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ANHYDROUS FERRIC CHLORIDE ADSORBED ON SILICA GEL INDUCED RING ENLARGEMENT OF TERTIARY CYCLOBUTANOLS

SYNTHESIS OF ISOLAUROLENE AND DERIVATIVES, CAMPHOLENIC ETHER AND (±) CUPARENE

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Abstract—The reagent obtained by mixing anhydrous $FeCl_3$ and silica gel induced, in dry medium, dehydration and specific $C_4 \rightarrow C_5$ ring enlargement of tertiary cyclobutanols, cyclization of olefinic alcohols and cleavage of tetrahydropyranyl ethers.

We report a specific ring enlargement of tertiary cyclobutanols into cyclopentene derivatives induced, in dry medium, by anhydrous ferric chloride adsorbed on silica gel and some synthetic applications.

It has been reported by Keinan and Mazur[1] that, when chromatographic grade silica gel is mixed with 10% its weight of hydrated ferric chloride ($FeCl_3 \cdot 6H_2O$) dissolved in a polar volatile solvent (ether, methanol, acetone, water) followed by removal of the solvent at 60° under vacuum (0.1 Torr) a dry yellowish brown powder is obtained, which is effective for dehydration of allylic, tertiary or sterically strained secondary alcohols.

We have observed that, when a mixture of anhydrous ferric chloride[2] (8%) and silica gel is simply stirred, without solvent at room temp for 24 hr, a pale yellowish green powder is obtained, which is also effective for dehydration of tertiary alcohols.

The dehydration is performed in dry medium by mixing directly the substrate with about 10 times its weight of the anhydrous $FeCl_3$–SiO_2 reagent, only.[3] The reaction, monitored by thin layer chromatography of an aliquot eluted with ether, is generally completed in a few hours at room temp; it can be accelerated either on heating at ~ 30–40° or when the mixture is left in a desiccator over P_2O_5.[1] Then, the product of the reaction is either distilled or eluted from the silica gel.

For instance, dehydration of tertiary cyclohexanols **1a, b** with anhydrous $FeCl_3$–SiO_2 led respectively to cyclohexenes **2a, b**, in 95% yield: and dehydration of terpineol **3** gave quantitatively *p*-cymene **4**. So, the efficiency of this reagent is comparable to the Mazur reagent. Moreover, we have found that tertiary cyclobutanols underwent dehydration and specific quantitative ring enlargement into cyclopentene derivatives.

Ring enlargement of 1-*t-butylcyclobutanol* **5** *into isolaurolene* **6** *and derivatives*

When 1-*t*-butylcyclobutanol **5**, prepared from the simple addition of *t*-butyllithium to the now readily available cyclobutanone,[4] was added to the pale yellowish green anhydrous $FeCl_3$–SiO_2 reagent, the mixture color turned to yellow-orange and after a few hours to brown. Elution with ether gave quantitatively the 1,5,5-trimethylcyclopentene or isolaurolene **6**, previously obtained as a degradation product of camphor.[5] Probably, this specific rearrangement involves the Lewis acid induced formation of the 1-*t*-butylcyclobutyl cation **A** and a methyl transfer giving the cyclobutylcarbinyl cation **B** followed by a $C_4 \rightarrow C_5$ ring enlargement into the cyclopentyl cation **C** and

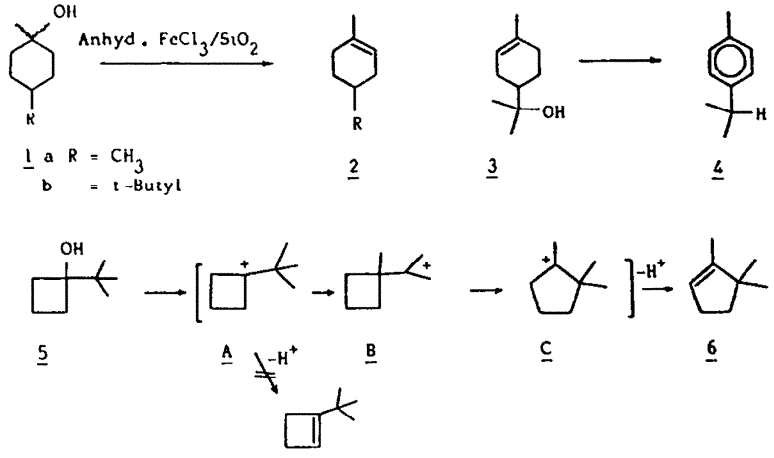
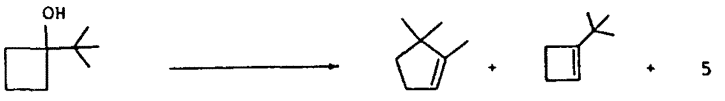


Table 1. Dehydration and ring enlargement of 1-*t*-butylcyclobutanol **5**



5	6	7	
DMSO, 160°	5	95	—
I_2, 160°	20	10	70
pTsOH, 120°	60	20	20
Anhy.$FeCl_3/SiO_2$, RT	100	—	—
△, 300°, 6 hr	—	—	78[a]

[a] The absence of compounds **6** and **7** in the thermolysis products of **5** was shown by the lack of any olefinic proton at δ 5.20 and 5.52 ppm, respectively; and, the formation of signals at δ 4.75 and 5.0 ppm.

deprotonation to give **6**. In these conditions, the formation of the 1-*t*-butylcyclobutene **7** involving deprotonation of **A** was not observed.

On the other hand, on heating either in DMSO at 160°,[6] or in the presence of iodine[7] or *p*-toluenesulfonic acid,[8] the tertiary cyclobutanol **5** underwent dehydration into a mixture of isolaurolene **6** and 1-*t*-butylcyclobutene **7**, with the ratios reported in Table 1. In sealed tube, neat **5** underwent 13 and 22% of dehydration only on heating at 240° for 16 hr and at 300° for 6 hr, respectively; important polymerization occurred on heating at 350°. Silica gel alone or alumina in the dry state were not effective for dehydration of **5**.

