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Highly efficient epoxidation of unsaturated steroids using magnesium bis(monoperoxyphthalate) hexahydrate

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ABSTRACT

Fast generation of epoxides from the corresponding homoallylic and allylic steroidal olefins was developed by using magnesium bis(monoperoxyphthalate) hexahydrate (MMPP) as oxidant suspended in acetonitrile (CH_3CN) at reflux temperature. The protocol involves the use of a safe readily available oxidant along with an easy work-up, which renders the process very efficient. Selective 4,5- and 5,6-epoxidations of steroids are reported. Among them, highly stereoselective epoxidation of Δ^5-B-nor-cholestanes was achieved. Moreover, the method is chemoselective for the 5,6-position and can be applied to the epoxidation of ring-A enones.

1. Introduction

Epoxysteroids are an important class of oxysterols, known for its biological activities, such as regulation of cell proliferation and cholesterol homeostasis.[1] For instance, 5α,6α- and 5β,6β-epoxides of cholesterol are cytotoxic[2] and mutagenic agents.[3] On the other hand, the synthetic versatility of epoxides[4] makes them useful intermediates for steroid semisynthesis, namely, as a strategy to access polyhydroxysteroids, with interesting biological activities.[5]

Extensive research has been conducted on the stereoselective epoxidation of Δ^5-steroids.[6] The synthesis of β-epoxides has been achieved through the use of halohydrins as intermediates[7] and of 3-halo substituents to block the entry of reagents from the α-face,[8] as different[11] strategies. Chromyl diacetate,[9] potassium permanganate/inorganic salts,[10] chiral ketones combined with oxone[11] and transition metal complexes in the presence of molecular oxygen and a sacrificial aldehyde[12] have been largely used as oxidative systems.

On the other hand, 5α,6α-epoxysteroids have generally been obtained by oxidation with peroxyacids, being 3-chloroperoxybenzoic acid (*m*-CPBA) the most common one.[13,14] The stereoselectivity of peroxyacids on these substrates is easily explained by the steric hindrance imposed by the C-10 and C-13 angular methyl groups.

Magnesium bis(monoperoxyphthalate) hexahydrate (MMPP) is a commercially available, inexpensive and relatively stable oxidant. Since its development in the early 80s, it has been used in the oxidation of various functional groups,[14,15] for instance, in the epoxidation of alkenes,[16] sulfur[17] and nitrogen oxidations,[18] Baeyer–Villiger oxidation[14,19] as well as in the oxidative cleavage of hydrazones.[20]

Compared to the widely used peroxyacid *m*-CPBA, MMPP has similar chemical properties, although it is gaining acceptance due to a number of advantageous properties. While *m*-CPBA is expensive, shock sensitive and potentially explosive, which limits the scale-up processes and its industrial application,[14,15,21] MMPP is stable in the solid state, has better safety in handling and is easier to use. Moreover, it can be produced and commercially available at a lower cost. Finally, due to its water solubility, work-up procedures are relatively easy.[14,15]

One of the reasons that have limited larger applications of MMPP is its low solubility in non-polar solvents. Reactions using MMPP have been usually carried out in water or low molecular weight alcohols as solvents. For insoluble substrates in polar solvents, reactions have been conducted in biphasic media combined with a phase transfer catalyst. However, reactions in ethanol or phase transfer media are often not efficacious. An attempt to overcome these limitations has been the use of a solid-phase-supported version of MMPP on wet silica gel or moist alumina.[22] Nonetheless, Foti et al. have demonstrated that only the presence of water is crucial, since the reaction occurs in the absence of silica or alumina.[23]

On the other hand, the use of non-supported moist MMPP suspended in dichloromethane at room temperature has been shown to be effective for the oxidation of sulfides to sulfoxides and the epoxidation of cyclohexene derivatives.[23,24]

Due to the relevance of Δ^4-, Δ^5- and ring-A enone epoxidations under the scope of steroid chemistry and within our continuing

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interest on new reactions and processes in steroids[25] we have decided to search for a more efficient process to access epoxysteroids.

In this paper, we report simple and effective approaches for the selective 4,5- and 5,6-epoxidation of steroids using MMPP in organic solvents. Epoxidation of ring-A enones, which represents a thrilling challenge due to the electrodeficiency of the double bond, has also been tackled using MMPP as oxidant.

2. Results and discussion

The advantages of MMPP and the need for efficient methods for steroid epoxidation prompted us to endeavour a systematic study to optimize the reaction conditions for the oxidation of unsaturated steroids.

In the first approach, we have studied the epoxidation of cholesterol, **1**, with unsupported moist MMPP suspended in dichloromethane at room temperature, a heterogeneous process described by Foti et al. (1999) for cyclohexenes[23] (Scheme 1, Table 1). In the absence of water, using dichloromethane as solvent, no reactivity was observed, even after 24 h. However simply by adding 100 μL of water per mmol of substrate, total consumption of the starting material was observed in 24 h (Table 1, entries 1 and 2).

The 5α,6α- and 5β,6β-epoxycholesterols, **1a** and **1b**, respectively, were isolated in 76% yield with a α/β ratio of 96:4. This result was remarkable compared to the known selectivity of most peroxyacids for this type of substrates (α/β ratio 4:1). These reaction conditions were applied to cholesteryl acetate, **2** (entry 3), cholesteryl hemisuccinate, **3** (entry 4), dehydroepiandrosterone, **4** (entry 5), dehydroepiandrosterone acetate, **5** (entry 6), pregnenolone, **6** (entry 7) and pregnenolone acetate, **7** (entry 8) as substrates and the corresponding 5α,6α- and 5β,6β-epoxysteroids were obtained in 73–93% yield with diastereoselectivities ranging from 77:23 to 94:6 (Table 3, entries 3–8).

Although good yields and high diastereoselectivities were obtained using moist MMPP in CH_2Cl_2 at rt, the low reaction rates of this procedure have prompted us to search for new conditions by changing the reaction solvent and temperature. Cholesteryl acetate, **2**, a very non-polar steroid, was chosen as the model substrate.

Out of several solvents tested, toluene, *tert*-butanol, *n*-butanol, methanol, dimethylformamide, acetone and acetonitrile, the last one gave the best results. Using CH_3CN as reaction solvent, either in the absence or in the presence of a small amount of water, the reaction was very slow at room temperature. After 48 h of reaction, only 15% of the substrate had been converted into the diastereomeric mixture of 5α,6α- and 5β,6β-epoxides at an α/β ratio of nearly 4:1 (Scheme 1, Table 2, entry 1).

At 50 °C, the substrate was totally consumed after 3 h of reaction (Scheme 1, Table 2, entry 2), and when heating the reaction mixture at reflux temperature, a remarkable effect on the reaction rate was observed (Scheme 1, Table 2, entry 3). The reaction was completed in 20 min with good diastereoselectivity (76:24 α/β) and very high yield (>90%). Moreover, the reaction outcome is reproducible when the scale is raised 10 times (Scheme 1, Table 2, entry 4).

Table 1
Epoxidation of sterols with moist MMPP in CH_2Cl_2[a]

Entry	Substrate (mmol)	Solvent	Product	Yield (%)[b]	Epoxide ratio α/β (%)[c]
1	**1**/0.150	CH_2Cl_2	**1a**+**1b**	—	—
2	**1**/0.150	CH_2Cl_2/H_2O	**1a**+**1b**	76	96:4
3	**2**/0.500	CH_2Cl_2/H_2O	**2a**+**2b**	91	93:7
4	**3**/0.200	CH_2Cl_2/H_2O	**3a**+**3b**	73	77:23
5	**4**/0.125	CH_2Cl_2/H_2O	**4a**+**4b**	81	92:8
6	**5**/0.125	CH_2Cl_2/H_2O	**5a**+**5b**	92	91:9
7	**6**/0.125	CH_2Cl_2/H_2O	**6a**+**6b**	82	89:11
8	**7**/0.125	CH_2Cl_2/H_2O	**7a**+**7b**	93	94:6

[a] Reaction conditions: 1 mmol of Δ^5-steroid; 1.1 mmol of MMPP; 100 μL H_2O; 15 mL CH_2Cl_2; room temperature; 24 h.
[b] Isolated yield by flash chromatography.
[c] Calculated by ^1H NMR integration of 6-H in the crude product.

