Cleavage of cyclopropyl ketones mediated by alkylmercury(II) hydrides † ‡

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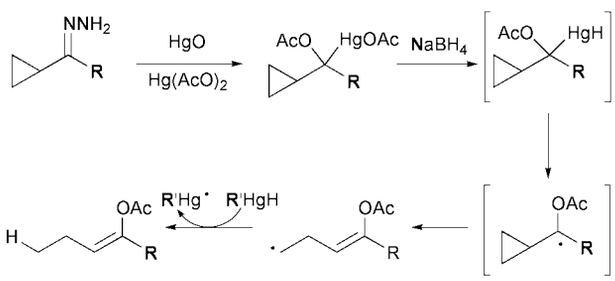
Cyclopropyl ketones are converted into their hydrazones which react with mercury(II) oxide and mercury(II) acetate to give α-(acetoxymercurio)alkyl acetates. These are reduced *in situ* to the corresponding α-acetoxyalkylmercury(II) hydrides which rearrange spontaneously with cleavage of the cyclopropane ring. The procedure is used to obtain D-homo- and 17(13⟶18)-*abeo*-pregnanes.

Introduction

In previous papers we have used steroidal cyclopropyl ketones for the synthesis of *abeo*-pregnane analogues of steroid hormones. A key transformation in these preparations was the rearrangement of cyclopropyl ketones fused to rings C or D of the steroid nucleus, under anionic[1] (NaOH–MeOH) or radical[2] (Bu_3SnH–AIBN) conditions. The latter methodology gave rise to 17(13⟶18)-*abeo*-pregnanes by reductive cleavage of the cyclopropyl ring, while the anionic method was used to rearrange (non-reductively) a 12β,18-cyclopropyl diketone into a 12(13⟶18)-*abeo*-pregnane with a seven-membered C ring. Although good yields were obtained with the Bu_3SnH–AIBN method, the reaction required high temperatures (110 °C), long reaction times (3 days), and tedious purifications to eliminate tin-containing by-products. Also, sterically hindered ketones did not react. Several methods have been applied to the cyclopropylcarbinyl ⟶ homoallyl radical transformation and a detailed study has been published.[3] In the case of cyclopropyl ketones, many examples of radical addition and electron-transfer reactions have been documented, most of them generating an organometallic oxycyclopropyl radical intermediate.[4] We considered the possibility of generating an acetoxycarbinyl radical next to a cyclopropane ring from a cyclopropyl ketone under the mild conditions of the organomercury chemistry developed by Giese,[5] by mercuriation of the hydrazone with $Hg(OAc)_2$–HgO (to give the α-substituted organomercury salt) followed by reduction to the alkylmercury(II) hydride with a hydrogen donor like Bu_3SnH or $NaBH_4$.[6] Hydrogen abstraction from this hydride should give an alkylmercury radical that decomposes spontaneously to mercury and an alkyl radical;[5,7] the latter can then rearrange (Scheme 1).



Scheme 1

Results and discussion

Table 1 summarizes our results for the rearrangement of cyclopropyl ketones by conversion to the corresponding alkylmercury(II) hydride *via* their hydrazones. Cyclopropyl ketones **1a** and **3a** were used as sources of conformationally mobile acetoxycarbinyl radicals, while 12β,18-cyclopropyl ketone **6a** and 'cyclopropylcarvone' **8a**, gave radicals with a fixed conformation. Hydrazones were obtained in 90–97% yield by treatment of an ethanolic solution of the ketone with hydrazine hydrate and BaO as catalyst.[8] The hydrazone of the 11-ketopregnane **6a** required more rigorous reaction conditions, using a slight modification of Barton's procedure with ethylene glycol as solvent (85% yield).[9] The low reactivity of the C-11 carbonyl in compound **6a** is due to the steric hindrance from both the 12β,18-cyclopropane and the C-10 angular methyl group. In a typical procedure, the crude hydrazone **1b** was treated with a mixture of HgO–$Hg(OAc)_2$ in dry 1,4-dioxane or THF to give the steroidal organomercury(II) salt. Subsequent addition of aqueous $NaBH_4$ yielded the enol acetate **2** (as a *ca.* 1 : 1 mixture of *E* and *Z* isomers) in which the endocyclic C-13–C-17 bond was regioselectively cleaved. Confirmation of the structure and stereochemistry at C-13 (C/D *trans*-fused rings) in the latter compound was carried out by hydrolysis of the enol acetate with NaOH–MeOH, yielding the *abeo*-pregnane **12** identical (TLC, NMR) with the sample described previously by us.[2] Use of the above sequence on cyclopropyl ketone **3a** gave predominant cleavage of the endocyclic C-16–C-17 bond, yielding a *ca.* 3 : 1 mixture of enol acetates **4** and **5** (as *E* : *Z* mixtures) which, after chromatographic separation and basic hydrolysis, gave the corresponding ketones **13** and **14**. The conformationally fixed radicals derived from ketones **6a** and **8a** gave exclusively cleavage of one of the exocyclic cyclopropane bonds. Hydrolysis of enol acetate **7** led to the known 11-ketopregnane **15**.[10] Ketone **10a** gave exclusively enol acetate **11**; that is, bond cleavage leading to the benzylic radical occurred exclusively.