Among the numerous methods developed to make cyclopentane derivatives, the expansion of four-membered ring into 5-membered ring has only recently been considered;[9] so, this specific rearrangement opens a new and convenient route for this challenging purpose.

Valuable derivatives of isolaurolene **6** are readily available by this route. So for instance, as ferric chloride in ether converts epoxide into 1,2-chlorohydrins,[10] we have observed that the epoxidation with *m*-chloroperbenzoic acid of the crude product obtained after treatment of **5** with anhydrous $FeCl_3$–SiO_2 and elution with ether from silica gel, so in the presence of $FeCl_3$, gave after filtration over neutral alumina, via the epoxide **8**, the 3,3-dimethyl-2-methylenecyclopentanol **9**, in 93% yield.

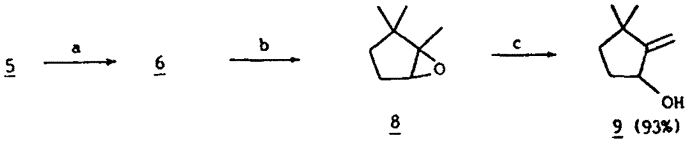
Oxidation of the cyclopentanol **9** with pyridinium chlorochromate (PCC)[11] led to the 3,3-dimethyl-2-methylenecyclopentanone **10**, in 75% yield. This α-methylene ketone **10**, previously obtained among the dehydration product of cyclopentanic acyloins,[12] can be as reported, converted, after Michael addition of malonic acid dimethyl ester, decarboxylation, and dehydration, to the terpenoïdic enol lactone of **11**.[13]

On the other hand, epoxidation of pure **6** directly distilled from the reaction medium, in the absence of $FeCl_3$, gave the 1,2-epoxy-1,5,5-trimethylcyclopentane **8**, in 85% yield. Then, treatment of **8** with a 0.2 N solution of sulfuric acid at room temp for 48 hr led to a mixture of the diol **12** (54% yield) and the cyclopentenol **13** (46% yield); whereas, in 1.2 N sulfuric acid at 60° for 1 hr, **13** was obtained in 94% yield. The formation of **13** involves acid induced dehydration and a methyl transfer.[14] Finally, oxidation of **13** with PCC[11] led to the 2,2,3-trimethyl-3-cyclopentanone **14**, in 96% yield.

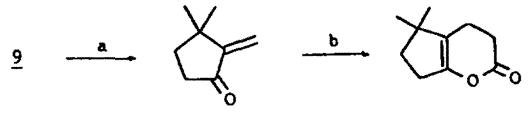
Ring enlargement of 1-t-*butyl*-2-(2-*hydroxyethyl*) *cyclobutanol* **16** *into campholenic ether* **18**

Hydroboration and oxidation[15] of 2-vinylcyclobutanone dimethylacetal prepared from 2-bromocyclobutanone acetal and vinylmagnesium bromide[16] gave, after deacetalisation, the 2-(2-hydroxyethyl) cyclobutanone **15**.

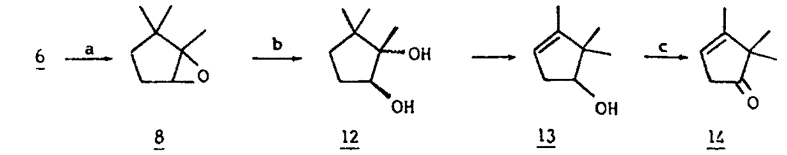
Addition of *t*-butyllithium to **15a** (R = H) in ether at −70°, led to 1-*t*-butyl-2-(2-hydroxyethyl) cyclobutanol



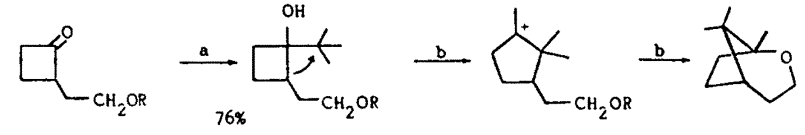
a) Anhydrous $FeCl_3$-SiO_2 ; b) $mClC_6H_5CO_3H$; c) neutral Al_2O_3.



a) Pyridinium chlorochromate, Na_2HPO_4 ; b) ref. 13.



a) $mClC_6H_5CO_3H$; b) H_2SO_4 0.2 N ; c) PCC, celite.



a) t-BuLi ; b) Anhydrous $FeCl_3$-SiO_2.

16a. Upon treatment with anhydrous $FeCl_3$–SiO_2 at 40° for 4 hr, **16a** gave, *via* the tertiary cyclopentyl cation **17**, after elution with ether, the 1,8,8-trimethyl 2-oxabicyclo [3.2.1] octane **18**, in 75% yield. In the same way, treatment of the tetrahydropyranyl ether **16b** prepared from the cyclobutanone **15b** and *t*-butyllithium, led to a mixture of the diol **16a** and ether **18**; and then, on further heating at 40°, exclusively to **18**. So, the anhydrous $FeCl_3$–SiO_2 reagent appears to be also effective in cleaving the tetrahydropyranyl ethers.[17]

The ether **18** was synthesized from the 2,2,3-trimethyl-3-cyclopentene-1-ethanol **19**, obtained by Meerwein–Ponndorf or lithium aluminium hydride reduction of α-campholene aldehyde, a product of zinc bromide catalyzed isomerization of α-pinene oxide.[14a] Upon treatment with anhydrous $FeCl_3$–SiO_2, **19** gave also the bicyclic ether **18**, in 85% yield after 19 hr at room temp, likely *via* the same intermediate **17** formed by addition of a proton resulting from the reaction of the alcohol **19** with $FeCl_3$. Examples of such acid induced formation of cyclic ethers have been recently reported.[18]

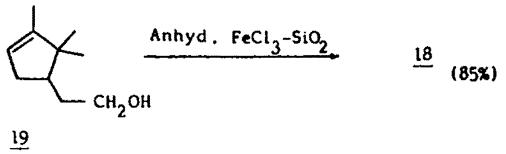
Ring enlargement of 1-(1-*methyl*-1-*aryl*) *ethylcyclobutanols* **22**. *Synthesis of* 3,3-*dimethyl*-2-p-*tolycyclopentene* **28b**, *a precursor of* (±) *cuparene* **31**

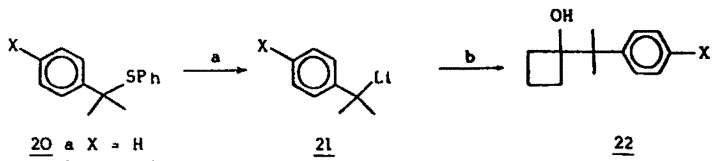
Addition of lithium naphthalene to the phenylsulfides **20**[19] gave, after cleavage and metalation, the tertiary benzylic lithium reagents **21**,[20] which were added to cyclobutanone to obtain the tertiary cyclobutanols **22**, in 50–70% yields.