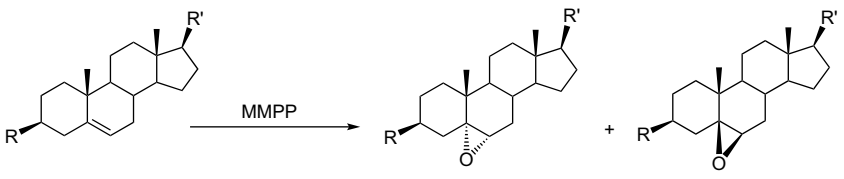
Using CH_3CN, the addition of a small amount of water as well as addition of the radical inhibitor 4,4′-thiobis(6-*tert*-butyl-*m*-cresol)[26] had no effect on the reaction outcomes.

Under these optimized conditions, we investigated the scope and limitations of the method in a set of Δ^5-steroids, **1** and **3**–**7**, and the results are summarized in Table 3.

All the substrates were readily converted into the respective epoxides, following the same pattern in terms of α/β diastereoselectivity of epoxidation. From the results displayed in Table 3, we can conclude that this protocol provides good reproducibility for 3β-hydroxy- and 3β-acetoxy-Δ^5-steroids. Indeed, for the whole reactions studied a 72–80% α-epoxidation and high yields (>80%) were obtained, with very short reaction times (5–10 min).

Then, we moved our attention to study the effect of an allylic group at C-4 in the epoxidation of Δ^5-steroids (Scheme 2).

3β,4β-Dihydroxycholest-5-ene **8** reacted with MMPP under the above conditions, rendering the diastereomeric epoxides **8a** and **8b** in a 43:57 α/β ratio (Scheme 2, Table 4, entry 1). Clearly, the hydrogen-bonding effect of the 4β-hydroxyl group to the oxidant favoured the attack by the β-face to yield the cis-diastereoisomer **8b**. The preferred α-diastereoselection in peroxyacid epoxidation of Δ^5-steroids due to the angular methyl groups at C-10 and C-13 has been partially reversed by the introduction of an allylic hydroxyl group at C-4. The diacetyl derivative **9** was much less reactive, and with an excess of MMPP afforded the usual epoxide mixture, with predominance of the α-isomer (76:24), in a high yield (93%). This reaction took 6 h to complete substrate consumption, but using a different methodology, where MMPP was added portionwise each hour (Scheme 2, Table 4, entry 2).



1.....R=OH, R'= C_8H_{17}.....**1a**.....**1b**
2.....R=OAc, R'=C_8H_{17}.....**2a**.....**2b**
3.....R=OCO$(CH_2)_2CO_2H$, R'=C_8H_{17}.....**3a**.....**3b**
4.....R=OH, R'=O.....**4a**.....**4b**
5.....R=OAc, R'=O.....**5a**.....**5b**
6.....R=OH, R'=$COCH_3$.....**6a**.....**6b**
7.....R=OAc, R'=$COCH_3$.....**7a**.....**7b**

Scheme 1.

Table 2
Epoxidation of cholesteryl acetate with MMPP in CH_3CN[a]

Entry	Substrate (mmol)	Temp	Time	Product	Yield (%)[b]	Epoxide ratio α/β (%)[c]
1	**2**/0.200	rt	48 h	**2a**+**2b**	15	79:21
2	**2**/0.300	50 °C	3.5 h	**2a**+**2b**	95	77:23
3	**2**/0.300	reflux	20 min	**2a**+**2b**	93	76:24
4	**2**/3.000	reflux	20 min	**2a**+**2b**	93	76:24

[a] Reaction conditions: 1 mmol of Δ^5-steroid; 1.1 mmol of MMPP; 15 mL CH_3CN; reflux temperature.
[b] Isolated yield by flash chromatography.
[c] Calculated by ^{1}H NMR integration of 6-H in the crude product.

Table 3
Epoxidation of steroids with MMPP at reflux temperature in acetonitrile[a]

Entry	Substrate (mmol)	Time (min)	Product	Yield (%)[b]	Epoxide ratio α/β (%)[c]
1	**1**/0.150	10	**1a**+**1b**	83	78:22
2	**3**/0.300	5	**3a**+**3b**	84	72:28
3	**4**/0.150	5	**4a**+**4b**	88	75:25
4	**5**/0.150	10	**5a**+**5b**	93	75:25
5	**6**/0.150	5	**6a**+**6b**	83	80:20
6	**7**/0.175	10	**7a**+**7b**	87	78:22

[a] Reaction conditions: 1 mmol of Δ^5-steroid; 1.1 mmol of MMPP; 15 mL CH_3CN; reflux temperature.
[b] Isolated yield by flash chromatography.
[c] Calculated by ^{1}H NMR integration of 6-H in the crude product.

The *syn*-directing effect of allylic hydroxyls is well known and the removal of this effect after acylation is well documented, being generally attributed to the steric hindrance created by the acetate group and to prevention of coordination between the oxidant and the hydroxyl group of the substrate[27] and are also responsible for the lower substrate reactivity.

The influence of allylic substituents was further investigated using Δ^4-steroids as substrates. 3β-Hydroxy-Δ^4-steroid **10** was readily converted into the corresponding epoxides, with predominance of the β-epimer **10b** (Scheme 2, Table 4, entry 3). The 3β-acetoxy derivative **11** (Scheme 2, Table 4, entry 4) reacted with MMPP under the same conditions, with total consumption of substrate in 50 min. Again, higher amounts of the oxidant were needed and the reaction time extended in the presence of an acetoxy group adjacent to the double bond, which can be explained by increased steric hindrance and lack of coordination between MMPP and the free hydroxyl group. α-Epoxidation was, to some extent, predominant when the hydroxyl was protected with an acetyl group.

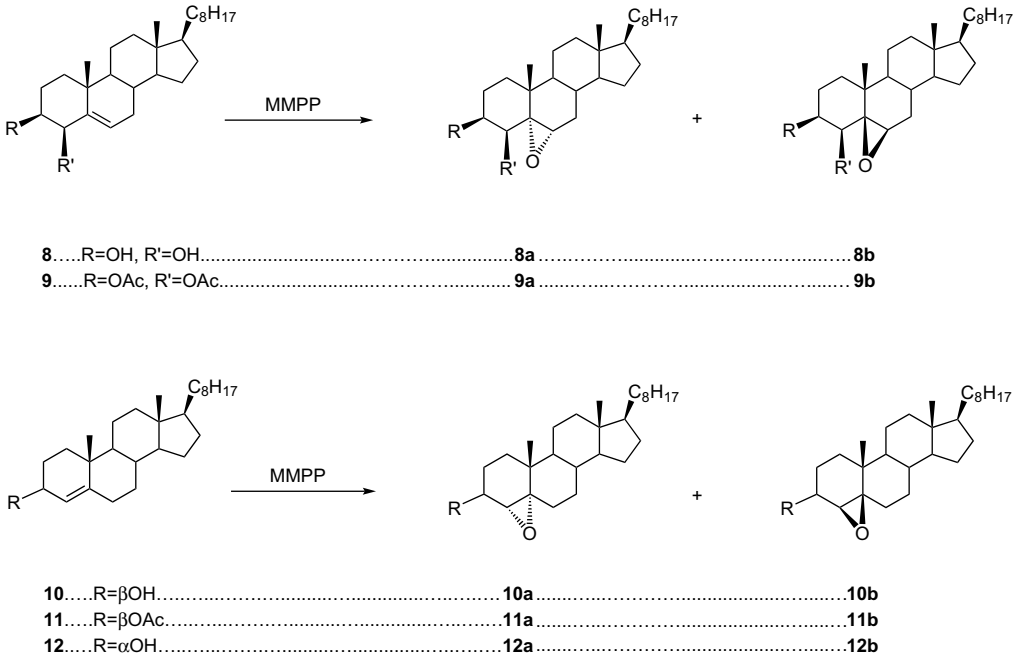
These results, in which a great influence of allylic substituents contributing to the reaction outcome was observed, prompted us to study the epoxidation of 3α-hydroxy-Δ^4-steroid **12**, where conjugation of the steric hindrance imposed by the C-10 and C-13 angular methyl groups and α-orientation provided by the allylic α-hydroxyl group would lead to a strong diastereoselection. However, β-epoxide was also formed in 16% (Scheme 2, Table 4, entry 5).