† A preliminary account of part of this work was presented at the 12th National Symposium of Organic Chemistry (XII SINAQO), Córdoba, Argentina, November 1999. Abstract published in *Molecules* (online computer file), 2000, **5**, 447.

‡ Electronic supplementary information (ESI) available: UHF/6-31G**-calculated structures, spin-density surfaces, cartesian coordinates, total atomic spin densities and Fermi-contact data for simplified models of radicals **18**, **19** and **20**. See http://www.rsc.org/suppdata/p1/b1/b107258g/

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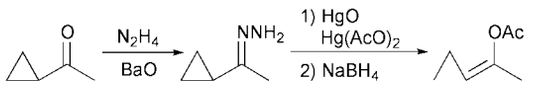
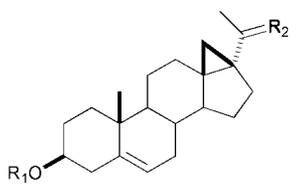
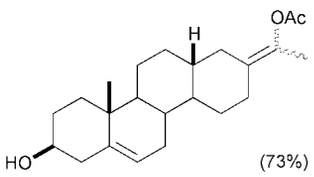
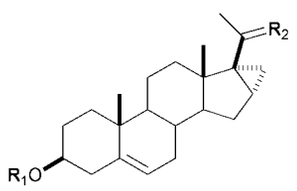
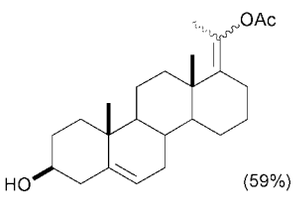
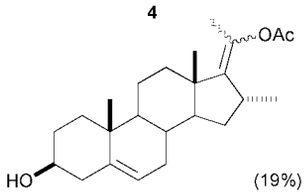
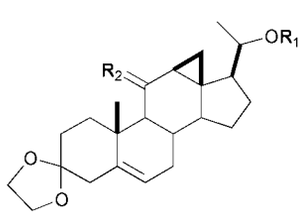
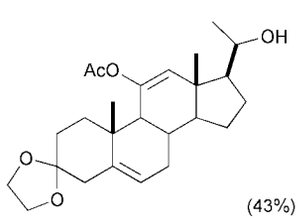
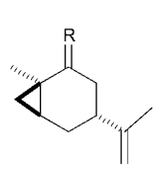
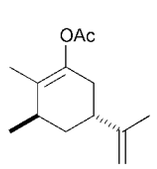
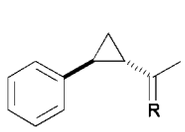
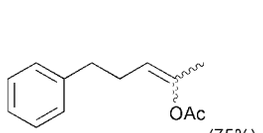
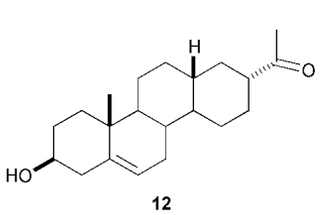
Table 1 Cleavage of cyclopropyl ketones

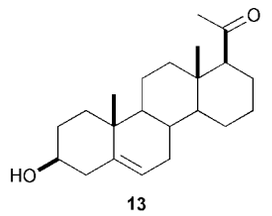


Cyclopropyl ketone	Product (isolated yield)
 **1a** R_1 = Ac, R_2 = O **1b** R_1 = H, R_2 = NNH_2	 (73%) **2**
 **3a** R_1 = Ac, R_2 = O **3b** R_1 = H, R_2 = NNH_2	 (59%) **4**
	 (19%) **5**
 **6a** R_1 = Ac, R_2 = O **6b** R_1 = H, R_2 = NNH_2	 (43%) **7**
 **8a** R=O **8b** R= NNH_2	 (84%) **9**
 **10a** R=O **10b** R= NNH_2	 (75%) **11**

Mechanism and regioselectivity

Alkylmercury(II) hydrides are excellent hydrogen donors,[5] thus in the above reactions the rearranged radical is rapidly quenched (last step in Scheme 1) rendering its formation esentially irreversible and resulting in kinetically controlled cleavage. This is at variance with certain cyclopropylcarbinyl ring-opening reactions that occur under conditions allowing reversible reclosure of the rearranged radicals, to give the thermodynamically favoured radical.[3,11]