Upon treatment with the anhydrous $FeCl_3$–SiO_2 reagent the cyclobutanols **22a**, **b** (X = H, CH_3) underwent dehydration and ring enlargement into a mixture of the isomeric cyclopentenes **28a**, **b** and **29a**, **b**, in 85 and 15% yields respectively, as shown by the NMR spectra of the crude products of the reaction by comparison of the areas of the vinylic protons of **28a**, **b** (a triplet at δ 5.62 ppm, J = 2.5 Hz[21]) with the areas of the vinylic protons of **29a**, **b** (a multiplet at δ 5.45 ppm).[22]

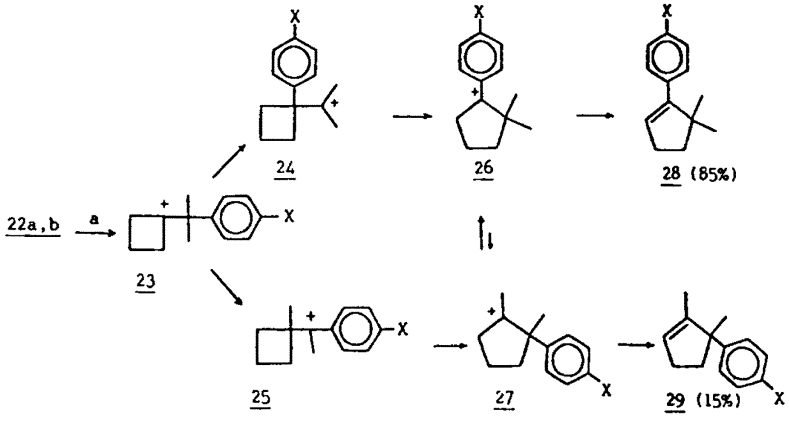
Therefore, the cyclobutyl cations **23** underwent either aryl migration to give the cations **24** or methyl transfer to give **25**; then, the $C_4 \rightarrow C_5$ ring enlargement led to cyclopentenes **28** and **29** after deprotonation of the intermediate cyclopentyl cations **26** and **27**, respectively. However, methyl or aryl transfers between the cations **26** and **27** cannot be excluded, too.

On the other hand, dehydration of the cyclobutanol **22** in DMSO at 160° gave a mixture of cyclobutene **30** (31%) presenting a vinylic proton at δ 5.22 ppm and of cyclopentene **28** (40%); the lack of any signal around 5.22 ppm in the NMR spectra of the product of the reaction of **22** with anhydrous $FeCl_3$–SiO_2 proved the specificity of this ring enlargement.

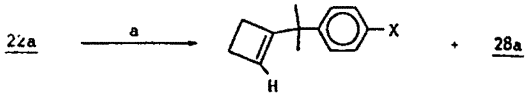




a) Lithium naphthalene, THF, -60°C ; b) Cyclobutanone, THF, -60°C.

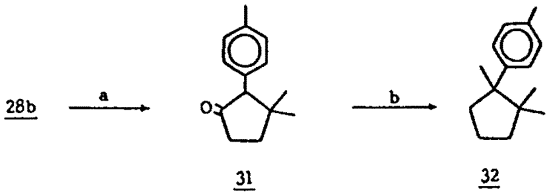


a) Anhyd. $FeCl_3$–SiO_2, in dry state.



a) DMSO, 160°, 1.5 hr.

Anhydrous $FeCl_3$–SiO_2 rearrangement of the readily available tertiary cyclobutanol **22b** provides a short and convenient route to the 3,3-dimethyl-2-*p*-tolylcyclopentene **28b**, separable from **29b** by gas chromatography, and after hydroboration and oxidation to the cyclopentanone **31**. Both compounds



a,b) ref. 21, 23.

28b[21] and **31**[23] have been used as precursors of the sesquiterpenoïd (±) cuparene **32**, while the minor compound **29b** is known as a precursor of the sesquiterpenoïd (±) laurene.[22]

Further synthetic applications of this anhydrous $FeCl_3$–SiO_2 reagent are currently under investigation and will be reported in due course.

EXPERIMENTAL

Preparation of the anhydrous $FeCl_3$–SiO_2 *reagent*

In a 250 ml flask, chromatographic grade silica gel (50 g) (70–230 mesh) and anhydrous ferric chloride (4 g) (8% of the weight of SiO_2) were vigorously stirred, without solvent, at room temp for 24 hr in order to achieve a homogeneous adsorption. A pale yellowish-green powder was obtained and used directly for the dehydration reactions.

General dehydration procedure

A 25 ml one-necked flask equipped with a magnetic stirrer was charged with anhydrous $FeCl_3$–SiO_2 (2.4 g) and 2 mmol of tertiary alcohol, about 10% of the weight of reagent. The reaction mixture was stirred at room temp. The color of the mixture turned from pale yellow to dark brown or dark red. The progress of the reaction was monitored by TLC or GC. When the reaction was completed the product was either directly distilled under vacuum from the dry reaction medium (volatile compounds) or eluted with ether–pentane (10:90) through a short column packed with Florisil (*ca* 6 g). After removal of solvent on a rotary evaporator the product was obtained practically pure or if necessary purified by liquid chromatography.