Next, we expanded the scope of this epoxidation method studying other B-ring olefins. Specifically, Δ^5-B-nor-steroid **13** and its acetate derivative **14**, which are more planar and sterically more hindered at the β face than cholesterol, reacted promptly with MMPP giving the corresponding epoxides quantitatively with very high diastereoselectivity and in high yield (Scheme 3, Table 5, entries 1 and 2).

To evaluate the chemoselectivity of this method, we applied the same reaction conditions to 16-dehydropregnenolone **15** and its acetate derivative **16**, which have an additional double bond in D-ring at C-16, and stigmasterol **17**, which has an additional C-22 double bond. In all cases, the oxidation took place exclusively at the Δ^5 position affording the corresponding epimeric epoxides similar to cholesterol (Scheme 3, Table 5, entries 3–5).

Due to the high reactivity of MMPP/CH_3CN system at reflux temperature, we decided to explore its ability to epoxidize electron-deficient ring-A steroid olefins, specifically Δ^4-enones. Peroxyacids are known to lack reactivity towards enones and epoxidation of such olefins requires, in general, nucleophilic oxidation under basic conditions, such as hydrogen peroxide and sodium hydroxide,[28] yielding preferentially the β-epoxide after very long reaction times.

Cholestenone **18**, progesterone **19** and testosterone **20** were converted into the corresponding epoxides in 53, 50 and 36% yields, respectively. Noteworthy, the α-isomer was predominant (α/



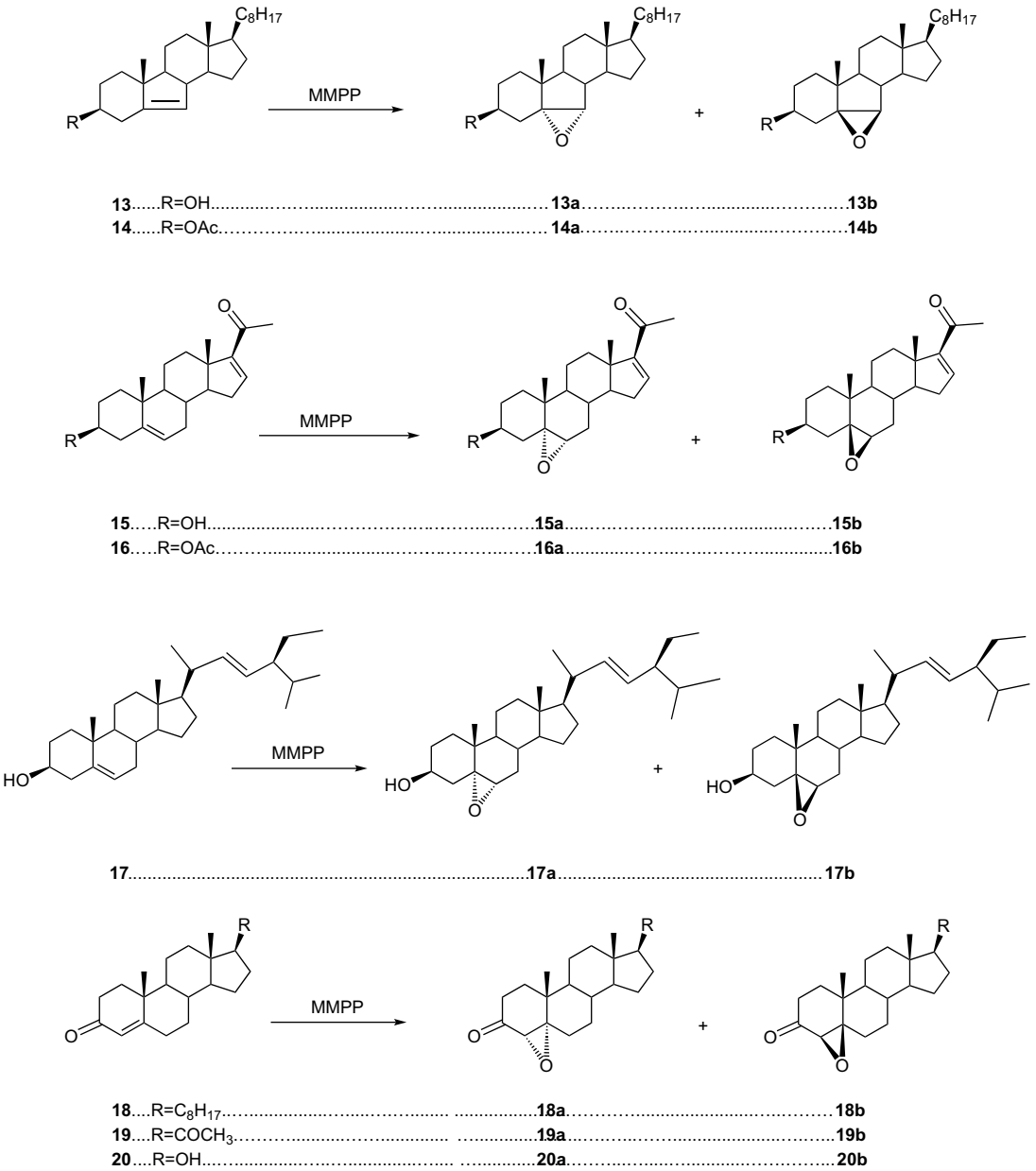
Scheme 2.

Table 4
Epoxidation of allylic steroid alcohols and acylated derivatives with MMPP under reflux temperature

Entry	Substrate (mmol)	MMPP[a]	Solvent (mL/mmol)	Time	Product	Yield (%)[b]	Epoxide ratio α/β (%)[c]
1	**8**/0.300	1.1	15/CH_3CN	30 min	**8a**+**8b**	82	43:57
2	**9**/0.300	6.1[d]	50/CH_3CN	6 h	**9a**+**9b**	93	76:24
3	**10**/0.200	1.1	25/CH_3CN	10 min	**10a**+**10b**	83	22:78
4	**11**/0.200	1.5	25/CH_3CN	50 min	**11a**+**11b**	90	61:39
5	**12**/0.100	1.1	15/CH_3CN	5 min	**12a**+**12b**	81	84:16

[a] mmol of MMPP per mmol of substrate.
[b] Isolated yield by flash chromatography.
[c] Calculated by ^1H NMR integration in the crude product.
[d] Addition of MMPP portionwise (1.017 mmol/h) until complete substrate consumption.

β >4:1) (Scheme 3, Table 5, entries 6–8) contrasting with the stereopreference of peroxide oxidation.[29] Due to the lower reactivity of the double bond, a larger amount of oxidant was needed for substrate consumption. Addition of MMPP was done portionwise, every hour, to overcome the possible degradation of MMPP at higher temperatures. Total consumption of substrate was observed after 5 h in all cases. Therefore, this protocol provides a stereoselective epoxidation of electron-deficient steroidal olefins under neutral conditions, and represents an alternative to perform such difficult epoxidations.



Scheme 3.

Table 5
Epoxidation of other steroidal substrates with MMPP under reflux temperature

Entry	Substrate (mmol)	MMPP[a]	Solvent (mL/mmol)	Time	Product	Yield (%)[b]	Epoxide ratio α/β (%)[c]
1	**13**/0.500	1.1	15/CH_3CN	2 min	**13a**+**13b**	80	99:1
2	**14**/0.500	1.1	25/CH_3CN	10 min	**14a**+**14b**	92	97:3
3	**15**/0.200	1.1	15/CH_3CN	5 min	**15a**+**15b**	88	74:26
4	**16**/0.200	1.1	15/CH_3CN	10 min	**16a**+**16b**	90	74:26
5	**17**/0.150	1.1	15/CH_3CN	5 min	**17a**+**17b**	80	74:26
6	**18**/1.000	4.1[d]	15/CH_3CN	5 h	**18a**+**18b**	53	85:15
7	**19**/1.000	4.1[d]	15/CH_3CN	5 h	**19a**+**19b**	50	83:17
8	**20**/1.000	4.1[d]	15/CH_3CN	5 h	**20a**+**20b**	36	84:16

[a] mmol of MMPP per mmol of substrate.
[b] Isolated yield by flash chromatography.
[c] Calculated by ^{1}H NMR integration of the crude product.
[d] Addition of MMPP portionwise (1.025 mmol/h) until complete substrate consumption.

3. Conclusions

Epoxidation of Δ^5-steroids with moist MMPP in CH_2Cl_2 at room temperature is very stereoselective, although with very low reaction rates. Therefore, it encouraged us to search for a fast method to access epoxysteroids.