12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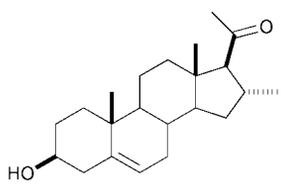
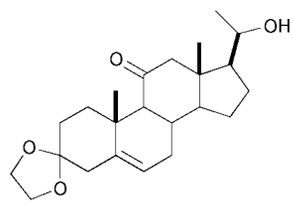
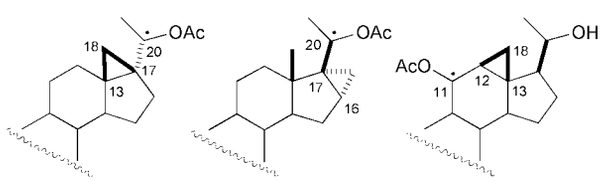
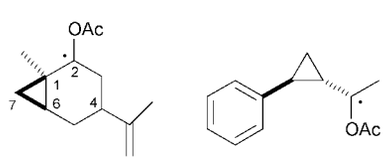

14


15

Maximum overlap of one of the β cyclopropane bond orbitals with the singly occupied p-orbital (SOMO) of the intermediate cyclopropylcarbinyl radical is required in the transition state for bond cleavage. Thus the bond that will be preferentially cleaved is determined by the lowest-energy transition state in which maximum overlap occurs.[3,12] For ketones **1a** and **3a**, the intermediate radicals (**16** and **17**) have their radical center *exo* to the ring system. The increased conformational mobility of the radical-bearing center around the C-17–C-20 bond allows SOMO overlap with either of the β-cyclopropyl bond orbitals. In radical **16**, preferential overlap with the endocyclic C-13–C-17 bond orbital is observed, leading to its regioselective cleavage as was the case for the Bu_3SnH–AIBN reaction.[2] For cyclopropylcarbinyl radical **17** both possible products **4** and **5** are obtained; however, the predominance of endocyclic cleavage is indicative of a lower-energy transition state leading to this product (**4**).


16 **17** **18**


19 **20**

Ab initio calculations (UHF/6-31G**)[13] on a simplified model of radical **18** (derived from **6a**) using Fermi contact analysis data as a gauge of the molecular-spin distribution[3] show, as expected, most of the radical character at C-11 (unpaired-spin value of 0.306 au, Fig. 1a). However, hyperconjugation of the radical into the adjacent cyclopropane σ-bonds is evident in the magnitude of the unpaired spin on the nuclei of the atoms encompassing them. Both cyclopropyl carbons β to the radical center show a similar degree of radical character, indicating partial overlap of the SOMO with both β-cyclopropyl bonds' orbitals in the minimum-energy conformation. ‡ Endocyclic cleavage of radical **18** would require ring C to adopt a boat-type conformation in the transition state (for overlapping of the SOMO on C-11 with the C-12–C-13 bond orbital), making ring expansion unlikely within the steroid framework. Thus, in this case overlap occurs with the exocyclic C-12–C-18 bond orbital, yielding a single cleavage product. Calculations carried out on a simplified model of radical **19**

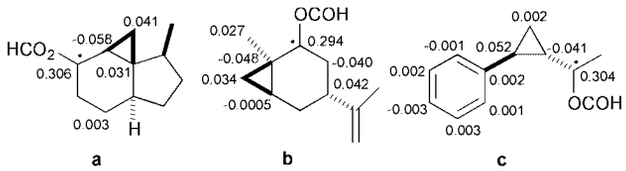


Fig. 1 Selected Fermi-contact analysis data (atomic units) from UHF/6–31G** calculations for minimum-energy conformations of simplified models of intermediate radicals a) **18**, b) **19** and c) **20** (data from the most stable conformer presenting delocalization of spin density on the phenyl ring are shown). ‡

show a minimum-energy conformation that already has predominant overlap of the SOMO with the exocyclic cyclopropane bond orbital ‡ (compare the unpaired-spin values for both β cyclopropyl carbons in Fig. 1b), the latter being regioselectively cleaved. Recently it has been argued that exocyclic cleavage can be avoided in bicyclo[*n*.1.0] radicals (n = 3–5),[14] although this was accomplished by introduction of a benzyloxycarbonyl substituent on the cyclopropane ring that stabilized the incipient radical in the *endo*-cleavage transition state.[15] In our case, the cleavage of radical **20**, derived from **10a**, exemplifies stabilization by a phenyl group (Fig. 1c), giving exclusively enol acetate **11**.

