Palladium(0)-Catalyzed Allylation of Heterocycles with Cyclopentene Derivatives

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Palladium(0)-catalyzed allylation of imidazoles, 6-methyluracil, 2-pyrimidinone, and Meldrum's acid with cyclopentadiene monoepoxide and *cis*-cyclopentene-3,5-diol mono and dicarbonate is described.

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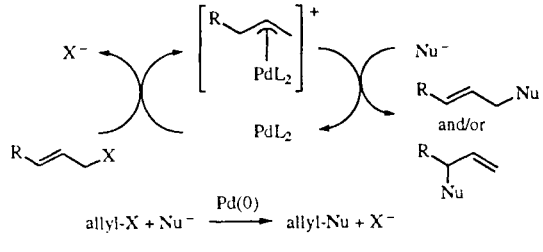
Introduction.

The palladium(0)-catalyzed allylation of nucleophiles (the Tsuji-Trost reaction) is a powerful method which has gained high recognition due to its versatility, broad scope, and easy experimental procedure [1]. The catalytic cycle is represented in Scheme 1; an allyl system reacts with palladium(0) species to form a strongly electrophilic cationic η^3-allylpalladium(II) complex, which is attacked by the nucleophile to form the final product or products, the catalytic species being recovered. Although many leaving groups X have been reported in the literature, the acetoxy (AcO-) and the alkoxycarbonyloxy (RO-CO-O-) groups remain the most popular since the corresponding acetates and mixed carbonates are very reactive and easily available. Moreover, mixed carbonates, as well as allylic epoxides, are excellent substrates also because no external base is required to activate the pronucleophile when working with them.

Scheme 1



Nucleosides and carbanucleosides as described in Figure 1, Het being an heterocyclic ring structurally related to purine or pyrimidine bases, have attracted a great deal of attention as intermediates for antiviral agents [2]. When X = methylene and n = 0, two different starting materials have been extensively used for the allylation of purines and pyrimidines under Pd(0)-catalysis, namely cyclopentadiene monoepoxide, **1**, [3] and *cis*-cyclopentene-3,5-diol, **2**, derivatives such as the enantiopure monoacetates and acetate-phosphate [4]. For X = 0 and n = 0, less information is available [5]. The general topic of the Pd(0)-catalyzed allylation of ambident nucleophilic aromatic heterocycles, including the preparation of compounds of Figure 1 for any n value has been reviewed [6].

Epoxide **1** reacts also under Pd(0)-catalysis with many non cyclic nucleophiles: carboxylates [7a,b] and phenoxides

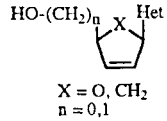


Figure 1

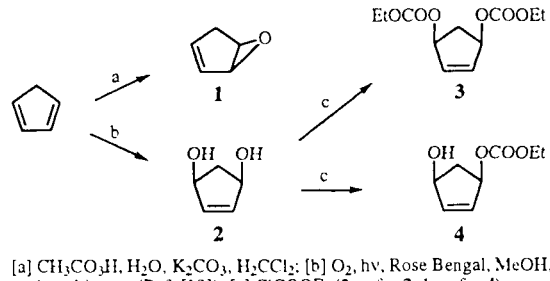
[7a-c], active methylene compounds [8], and nitromethane [9]. It should be mentioned that epoxide **1** reacts with certain aryloxides whereas the monoacetate of diol **2** does not [7c]. Also Pd(0)-catalyzed reactions of enantiopure diol **2** monoacetate with nucleophiles featuring active methylene groups, phenoxide, benzenethiolate, azide and phthalimide have been succesfully studied [10]. In all cases reported both epoxide **1** and derivatives of diol **2** react with clean overall retention of configuration through two consecutive inversions as it usually happens in Pd(0)-catalyzed allylation of this sort of nucleophiles, thus affording *cis*-3,5-disubstituted cyclopentenes. The reported Pd(0)-catalyzed reactions of **1** give in general low yields of the target products and discussion on their limitations is confined to reports on the Pd(0)-catalyzed isomerization of **1** into 3-cyclopentenone [8a,11].

Results.

We present here the preparation of a series of compounds of the general formula of Figure 1 featuring X = methylene and n = 0, and Het being a ring bound through nitrogen or carbon as well as some examples of the double replacement of both functional groups in dicarbonate **3** by nitroimidazoles. The scope and limitations on the use of **1** are also discussed.

The preparation of epoxide **1**, diol **2**, and the mixed carbonates **3** and **4** is in Scheme 2. The reactions of epoxide **1**