1,4-*Dimethylcyclohexene* **2a**

A mixture of *cis*- and *trans*-1,4-dimethylcyclohexanol **1a** (256 mg; 2 mmol), prepared by addition of methyllithium to 4-methylcyclohexanone and anhydrous $FeCl_3$–SiO_2 (2.4 g) was stirred at room temp for 36 hr, while the color of the mixture turned from yellow to light brown. Then 1,4-dimethylcyclohexene **2a** (210 mg, 95%) were distilled from the dry medium.

The same mixture stirred at room temp for 10 min, was then left in a desiccator over P_2O_5 for 10 hr. Then distillation of the mixture gave of cyclohexen **2a** (200 mg, 91%) presenting spectral data similar to those of an authentic sample.

4-t-*Butyl*-1-*methylcyclohexene* **2b**

A mixture of *cis*- and *trans*-4-*t*-butyl-1-methylcyclobutanol **1b** (340 mg), prepared by addition of methyllithium to 4-*t*-butylcyclohexanone and 2.4 g of anhydrous $FeCl_3$–SiO_2 was stirred at room temp overnight, while the color turned to dark brown. Then, 4-*t*-butyl-1-methylcyclohexene **2b** (280 mg, *ca* 93%) was distilled from the reaction medium, presenting spectral data similar with those of an authentic sample.[24]

p-Cymene **4**

A mixture of freshly distilled α-terpineol (308 mg, 2 mmol) and anhydrous $FeCl_3$–SiO_2 (2.4 g) was stirred at room temp for 3 hr. The reaction was exothermic and the color turned from yellow to dark blue. Elution through Florisil yielded *p*-cymene (240 mg, *ca* 90%) with spectral data identical with those of an authentical sample.

1-t-*Butylcyclobutanol* **5**

To a solution of cyclobutanone[4] (2.1 g, 30 mmol) in anhydrous ether (30 ml) cooled at −70°, was added dropwise over 2 hr, under an argon atmosphere a solution of *t*-BuLi (30 ml, 1.17 N) (34.5 mmol). The reaction mixture was stirred at −50° for 1 hr and at room temp overnight. Then, a cold saturated solution of NH_4Cl (10 ml) was added, the organic layer was decanted and the aqueous layer extracted four times with ether (80 ml). The combined organic layers were washed quickly with a solution of HCl (0.5 N) and then with saturated brine (1 ml), dried over $MgSO_4$, filtered, concentrated on a rotary evaporator to give the crude 1-*t*-butylcyclobutanol **5** (4 g, 85%): NMR (CCl_4): δ 2.5–1.3 (m, 6H); 2.1 (s, OH); 0.9 (s, 9H). IR (CCl_4): 3420 cm^{-1} (ν_{OH}), 1255 and 1142 cm^{-1}. M.S.: *m/e* (rel. intensity): 100 (22.5); 85 (100); 57 (53); 43 (72); 41 (62). Found: C, 75.32; H, 12.47; $C_8H_{16}O$ requires: C, 74.95; H, 12.57%.

Dehydration of 1-t-*butylcyclobutanol* **5** *into* 1-t-*butylcyclobutene* **7**

A solution of 1-*t*-butylcyclobutanol **5** (520 mg, 4 mmol) in anhydrous DMSO (6 ml) was heated at 160–170°[6] in a flask fitted with a Claisen condenser and a trap. After 3 hr 1-*t*-butylcyclobutene **7** (426 mg, 95.3%) containing 5% of isolaurolene **6**, as shown by GC were received in the trap cooled at 0°. A sample of 1-*t*-butylcyclobutene **7** was purified by liquid chromatography. NMR (CCl_4): δ 5.52 (s, H); 2.6–2 (m, 4H); 1.02 (s, 9H). IR (CCl_4): 1630 cm^{-1} ($\nu_{C=C}$). M.S.: *m/e* (rel. intensity): 110 (M^+, 16); 95 (100); 67 (57).

In the same flask **5** (520 mg, 4 mmol) was heated at 160° in the presence of a crystal of iodine.[7] After 2 hr a mixture (122 mg, 30%) of **5** and **6**, in 33:67 ratio, was obtained in the trap.

The distillation of **5** (520 mg, 4 mmol) in the presence of *p*-toluenesulfonic acid[8] gave, after 2 hr, a mixture (350 mg, 80%) containing **7** and isolaurolene **6** in the ratio 25:75.

On heating in a sealed tube **5** (65 mg, 0.5 mmol) at 240° for 16 hr only 13% of dehydration occurred as determined by GC. However NMR of the crude product showed 2 multiplets of 5.0 and 4.75 ppm.

On heating at 300° for 6 hr in a sealed tube **5**, (65 mg) 22% of dehydration occurred, while on further heating, *ca* 350°, polymerization was observed.

Dehydration of 1-t-*butylcyclobutanol* **5** *into* 1,5,5-*trimethylcyclopentene* (*isolaurolene*) **6**

To yellowish-green anhydrous $FeCl_3$–silica gel reagent (10 g) was added rapidly **5** (1.24 g, 8 mmol) and the mixture was stirred for 24 hr at room temp. The mixture color turned to yellow–orange and after a few hours to brown. Then, the product was either eluted from silica gel with pentane or ether, or directly distilled under reduced pressure to give isolaurolene **6** (710 mg, 90%): NMR (CCl_4): δ 5.20 (m, H); 2.18 (m, 2H); 2–1.25 (m, 2H); 1.6 (d, 3H); 1.0 (s, 6H). IR (CCl_4): 1660 cm^{-1} ($\nu_{C=C}$). M.S.: *m/e* (rel. intensity): 110 (M^+, 19.4); 95 (100); 67 (44.8); 41 (30); 39 (30).

