz) δ $CDCl_3$ 2.66 (3H, s, Ar-$COCH_3$), 3.9 (3H, s, $ArOCH_3$), 7.06 (2H, d, J=8 Hz, ArH), 7.63 (2H, d, J=8 Hz, ArH), 7.7 (2H, d, J=8 Hz, ArH), 8.04 (2H, d, J=8 Hz, ArH). Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.6; H, 6.2. Found: C, 79.6; H, 6.3%.

SeO_2 Oxidation of the Bridged Ketones 5 and 6. 1-Methyl-4-p-methoxyphenyl bicyclo[2.2.2]octan-2,3-dione (9). A mixture of the bridged-ketone 5 (200 mg, 0.82 mmol) and freshly sublimed and powdered SeO_2 (400 mg, 3.65 mmol) in Ac_2O (7 ml) was reluxed with stirring under N_2 atmosphere for 8 h at 160°C on an oil bath. The cold solution was diluted with Et_2O (100 ml) and filtered free of precipitated Se. The yellow solution was repeatedly extracted with 5% $NaHCO_3$ aq. until it was free of all the Ac_2O. The Et_2O layer was then washed once with brine and dried (Na_2SO_4). Evaporation of solvent yielded the diketone 9 as a yellow solid (190 mg, 90%) mp 160°C (ether-petroleum, 1:3); ν_{max} (KBr) 2930, 1745 (sh), 1725, 1610, 1515 cm^{-1}; ^{1}H NMR (200 MHz) δ $CDCl_3$ 1.16 (3H, s, CH_3), 1.78-2.16 (4H, m), 2.18-2.46 (4H, m), 3.80 (3H, s, $ArOCH_3$), 6.93 (2H, d, J=8 Hz, ArH), 7.16 (2H, d, J=8 Hz, ArH). Anal. Calcd. for $C_{16}H_{18}O_3$: C, 74.4; H, 7.0. Found: C, 74.3; H, 7.0%.

4-p-Methoxyphenylbicyclo[2.2.2]octane-2,3-dione (16). A mixture of the bridged ketone 6 (200 mg, 0.87 mmol) and SeO_2 (400 mg, 3.65 mmol) in Ac_2O (7 ml) was refluxed with stirring under N_2 for 8 h at 160°C. The reaction mixture on work-up as described above afforded the diketone 16 as a crystalline yellow solid (195 mg, 92%); mp 130-132°C (ether-petroleum, 1:3); ν_{max} (KBr) 2950, 1750 (sh), 1725, 1610, 1510 cm^{-1}; ^1H NMR (200 MHz) δ $CDCl_3$ 2.06-2.44 (8H, m), 2.9 (1H, m), 3.80 (3H, s, $ArOCH_3$), 6.94 (2H, d, J=8 Hz, ArH), 7.16 (2H, d, J=8 Hz, ArH). Anal. Calcd. for $C_{15}H_{16}O_3$: C, 73.8; H, 6.6. Found: C, 73.8; H, 6.5%.

1-Methyl-4-p-methoxyphenylcyclohexane-cis-1,4-dicarboxylic Acid (10). To a solution of the diketone (9) (1 g, 3.7 mmol) in t-BuOH (50 ml) was added with stirring 30% H_2O_2 aq. (50 ml) followed by 10% NaOH aq. (125 ml) dropwise. After stirring for 30 min, a second aliquot of 30% H_2O_2 (50 ml) followed by 10% NaOH aq. (125 ml) was added dropwise. The mixture was stirred for an additional 1 h and the excess peroxide was then decomposed by addition of a small amount of Pd-C(10%) catalyst and the solution filtered. The filtrate was washed with Et_2O (2 x 80 ml). The basic aqueous part was then acidified with ice-cold 6N HCl. The precipitated acid was extracted with $CHCl_3$. The dried ($CaCl_2$) $CHCl_3$ extract on evaporation under vacuum afforded the diacid 10 (1.0 g, 90%). Recrystallization from EtOAc afforded an analytical sample mp 196-197°C; ν_{max} 1700 cm^{-1}. Anal. Calcd. for $C_{16}H_{20}O_5$: C, 65.75; H, 6.8. Found: C, 65.5; H, 6.9%.