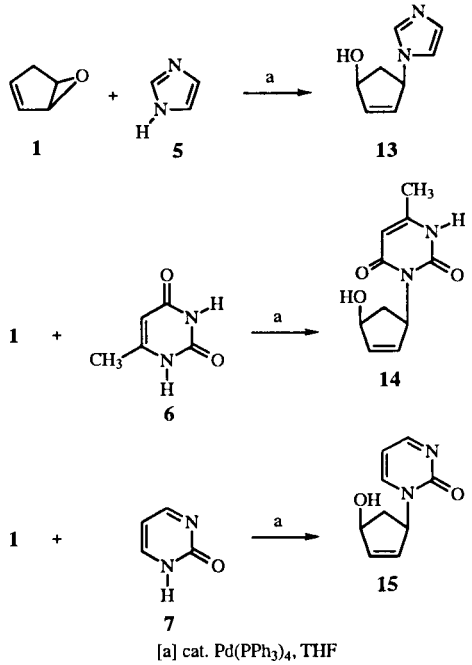
Scheme 2



[a] CH_3CO_3H, H_2O, K_2CO_3, H_2CCl_2; [b] O_2, hv, Rose Bengal, MeOH, rt, then thiourea (Ref. [18]); [c] ClCOOEt (3 eq for **3**, 1 eq for **4**), pyr., diethyl ether, rt.

with several heterocyclic nucleophiles are in Schemes 3 and 4. The reaction of **1** with imidazole, **5**, (Scheme 3) in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium in tetrahydrofuran at room temperature afforded *cis*-1-(4-hydroxy-2-cyclopentenyl)imidazole, **13**, in 35 and 22% isolated yield in two different operations carried out with 1:1 ratio of reagents, 2.7 and 2.0% of palladium, at 0.5 and 1.2*M* concentration of starting materials, and mixing of reagents at room temperature and at 0°, respectively. Part of the epoxide was consumed in the formation of a liquid compound, probably a dimer of **1** according to its mass spectrum, which was not further characterized. An insoluble solid was also formed in both reactions, but according to our experience this is frequent in reactions in which palladium and heterocycles with good complexing properties are present together. Unreacted imidazole was recovered in both cases. Thus, at least two different side reactions were identified, one of them consuming epoxide **1**.

Scheme 3



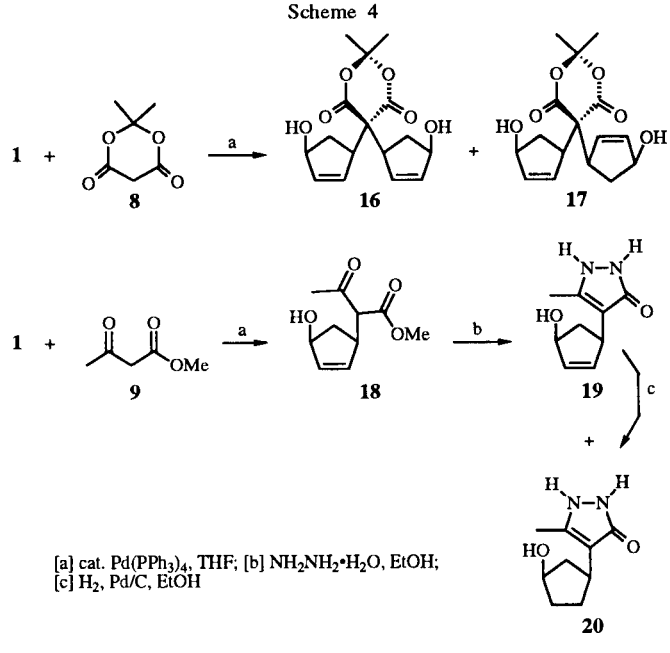
[a] cat. $Pd(PPh_3)_4$, THF

Addition of reagents under ice-cooling (see experimental) was decided for the reaction of **1** with 6-methyluracil, **6**, (Scheme 3) which afforded *cis*-3-(4-hydroxy-2-cyclopentenyl)-6-methyluracil, **14**, in 55% isolated yield. Although uracil and 5-methyluracil (thymine) react under Pd(0)-catalysis at N-1, 6-methyluracil reacts at N-3 due to the steric hindrance at N-1 [12]. Confirmation of the regiochemistry was achieved by applying the nmr SDEPT method to compound **14** [13]. Other operations with **6** at higher dilution and mixing the reagents at room temperature gave lower yields.

The reaction of **1** with 2-pyrimidinone, **7**, (Scheme 3) was also performed mixing the reagents under ice-cooling. It afforded cis-1-(4-hydroxy-2-cyclopentenyl)-2-pyrimidinone, **15**, in 69% isolated yield.

2,2-Dimethyl-1,3-dioxane-4,6-dione (Meldrum's acid), **8**, (Scheme 4) is a nucleophile difficult to control in the Tsuji-Trost reaction. Indeed, the products directly formed in the initial monoallylation step are more reactive than **8**, so that products of double allylation are always formed [14]; this is an important limitation shared in Pd(0) chemistry by many cyclic nucleophiles featuring intercarbonylic methylene groups [6,14,15], unless the electrophile is sterically hindered [16]. Our experiments with **1** and **8** showed the same trend (Scheme 4). They were difficult to control and non easily reproduceable. In no case the product of monoallylation could be detected, and always a mixture (1:1 ratio) of the two possible diallylation products, **16** and **17**, was formed.