1,5,5-*Trimethyl*-1,2-*epoxycyclopentane* **8**

To a solution of isolaurolene **6** (550 mg, 5 mmol) in anhydrous ether (15 ml) containing $NaHCO_3$ (1 g) was added at 15° a solution of *m*-chloroperbenzoïc acid (MCPBA) (1.11 g, 5.5 mmol, 85%) in anhydrous ether (15 ml) and the mixture was stirred vigourously for 2 hr. The consumption of MCPBA was monitored by a KI test. The excess of MCPBA was eliminated by a 10% aqueous solution of sodium sulfite, the organic layer was decanted and the aqueous layer extracted with ether (50 ml). The combined organic layers were washed twice with brine (1 ml), dried over $MgSO_4$, filtered and concentrated by distillation of the solvent. The residue was chromatographed on silica gel (25 g); elution with pentane–ether (90:10) gave 1,5,5-*trimethylepoxycyclopentane* **8** (535 mg, 85%): NMR (CCl_4): δ 3.13 (s, H); 2.0–1.0 (m, 4H); 1.26 (s, 3H); 1.04 (s, 3H); 0.93 (s, 3H) IR (CCl_4): ν 1380, 1370, 1090, 905 cm^{-1}. M.S.: *m/e* (rel. intensity): 126 (M^+, 12.4); 111 (49.8); 83 (32.7); 69 (39); 67 (30.6); 55 (95); 43 (100); 41 (89.5); 39 (55.8).

2,2,3-*Trimethylcyclopent*-3-*enol* **13**

A solution of epoxide **8** (126 mg, 1 mmol) and H_2SO_4[14] (1.3 ml 1.2 N solution) was stirred at 60° for 16 hr. Then, the reaction mixture was neutralized by a saturated solution of K_2CO_3. The aqueous layer was extracted three times with ether (30 ml), and the organic layer was washed twice with brine (2 ml), dried over $MgSO_4$, and the solvent was removed. The residue was chromatographed on silica gel (18 g) and eluted with pentane–ether (80:20) to give 2,2,3-trimethylcyclopent-3-enol **13** (15 mg, 94.4%): NMR (CCl_4): δ 5.14 (m, H); 3.85 (t, 6.6 Hz, H); 2.9 (m, OH); 2.6–2 (m, 2H); 1.58 (d, 3H); 0.96 (s, 3H); 0.90 (s, 3H). IR (CCl_4): 3640 and 3500 cm^{-1} (ν_{OH}); 1652 cm^{-1} ($\nu_{C=C}$); 1070. M.S.: *m/e* (rel. intensity): 126 (M^+, 66); 111 (M^+—CH_3, 84); 109 (30.5); 108 (42); 93 (63); 91 (49); 83 (45.5); 81 (52.9); 79 (93.6); 77 (56.7); 55 (100); 53 (42.8); 43 (77.5); 41 (63); 39 (77); 27 (55).

Upon treatment of **8** (126 mg) with H_2SO_4, (0.2 N solution) at room temperature for 48 hr alcohol **13** (51 mg, 40%) and 1,2-dihydroxy-2,3,3-trimethylcyclopentane **12** (77 mg, 53.4%) were obtained: NMR (CCl_4): δ 3.65 (m, H); 3.5 (m, 20H); 1.76 (m, 4H); 1.1 (s, 3H); 0.97 (s, 3H); 0.75 (s, 3H). IR (CCl_4): 3630 and 3545 cm^{-1} (ν_{OH}), 1045 cm^{-1}.

2,2,3-*Trimethylcyclopent*-3-*enone* **14**

To a mixture of pyridinium chlorochromate (433 mg, 2 mmol) (PCC),[11] celite[26] (200 mg) and Na_2HPO_4 (285 mg, 2 mmol) in anhydrous methylene chloride (12 ml), was added in one portion a solution of cyclopentenol **13** (126 mg, 1 mmol) in CH_2Cl_2 (4 ml) and the mixture was stirred at room temp for 10 hr. The ketone formation was monitored by TLC. The mixture was filtered through Florisil (6 g) eluted with ether (50 ml). The solvent was distilled to yield pure cyclopentenone **14** (120 mg, 96%): NMR (CCl_4): δ 5.65 (m, H); 2.8 (t, 2H); 1.85 (t, m, 3H); 1.03 (s, 6H). IR (CCl_4): 1750 ($\nu_{C=O}$); 1650 cm^{-1} ($\nu_{C=C}$). M.S.: *m/e* (rel. intensity): 124 (M^+, 16.7); 96 (33); 81 (100); 79 (70.8); 77 (29); 53 (23). Found: 124.0891. $C_8H_{12}O$ requires: 124.08881%.

3,3,-*Dimethyl*-2-*methylenecyclopentanol* **9**

A mixture of 1-*t*-butylcyclobutanol **5** (2.1 g, 16.4 mmol) and anhydrous $FeCl_3$–SiO_2 reagent (30 g) was stirred overnight at room temp. Then, the reaction mixture was filtered through Florisil (80–200 mesh) (5 g) and eluted with anhydrous ether (150 ml). To the filtrate was added $NaHCO_3$ (3 g) and a solution of MCPBA (3.63 g, 18 mmol, 85%) in anhydrous ether (30 ml) was added dropwise. After the addition was completed, the reaction mixture was stirred at room temp overnight. Then the excess of MCPBA was eliminated by a 10% solution of sodium sulfite (negative KI test). The organic layer was decanted and the aqueous phase was extracted twice with ether (60 ml). The combined organic layers were washed with 1 ml portions of a half-saturated solution of NaCl until neutrality, dried over $MgSO_4$ filtered through neutral activated alumina (30 g) to remove iron salts and eluted with ether (200 ml) and then concentrated by distillation of the solvent. The residue was chromatographed on silica gel (80 g) and eluted with pentane–ether (95:5) to give of 3,3-dimethyl-2-methylenecyclopentanol **9** (1.95 g, 93%): NMR (CCl_4): δ 5.07 (d, 2 Hz, H); 4.87 (d, 2 Hz, H); 4.4 (t, m, H); 2.8 (s, b, OH); 2.4–1.3 (m, culminating at 1.57, 4H); 1.13 (s, 3H); 1.05 (s, 3H), IR (CCl_4): 3630 (m), 3480 (m) (ν_{OH}), 1660 (w) ($\nu_{C=C}$), 1075 (s), 900 (s). M.S.: *m/e* (rel. intensity): 126 (M^+, 3.4%); 111 (40); 109 (8.5); 93 (25.6); 70 (100); 67 (39.9) 55 (33); 43 (34); 41 (60.7); 39 (53); 27 (55.7). Found: 126.1054; $C_8H_{14}O$ requires: 126.104459%.