With this study we demonstrate that the use of the non-expensive and readily available MMPP in CH_3CN at reflux temperature provides a method for selective epoxidation of Δ^4- and Δ^5-steroids, whereas the C-16 and C-22 olefins and oxo functionalities at C-17 and C-20 remain unchanged. Excellent yields and good stereoselectivities were obtained under simple reaction conditions within very short reaction times. Moreover, epoxidation of electron-deficient olefins was successfully performed using a peroxyacid under neutral conditions and with good selectivity for α-epoxide.

This new protocol, in which MMPP was used to epoxidize low polar substrates in an aprotic solvent, offers a fast, efficient and cost effective alternative over other epoxidation systems, being the oxidant safe to use and easily removed by aqueous work-up.

4. Experimental

4.1. General

Cholesteryl acetate, pregnenolone acetate, dehydroisoandrosterone acetate, 16-dehydropregnenolone acetate, cholesteryl hemisuccinate, stigmasterol, cholestenone, testosterone and progesterone were purchased from Sigma–Aldrich Co. 7-Norcholest-5-en-3β-yl acetate was kindly supplied by Dr. Alexander Kasal. Cholesterol, pregnenolone, dehydroisoandrosterone and 16-dehydropregnenolone were obtained by simple alkaline hydrolysis of the correspondent acetate derivatives, using the procedure described below for the synthesis of 7-norcholest-5-en-3-β-ol. The other starting materials were obtained by synthesis as described below in Section 4.2. All reagents and solvents were purchased from Sigma–Aldrich Co, except 4,4′-thiobis(6-*tert*-butyl-*m*-cresol), which was from TCI Europe nv. All commercially available chemicals were used without purification. Kieselgel 60HF_{254}/Kieselgel 60G was used as TLC plates. Flash column chromatography was performed in a Büchi automated system using a borosilikat 3.3 column and silica gel 60 (230–400 mesh ASTM). Melting points were determined on a Buchi Melting Point B-540 and are uncorrected. IR spectroscopy was performed on a Jasco FT/IR 420 spectrophotometer. ^{1}H, ^{13}C and DEPT NMR spectra were recorded in a Bruker Avance 300 MHz and in a 500 MHz. Sample solutions were prepared in $CDCl_3$ with tetramethylsilane (TMS) as internal reference. Mass spectra were recorded on a Thermo Finnigan Mass Spectrometer, model LCQ Advantage MAX.

4.2. Substrate synthesis

4.2.1. *Cholest-5-ene-3β,4β-diol (**8**)*

To a solution of cholesterol **1** (600 mg, 1.552 mmol) in toluene (8 mL) a hot solution of selenium dioxide (480 mg, 4.326 mmol) in acetic acid 98% (6 mL) was added. The reaction mixture was stirred for 90 min at 90 °C and then stopped by the addition of sodium acetate (1.2 g). Reaction mixture was stirred for 10 min at room temperature and then filtered and extracted with toluene. The toluene solution was washed with water, dried under anhydrous Na_2SO_4 and concentrated under vacuum to give a brown crude product. Flash chromatography (gradient of petroleum ether–ethyl acetate, starting from 8:1) afforded **8** as pure compound (315 mg, 50%). IR 3408, 2940, 2870, 1457, 1365, 1072, 966, 841, 762, 641 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.68 (3H, s, 18-CH_3), 0.86 and 0.87 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.91 (3H, d, J=6.6 Hz, 21-CH_3), 1.18 (3H, s, 19-CH_3), 3.56 (1H, td, J=11.8, 4.0, 4.0 Hz, 3α-H), 4.13 (1H, d, J=4.0 Hz, 4α-H), 5.68 (1H, dd, J=4.9, 1.9 Hz, 6-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 11.8, 18.7, 20.5, 21.0, 22.5, 22.8, 23.8, 24.2, 25.3, 28.0, 28.2, 31.8, 32.0, 35.8, 36.0 (C-10), 36.1, 36.9, 39.5, 39.6, 42.26 (C-13), 50.1, 56.0, 56.9, 72.4, 77.2, 128.8 (C-6), 142.7 (C-5); MS [m/z (%)] 401.7 (68) [M−H]$^+$, 387.7 (24), 293.7 (35), 270.4 (27), 265.2 (100), 201.0 (27).

4.2.2. *Cholest-5-ene-3β,4β-diyl-diacetate (**9**)*

To a solution of cholest-5-ene-3β,4β-diol **8** (161 mg, 0.4 mmol) and 4-dimethylaminopyridine (48.9 mg; 0.4 mmol) in tetrahydrofuran (1.5 mL) was added acetic anhydride (189 μL, 2 mmol). The reaction mixture was stirred at room temperature for 5 h and then evaporated to dryness. The residue was extracted with diethyl ether, and the organic phase washed with NH_4Cl (satd aq soln), $NaHCO_3$ (satd aq soln) and water, dried over anhydrous Na_2SO_4, filtered and evaporated to afford **9** as white powder crude product (190 mg, 98%). IR 2936, 2902, 2870, 1741, 1729, 1468, 1375, 1254, 1218, 1051, 1017, 973, 894, 758 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.67 (3H, s, 18-CH_3), 0.86 and 0.87 (each 3H, 2d, J=6.5 Hz, 26-CH_3 and 27-CH_3), 0.91 (3H, d, J=6.5 Hz, 21-CH_3), 1.13 (3H, s, 19-CH_3), 2.01 and 2.07 (each 3H, 2s, 3β-CH_3COO and 4β-CH_3COO), 4.74 (1H, ddd, J=12.5, 4.5, 3.6 Hz, 3α-H), 5.50 (1H, dd, J=3.6, 1.3 Hz, 4α-H), 5.81 (1H, dd, J=5.0, 2.0 Hz, 6-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 11.8, 18.7, 20.4, 20.5, 21.1, 21.5, 22.5, 22.5, 22.8, 23.8, 24.2, 28.0, 28.2, 31.6, 32.0, 35.7, 36.1 (C-10), 36.1, 36.7, 39.5, 39.6, 42.2 (C-13), 50.1, 56.0, 56.7, 72.8, 75.9, 131.7 (C-6), 138.2 (C-5), 170.1 and 170.3 (3β-CH_3COO and 4β-CH_3COO); MS [m/z (%)] 485.7 (55) [M−H]$^+$, 467.6 (82), 444.4 (100), 431.7 (77), 401.2 (72), 330.1 (41).

4.2.3. *Cholest-4-en-3β-ol (**10**) and cholest-4-en-3α-ol (**12**)*

To a solution of 4-cholesten-3-one (400 mg, 1.04 mmol) in tetrahydrofuran (10 mL) at −70 °C (methanol bath cooled in

a Cryocool apparatus) under nitrogen atmosphere was added 1 M L-selectride (6.80 mL, 6.80 mmol). The reaction mixture was stirred at −70 °C for 24 h. The reaction was quenched with water (15 mL), warmed up to 0 °C and the organoborane was oxidized by addition of sodium hydroxide 6 M (15 mL) and hydrogen peroxide 30% (15 mL) for 2 h. Then, THF was removed under reduced pressure and the crude product extracted with dichloromethane. The resulting organic phase was washed with water, dried over anhydrous Na_2SO_4, filtered and evaporated to yield a white crude product. Flash chromatography of the crude (petroleum ether–ethyl acetate, 20:1) afforded the pure products **10** (294 mg, 73%) and **12** (78.5 mg, 19.5%).

*4.2.4. Cholest-4-en-3β-ol (**10**)*

IR 3354, 2928, 2867, 1654, 1465, 1377, 1045, 878, 854, 753 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm 0.67 (3H, s, 18-CH_3), 0.86 and 0.86 (each 3H, 2d, J=6.5 Hz, 26-CH_3 and 27-CH_3), 0.90 (3H, d, J=6.5 Hz, 21-CH_3), 1.05 (3H, s, 19-CH_3), 4.15 (1H, m, 3α-H), 5.27 (1H, d, J=1.7 Hz, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 11.9, 18.6, 18.9, 21.0, 22.5, 22.8, 23.8, 24.2, 28.0, 28.2, 29.5, 32.2, 33.1, 35.3, 35.8, 35.9, 36.1, 37.3 (C-10), 39.5, 39.8, 42.4 (C-13), 54.4, 56.1, 56.1, 68.0 (C-3), 123.2 (C-4), 147.8 (C-5); MS [m/z (%)] 385.6 (83) $[M-H]^+$, 329.1 (65), 311.5 (84), 294.8 (57), 279.3 (66), 249.1 (100), 111.0 (96).