Scheme 4



[a] cat. $Pd(PPh_3)_4$, THF; [b] $NH_2NH_2{\cdot}H_2O$, EtOH; [c] H_2, Pd/C, EtOH

4-(1-Methoxycarbonyl-2-oxopropyl)-2-cyclopenten-1-ol, **18**,was prepared as previously described for the ethyl ester [8c] by the Pd(0)-catalyzed reaction of **1** with methyl acetoacetate, **9** (Scheme 4). When **18** was treated with hydrazine hydrate it was converted into a mixture of *cis*-4-(4-hydroxy-2-cyclopentenyl)-3-methyl-5-pyrazolone, **19**, and its dihydro derivative **20**. The result can not be easily explained, but it was reproduced using hydrazine from a different bottle and samples of **18** purified by column chromatography showing no traces of palladium. The mixture of **19** and **20** was hydrogenated to **20** under Pd in charcoal catalysis in ethanol.

It can be concluded that reactions with **1** should be performed at low temperature and at rather high concentration to avoid isomerization [8a, 11].

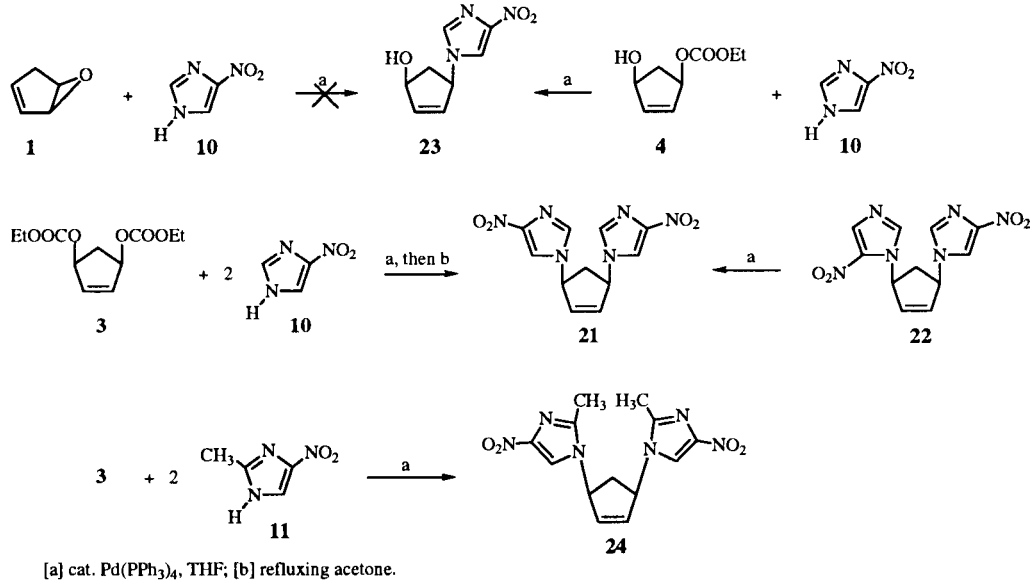
4-Nitroimidazole, **10**, and its 2-methyl derivative, **11** (Scheme 5) have also been successfully used in the Tsuji-Trost reaction. However, their conjugate bases being quite stable, they require harder reaction conditions [17]. Therefore, considering the limited stability of epoxide **1** we were not surprised when attempts to prepare *cis*- 1-(4-hydroxy-2-cyclopentenyl)-4-nitroimidazole, **23**, by reaction of **1** with **10** were not successful (Scheme 5). Moreover, reactions of dicarbonate **3** with **10** in a molar ratio 1:1 showed propensity to afford the diallylation product **21** rather than **23**. *cis*-Bis-3,5-(4-nitro-1-imidazolyl)-1-cyclopentene, **21**, was best obtained by the Pd(0)-catalyzed reaction of **3** with two equivalents of **10** at *initial* room temperature, although some experimentals details are crucial. Thus, we noted that the solution took a deep violet colour due to traces of unidentified impurities. In order to eliminate the colour we changed the solvent to acetone, added activated charcoal and refluxed the new solution still containing the Pd(0) species for large periods of time (see experimental). By following this procedure we obtained **21** in a reasonably good condition as a dirty white solid. When the mixture was not refluxed with activated charcoal in acetone in the presence of the catalysts and, instead the reaction was carried out at milder conditions, significant amounts were produced of isomer **22** in which both nitroimidazole rings were linked to the cyclopentene in such a way that the nitro groups appeared at C-4 and C-5 respectively in the heterocyclic rings. It has been previously reported that a mixture of 1-cinnamyl-4-nitroimidazole and 1-cinnamyl-5-nitroimidazole was converted into the 1,4-isomer by catalytic Pd(0) in refluxing tetrahydrofuran [17]. In other words, the product of thermodynamic control can be obtained under forcing conditions, Pd(0)-catalysis and enough time since many Pd(0)-catalyzed allylations are reversible [6, 17]. This was shown to be the case since **22** was slowly converted into **21** under Pd(0)-catalysis and forcing experimental conditions.

cis-4-(4-nitro-1-imidazolyl)-2-cyclopenten-1-ol, **23**, could be prepared by reaction of **10** with monocarbonate **4** under the usual Pd(0)-catalysis (Scheme 5). No violet colour was observed in this reaction.

cis-Bis-3,5-(2-methyl-4-nitro-1-imidazolyl)-1-cyclopentene, **24**, (Scheme 5) was obtained by reacting **3** with 2-methyl-4-nitroimidazole, **11**, under Pd(0)-catalysis for large periods of time to achieve the thermodynamic control, separation of the crude, violet-coloured precipitated **24**, and treatment with activated charcoal in refluxing ethanol.