Conclusions

Use of alkylmercury(II) hydrides has several advantages over the Bu_3SnH method: (a) the reaction is simple and proceeds rapidly at room temperature or below; (b) the separation of products from reagents is straightforward (inorganic mercury by-products are removed by filtration and extraction with water); (c) the organomercurials are formed *in situ* and never isolated; (d) the reagent can be used on sterically hindered ketones.

The latter point is dramatically exemplified by the attempted reaction of ketones **3a** and **6a** with Bu_3SnH–AIBN.§ While ketone **6a** completely failed to react, ketone **3a** gave only *ca.* 5% of methyl ketone **14** and unchanged starting material. The change in product distribution observed for **3a** is probably due to the steric bulk of the tributyltin substituent that rotates the side chain around the C-17–C-20 bond so that the SOMO of the stannyloxy radical, analogous to **17**, can only overlap with the exocyclic cyclopropyl bond orbital.

In summary, alkylmercury(II) hydrides represent a new procedure for radical rearrangement of cyclopropyl ketones (*via* their hydrazones) under mild conditions, with synthetic potential for ring-enlargement applications in sterically hindered systems and the generation of radical intermediates for the addition to double and triple bonds.[16]

Experimental

Mps were taken on a Fisher-Johns apparatus and are uncorrected. IR spectra were recorded for KBr pellets on a Nicolet Magna IR 550 FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were measured in a Bruker AC-200 (200.13 and 50.32 MHz) or AM-500 (500.13 and 125.72 MHz) NMR spectrometer for samples in deuteriochloroform (using tetramethylsilane as internal standard). *J*-Values are given in hertz. Electron-impact mass spectra (EI) were measured in a GC-MS Shimadzu QP-5000 mass spectrometer at 70 eV by direct inlet. Electron-impact high-resolution mass spectra were obtained in a VG ZAB BEQQ mass spectrometer. *Ab initio* calculations were performed with Gaussian 98W (Gaussian Inc.).[13] All solvents used were reagent grade. Solvents were evaporated at $\theta \approx 45$ °C under reduced pressure. Extractive work-up included exhaustive extraction with the solvent indicated, washing successively with brine and water, drying with anhydrous sodium sulfate, and evaporation of the solvent. Flash chromatography was performed on silica gel Merck 9385 (40–63 μ). Reversed-phase column chromatography was performed on octadecyl-functionalized silica gel (Aldrich). Homogeneity of all compounds was confirmed by TLC.

Ketone **1a** was synthesized in 40% yield from pregnenolone acetate,[2] and ketone **6a** was obtained in 11% yield from 11α-hydroxyprogesterone.[1] Ketones **3a**, **8a** and **10a** were obtained by addition of dimethyloxosulfonium methylide to the corresponding α,β-unsaturated ketones.[17]

3β-Acetoxy-17β,18-cyclopregn-5-en-20-one hydrazone 1b (Typical procedure)

To a solution of cyclopropyl ketone **1a** (0.100 g, 0.32 mmol) in ethanol (3.2 cm^3) were added hydrazine hydrate (80%; 0.59 cm^3, 9.7 mmol) and barium oxide (2 mg). The mixture was stirred at 60 °C until disappearance of starting ketone (TLC, 2 h), poured over water, and extracted with dichloromethane. Purification by reversed-phase flash chromatography (MeOH–water, 75 : 25) gave pure *hydrazone* **1b** (0.084 g, 90%) as an amorphous white solid; ν_{max} (KBr)/cm^{-1} 3490 (OH and NH), 2960, 1652 (C=N) and 754; δ_H (200 MHz) 0.62 (1H, d, J = 4.4, 18-H^a), 0.70 (1H, d, J = 4.4, 18-H^b), 0.98 (3H, s, 10-CH_3), 1.75 (3H, s, 20-CH_3), 3.60 (1H, m, 3-H), 5.38 (1H, br d, J = 4, 6-H); *m*/*z* (EI) 328.2514 (M$^+$, 100%. $C_{21}H_{32}N_2O$ requires *M*, 328.2515), 313 (12%), 312 (15), 91 (50).

3β-Hydroxy-16α,17α-methylenepregn-5-en-20-one hydrazone 3b

Ketone **3a** (0.90 g, 2.43 mmol), hydrazine hydrate (80%; 4.2 cm^3, 69 mmol) and barium oxide (4 mg) in ethanol (40 cm^3) were heated under reflux for 48 h to give *hydrazone* **3b** (0.80 g, 96%); ν_{max} (KBr)/cm^{-1} 3373 (OH and NH), 2930, 1636 (C=N), 1051 and 733; δ_H (200 MHz) 0.27 (2H, m, 16a-H_2), 0.82 (3H, s, 13-CH_3), 1.03 (3H, s, 10-CH_3), 1.81 (3H, s, 20-CH_3), 3.52 (1H, m, 3-H), 5.33 (1H, br d, J = 4, 6-H); *m*/*z* (EI) 342.2676 (M$^+$. $C_{22}H_{34}N_2O$ requires *M*, 342.2671), 327 (77%), 326 (55), 84 (72), 49 (100).