The dimethyl ester 11 was prepared by esterification of 10 with CH_2N_2 in Et_2O; ν_{max} (neat) 2955, 1725, 1605, 1590, 1510, 1460, 1300, 1250, 1185, 1110, 1035, 830 cm^{-1}; ^1H NMR (CCl_4) δ 1.03 (3H, s, $-CH_3$), 1.16-2.13 (8H, m), 3.46 (3H, s, $-CO_2CH_3$), 3.56 (3H, s, $-CO_2CH_3$), 3.7 (3H, s, $ArOCH_3$), 6.7 (2H, q, J_{ortho}=9 Hz, J_{meta}=2 Hz, ArH) and 7.2 (2H, q, J_{ortho}=9 Hz, J_{meta}=2 Hz, ArH).

Reduction of the ketone (5).2-Hydroxy-1-methyl-4-p-methoxyphenylbicyclo[2.2.2]octane (20). Diborane gas [generated from $NaBH_4$ (5 g, 132.2 mmol) and $BF_3.Et_2O$ (20 ml, 162.6 mmol) in diglyme (20 ml)] was bubbled through a cold (0°C) solution of the ketone 5 (4 g, 16.39 mmol) in anhydrous THF (20 ml) for 2 h under a slow stream of N_2. The reaction mixture was then carefully decomposed with H_2O and was extracted with Et_2O after saturation with NaCl. The ethereal extract was washed with brine and dried (Na_2SO_4). Removal of Et_2O afforded a solid (3.28 g, 81%) which was purified by crystallization from light petroleum to afford pure 20 mp 100°C; ν_{max} (KBr) 3540, 3440, 1610 cm^{-1}; ^1H NMR (CCl_4) δ 0.86 (3H, s, CH_3), 1.03-2.33 (11H, m), 3.50 (1H, m, CHOH), 3.68 (3H, s, $ArOCH_3$), 6.65 (2H, d, J=9 Hz, ArH), 7.01 (2H, d, J=9 Hz, ArH). Anal. Calcd. for $C_{16}H_{22}O_2$: C, 78.0; H, 9.0. Found: C, 78.0; H, 9.0%.

1-p-Methoxyphenyl-4-methylbicyclo[3.2.1]oct-3-ene (22). To a well stirred, cold (0°C) solution of the carbinol 20 (3.02 g, 12.3 mmol) in anhydrous CH_2Cl_2 (50 ml) containing NEt_3 (7 ml, 50 mmol), was added dropwise freshly distilled CH_3SO_2Cl (3.5 ml, 45.2 mmol) for a period of 5 min. After stirring at 0°C for 15 min, the reaction mixture was quenched with ice-cold H_2O. The organic layer was separated and washed thoroughly with H_2O and dried (Na_2SO_4). The brownish residue after removal of the solvent was chromatographed through a column of neutral alumina (40 g). Elution with light petroleum and subsequent distillation of the product afforded 22 (2.76 g, 98%) as a pale yellow homogenous liquid, bp (bath temperature) 120°C (0.3 mm Hg); ν_{max} (neat) 2960, 2860, 1610, 1510, 1470, 1440 cm^{-1}; ^1H NMR (CCl_4) δ 1.51-2.35 (12H, m,), 1.68 (3H, d, J=2 Hz, CH_3), 3.70 (3H, s, $ArOCH_3$), 5.01 (1H, m, vinylic), 6.65 (2H, d, J=9 Hz, ArH), 7.03 (2H, d, J=9 Hz, ArH); GLC (column temp. 170°C) with t_R 3.1 min. Anal. Calcd. for $C_{16}H_{20}O$: C, 84.2; H, 8.8. Found: C, 84.1; H, 8.8%.