3,3,-*Dimethyl*-2-*methylenecyclopentanone* **10**

To a mixture of pyridinium chlorochromate (PCC)[11] (433 mg, 2 mmol) celite[26] (200 mg) and Na_2HPO_4 (285 mg, 2 mmol) anhydrous methylene choride (12 ml) was added in one portion a solution of methylenecyclopentanol **9** (126 mg, 1 mmol) in CH_2Cl_2 (4 ml). The mixture was stirred at room temp

for 2 hr. Then, the mixture was filtered through Florisil (6 g) eluted with ether (50 ml). The solvent was distilled to yield a crude product (115 mg, 91%). Purification by chromatography on silica gel (15 g) and elution with pentane–ether (90:10) gave pure methylenecyclopentanone **10** (93 mg, 75%): NMR (CCl_4): δ 5.88 (d, H); 5.13 (d, H); 2.28 (t, d, 2H); 1.74 (t, d, 2H); 1.2 (s, 6H). IR (CCl_4): 1735 ($\nu_{C=O}$); 1646 ($\nu_{C=C}$); 1100; 944. M.S.: *m/e* (rel. intensity): 124 (M^+, 37.7%); 109 (49); 96 (19.7); 82 (54); 81 (54); 79 (32.8); 68 (62); 67 (100); 53 (54); 41 (49); 39 (59).

2-(2-Hydroxyethyl) cyclobutanone **15a**

A 100 ml two-necked flask equipped with magnetic stirring bar, argon inlet, and septum, was charged with a solution of BH_3, THF (6.6 ml, 4 mmol, 0.606 M in THF) and anhydrous THF[18b,25] (20 ml). To this solution cooled at $-10°$ was added dropwise a solution of 2-vinylcyclobutanonedimethylacetal[16] (426 mg, 3 mmol) in freshly distilled tetrahydrofuran (8 ml). The reaction mixture was stirred for 3 hr at $-10°$, then was added successively water (2.5 ml), a solution of NaOH (10 ml, 30 mmol, 3m), at 5°, followed by the dropwise addition of H_2O_2 (6 ml, 30%) in water (47 mmol). The reaction mixture was stirred overnight at room temp. Then, the mixture was poured on crushed ice (50 g). The organic layer was decanted and the aqueous layer was extracted three times with ether (100 ml). The organic layers were washed with brine until neutrality, dried over $MgSO_4$, filtered and concentrated to give of pure 1,1-dimethoxy-2 (2-hydroxyethyl) cyclobutane (500 mg, 98%): NMR (CCl_4): δ 3.7 (s, OH); 3.53 (t, 2H); 3.14 (s, 3H); 3.10 (s, 3H); 2.7–1 (m, 5H + 2H). IR (CCl_4): 3650 (m) (ν_{OH}) and 1040 (s) cm^{-1}. M.S.: *m/e* (rel. intensity): 160 (no pic parent); 132 ($M^+ - 28$, 6.6%); 101 (82.5); 100 (31.7); 88 (100); 58 (49); 55 (78.7); 43 (94); 41 (54); 31 (43); 29 (61).

To a stirred mixture of silica gel (2 g), a solution of oxalic acid in water (0.2 g, 10%) and of CH_2Cl_2[27] (5 ml) was added rapidly at room temp a solution of 1,1-dimethoxy-2(2-hydroxyethyl) cyclobutane (320 mg, 2 mmol) in CH_2Cl_2 (1 ml). The reaction was completed within 1 hr. Then, $NaHCO_3$ (75 mg) was added to the reaction mixture, which was stirred for 5 min, filtered and the solid washed with ether (40 ml). After removal of the solvent, the residue was chromatographed on silica gel (10 g) and eluted with ether–pentane (40:60) to give 2-(2-hydroxyethyl) cyclobutanone **15a** (220 mg, 97%): NMR (CCl_4): δ 3.9–2.6 (m, 5H); 3.26 (s, OH); 2.2–1.4 (m, 2H); 1.17 (m, 2H). IR (CCl_4): 3650 (w) (ν_{OH}); 1787 (s) ($\nu_{C=O}$). M.S.: *m/e* (rel. intensity): 114 (M^+, 5%); 97 (7.6); 86 ($M^+ - 28$, 100); 55 (74); 41 (82); 29 (90).

2-(2-Tetrahydropyranyloxyethyl)cyclobutanone **15b**

To a solution of **15a** (230 mg, 2 mmol) in anhydrous CH_2Cl_2 (7 ml) was added dihydropyran (420 mg, 5 mmol) and pyridinium *p*-toluenesulfonate (PPTS)[28] (50 mg) and the reaction mixture was stirred at room temp. The reaction, monitored by TLC, was completed within 14 hr. After removal of the solvent the residue was extracted with ether (100 ml). The organic layer was washed with half-saturated brine (2 ml), dried over $MgSO_4$ and filtered. After evaporation of ether the residue was chromatographed on silica gel (20 g) to yield of 2-(2-tetrahydropyranyloxyethyl) cyclobutanone **15b** (240 mg, 60%): NMR (CCl_4): δ 4.53 (m, H); 4.1–2.65 (m, 7H); 2.65–1.1 (m, 10H). IR (CCl_4): 1780 (s) ($\nu_{C=O}$); 1125 (s); 1080 (s); 1055 (s) cm^{-1}. M.S.: *m/e* (rel. intensity): 198 (no pic parent); 170 ($M^+ - 28$, 1.2); 85 (THP$^+$, 100); 67 (26); 55 (85); 41 (66); 39 (45); 29 (65).

1-t-Butyl-2 (2-hydroxyethyl) cyclobutanol **16a**

The diol **16a** was prepared from **15a** (114 mg, 1 mmol) and *t*-butyllithium (2.2 equiv.), following the procedure used to prepare the 1-*t*-butylcyclobutanol **5**, to yield **16a** (130 mg, 76%): NMR ($CDCl_3$): δ 3.9–3.3 (m, 2H); 2.8–2.6 (m, 3H); 2.6–1.2 (m, 20H + 4H); 0.94 (s, 9H). IR ($CDCl_3$): 3625 (m) and 3435 (m) (ν_{OH}); 1140 (s); 1105 (s); 1060 (s); 860 (s) cm^{-1}. M.S.: *m/e* (rel. intensity): 172 (no pic parent); 155 (0.5%); 113 (33); 85 (75); 67 (52.6); 55 (29); 43 (100); 41 (57); 29 (48).