3,3-Ethylenedioxy-20(*R*)-hydroxy-12β,18-cyclopregn-5-en-11-one hydrazone 6b

Ketone **6a** (0.20 g, 0.48 mmol), hydrazine hydrate (80%; 3.1 cm^3, 51 mmol) and barium oxide (2 mg) in ethylene glycol (12 cm^3) were heated for 4 days at 160 °C to give *hydrazone* **6b** (0.16 g, 85%); ν_{max} (KBr)/cm^{-1} 3379 (OH and NH), 2960, 1668 (C=N), 1105 (O–C–O) and 763; δ_H (200 MHz) 1.01 (3H, s, 10-CH_3), 1.16 (3H, d, J = 6, 20-CH_3), 2.10 (1H, dd, J = 14 and 2, 12-H), 2.48 (1H, dd, J = 13 and 2, 4β-H), 2.65 (1H, dt, J = 13 and 3, 1β-H), 3.48 (1H, m, 20-H), 3.93 (4H, m, 3-OCH_2CH_2O), 5.41 (1H, br d, J = 4, 6-H); *m*/*z* (EI) 386.2569 (M$^+$. $C_{23}H_{34}N_2O_3$ requires *M*, 386.2569), 370 (6%), 207 (29), 99 ($C_5H_7O_2$, 100).

4-Isopropenyl-1-methylbicyclo[4.1.0]heptan-2-one hydrazone 8b

Ketone **8a** (2.09 g, 13 mmol), hydrazine hydrate (80%; 32 cm^3, 526 mmol) and barium oxide (10 mg) in ethanol (150 cm^3) were heated for 18 h at 55 °C to give *hydrazone* **8b** (2.3 g, 95%) as a yellow oil that was used immediately; ν_{max} (KBr)/cm^{-1} 3385 (NH), 2965, 2924, 1685 (C=N), 1445, 889; δ_H (200 MHz) 0.62 (1H, dd, J = 8 and 5, 6-H), 0.90 (2H, m, 7-H_2), 1.24 (3H, s, 1-CH_3), 1.73 (3H, s, =CCH_3), 4.71 (1H, s, =C–H^a), 4.75 (1H, s, =C–H^b), 5.00 (2H, br s, NH_2); *m*/*z* (EI) 178.1467 (M$^+$. $C_{11}H_{18}N_2$ requires *M*, 178.1470), 163 (2%), 162 (20), 41 (100).

1-[*trans*-2-Phenylcyclopropyl]ethanone hydrazone 10b

Ketone **10a** (0.54 g, 3.37 mmol), hydrazine hydrate (80%; 8.0 cm^3, 131.5 mmol) and barium oxide (5 mg) in ethanol

§ Toluene, 3 days at 110 °C (see ref. 2).

(44 cm^3) were heated for 2 h at 45 °C to give *hydrazone* **10b** (0.57 g, 97%); ν_{max} (KBr)/cm^{-1} 3292 (OH and NH), 2980, 1668 (C=N), 1630, 1605 (phenyl), 745 and 698; δ_H (200 MHz) 1.29 (2H, m, H_2C), 1.64 (1H, dt, J = 9.5 and 4.6 Hz, H–C–C=N), 1.92 (3H, s, H_3CC=N), 2.39 (1H, dt, J = 9.5 and 4.6, *H*C–Ph), 7.00–7.40 (5H, m, ArH); *m*/*z* (EI) 174.1154 (M^+. $C_{11}H_{14}N_2$ requires *M*, 174.1157), 159 (3%), 158 (25), 63 (100).

Cleavage of cyclopropyl hydrazones (typical procedure). (3*R*,5*R*)-5-Isopropenyl-2,3-dimethylcyclohex-1-enyl acetate 9