Compounds **2**, **3**, and **4** have *cis* stereochemistry imposed by their origin, the reaction of cyclopentadiene with singlet oxygen to form the bicyclic peroxide which, upon reduction, affords **2** [18]. Differences in chemical shifts for the non equivalent methylene protons of the cyclopentene ring are 1.3 (for **2**), 1.0 (for **3**) and 1.1 (for **4**). The symmetrical compounds **21** and **24** present different signals for the methylene protons, and therefore the *cis* stereochemistry is assigned to them, differences in chemical shifts being 1.3 for **21** and 1.7 for **24**. No compelling stereochemical evidences are available for other compounds here prepared, but the general propensity of our allylic substrates, the general resemblance of the pmr spectra, and the differences in chemical shifts for the methylene protons in compounds **13** (1.2), **14** (0.8), **15**

Scheme 5



[a] cat. $Pd(PPh_3)_4$, THF; [b] refluxing acetone.

(1.3 and 1.3 in its picrate), **16** and **17** (0.7 and 0.3 or the reverse), **19** (0.5) and **23** (1.2) clearly point out to a *cis* geometry for all of them.

In summary, good experimental conditions have been defined for the Pd(0)-catalyzed reactions of cyclopentadiene monoepoxide, **1**, permitting the preparation of cyclopentenols substituted with heterocyclic rings linked through nitrogen or carbon atom. 4-Nitroimidazoles **10** and **11** react better with cyclopentene-3,5-diol mixed dicarbonate **3** to afford cyclopentenes symmetrically *cis*-disubstituted with the 4-nitro-1-imidazolyl group under thermodynamically controlled experimental conditions.

EXPERIMENTAL

The pmr (cmr) spectra were registered at 250 MHz (62.5 MHz) using tetramethylsilane as internal standard and data are in δ units. Mass spectra were determined under electron impact at 70 eV unless otherwise stated. All manipulations concerning Pd-catalyzed allylations were performed under nitrogen and with anhydrous solvents.

6-Oxabicyclo[3.1.0]hex-3-ene (Cyclopentadiene Monoepoxide) (**1**) [19].

A solution of sodium acetate (1.36 g) in 65 g (58 ml) of peracetic acid solution (32% w/w in water) was added during 50 minutes on a mechanically stirred mixture of cyclopentadiene (34 g, 0.52 mole), anhydrous potassium carbonate (94 g, 0.68 mole) and dichloromethane (300 ml) maintaining the temperature below 25°. Then the mixture was stirred for 5 hours, anhydrous sodium carbonate (70 g, 0.66 mole) was added, the mixture stirred for 4 hours and filtered, the solid was washed with dichloromethane (3 x 30 ml). The combined organic solutions were distilled through a fractionation column at atmospheric pressure to eliminate the dichloromethane. The residue was distilled at 40-43°/55-60 mm Hg, to afford epoxide **1** (6.74 g, 30%); ir (film): 3049, 2964, 2930, 2845, 1678, 1442, 1342, 1249, 911, 822, 756 cm^{-1}; pmr (deuteriochloroform, 250 MHz): 2.36 (ddt, J = 19.0, 3.3 and 2.2 Hz, 1H), 2.62 (ddd, J = 19.0, 4.0 and 2.2 Hz, 1H), 3.79 (m, 1H), 3.88 (dt, J = 3.3 and 2.2 Hz, 1H), 5.96 (m, 1H), 6.12 (ddt, J = 5.8, 3.3 and 1.1 Hz, 1H); cmr (deuteriochloroform, 62.5 MHz): 35.5, 56.7, 59.1, 131.2, 137.7.

cis-Cyclopentene-3,5-diol (**2**).

This compound was prepared as previously described [18]. It had mp 58-60° (lit [18] mp 59-60°);ir(film): 3339,3065, 2980, 2945, 2882, 1658, 1426, 1349, 1314, 1265, 1117, 1068, 1005, 898, 772 cm^{-1}; pmr (deuteriomethanol, 250 MHz): 1.50 (dt, J = 13.5 and 5.5 Hz, 1H), 2.81 (dt, J = 13.5 and 7.3 Hz, 1H), 4.67 (dd, J = 7.3 and 5.5 Hz, 2H), 4.97 (br s, 2H), 5.98 (s, 2H); cmr (deuteriomethanol, 62.5 MHz): 44.5, 75.3, 137.1.

cis-3,5-Bis(ethoxycarbonyloxy)cyclopentene (**3**).