1-t-Butyl-2-(2-tetrahydropyranyloxyethyl)cyclobutanol **16b**

This alcohol **16b** was prepared from **15b** (198 mg, 1 mmol) and *t*-butyllithium (1.1 equiv.), following the procedure used to obtain **5**. Purification by chromatography on silica gel (10 g) yielded of tetrahydropyranylether **16b** (90 mg, 35%): NMR (CCl_4): δ 4.56 (m, H); 4.15–2.9 (m, 4H); 2.9–1.1 (m, 13H + OH); 0.9 (s, 9H). IR (CCl_4): 3620 and 3465 (ν_{OH}); 1125; 1080; 1030 cm^{-1}. M.S.: *m/e* (rel. intensity): 256 (no pic parent); 199 (0.6%); 85 (THP$^+$, 100); 57 (61); 55 (53); 43 (51); 41 (81); 29 (73); 27 (44).

1,8,8-Trimethyl-2-oxabicyclo[3.2.1]*octane* **18**

A mixture of 1-*t*-butyl-2 (2-hydroxyethyl) cyclobutanol **16a** (154 mg, 1 mmol) and anhydrous $FeCl_3$–SiO_2 (1.2 g) was stirred at 40° for 4 hr. While the color of the medium turned from yellow to light brown. Elution with ether and chromatography on silica gel (6 g) yielded the 1,8,8-trimethyl-2-oxabicyclo[3.2.1]octane **18** (115 mg, 75%): NMR (CCl_4): δ 3.77 (t, 2H); 2.6–1.2 (m, 7H); 1.01 (s, 3H); 0.97 (s, 3H); 0.85 (s, 3H). IR (CCl_4): ν 1260 (m); 1140 (s); 1075 (m). M.S.: *m/e* (rel. intensity): 154 (M^+, 3.1); 97 (100); 55 (25.7); 43 (99); 41 (42). Found: C, 77.25; H, 11.76; $C_{10}H_{18}O$ requires: C, 77.85; H, 11.76%.

Synthesis of **18**

A mixture of campholenic alcohol **19** (308 mg, 2 mmol) and of anhydrous $FeCl_3$–SiO_2 (2.4 g) was stirred at 25° for 19 hr, while the color of the mixture turned to greenish-grey. Elution with ether and chromatography on silica gel (15 g) gave a bicyclic ether (175 mg, 85%) with spectral data identical with those obtained for **18** prepared from **16a**.

Ring enlargement of **16b** *induced by* $FeCl_3$–SiO_2

A mixture of **16b** (90 mg, 0.35 mmol) and anhydrous $FeCl_3$–SiO_2 (400 mg) was stirred for 12 hr at room temp, while the color turned from yellow to brownish yellow. Elution with ether and chromatography led to the tertiary alcohol **16a** (26 mg, 43%) and the bicyclic ether **18** (20 mg, 35%).

The same mixture stirred at 40° for 4 hr led exclusively, after work-up to the bicyclic ether **18** (40 mg, 70%).

(1-Phenyl-1-methylethyl) phenylsulfide **20a**

A 500 ml round-bottomed flask fitted with a Dean-Stark apparatus was charged with a mixture of 1-phenyl-1-methylethanol (27.2 g, 0.2 mol), of thiophenol (22 ml, 0.2 mol), dry benzene (180 ml) and perchloric acid[19] (1 ml, 70%). The mixture was heated rapidly to reflux. Although water (2 ml) had been collected after 2 min of reflux, the reaction was completed within 1 hr, while the color turned to brown red. Then, sodium hydroxide solution (100 ml, 10%) was added, and the mixture was stirred for a few minutes. The benzene layer was separated, washed with water until neutrality, dried over anhydrous magnesium sulfate, and concentrated to yield (practically pure) (1-phenyl-1-methylethyl) phenylsulfide **20a**[19] (44 g, 96.5%). RMN (CCl_4): δ 7.5–7.1 (m, 5H); 7.1 (s, b, 5H, S-ph); 1.65 (s, 6H). IR (neat): 1603 (w) and 1585 (w) ($\nu_{C=C}$); 750 (s); 692 (s) cm^{-1}.

(1-p-tolyl-1-methylethyl) phenylsulfide **20b**

The same procedure used above for **20a**.

A mixture of 1-*p*-tolyl-1-methylethanol (12 g, 80 mmol; readily available from the addition of methyllithium to *p*-tolylmethylketone), of thiophenol (9.7 ml, 80 mmol), dry benzene (80 ml) and $HClO_4$ (0.7 ml, 70%) was refluxed for 1 hr. The work-up, used to prepare the sulfide **20a**, led to pure (1-*p*-tolyl-1-methylethyl) phenylsulfide **20b** (19 g, 98%). NMR (CCl_4): δ 7.45–6.7 (m, 4H); 7.16 (s, 5H, S-ph); 2.31 (s, 3H); 1.63 (s, 6H). IR (neat) $\nu_{C=C}$ 1610 (w); $\nu_{C=C}$ 1585 (w); 1090 (s); 818 (s); 750 (s): 690 (s) cm^{-1}. Found: C, 79.19; H, 7.50; S, 13.32; $C_{16}H_{18}S$ requires: C, 79.28; H, 7.48; S, 13.23%.