A solution of hydrazone **8b** (1.97 g, 11.05 mmol) in anhydrous THF (15 cm^3) was added at 25 °C under N_2 to a suspension of HgO (2.4 g, 11.05 mmol) and $Hg(OAc)_2$ (7.04 g, 22.1 mmol) in anhydrous THF (15 cm^3). The reaction mixture was vigorously stirred until it turned yellow (*ca.* 15 min), and was placed in an ice-bath. A cold aqueous solution of $NaBH_4$ (8 M; 25 cm^3) was added slowly and the suspension stirred until gas evolution ceased (*ca.* 0.5 h). The reaction mixture was filtered, diluted with water (150 cm^3), and extracted with dichloromethane to give *enol acetate* **9** (2.03 g, 88%), ν_{max} (KBr)/cm^{-1} 3482, 2924, 2871, 1751, 1221; δ_H (500 MHz) 1.10 (3H, d, J = 6.6 Hz, 3-CH_3), 1.53 (3H, s, 2-CH_3), 1.54–1.69 (2H, m, 4-H_2), 1.73 (3H, s, CH_3-C=CH_2), 2.00–2.19 (2H, m, 6-H_2), 2.12 (3H, s, acetate), 2.26 (1H, br q, J = 6.6, 3-H), 2.46 (1H, m, 5-H), 4.73 (2H, br s, =CH_2); δ_C (125 MHz) 14.33 (2-CH_3), 19.32 (3-CH_3), 20.79 (acetate), 20.80 (*C*H_3-C=CH_2), 32.57 (C-6), 33.63 (C-3), 34.76 (C-4), 36.86 (C-5), 109.18 (=CH_2), 124.13 (C-2), 141.46 (C-1), 148.68 (CH_3-*C*=CH_2), 168.97 (acetate); *m*/*z* (EI) 208.1466 (M^+. $C_{13}H_{20}O_2$ requires *M*, 208.1463), 166 (M − CH_2CO, 8%), 151 (5), 123 (49), 109 (14), 83 (9), 69 (14), 55 (21), 43 (100).

3β-Hydroxy-17(13→18)-*abeo*-17β(H)-pregn-5-en-20-one 12

Hydrazone **1b** (0.080 g, 0.244 mmol) gave an *E*/*Z* mixture (1 : 1) of *enol acetate* **2** (0.071 g, 81%); δ_H (200 MHz) 0.98 (3H, s, 10-CH_3), 1.84 and 1.85 (3H, s, 20-CH_3), 2.12 and 2.13 (3H, s, CH_3COO), 3.55 (1H, m, 3-H), 5.38 (1H, m, 6-H); *m*/*z* (EI) 358 (M^+, 2%), 316 (49), 314 (6), 298 (6), 91 (30), 43 (100).

The enol acetate was dissolved in methanol (3.2 cm^3), 10% aq. sodium hydroxide (0.4 cm^3) was added, and the solution was stirred for 1 h under a nitrogen atmosphere. Dilution with water and extraction with dichloromethane gave the *abeo*-pregnane **12** identical (TLC, NMR) with an authentic standard.[2]

3β-Hydroxy-D-homopregn-5-en-20-one 13 and 3β-hydroxy-16α-methylpregn-5-en-20-one 14

Hydrazone **3b** (0.76 g, 2.22 mmol) gave *enol acetate* **5** (*E*/*Z* mixture, 0.164 g, 20%); δ_H (500 MHz) 0.862 and 0.928 (3H, s, 13-CH_3), 1.007 and 1.020 (3H, s, 10-CH_3), 1.007 and 1.080 (3H, d, J = 7.3, 16α-CH_3), 1.864 and 1.907 (3H, s, 20-CH_3), 2.097 (3H, s, CH_3COO), 2.703 (1H, m, 16β-H), 3.518 (1H, m, 3-H), 5.36 (1H, br d, J = 4.7, 6-H); *m*/*z* (EI) 372 (M^+, 3%), 330 (19), 315 (25), 312 (9), 84 (25), 43 (100).

The enol acetate (0.040 g) was dissolved in methanol (4 cm^3), 10% aq. sodium hydroxide (0.4 cm^3) was added, and the solution was stirred for 2 h under a nitrogen atmosphere. Dilution with water and extraction with dichloromethane gave *ketone* **14** (0.034 g, 96%); mp 183–185 °C (from hexane–ethyl acetate); ν_{max} KBr/cm^{-1} 3427 (OH), 2931 (CH), 1686 (C=O), 1074 (C–O); δ_H (200 MHz) 0.66 (3H, s, 13-CH_3), 0.94 (3H, d, J = 6.8, 16α-CH_3), 1.00 (3H, s, 10-CH_3), 2.13 (3H, s, 20-CH_3), 2.15 (1H, d, J = 8.0, 17-H), 2.67 (1H, m, 16β-H), 3.52 (1H, m, 3-H), 5.34 (1H, dt, J = 5.0 and 2.7, 6-H); δ_C (125 MHz) 13.9 (C-18), 19.4 (C-19), 21.0 (C-11), 22.3 (16-CH_3), 31.1 (C-16), 31.65 (C-2), 31.72 (C-7), 31.74 (C-8), 32.1 (C-15), 33.4 (C-21), 36.6 (C-10), 37.3 (C-1), 39.1 (C-12), 42.3 (C-4), 45.7 (C-13), 50.1 (C-9), 55.4 (C-14), 71.8 (C-3), 73.3 (C-17), 121.4 (C-6), 140.8 (C-5), 209.3 (C-20); *m*/*z* (EI) 330.2551 (M^+. $C_{22}H_{34}O_2$ requires *M*, 330.2558), 312 (5%), 43 (100).