Pyridine (3.67 g, 3.7 ml, 46.4 mmoles) and ethyl chloroformate (3.78 g, 4.3 ml, 34.8 mmoles) were sequentially and dropwise added to a magnetically stirred, ice-cooled mixture of diol **2** (1.16 g, 11.6 mmoles) and diethyl ether (35 ml). The new mixture was stirred overnight at room temperature, diluted with diethyl ether (35 ml) and washed with 1*M* hydrochloric acid and with water. The organic layer was dried and evaporated to afford dicarbonate **3** (2.27 g, 81%), bp 139° (oven temperature)/1-2 mm Hg; ir (film): 1743 cm^{-1}; pmr (deuteriochloroform, 250 MHz): 1.27 (t, J = 7.3 Hz, 6H), 1.88 (dt, J = 15.0 and 4.0 Hz, 1H); 2.90 (dt, J = 15.0 and 7.3 Hz, 1H), 4.16 (q, J = 7.3 Hz, 4H), 5.42 (ddd, J = 7.3, 4.0 and 1.0 Hz, 2H), 6.12 (d, J = 1.0 Hz, 2H); cmr (deuteriochloroform, 62.5 MHz): 14.2, 36.9, 64.0, 79.5, 134.5, 154.6.

Anal. Calcd. for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 53.47; H, 6.39.

cis-3-(Ethoxycarbonyloxy)-5-hydroxycyclopentene (**4**).

Monocarbonate **4** was prepared as for **3** using a 1:1 molar ratio of **2** and ethyl chloroformate. A mixture was formed from which **3** (16%), **4** (50%) and unreacted diol **2** (17%) were separated by column chromatography on silica gel.

Monocarbonate **4** was a liquid presenting pmr (deuteriochloroform, 250 MHz): 1.27 (t, J = 7.3 Hz, 3H), 1.68 (dt, J = 14.6 and 4.0 Hz, 1H), 2.79 (dt, J = 14.6 and 7.3 Hz, 1H), 4.15 (q, J = 7.3 Hz, 2H), 4.64-4.67 (m, 1H), 5.32-5.34 (m, 1H), 5.96 (dq, J = 5.5 and 1.1 Hz, 1H), 6.08 (dq, J = 5.5 and 1.1 Hz, 1H); cmr (deuteriochloroform, 62.5 MHz): 14.0, 40.0, 63.8, 74.3, 80.2, 131.5, 139.0, 154.5.

cis- 1-(4-Hydroxy-2-cyclopentenyl)imidazole (**13**).

Epoxide **1** (1.50 g, 18.3 mmoles) in tetrahydrofuran (5 ml) was slowly added (1 hour) into a mixture of imidazole (1.16 g, 17.0 mmoles), tetrakis(triphenylphosphine)palladium (0.58 g, 0.5 mmole) and tetrahydrofuran (30 ml). The mixture was maintained at room temperature for 64 hours. The formed solid was filtered off (0.17 g) and the filtrate was evaporated to give a residue which was chromatographed through silica-gel with mixtures of hexanes-ethyl acetate and ethyl acetate-ethanol of increasing polarity. The following compounds were eluted.

Triphenylphosphine (0.13 g) was first obtained.

A liquid dimer of **1** (0.25 g) which had bp 125-150° (oven temperature)/0.2-0.5 mm Hg eluted as the second product; ir (film): 3409, 2931, 1693, 1623, 1440, 1363 cm^{-1}; pmr (deuteriochloroform, 250 MHz): 1.60 (dt, J = 13.9 and 3.4 Hz, 1H), 2.40-2.46 (m, 2H), 2.52-2.65 (m, 3H), 3.52 (d, J = 5.8 Hz, 1H), 3.99 (br s, 1H), 4.79 (d, J = 7.3 Hz, 1H), 5.75 (dd, J = 5.8 and 2.2 Hz, 1H), 5.94 (dt, J = 5.8 and 2.2 Hz, 1H), 7.44 (t, J = 2.6 Hz, 1H); cmr (deuteriochloroform, 62.5 MHz): 26.0, 35.1, 38.6, 40.7, 76.4, 134.1, 134.7, 147.3, 159.3, 209.8; ms: m/z 164 (M, 5), 146 (100), 117 (64), 91 (33), 79 (31), 55 (17).

Triphenylphosphine oxide (0.34 g) was the third compound obtained.

Unreacted imidazole (0.17 g) was the fourth product.

Compound **13** (0.90 g, 35 %) which had mp 108-110° was the final compound obtained; ir (potassium bromide): 3134 (br), 2893, 1641, 1507, 1263, 1225, 1110, 1075, 1007, 832, 793 cm^{-1}; pmr (deuteriochloroform, 250 MHz): 1.74 (dt, J = 14.2 and 4.8 Hz, 1H), 2.94 (ddd, J = 14.2, 8.1 and 7.3 Hz, 1H), 4.85 (m, 1H), 5.02 (m, 1H), 5.93 (ddd, J = 5.5, 2.1 and 1.1 Hz, 1H), 6.18 (dt, J = 5.5 and 2.0 Hz, 1H), 6.95 (t, J = 1.1 Hz, 1H), 7.00 (t, J = 1.1 Hz, 1H), 7.47 (br s, 1H); cmr (deuteriochloroform, 62.5 MHz): 42.7, 60.6, 74.1, 117.6, 128.6, 130.9, 135.4, 139.3; ms: m/z 151 (M+1, 14), 150 (M, 89), 121 (15), 83 (52), 68 (100), 69 (87), 55 (77).

Anal. Calcd. for $C_8H_{10}N_2O$: C, 63.98; H, 6.71; N, 18.65. Found: C, 63.58; H, 6.41; N, 18.43.

cis-3-(4-Hydroxy-2-cyclopentenyl)-6-methyluracil (**14**).