1-(1-phenylethyl) cyclobutanol **22a**

To a stirred solution of lithium naphthalene under argon [prepared from naphthalene (5.76 g, 45 mmol), lithium

metal (0.315 g, 45 mg-atom) and freshly distilled THF (30 ml)] was added at −65° dropwise within 2 hr a solution of (1-phenyl-1-methylethyl) phenylsulfide **20a** (5.20 g, 22.5 mmol) in THF (8 ml). When the addition was over, the resulting dark red solution was allowed to warm to −30° within 1 hr. Then the mixture was cooled to −60° and a solution of cyclobutanone[4] (1.05 g, 15 mmol) in THF (8 ml) was added dropwise within 2 hr. The mixture was stirred for an additional hour at −30° and overnight at room temp. It was poured into a mixture of NH_4Cl and crushed ice and extracted 3 times with ether (60 ml). The organic layers were washed with half-saturated brine and dried over $MgSO_4$. Evaporation of the ethereal solution, removal of solvent in vacuo left a crude oil containing naphthalene and dihydronaphthalene derivatives, which was chromatographed on silica gel (120 g) and eluted with ether–pentane (8:92) to yield 1-(1-phenyl-1-methylethyl) cyclobutanol **22a** (2 g, 70%). NMR (CCl_4): δ 7.5–6.95 (m, 5H); 2.55–1.1 (m, 6H + OH); 1.32 (s, 6H). IR (neat): 3570 and 3470 (ν_{OH}); 1603 and 1585 ($\nu_{C=C}$); 1252; 1138; 1030; 772; 700. M.S.: *m/e* (rel. intensity): 190 (no pic parent); 173 (M^+–OH, 8.6%); 172 (M^+ − 18, 8.2); 171 (61.6); 147 (21.6); 129 (20.7); 120 (68.7); 119 (41.8); 105 (pHCO$^{\cdot+}$, 100); 91 (70); 77 (35); 51 (28); 43 (46.8); 41 (60); 39 (45). Found: C, 82.33; H, 9.26; $C_{13}H_{18}O$ requires: C, 82.06; H, 9.53%.

1-(1-p-*tolyl*-1-*methylethyl*) *cyclobutanol* **22b**

To a solution of lithium naphthalene (15 mmol) prepared as above in THF (15 ml) was added dropwise under argon at −60° a solution of (1-*p*-tolyl-1-methylethyl) phenylsulfide **20b** (1.82 g, 7.5 mmol) in THF (5 ml) under stirring within 2 hr. The mixture was allowed to warm to −30° in order to ensure completion of the reaction. Then the mixture was cooled to −45°, and a solution of cyclobutanone (0.35 g, 5 mmol) in THF (5 ml) was added dropwise within 2 hr. The mixture was stirred at −30° for 1 hr and overnight at room temp. The work-up used to prepare **22a**, led after chromatography on silica gel to the title compound **22b** (510 mg, 50%). NMR (CCl_4): δ 7.14 (2d, 4H); 2.6–1 (m, 6H + OH); 2.3 (s, 3H); 1.32 (s, 6H). IR (neat): 3560 and 3460 (ν_{OH}); 1608 and 1575 ($\nu_{C=C}$); 1240; 1140; 815 cm^{-1}. Found: C, 82.35; H, 9.39. $C_{14}H_{20}O$ requires: C, 82.30; H. 9.86%.

5,5-*Dimethyl*-1-*phenylcyclopentene* **28a** *and* **29a**

A mixture of the tertiary cyclobutanol **22a** (190 mg, 1 mmol) and anhydrous $FeCl_3$–SiO_2 (1.2 g) was stirred at room temp. The reaction monitored by TLC was completed within 2 hr, while the color of the mixture turned from yellow to dark greenish brown. Elution with ether gave a mixture of 5,5-dimethyl-1-phenylcyclopentene **28a** and of 1,5-dimethyl-5-phenylcyclopentene **29a** (170 mg; 85 and 15% yields respectively) as shown in the NMR spectra of the crude product by comparison of the areas of the vinylic protons. The spectral data of **28a** were identical with those reported for 5,5-dimethyl-1-phenylcyclopentene[29] and for 1,5-dimethyl-5-phenylcyclopentene **29a** the data are: NMR (CCl_4): δ 7.5–6.9 (m, 5H); 5.5 (m, H); 2.6–1.25 (m, 4H); 1.5 (d, 3H); 1.45 (s, 3H). IR (neat): 1625; 1603 ($\nu_{C=C}$) cm^{-1}. M.S.: *m/e* (rel. intensity): 172 (M^+, 44); 157 (100); 129 (52); 115 (25.7); 91 (20).

5,5-*Dimethyl*-1-p-*tolylcyclopentene* **28b** *and* **29b**

A mixture of the tertiary cyclobutanol **22b** (204 mg, 1 mmol) and anhydrous $FeCl_3$–SiO_2 (1.2 g) was stirred at room temp. The reaction monitored by TLC was completed within 3 hr, while the color of the mixture turned from yellow to dark brownish red. Elution with ether gave a mixture of 5,5-dimethyl-1-*p*-tolylcyclopentene **28b** and 1,5-dimethyl-5-*p*-tolylcyclopentene **29b** in (182 mg; 84 and 14% yields respectively) as shown in the NMR spectra of the crude product by comparison of the areas of the vinyl protons. The spectral data of **28b** and **29b** are identical with those reported for 5,5-dimethyl-1-*p*-tolylcyclopentene[21] and 1,5-dimethyl-5-*p*-tolylcyclopentene.[22]

1-(1-*Methyl*-1-*phenylethyl*) *cyclobutene* **30**

A solution of the tertiary cyclobutanol **22a** (95 mg, 0.5 mmol) and anhydrous DMSO (0.5 ml) was heated at 160–170°.[6] The reaction monitored by TLC and GC was completed within 1.5 hr. The reaction mixture was taken up with ether–pentene (10–90; 40 ml) washed 3 times with water, (1 ml) dried over $MgSO_4$ and concentrated in vacuo to give 85 mg of a mixture of cyclobutene **30** (31%) and cyclopentene **28a** (40%) as shown in the NMR spectra, by comparison of the vinyl protons. NMR (CCl_4): δ 7.25 (m, 5H); 5.22 (s, b, H); 2.6–1.2 (m, 4H); 1.15 (s, 6H). IR (neat): 1645 and 1603 ($\nu_{C=C}$) cm^{-1}. M.S.: *m/e* (rel. intensity): 172 (M^+, 22.5%); 157 (56.9); 129 (100); 119 (46); 115 (21); 104 (46); 91 (80.6); 79 (20.4); 77 (25.8); 41 (38.7).

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