endo-1-p-Methoxyphenyl-4-methylbicyclo[3.2.1]octane (23). The olefin 22 (250 Mg, 1.1 mmol) was hydrogenated in EtOH (15 ml) in the presence of 10% Pd-C (72 mg) at room temperature and pressure. The hydrogen uptake was completed within 1 h. Filtration of the catalyst and removal of the solvent afforded a white solid (233 mg, 92%), mp 58-59°C. Two recrystallizations of this material from light petroleum in cold (10-15°C) afforded the pure hydrocarbon 23, mp 60°C; IR (KBr) 2960, 2920, 2860, 1610, 1510, 1450, 1310, 1250, 1180, 1040, 830, 590, and 540 cm^{-1}; ^1H NMR (100 MHz) (CCl_4) δ 0.83 (3H, d, J=7 Hz, $-CHCH_3$), 1.05-2.05 (12H, m), 3.68 (3H, s, $ArOCH_3$), 6.62 (2H, d, J=8 Hz, ArH), 6.97 (2H, d, J=8 Hz, ArH). Anal. Calcd. for $C_{16}H_{22}O$: C, 83.4; H, 9.6. Found: C, 83.3; H, 9.8%.

endo-1-p-Methoxyphenyl-4-methylbicyclo[3.2.1]octan-3-one(25). Diborane gas [generated from $NaBH_4$ (2 g, 52.8 mmol) and $BF_3.Et_2O$ (8 ml, 65 mmol) in diglyme (8 ml)] was bubbled through a cold (0°C) solution of the olefin 22 (2.42 g, 10.6 mmol) in anhydrous THF (10 ml) during 2 h under a slow stream of N_2. The cold (10-15°C) reaction mixture was decomposed by slow addition of H_2O. To this solution, was added 3N aqueous NaOH (45 ml) followed by dropwise addition of 30% H_2O_2 (30 ml) with stirring at 10-15°C. Stirring at that temperature was continued for an additional 30 min. Then a second lot of 30% H_2O_2 (15 ml) was added similarly. The bath temperature was gradually raised and the reaction mixtgure was left overnight. On the next day, it was extracted with Et_2O and the ethereal extract was washed with H_2O and dried (Na_2SO_4). Removal of the solvent left a pale yellow thick liquid (2.37 g) which was directly oxidized as follows:

To a magnetically stirred, cold (5-10°C) solution of the aforementioned material in $(CH_3)_2CO$ (30 ml), Jones reagent[16] (4 ml, 10.68 mmol) was added dropwise. Stirring in cold was continued for additional 45 min. The reaction mixture was diluted with saturated aqueous NaCl and extracted with Et_2O. The ethereal extract was washed with 5% $NaHCO_3$ aq. H_2O and dried (Na_2SO_4). The semi-solid residue after removal of solvent was chromatographed through a column of neutral alumina (30 g). Elution with petroleum afforded a gummy solid (1.62 g, 63%) which by GLC analysis (column temp. 170°C) was found to be a mixture of two components 26 and 25 in the ratio of ~10:90 (t_R 3.5 and 6.7 min). The major isomer was crystallized out from petroleum ether (bp 40-60°C) to afford the ketone 25 (1.49 g, 58%), mp 74°C, t_R 6.7 min, ν_{max} (KBr) 2960, 2920, 1700,1610, 1510, 1450, 1440, 1375, 1290, 1250, 1180, 1030, 840, 820, and 530 cm^{-1}; ^1H NMR (CCl_4) δ 0.98 (3H, d, J=6 Hz, $-CHCH_3$), 1.43-2.57 (10H, m), 3.70 (3H, s, $ArOCH_3$), 6.66 (2H, d, J=9 Hz, ArH) and 7.04 (2H, d, J=9 Hz, ArH). Anal. Calcd. for $C_{16}H_{20}O_2$: C, 78.65, H, 8.25. Found: C, 78.5; H, 8.2%.

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