Epoxide **1** (0.50 g, 6.1 mmoles) in tetrahydrofuran (2 ml) was slowly added (15 minutes) to a stirred and ice-cooled mixture of

6-methyluracil (1.15 g, 9.1 mmoles), tetrakis(triphenylphosphine)-palladium (0.12 g, 0.11 mmole) and tetrahydrofuran (7 ml). The mixture was heated at room temperature and finally at reflux for 30 hours. The solvent was evaporated and the residue was chromatographed through a column of silica-gel using ethyl acetate and mixtures of ethyl acetate-methanol to afford compound **14** (0.70 g, 55%); mp 175-176° (from chloroform-hexanes); ir (potassium bromide): 3404, 3376 (br), 1737, 1708, 1642, 1602, 1504, 1417, 1342, 1085, 759 cm^{-1}; pmr (deuteriochloroform, 250 MHz): 1.92 (d, J = 15.0 Hz, 1H), 2.14 (d, J = 1.0 Hz, 3H), 2.72 (ddd, J = 15.0, 9.9 and 8.2 Hz, 1H), 4.11 (d, J = 11.7 Hz, 1H), 4.68 (m, 1H), 5.53 (q, J = 1.0 Hz, 1H), 5.70 (dd, J = 5.4 and 2.6 Hz, 1H), 5.85 (ddd, J = 9.9, 4.8 and 2.6 Hz, 1H), 6.10 (dt, J = 5.4 and 2.6 Hz, 1H), 8.10 (br s, 1H); cmr (deuteriochloroform, 62.5 MHz): 18.5, 37.3, 54.9, 76.1, 100.8, 130.6, 137.0, 149.9, 152.8, 163.4; cmr under SDEPT conditions (deuteriodimethylsulfoxide, 250 MHz): transfer of magnetization from the proton at δ 5.6, attached at C-1 of the carbocyclic ring, results in enhanced signals for both C=0 carbon atoms at δ 151.6 (C-2) and 163.3 (C-4) of the heterocyclic ring; ms: (chemical ionization with ammonia) m/z 226 (M+18, 2), 209 (M+1, 19), 191 (100).

Anal. Calcd. for $C_{10}H_{12}N_2O_3$: C, 57.69; H, 5.81; N, 13.45. Found: C, 57.30; H, 5.54; N, 13.22.

cis-1-(4-Hydroxy-2-cyclopentenyl)-2-pyrimidinone (**15**).

Epoxide **1** (0.54 g, 6.6 mmoles) in tetrahydrofuran (2 ml) was slowly added (20 minutes) to a stirred and ice-cooled mixture of 2-pyrimidinone (0.76 g, 7.9 mmoles), tetrakis(triphenylphosphine)palladium (0.13 g, 0.11 mmole) and tetrahydrofuran (6 ml). The mixture was maintained at room temperature for 40 hours. The solvent was evaporated and the residue was chromatographed through a column of silica-gel to give **15** [3a] (0.80 g, 69%); ir (potassium bromide): 3374 (br), 2931, 1651, 1539, 1450, 1395, 1247, 1082, 795 cm^{-1}; pmr (deuteriochloroform, 250 MHz): 1.69 (dt, J = 15.3 and 3.3 Hz, 1H), 2.96 (ddd, J = 15.3, 8.4 and 7.3 Hz, 1H), 4.90 (m, 1H), 5.62 (m, 1H), 5.81 (dd, J = 5.5 Hz and 2.2 Hz, 1H), 6.27-6.38 (m, 2H), 7.90 (dd, J = 6.6 and 2.9 Hz, 1H), 8.48 (dd, J = 4.0 and 2.9 Hz, 1H); cmr (deuteriochloroform, 62.5 MHz): 40.5, 62.6, 74.9, 104.6, 131.3, 140.0, 145.7, 165.4.

The picrate of **15** had mp 154-155°; ir (potassium bromide): 3438 (br), 3043 (br), 2922 (br), 1725, 1632, 1591, 1558, 1337, 1265, 1082, 913, 721, 709 cm^{-1}; pmr (deuteriodimethylsulfoxide, 250 MHz): 1.56 (dt, J = 14.3 and 4.0 Hz, 1H), 2.84 (ddd, J = 14.3, 8.9 and 7.1 Hz, 1H), 4.68 (m, 1H), 5.51 (m, 1H), 5.87 (ddd, J = 5.5, 2.2 and 1.9 Hz, 1H), 6.29 (dt, J = 5.5 and 1.9 Hz, 1H), 6.87 (t, J = 5.5 Hz, 1H), 8.57 (s, 2H), 8.60 (m, 1H), 8.72 (dd, J = 5.5 and 2.6 Hz, 1H); cmr (deuteriodimethylsulfoxide + deuteriomethanol, 62.5 MHz): 40.8, 63.1, 73.8, 104.9, 124.9, 125.5, 129.5, 142.3, 142.5, 149.7, 155.4, 159.9, 161.2.

Anal. Calcd. for $C_{15}H_{13}N_5O_9$: C, 44.23; H, 3.22; N, 17.19. Found: C, 44.07; H, 2.96; N, 16.92.

cis-5,5-Bis-(4-hydroxy-2-cyclopentenyl)-2,2-dimethyl-1,3-dioxane-4,6-diones **16** and **17**.