Further elution from the chromatographic separation of the product of the cleavage reaction of hydrazone **3b** gave *enol acetate* **4** (*E*/*Z* mixture, 0.509 g, 62%); δ_H (500 MHz) 0.972 and 0.987 (3H, s, 10-CH_3), 1.062 and 1.134 (3H, s, 13-CH_3), 1.868 and 1.869 (3H, s, 20-CH_3), 2.095 (3H, s, acetate), 3.522 (1H, m, 3-H), 5.334 (1H, br d, J = 4.0, 6-H); *m*/*z* (EI) 372 (M^+, 4%), 330 (47), 315 (19), 312 (5), 84 (100), 43 (79).

The enol acetate (0.046 g) was dissolved in methanol (4 cm^3), 10% aq. sodium hydroxide (0.4 cm^3) was added, and the solution was stirred for 2 h under a nitrogen atmosphere. Dilution with water and extraction with dichloromethane gave *ketone* **13** (0.040 g, 99%); mp 193–196 °C (from hexane–ethyl acetate) (Found: C, 79.7; H, 10.6. $C_{22}H_{34}O_2$ requires C, 80.0; H, 10.4%); ν_{max} (KBr)/cm^{-1} 3416 (OH), 1684 (C=O), 1065 (C–O); δ_H (500 MHz) 0.83 (1H, dt, J = 9.5 and 2.9, 14-H), 0.96 (3H, s, 13-CH_3), 1.03 (3H, s, 10-CH_3), 2.13 (3H, s, 20-CH_3), 2.28 (1H, dd, J = 12.5 and 3.4, 17-H), 3.53 (1H, m, 3-H), 5.34 (1H, dd, J = 3.2 and 2.7, 6-H); δ_C (125 MHz) 13.5 (C-18), 19.7 (C-19), 20.5 (C-11), 24.2 (C-15), 24.9 (C-16a), 26.3 (C-16), 31.9 (C-8), 32.0 (C-2), 32.2 (C-7), 33.1 (C-21), 37.2 (C-10 and C-13), 37.3 (C-1), 39.8 (C-12), 42.4 (C-4), 50.1 (C-9), 52.8 (C-14), 62.5 (C-17), 72.0 (C-3), 121.8 (C-6), 140.8 (C-5), 213.2 (C-20); *m*/*z* (EI) 330 (M^+, 32%), 312 (22), 245 (11) and 43 (100).

3,3-Ethylenedioxy-20(*R*)-hydroxypregn-5-en-11-one 15

Hydrazone **6b** (0.130 g, 0.336 mmol) gave *enol acetate* **7** (0.070 g, 50%) as an amorphous white solid; δ_H (200 MHz) 0.90 (3H, s, 13-CH_3), 1.15 (3H, d, J = 6, 20-CH_3), 1.16 (3H, s, 10-CH_3), 2.05 (3H, s, CH_3COO), 3.65 (1H, m, 20-H), 3.93 (4H, m, 3-OCH_2CH_2O), 5.38 (1H, s, 12-H), 5.47 (1H, m, 6-H); δ_C (50 MHz) 16.1 (C-18), 18.6 (C-19), 21.6 (acetate), 23.3 (C-16), 23.8 (C-21), 25.8 (C-15), 31.1 (C-7), 31.3 (C-2), 32.3 (C-8), 36.5 (C-1), 39.4 (C-10), 42.3 (C-4 and C-13), 51.0 (C-9), 53.1 (C-17), 54.3 (C-14), 64.2 and 64.4 (O-CH_2CH_2-O), 71.3 (C-20), 109.0 (C-3), 123.2 (C-6), 129.9 (C-12), 140.9 (C-5), 142.8 (C-11), 169.9 (acetate); *m*/*z* (EI) 416.2560 (M^+. $C_{25}H_{36}O_5$ requires *M*, 416.2563), 374 (11%), 356 (3), 312 (5), 262 (3), 99 (100).

The enol acetate (0.050 g) was dissolved in methanol (3.0 cm^3), 10% aq. sodium hydroxide (0.37 cm^3) was added, and the solution was stirred for 18 h under a nitrogen atmosphere. Dilution with water and extraction with dichloromethane gave 3,3-ethylenedioxy-20(*R*)-hydroxypregn-5-en-11-one **15**; mp 183–184 °C (from chloroform–hexane) (lit.,[10] 182–184 °C); δ_H (200 MHz) 0.72 (3H, s, 13-CH_3), 1.14 (3H, d, J = 6, 20-CH_3), 1.22 (3H, s, 10-CH_3), 2.25 (1H, br d, J = 14, 12α-H), 2.56 (1H, dd, J = 16 and 2, 4β-H), 2.63 (1H, dt, J = 13 and 3, 1β-H), 2.78 (1H, d, J = 14, 12β-H), 3.72 (1H, m, 20-H), 3.93 (4H, m, 3-OCH_2CH_2O) and 5.32 (1H, br d, J = 5, 6-H).