*4.2.5. Cholest-4-en-3α-ol (**12**)*

IR 3338, 2931, 2867, 1655, 1466, 1379, 1014, 990, 857 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm 0.68 (3H, s, 18-CH_3), 0.86 and 0.86 (each 3H, 2d, J=6.5 Hz, 26-CH_3 and 27-CH_3), 0.90 (3H, d, J=6.5 Hz, 21-CH_3), 0.98 (3H, s, 19-CH_3), 4.07 (1H, dt, J=5.0, 5.0, 3.1 Hz, 3β-H), 5.45 (1H, dd, J=5.0, 1.9 Hz, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 12.0, 18.1, 18.6, 21.5, 22.5, 22.8, 23.8, 24.2, 27.8, 28.0, 28.2, 31.6, 32.4, 32.8, 35.8, 35.8, 36.1, 37.5 (C10), 39.5, 39.9, 42.5 (C-13), 54.1, 56.1, 56.1, 64.3 (C-3), 120.5 (C-4), 150.5 (C-5); MS [m/z (%)] 385.7 (89) $[M-H]^+$, 378.1 (76), 366.6 (64), 353.1 (71), 325.4 (83), 292.5 (86), 265.5 (74), 161.75 (100).

*4.2.6. Cholest-4-en-3β-yl acetate (**11**)*

To a solution of cholest-4-en-3β-ol **10** (150 mg, 0.390 mmol) and 4-dimethylaminopyridine (23.8 mg, 0.195 mmol) in tetrahydrofuran (3 mL) acetic anhydride (73.7 μL, 0.780 mmol) was added. The reaction mixture was stirred at room temperature for 2 h and then evaporated to dryness. The residue was extracted with diethyl ether, and organic phase washed successively with NH_4Cl (satd aq soln), $NaHCO_3$ (satd aq soln) and water; dried over anhydrous Na_2SO_4, filtered and evaporated to yield compound **11** as a white crystalline crude product (165 mg, 99%). IR 2934, 2869, 1738, 1468, 1372, 1239, 1021, 757 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm 0.67 (3H, s, 18-CH_3), 0.86 and 0.86 (each 3H, 2d, J=6.5 Hz, 26-CH_3 and 27-CH_3), 0.90 (3H, d, J=6.5 Hz, 21-CH_3), 1.06 (3H, s, 19-CH_3), 2.05 (3H, s, 3β-CH_3COO), 5.22 (1H, s, 4-H), 5.23 (1H, m, 3α-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 11.9, 18.6, 18.8, 20.9, 21.4, 22.5, 22.8, 23.8, 24.2, 25.1, 28.0, 28.2, 32.2, 32.9, 34.9, 35.7, 35.9, 36.1, 37.3 (C-10), 39.5, 39.8, 42.4 (C-13), 54.2, 56.0, 56.1, 70.9 (C-3), 118.8 (C-6), 149.6 (C-5), 171.0 (CH_3COO); MS [m/z (%)] 427.7 (53) $[M-H]^+$, 322.7 (75), 288.4 (100), 173.3 (56), 159.0 (75).

*4.2.7. 7-Norcholest-5-en-3-β-ol (**13**)*

To a solution of 7-norcholest-5-en-3β-yl acetate **14** (300 mg, 0.723 mmol) in a mixture of methanol (13 mL) was added a methanolic solution of 0.5 M sodium methoxide (723 μL, 0.362 mmol). The reaction mixture was stirred at room temperature for 4 h, stopped with the addition of dowex 50x8 until neutralization, filtered and evaporated to dryness. The residue was dissolved in ethyl acetate and washed with $NaHCO_3$ (satd aq) and water, dried over anhydrous Na_2SO_4 and evaporated to yield a white powder, product **13** (264 mg, 98%). IR 3393, 3032, 2950, 2867, 1457, 1376, 1040 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm 0.68 (3H, s, 18-CH_3), 0.86 and 0.87 (each 3H, 2d, J=6.5 Hz, 26-CH_3 and 27-CH_3), 0.88 (3H, s, 19-CH_3), 0.92 (3H, d, J=6.5 Hz, 21-CH_3), 3.57 (1H, tt, J=11.2, 11.2, 4.5, 4.5 Hz, 3α-H), 5.36 (1H, br s, 6-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 12.3, 15.0, 18.8, 21.2, 22.5, 22.8, 23.9, 24.3, 28.0, 28.6, 32.0, 35.6, 36.2, 36.6, 37.2, 39.5, 40.1, 44.4 (C-10), 44.8 (C-13), 46.2, 54.4, 55.8, 62.4, 71.7 (C-3), 125.5 (C-6), 148.9 (C-5); MS [m/z (%)] 372.0 (44) $[M-H]^+$, 355.0 (49), 339.3 (60), 324.4 (100), 311.6 (54), 228.8 (63), 195.2 (54), 125.9 (85).

4.3. General procedure for epoxidation using MMPP

To a solution of steroid olefin in the appropriate solvent, MMPP was added as a single portion. The suspension was stirred for the periods of time and temperatures indicated in Tables 1–5. Reactions were monitored by TLC. After substrate consumption, reaction mixture was cooled, filtered and concentrated under vacuum. The white solid residue was dissolved in diethyl ether, ethyl acetate or chloroform (saturated in water), according to the substrate polarity, and the resulting organic phase was washed with Na_2SO_3 (10% aq soln), $NaHCO_3$ (satd aq soln), and water, dried over anhydrous Na_2SO_4, filtered and evaporated to yield a white foam crude product. The diastereomeric mixture was determined by proton integration of the 4-H or 6-H of the crude product. Yield was determined by the epoxide mixture obtained through flash silica column chromatography with ethyl acetate/*n*-hexane mixtures as eluent (except for compound **3**: chloroform/ethanol 20:1).

*4.3.1. 5α,6α-Epoxycholestan-3β-ol (**1a**)*

Mp 141–142 °C (EtOH); lit.[29] 141–143 °C; ^1H NMR (300 MHz, $CDCl_3$) δ ppm 0.61 (3H, s, 18-CH_3), 0.86 and 0.87 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.89 (3H, d, J=6.6 Hz, 21-CH_3), 1.07 (3H, s, 19-CH_3), 2.91 (1H, d, J=4.4 Hz, 6β-H), 3.92 (1H, tt, J=11.4, 11.4, 5, 5 Hz, 3α-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 11.8, 15.9, 18.6, 20.6, 22.5, 22.8, 23.8, 24.0, 28.0, 28.0, 28.8, 29.8, 31.0, 32.4, 34.8 (C-10), 35.7, 36.1, 39.4, 39.5, 39.8, 42.3 (C-13), 42.5, 55.8, 56.8, 59.3, 65.7 (C-5), 68.7.

*4.3.2. 5β,6β-Epoxycholestan-3β-ol (**1b**)*

^1H NMR (300 MHz, $CDCl_3$) δ ppm 0.64 (3H, s, 18-CH_3), 0.86 and 0.87 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.89 (3H, d, J=6.6 Hz, 21-CH_3), 1.00 (3H, s, 19-CH_3), 3.07 (1H, d, J=2.4 Hz, 6α-H), 3.70 (1H, m, 3α-H).

*4.3.3. 5α,6α-Epoxycholestan-3β-yl acetate (**2a**)*

Mp 98–99 °C (EtOH); lit.[29] 101–103 °C; ^1H NMR (300 MHz, $CDCl_3$) δ ppm 0.61 (3H, s, 18-CH_3), 0.86 and 0.86 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.88 (3H, d, J=6.6 Hz, 21-CH_3), 1.07 (3H, s, 19-CH_3), 2.02 (3H, s, 3β-CH_3COO), 2.89 (1H, d, J=4.4 Hz, 6β-H), 4.95 (tt, J=11.4, 11.4, 5.0, 5.0 Hz, 3α-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 11.8, 15.8, 18.6, 20.5, 21.3, 22.5, 22.8, 23.8, 24.0, 27.2, 28.0, 28.1, 28.7, 29.8, 32.1, 35.0 (C-10), 35.7, 36.1, 36.1, 39.3, 39.5, 42.3 (C-13), 42.4, 55.8, 56.7, 59.2, 65.2 (C-5), 71.4, 170.2 (CH_3COO).