Epoxide **1** (0.51 g, 6.1 mmoles) in tetrahydrofuran (10 ml) was slowly added (15 minutes) to a stirred and ice-cooled mixture of Meldrum's acid (0.81 g, 5.5 mmoles), tetrakis(triphenylphosphine)-palladium (0.21 g, 0.19 mmole) and tetrahydrofuran (10 ml). The mixture was maintained at room temperature for 40 hours. The solvent was evaporated and the residue was chromatographed through a silica-gel column to afford 0.21 g (23%) of the mixture of isomers **16** and **17**; mp 149- 150°; ir (potassium bromide): 3411 (br), 2925, 1765, 1732, 1443, 1393, 1328, 1261, 1113, 1081, 977 cm^{-1}; pmr (deuteriochloroform, 250 MHz): 1.71 (s, 6H) and 1.72 (s, 6H), 1.80 (ddd, J = 14.8, 4.7 and 3.6 Hz, 2H) and 2.19 (dt, J = 14.8 and 3.5 Hz, 2H), 2.53 (m, 2H + 2H), 3.50 (m, 2H + 2H), 4.72 (m, 2H + 2H), 5.73 (ddd, J = 5.6, 2.2 and 0.9 Hz, 2H) and 5.86 (ddd, J = 5.7, 2.2 and 1.1 Hz, 2H), 6.01 (m, 2H + 2H); cmr (deuteriochloroform, 62.5 MHz): 29.8 and 29.9, 34.7 and 35.7, 50.5 and 51.1, 59.9 and 60.2, 75.7 and 75.8, 106.0 and 106.1, 130.9 and 131.6, 136.9 and 137.5, 168.4 and 168.6.

Anal. Calcd. for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 61.67, H, 6.07.

cis-4-(4-Hydroxy-2-cyclopentenyl)-3-methyl-5-pyrazolone (**19**) and *cis*-4-(3-Hydroxycyclopentyl)-3-methyl-5-pyrazolone (**20**).

A mixture of 4-(1-methoxycarbonyl-2-oxopropyl)-2-cyclopenten-1-ol, **18**, (See [8c] for the preparation of the corresponding ethyl ester) (0.5 g, 2.53 mmoles), 99% hydrazine hydrate (0.126 g, 2.53 mmoles) and ethanol (5 ml) was refluxed under stirring for 20 hours. The precipitate (0.34 g) was filtered out and it was shown to be a mixture of **19** and **20** in a ratio 5:2. Compound **19** had pmr (deuteriomethanol, 250 MHz): 1.67 (dt, J = 14.0 and 3.5 Hz, 1H), 2.17 (s, 3H), 2.61 (ddd, J = 14.0, 9.0 and 7.5 Hz, 1H), 3.63 (m, 1H), 4.71 (m, 1H), 5.77 (ddd, J = 5.5, 2.2 and 0.7 Hz, 1H), 5.86 (dt, J = 5.5 and 2.2, 1H); cmr (deuteriomethanol, 62.5 MHz): 10.5, 39.0, 41.2, 77.3, 105.0, 133.8, 137.3, 142.7, 163.3.

The mixture of **19** and **20** (0.34 g), 10% palladium on charcoal (35 mg) and ethanol (20 ml) was treated with hydrogen at atmospheric pressure till one equivalent (11.2 ml) of hydrogen was taken. The mixture was filtered and the solvent evaporated to afford **20** (0.34 g, 100%); mp 198-200°; ir (potassium bromide): 3431 (br), 3143 (br), 2936, 1612, 1539, 1516, 1456, 1214, 1067, 1007, 979, 830, 773 cm^{-1}; pmr (deuteriomethanol, 250 MHz): 1.60-2.00 (m, 5H), 2.14 (s, 3H), 2.22 (m, 1H), 3.01 (m, 1H), 4.27 (m, 1H); cmr (deuteriomethanol, 62.5 MHz): 10.3, 31.7, 36.9, 41.9, 74.6, 107.4, 141.4, 163.3.

Anal. Calcd. for $C_9H_{14}N_2O_2$: C, 59.32; H, 7.74; N, 15.37. Found: C, 58.92; H, 7.41; N, 14.66.

cis-Bis-3,5-(4-nitro-1-imidazolyl)-1-cyclopentene (**21**).