Cleavage of 1-[*trans*-2-phenylcyclopropyl]ethanone hydrazone 10b

Hydrazone **10b** (0.129 g, 0.74 mmol) gave *enol acetate* **11** (*E*/*Z* mixture, 0.116 g, 77%); δ_H (200 MHz) 1.76 (3H, br s, H_3C–C=, *E* isomer), 1.84 (3H, br s, H_3C–C=, *Z* isomer), 2.06 (3H, s, acetate, *E* isomer), 2.10 (3H, s, acetate, *Z* isomer), 2.26 (4H, m, H_2C–C=, *E* and *Z* isomers), 2.64 (2H, t, J = 8, H_2C–Ph, *E* isomer), 2.66 (2H, t, J = 8, H_2C–Ph, *Z* isomer), 5.02 (1H, br t, J = 6.7, HC=C, *Z* isomer), 5.14 (1H, br t, J = 6.7, HC=C, *E* isomer), 6.95–7.45 (10H, m, ArH).

To the enol acetate (0.100 g, 0.49 mmol) was added a solution of potassium hydroxide (0.050 g) in ethanol (5.0 cm^3) and the mixture was stirred for 15 min at 25 °C under a nitrogen atmosphere. Dilution with water and extraction with dichloromethane gave 5-phenylpentan-2-one (0.056 g, 71%), identical (TLC, NMR) with an authentic standard.

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References

1 A. Ferrara and G. Burton, *Tetrahedron Lett.*, 1996, **37**, 929.
2 A. Ferrara, M. O. V. Benedetti, A. A. Ghini and G. Burton, *J. Chem. Res. (S)*, 1993, 276.
3 E. J. Kantorowski, S. W. E. Eisenberg, W. H. Fink and M. J. Kurth, *J. Org. Chem.*, 1999, **64**, 570.
4 W. G. Dauben and E. J. Deviny, *J. Org. Chem.*, 1966, **31**, 3794; W. G. Dauben and R. E. Wolf, *J. Org. Chem.*, 1970, **35**, 374; M. Pereyre and J. Y. Godet, *Tetrahedron Lett.*, 1970, 3653; M. Pereyre and J. P. Quintard, *Pure Appl. Chem.*, 1981, **53**, 2401; K. J. Kulicke and B. Giese, *Synlett*, 1990, 91; R. A. Batey and W. B. Motherwell, *Tetrahedron Lett.*, 1991, **32**, 6211.
5 B. Giese, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 553.
6 B. Giese and U. Erfort, *Chem. Ber.*, 1983, **116**, 1240.
7 B. Giese, *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*, Pergamon Press, Oxford, 1986, ch. 3; D. Curran, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 4, p. 715.
8 T. L. Holton and H. Shecheter, *J. Org. Chem.*, 1995, **60**, 4725.
9 D. H. R. Barton, J. F. McGhie and P. L. Balton, *J. Chem. Soc. C*, 1970, 1033.
10 K. Heusler, J. Kalvoda, P. Weiland and A. Wettstein, *Helv. Chim. Acta*, 1961, **44**, 179.
11 R. A. Batey, P. Grice, J. D. Harling, W. B. Motherwell and H. S. Rzepa, *J. Chem. Soc., Chem. Commun.*, 1992, 942.
12 K. U. Ingold and J. C. Walton, *Acc. Chem. Res.*, 1986, **19**, 72.
13 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, B. B. Baboul, G. Stefanov, A. Liu, P. Liashenko, I. Piskorz, R. Komaromi, A. G. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle and J. A. Pople, *Gaussian 98 (Revision A.7)*, Gaussian, Inc., Pittsburgh, PA, 1998.
14 P. H. Lee, B. Lee, J. Lee and S. K. Park, *Tetrahedron Lett.*, 1999, **40**, 3427.
15 F. N. Martinez, H. B. Schlegel and M. Newcomb, *J. Org. Chem.*, 1998, **63**, 3618.
16 R. A. Batey, J. D. Harling and W. B. Motherwell, *Tetrahedron*, 1992, **48**, 8031; D. L. J. Clive and S. Daigneault, *J. Org. Chem.*, 1991, **56**, 3801.
17 E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, 1965, **87**, 1353; N. G. Steinberg, G. H. Rasmusson and R. A. Reamer, *J. Org. Chem.*, 1979, **44**, 2294.