*4.3.4. 5β,6β-Epoxycholestan-3β-yl acetate (**2b**)*

^1H NMR (300 MHz, $CDCl_3$) δ ppm 0.64 (3H, s, 18-CH_3), 0.86 and 0.86 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.88 (3H, d, J=6.6 Hz, 21-CH_3), 1.00 (3H, s, 19-CH_3), 2.03 (3H, s, 3β-CH_3COO), 3.08 (1H, d, J=2.4 Hz, 6α-H), 4.77 (1H, tdd, J=11.9, 10.0, 4.8, 4.8 Hz, 3α-H).

*4.3.5. 5α,6α-Epoxycholestan-3β-yl-hemisuccinate (**3a**)*

Mp 175.5–177 °C (EtOH); IR 3393, 2933, 2869, 1725, 1707, 1468, 1439, 1379, 1171, 1047, 874, 800 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm 0.61 (3H, s, 18-CH_3), 0.86 and 0.86 (each 3H, 2d,

J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.89 (3H, d, J=6.6 Hz, 21-CH_3), 1.08 (3H, s, 19-CH_3), 2.58 and 2.67 (each 2H, 2dd, J=10.0, 4.0 Hz, HOOC$(CH_2)_2$–), 2.91 (1H, d, J=4.4 Hz, 6β-H), 4.98 (1H, tt, J=11.2, 11.2, 4.7, 4.7 Hz, 3α-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 11.8, 15.8, 18.6, 20.6, 22.5, 22.8, 23.8, 24.0, 27.1, 28.0, 28.1, 28.7, 28.9, 29.1, 29.8, 32.1, 35.0 (C-10), 35.7, 36.0, 36.1, 39.3, 39.5, 42.3 (C-13), 42.4, 55.8, 56.7, 59.2, 65.3 (C-5), 71.9, 171.3 (C═O), 177.6 (C═O); MS [m/z (%)] 501.3 (100) $[M-H]^+$, 452.9 (23), 338.2 (27), 164.4 (51), 98.6 (36).

*4.3.6. 5β,6β-Epoxycholestan-3β-yl-hemisuccinate (**3b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.64 (3H, s, 18-CH_3), 0.86 and 0.86 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.89 (3H, d, J=6.6 Hz, 21-CH_3), 1.00 (3H, s, 19-CH_3), 2.55–2.60 and 2.64–2.70 (each 2H, 2 m, HOOC$(CH_2)_2$–), 3.1 (1H, d, J=2.4 Hz, 6α-H), 4.80 (1H, tdd, J=11.9, 9.8, 4.9, 4.9 Hz, 3α-H).

*4.3.7. 5α,6α-Epoxy-3β-hydroxy-androstan-17-one (**4a**)*

Mp 228–229 °C (EtOH); lit.[30] 229–230 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.82 (3H, s, 18-CH_3), 1.09 (3H, s, 19-CH_3), 2.96 (1H, d, J=4.4 Hz, 6β-H), 3.92 (1H, tt, J=11.2, 11.2, 4.8, 4.8 Hz, 3α-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 13.5, 15.9, 19.9, 21.7, 27.7, 29.5, 31.0, 31.0, 32.4, 35.0 (C-10), 35.7, 39.7, 42.7, 47.6 (C-13), 51.8, 58.7, 65.7, 68.5 (C-5), 220.7 (C-17).

*4.3.8. 5β,6β-Epoxy-3β-hydroxy-androstan-17-one (**4b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.85 (3H, s, 18-CH_3), 1.03 (3H, s, 19-CH_3), 3.13 (1H, d, J=2.5 Hz, 6α-H), 3.71 (1H, tdd, J=11.6, 10.1, 4.6, 4.6 Hz, 3α-H).

*4.3.9. 5α,6α-Epoxy-17-oxo-androstan-3β-yl acetate (**5a**)*

Mp 221.5–222.5 °C (EtOH); lit.[31] 223–224 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.82 (3H, s, 18-CH_3), 1.10 (3H, s, 19-CH_3), 2.02 (3H, s, 3β-CH_3COO), 2.94 (1H, d, J=4.4 Hz, 6β-H), 4.95 (1H, tt, J=11.6, 11.6, 5.0, 5.0 Hz, 3α-H), ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 13.5, 15.8, 19.9, 21.3, 21.7, 27.1, 27.6, 29.5, 31.0, 32.1, 35.1 (C-10), 35.7, 36.0, 42.6, 47.6 (C-13), 51.7, 58.6, 65.2 (C-5), 71.1, 170.2 (CH_3COO), 220.5 (C-17).

*4.3.10. 5β,6β-Epoxy-17-oxo-androstan-3β-yl acetate (**5b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.85 (3H, s, 18-CH_3), 1.04 (3H, s, 19-CH_3), 2.04 (3H, s, 3β-CH_3COO), 3.15 (1H, d, J=2.5 Hz, 6α-H), 4.77 (1H, tdd, J=11.8, 9.8, 4.7, 4.7 Hz, 3α-H).

*4.3.11. 5α,6α-Epoxy-3β-hydroxy-pregnan-20-one (**6a**)*

Mp 190–192 °C (EtOH); lit.[32] 190–191 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.56 (3H, s, 18-CH_3), 1.06 (3H, s, 19-CH_3), 2.11 (3H, s, 21-CH_3), 2.91 (1H, d, J=4.4 Hz, 6β-H), 3.92 (1H, tt, J=11.2, 11.2, 4.8, 4.8 Hz, 3α-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 13.2, 15.9, 20.6, 22.6, 24.2, 28.6, 29.8, 31.0, 31.5, 32.4, 34.8 (C-10), 38.4, 39.7, 42.4, 43.9 (C-13), 57.0, 59.1, 63.3, 65.7 (C-5), 68.6, 209.5 (C-20).

*4.3.12. 5β,6β-Epoxy-3β-hydroxy-pregnan-20-one (**6b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.60 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 2.12 (3H, s, 21-CH_3), 3.08 (1H, d, J=2.5 Hz, 6α-H), 3.71 (1H, tdd, J=11.6, 9.7, 4.8, 4.8 Hz, 3α-H).

*4.3.13. 5α,6α-Epoxy-20-oxo-pregnan-3β-yl acetate (**7a**)*

Mp 167.5–168.5 °C (EtOH); lit.[32] 167–168 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.56 (3H, s, 18-CH_3), 1.08 (3H, s, 19-CH_3), 2.02 (3H, s, 3β-CH_3COO), 2.11 (3H, s, 21-CH_3), 2.91 (1H, d, J=4.4 Hz, 6β-H), 4.95 (tt, J=11.4, 11.4, 4.9, 4.9 Hz, 3α-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 13.2, 15.8, 20.6, 21.3, 22.6, 24.2, 27.1, 28.6, 29.8, 31.5, 32.1, 35.0 (C-10), 36.0, 38.4, 42.3, 43.9 (C-13), 56.9, 58.9, 63.3, 65.2 (C-5), 71.2, 170.3 (CH_3COO), 209.5 (C-20).

*4.3.14. 5β,6β-Epoxy-20-oxo-pregnan-3β-yl acetate (**7b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.59 (3H, s, 18-CH_3), 1.01 (3H, s, 19-CH_3), 2.04 (3H, s, 3β-CH_3COO), 2.13 (3H, s, 21-CH_3), 3.10 (1H, d, J=2.5 Hz, 6α-H), 4.77 (1H, m, 3α-H).

*4.3.15. 5α,6α-Epoxycholestane-3β,4β-diol (**8a**)*

Mp 205–206 °C (EtOH); lit.[33] 195.5–198 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 0.61 (3H, s, 18-CH_3), 0.86 and 0.86 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.88 (3H, d, J=6.6 Hz, 21-CH_3), 1.22 (3H, s, 19-CH_3), 3.03 (1H, dd, J=4.2 Hz, 6β-H), 3.19 (1H, dd, J=3.5, 1.0 Hz, 4α-H), 3.86 (1H, ddd, J=12.0, 5.0, 3.6 Hz, 3α-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 11.9, 15.3, 18.7, 20.0, 22.6, 22.8, 23.9, 24.0, 25.6, 28.0, 28.1, 28.3, 30.0, 32.7, 34.3 (C-10), 35.8, 36.2, 39.4, 39.5, 42.45 (C-13), 43.4, 55.9, 57.0, 59.3, 64.7 (C-5), 70.1, 77.4.