Dicarbonate **3** (0.49 g, 2.0 mmoles) in tetrahydrofuran (10 ml) was slowly added to a stirred mixture of 4-nitroimidazole (0.45 g, 4.0 mmoles), tetrakis(triphenylphosphine)palladium (0.14 g, 0.10 mmoles) and tetrahydrofuran (10 ml). The mixture was maintained at room temperature for 4 hours while the solution became deeply violet. Then it was evaporated and the residue was dissolved in acetone (50 ml), activated charcoal was added and the mixture was refluxed for 60 hours and then filtered while hot. The filtrate was evaporated to afford 0.45 g of a brown-blue solid consisting of a mixture of **21** and triphenylphosphine oxide (pmr monitoring), which was digested in benzene to give insoluble **21** (0.40 g, 69%). A more pure sample was obtained by treating this solid with refluxing ethanol in the presence of activated charcoal, and it presented mp 184-186°; ir (potassium bromide): 3135, 1539, 1510, 1489, 1391, 1342, 1285, 1222, 1124, 983, 857, 821 cm^{-1}; pmr (deuterioacetone, 250 MHz): 2.27 (dt, J = 13.9 and 7.3 Hz, 1H), 3.60 (dt, J = 13.9 and 7.3 Hz, 1H), 5.72 (t, J = 7.3 Hz, 2H), 6.49 (s, 2H), 7.89 (d, J = 1.5 Hz, 2H), 8.32 (d, J = 1.5 Hz, 2H); cmr (deuterioacetone, 62.5 MHz): 42.9, 62.9, 119.7, 135.4, 136.7, 149.2. No good elemental analysis could be obtained for this compound.

In a different reaction under milder conditions a sample of the isomeric *cis*-3-(4-nitro-1-imidazolyl)-5-(5-nitro-1-imidazolyl)-1-cyclopentene (**22**) was isolated. It presented pmr (deuteriodimethylsulfoxide, 250 MHz): 2.06 (dt, J = 13.9 and 5.8 Hz, 1H), ca. 3.3 (overlapped with the signal of water contaminating the deuteriodimethyl sulfoxide, 1H), 5.55 (t, J = 6.6 Hz, 1H), 5.89 (t, J = 5.89 Hz, 1H), 6.39 (s, 2H), 7.94 (br d, 1H), 8.12 (s, 1H), 8.24 (s, 1H), 8.45 (s, 1H). Upon prolonged refluxing in tetrahydrofuran in the presence of tetrakis(triphenylphosphine)-palladium(0) **22** was slowly converted into **21** (pmr monitoring).

cis- 1-(4-Hydroxy-2-cyclopentenyl)-4-nitroimidazole (**23**).

Monocarbonate **4** (0.64 g, 3.7 mmoles) in tetrahydrofuran (10 ml) was slowly added to a stirred mixture of 4-nitroimidazole (0.42 g, 3.7 mmoles), tetrakis(triphenylphosphine)palladium (0.21 g, 0.20 mmoles) and tetrahydrofuran (10 ml). The mixture was refluxed for 22 hours, no violet colour being observed. The mixture was evaporated and the residue was chromatographed through silica-gel to afford **23** (0.18 g, 22%); mp 98-100°; ir (potassium bromide): 3353, 3142, 2952, 1532, 1510, 1496, 1412, 1384, 1342, 1285, 1271, 1131, 1075,990 cm^{-1}; pmr(deuterioacetone, 250 MHz): 1.79 (dt, J = 14.6 and 3.6 Hz, 1H), 2.98 (dt, J = 14.6 and 7.3 Hz, 1H), 4.51 (d, J = 5.85 Hz, 1H), 4.86 (s, 1H), 5.36-5.41 (m, 1H), 6.05 (dd, J = 5.8 and 1.5 Hz, 1H), 6.26 (dt, J = 5.1 and 2.2 Hz, 1H), 7.76 (d, J = 1.5 Hz, 1H), 8.14 (d, J = 1.5 Hz, 1H); cmr (deuterioacetone, 62.5 MHz): 42.9, 62.9, 75.1, 119.7, 131.7, 136.5, 141.0.

Anal. Calcd for $C_8H_9N_3O_3$: C, 49.23; H, 4.65; N, 21.53. Found: C, 49.24; H, 4.47; N, 21.58.

cis-Bis-3,5-(2-methyl-4-nitro-1-imidazolyl)-1-cyclopentene (**24**).

Dicarbonate **3** (0.61 g, 2.5 mmoles) in tetrahydrofuran (5 ml) was slowly added into a stirred mixture of 2-methyl-4-nitroimidazole (0.63 g, 5.0 mmoles), tetrakis(triphenylphosphine)palladium (0.14 g, 0.12 mmoles) and tetrahydrofuran (10 ml). The mixture was refluxed for 15 hours while a precipitate appeared, the liquid and the precipitate were deeply violet. The precipitate was filtered out to afford crude **24** (0.59 g, 74%). Purification was achieved by treatment with activated charcoal in boiling ethanol for 6 hours, then the mixture was filtered when hot and the filtrate was evaporated to give white **24**; mp > 300° (from ethanol); ir (potassium bromide): 3128, 1539, 1489, 1391, 1349, 1285, 1264, 1152, 990, 835 cm^{-1}; pmr (deuteriomethanol, 250 MHz): 1.81 (dt, J = 13.5 and 7.0 Hz, 1H), 2.57 (s, 6H), 3.53 (dt, J = 13.5 and 7.0 Hz, 1H), 5.58 (t, J = 7.5 Hz, 2H), 6.43 (s, 2H), 8.35 (s, 2H); cmr (deuteriodimethylsulfoxide, 62.5 MHz): 13.1, 40.5, 60.4, 120.1, 134.1, 144.9, 146.0.

Anal. Calcd. for $C_{13}H_{14}N_6O_4$: C, 49.06; H, 4.43; N, 26.40. Found: C, 48.83; H, 4.33; N, 26.13.

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