*4.3.16. 5β,6β-Epoxycholestane-3β,4β-diol (**8b**)*

Mp 175.5–176.5 °C (EtOH); lit.[34] 173–175 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 0.59 (1H, m), 0.63 (3H, s, 18-CH_3), 0.85 and 0.86 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.89 (3H, d, J=6.6 Hz, 21-CH_3), 1.12 (3H, s, 19-CH_3), 3.19 (1H, d, J=2.2 Hz, 6α-H), 3.35 (1H, d, J=3.6 Hz, 4α-H), 3.61 (1H, td, J=11.6, 4.5, 3.6 Hz, 3α-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 11.7, 17.8, 18.7, 21.2, 22.5, 22.8, 23.8, 24.2, 24.8, 28.0, 28.1, 29.6, 32.5, 34.7 (C-10), 35.7, 36.1, 36.9, 39.5, 39.6, 42.2 (C-13), 51.5, 56.1, 56.2, 64.0, 65.4 (C-5), 71.2, 77.1.

*4.3.17. 5α,6α-Epoxycholestane-3β,4β-diyl-diacetate (**9a**)*

Mp 145–146.5 °C (EtOH); lit.[35] 145–146 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.59 (3H, s, 18-CH_3), 0.85 and 0.86 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.88 (3H, d, J=6.6 Hz, 21-CH_3), 1.16 (3H, s, 19-CH_3), 1.99 and 2.12 (each 3H, 2s, 3β-CH_3COO and 4β-CH_3COO), 3.16 (1H, d, J=4.2 Hz, 6β-H), 4.50 (1H, dd, J=3.5, 1.1 Hz, 4α-H), 5.03 (1H, ddd, J=12.3, 4.9, 3.5 Hz, 3α-H); ^{13}C NMR (75 MHz MHz, $CDCl_3$) δ ppm 11.8, 15.1, 18.6, 19.8, 21.0, 21.2, 22.5, 22.8, 22.8, 23.8, 24.0, 28.0, 28.0, 28.0, 29.8, 32.3, 34.5, 35.7, 36.1, 39.2, 39.5, 42.3, 43.1, 55.8, 56.7, 60.1, 63.4, 70.6, 75.5, 169.9 and 170.0 (3β-CH_3COO and 4β-CH_3COO).

*4.3.18. 5β,6β-Epoxycholestane-3β,4β-diyl-diacetate (**9b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.62 (3H, s, 18-CH_3), 0.86 and 0.86 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.88 (3H, d, J=6.6 Hz, 21-CH_3), 1.14 (3H, s, 19-CH_3), 1.99 and 2.13 (each 3H, 2s, 3β-CH_3COO and 4β-CH_3COO), 3.24 (1H, d, J=2.2 Hz, 6α-H), 4.80 (1H, d, J=3.5 Hz, 4α-H), 4.84 (1H, m, 3α-H).

*4.3.19. 4α,5α-Epoxycholestan-3β-ol (**10a**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.68 (3H, s, 18-CH_3), 0.86 and 0.87 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.90 (3H, d, J=6.6 Hz, 21-CH_3), 1.11 (3H, s, 19-CH_3), 2.90 (1H, d, J=1.0 Hz, 4β-H), 3.99 (1H, m, 3α-H).

*4.3.20. 4β,5β-Epoxycholestan-3β-ol (**10b**)*

Mp 96–97 °C (EtOH); lit.[36] 96–97 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 0.68 (3H, s, 18-CH_3), 0.86 and 0.87 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.90 (3H, d, J=6.6 Hz, 21-CH_3), 1.03 (3H, s, 19-CH_3), 3.14 (1H, d, J=4.8 Hz, 4α-H), 4.06 (1H, dt, J=4.8, 4.8, 2.5 Hz, 3α-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 11.9, 18.6, 19.1, 21.3, 22.8, 23.8, 24.3, 25.9, 26.0, 28.0, 28.2, 30.3, 31.1, 35.0, 35.7 (C-10), 36.1, 36.1, 39.5, 39.7, 42.5 (C-13), 47.0, 56.1, 56.2, 63.7, 64.2, 69.0 (C-5).

*4.3.21. 4α,5α-Epoxycholestan-3β-yl acetate (**11a**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.68 (3H, s, 18-CH_3), 0.86 and 0.87 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.90 (3H, d, J=6.6 Hz, 21-CH_3), 1.11 (3H, s, 19-CH_3), 2.08 (1H, s, 3β-CH_3COO), 2.87 (1H, s, 4β-H), 4.95 (1H, t, J=8.2, 8.2 Hz, 3α-H).

*4.3.22. 4β,5β-Epoxycholestan-3β-yl acetate (**11b**)*

Mp 89–90 °C (EtOH); lit.[37] 89–90 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.68 (3H, s, 18-CH_3), 0.86 and 0.87 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.90 (3H, d, J=6.6 Hz, 21-CH_3), 1.04 (3H, s, 19-CH_3), 2.10 (1H, s, 3β-CH_3COO), 3.16 (1H, d, J=3.6 Hz, 4α-H), 5.13 (1H, m, 3α-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 11.9, 18.4, 18.6, 21.2, 21.4, 22.5 (2C), 22.8, 23.8, 24.2, 28.0, 28.1, 29.6, 30.3, 31.2, 35.2, 35.7, 35.8 (C-10), 36.1, 39.5, 39.7, 42.5 (C-13), 49.0, 56.0, 56.2, 61.3, 66.8 (C-5), 69.0, 171.0 (CH_3COO).

*4.3.23. 4α,5α-Epoxycholestan-3α-ol (**12a**)*

Mp 92–93 °C (EtOH); lit.[38] 92–94 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.68 (3H, s, 18-CH_3), 0.86 and 0.87 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.90 (3H, d, J=6.6 Hz, 21-CH_3), 1.02 (3H, s, 19-CH_3), 3.19 (1H, dd, J=4.5, 0.6 Hz, 4β-H), 4.03 (1H, ddd, J=5.1, 4.5, 0.6 Hz, 3β-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 12.0, 17.3, 18.6, 20.7, 22.5, 22.8, 23.8, 24.1, 27.0, 27.7, 28.0, 28.2, 28.5, 29.8, 35.4, 35.4 (C-10), 35.8, 36.1, 39.5, 39.7, 42.6 (C-13), 50.4, 55.7, 56.1, 63.1, 63.1, 69.6 (C-5).

*4.3.24. 4β,5β-Epoxycholestan-3α-ol (**12b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.68 (3H, s, 18-CH_3), 0.87 and 0.87 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.94 (3H, d, J=6.6 Hz, 21-CH_3), 1.01 (3H, s, 19-CH_3), 2.85 (1H, d, J=0.9 Hz, 4α-H), 3.98 (1H, m, 3β-H).

*4.3.25. 5α,6α-Epoxy-7-norcholestan-3β-ol (**13a**)*

Mp 138.5–139.5 °C (EtOH); lit.[39] 139–140 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm 0.63 (3H, s, 18-CH_3), 0.86 and 0.87 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.89 (3H, s, 19-CH_3), 0.90 (3H, d, J=6.6 Hz, 21-CH_3), 3.26 (1H, s, 6β-H), 3.96 (1H, m, 3α-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 12.1, 15.4, 18.7, 20.9, 22.5, 22.8, 23.9, 24.2, 28.0, 28.5, 30.9, 31.2, 34.6, 35.7, 36.2, 38.8 (C-10), 39.4, 39.8, 42.5, 44.4 (C-13), 48.2, 50.6, 55.5, 60.4, 69.1 (C-5), 69.8.

*4.3.26. 5α,6α-Epoxy-7-norcholestan-3β-yl acetate (**14a**)*

Mp 113–113.5 °C (EtOH); lit.[40] 111–112 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm 0.63 (3H, s, 18-CH_3), 0.86 and 0.87 (each 3H, 2d, J=6.6 Hz, 26-CH_3 and 27-CH_3), 0.90 (3H, s, 19-CH_3), 0.91 (3H, d, J=6.6 Hz, CH_3-21), 2.03 (3H, s, 3β-CH_3COO), 3.26 (1H, s, 6β-H), 4.98 (1H, tt, J=11.2, 11.2, 4.8, 4.8 Hz, 3α-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 12.0, 15.3, 18.6, 20.8, 21.3, 22.5, 22.7, 23.8, 24.2, 26.9, 27.9, 28.5, 30.9, 31.1, 35.6, 36.1, 38.7 (C-10), 39.4, 39.7, 42.4, 44.4 (C-13), 48.0, 50.5, 55.5, 60.3, 68.3 (C-5), 72.1, 170.1 (CH_3COO).

*4.3.27. 5α,6α-Epoxy-3β-hydroxy-pregn-16-en-20-one (**15a**)*

Mp 172–174 °C (EtOH); lit.[41] 140–143 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.85 (3H, s, 18-CH_3), 1.10 (19-CH_3), 2.25 (3H, s, 21-CH_3), 2.93 (1H, d, J=4.5 Hz, 6β-H), 3.91 (1H, tt, J=11.3, 11.3, 4.8, 4.8 Hz, 3α-H), 6.68 (1H, dd, J=3.4, 1.9 Hz, 16-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 15.6, 15.9, 20.3, 27.1, 28.2, 28.4, 31.0, 32.0, 32.2, 34.2, 35.0 (C-10), 39.8, 42.7, 46.0 (C-13), 56.3, 58.9, 65.9, 68.6, 144.2 (C-16), 155.1 (C-17), 196.8 (C-20).

*4.3.28. 5β,6β-Epoxy-3β-hydroxy-pregn-16-en-20-one (**15b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.88 (3H, s, 18-CH_3), 1.03 (3H, s, 19-CH_3), 2.25 (3H, s, 21-CH_3), 3.10 (1H, d, J=2.5 Hz, 6α-H), 3.70 (1H, m, 3α-H), 6.69 (1H, m, 16-H).

*4.3.29. 5α,6α-Epoxy-20-oxo-pregn-16-en-3β-yl acetate (**16a**)*

Mp 189–190 °C (EtOH); lit.[42] 170–172 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.84 (3H, s, 18-CH_3), 1.11 (3H, s, 19-CH_3), 2.01 (3H, s, 3β-CH_3COO), 2.24 (3H, s, 21-CH_3), 2.92 (1H, d, J=4.5 Hz, 6β-H), 4.94 (tt, J=11.4, 11.4, 5.0, 5.0 Hz, 3α-H), 6.67 (1H, dd, J=3.2, 1.9 Hz, 16-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 15.6, 15.8, 20.3, 21.3, 27.1, 27.1, 28.1, 28.3, 31.9, 31.9, 34.1, 35.1 (C-10), 36.0, 42.6, 46.0 (C-13), 56.2, 58.7, 65.3 (C-5), 71.2, 144.1 (C-16), 155.1 (C-17), 170.2 (CH_3COO), 196.7 (C-20).

*4.3.30. 5β,6β-Epoxy-20-oxo-pregn-16-en-3β-yl acetate (**16b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.87 (3H, s, 18-CH_3), 1.04 (3H, s, 19-CH_3), 2.03 (3H, s, 3β-CH_3COO), 2.25 (3H, s, 21-CH_3), 3.11 (1H, d, J=2.4 Hz, 6α-H), 4.77 (1H, tdd, J=11.4, 9.6, 4.7, 4.7 Hz, 3α-H), 6.68 (dd, J=3.2, 1.9 Hz, 16-H).

*4.3.31. (22E)-5α,6α-Epoxystigmast-22-en-3β-ol (**17a**)*

Mp 155–155.5 °C (EtOH); lit.[43] 149–151 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.63 (3H, s, 18-CH_3), 0.79 (3H, d, J=6.6 Hz, 26-CH_3), 0.80 (3H, t, J=6.6, 6.6 Hz, 24^2-CH_3), 0.84 (3H, d, J=6.6 Hz, 27-CH_3), 0.99 (3H, d, J=6.6 Hz, 21-CH_3), 1.06 (3H, s, 19-CH_3), 2.90 (1H, d, J=4.4 Hz, 6β-H), 3.91 (1H, tt, J=11.2, 11.2, 4.8, 4.8 Hz, 3α-H), 5.00 and 5.13 (each 1H, 2dd, J=15.2, 8.4 Hz, 22-H and 23-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 12.0, 12.2, 15.9, 18.9, 20.6, 21.1, 21.1, 24.1, 25.4, 28.8, 29.9, 31.0, 31.8, 32.4, 34.8, 39.3, 39.8, 40.4, 42.2 (C-13), 42.6, 51.2, 51.3, 55.6, 56.9, 59.3, 65.7 (C-5), 68.7, 129.3 and 138.2 (C-22 and C-23).

*4.3.32. (22E)-5β,6β-Epoxystigmast-22-en-3β-ol (**17b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.66 (3H, s, 18-CH_3), 0.79 (3H, d, J=6.6 Hz, 26-CH_3), 0.80 (3H, t, J=6.6, 6.6 Hz, 24^2-CH_3), 0.84 (3H, d, J=6.6 Hz, 27-CH_3), 0.99 (3H, d, J=6.6 Hz, 21-CH_3), 1.00 (3H, s, 19-CH_3), 3.06 (1H, d, J=2.5 Hz, 6α-H), 3.70 (1H, m, 3α-H), 5.00 and 5.13 (each 1H, 2dd, J=15.2, 8.5 Hz, 22-H and 23-H).

*4.3.33. 4α,5α-Epoxycholestan-3-one (**18a**)*

Mp 121–123 °C (EtOH); lit.[44] 120–121 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.70 (3H, s, 18-CH_3), 0.86 and 0.87 (each 3H, 2d, J=6.5 Hz, 26-CH_3 and 27-CH_3), 0.91 (3H, d, J=6.5 Hz, 21-CH_3), 1.05 (3H, s, 19-CH_3), 3.04 (1H, s, 4β-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 12.0, 16.5, 18.6, 21.4, 22.5, 22.8, 23.8, 24.2, 28.0, 28.1, 28.9, 28.9, 29.1, 33.1, 35.4, 35.8, 36.1, 36.7 (C-10), 39.5, 39.7, 42.5 (C-13), 50.7, 55.6, 56.2, 62.9 (C-4), 70.2 (C-5), 207.1 (C-3).

*4.3.34. 4β,5β-Epoxycholestan-3-one (**18b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.68 (3H, s, 18-CH_3), 0.86 and 0.87 (each 3H, 2d, J=6.5 Hz, 26-CH_3 and 27-CH_3), 0.90 (3H, d, J=6.5 Hz, 21-CH_3), 1.15 (3H, s, 19-CH_3), 2.98 (1H, s, 4α-H).

*4.3.35. 4α,5α-Epoxypregnane-3,20-dione (**19a**)*

Mp 178–179 °C (EtOH); lit.[28] 177–178 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.65 (3H, s, 18-CH_3), 1.05 (3H, s, 19-CH_3), 2.12 (3H, s, 21-CH_3), 3.04 (1H, s, 4β-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 13.3, 16.5, 21.4, 22.8, 24.4, 28.8, 29.1, 29.6, 31.5, 33.0, 35.3, 36.7 (C-10), 38.7, 44.0 (C-13), 50.5, 55.8, 62.8, 63.6, 70.0 (C-5), 206.9 (C=O), 209.5 (C=O).

*4.3.36. 4β,5β-Epoxypregnane-3,20-dione (**19b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.64 (3H, s, 18-CH_3), 1.15 (3H, s, 19-CH_3), 2.12 (3H, s, 21-CH_3), 2.99 (1H, s, 4α-H).

*4.3.37. 4α,5α-Epoxy-17β-hydroxy-androstan-3-one (**20a**)*

Mp 169–170 °C (EtOH); lit.[28] 169–171 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.78 (3H, s, 18-CH_3), 1.07 (3H, s, 19-CH_3), 3.04 (1H, s, 4β-H), 3.67 (1H, t, J=8.5, 8.5 Hz, 17α-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 11.0, 16.5, 21.0, 23.3, 28.5, 29.1, 29.6, 30.4, 33.1, 35.4, 36.4, 36.7 (C-10), 42.9 (C-13), 50.2, 50.8, 62.8, 70.1 (C-5), 81.6, 207.0 (C=O).

*4.3.38. 4β,5β-Epoxy-17β-hydroxy-androstan-3-one (**20b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.77 (3H, s, 18-CH_3), 1.16 (3H, s, 19-CH_3), 2.98 (1H, s, 4β-H), 3.67 (1H, t, J=8.5, 8.5 Hz, 17α-H).

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