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# Synthesis of deoxycholic-derived chiral stationary phases possessing both arylcarbamate and arylamide moieties: evaluation of their chiral discrimination properties in the HPLC resolution of racemic compounds†

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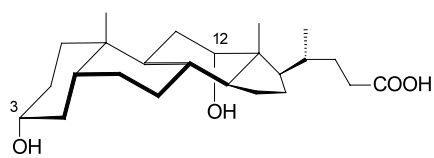
**Abstract**—Two families of chiral selectors derived from deoxycholic acid, possessing both an arylamide and an arylcarbamate group on the cholestanic backbone were synthesized and covalently bonded to silica gel to afford new chiral stationary phases (CSPs **A1**–**D1** and **A2**–**D2**) for the HPLC resolution of racemic compounds. The chromatographic data concerning the resolution of selected racemic compounds on CSPs **A1**–**D1** and **A2**–**D2** were compared with those obtained using analogous CSPs possessing only arylcarbamate groups on the cholestanic system (CSPs **A**–**D**). This has allowed us to establish that the resolution capability of CSPs **A1**–**D1** and **A2**–**D2** depends not only on the position of the arylamide group on the cholestanic backbone, but also on the electronic characteristics of the aromatic substituents. 

## 1. Introduction

Chiral natural products represent a very attractive class of compounds for use in the field of chiral recognition. Their molecular structure, endowed with a variety of functional groups and multiple stereogenic centers, gives them interesting enantiodiscrimination properties. The presence of reactive groups allows further derivatizations to be performed, affording new materials, whose properties depend on the nature of the newly introduced moieties. Exploiting these features, a variety of natural products have been suitably derivatized and linked to silica gel to give chiral stationary phases (CSPs) for the chromatographic resolution of racemic compounds: tartaric acid derivatives,[1] cinchona alkaloids,[2] ergot alkaloids,[3] derivatized polysaccharides[4] and glycopeptide antibiotics[5] have been successfully used in enantioselective HPLC.

Among natural products, bile acids have been widely employed as chiral auxiliaries in various molecular recognition processes. Their success lies in the presence of hydroxyl groups on the cholestanic backbone having different reactivity because of their different steric environment; this feature allows derivatization with different molecular units to be performed. Molecular tweezers,[6] supramolecular receptors,[7] chiral auxiliaries for asymmetric reactions,[8] chiral stationary phases[9] have been prepared starting from bile acids. We have recently directed our attention towards the use of deoxycholic acid **1** (Fig. 1) for preparing new chiral stationary phases for the HPLC resolution of racemic compounds.[9b] By derivatizing the hydroxyl groups of **1** with 3,5-dichlorophenylisocyanate and 3,5-dimethylphenylisocyanate and using the carboxylic




**1**

**Figure 1.** Structure of the deoxycholic acid.

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† Dedicated to Professor Luciano Lardicci on the occasion of his 75th birthday.

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group for linking the chiral selectors to silica gel, four CSPs have been obtained, two homoderivatized (A and B) and two heteroderivatized (C and D) (Fig. 2).[9b] These CSPs have proven to be effective in the resolution of various racemic compounds, depending not only on the nature of the derivatizing aromatic groups, but also on their arrangement on the cholestanic skeleton.[9b]

The enantiodiscrimination properties exhibited by these CSPs prompted us to search for other derivatives of deoxycholic acid for use as chiral selectors in enantioselective HPLC. We decided to synthesize analogues of CSPs **A**–**D** where one of the two arylcarbamate moieties has been replaced with an arylamide group, in order to assess the influence of this structural change on the enantiorecognition properties of this class of chiral selector. Two new families of CSPs based on amino analogues of deoxycholic acid were prepared to this end: the former possessing an arylamide group at C(3) of the cholestanic skeleton, the latter with an arylamide moiety at the C(12) of **1**. Furthermore, in order to compare the efficiency of the new CSPs to that of CSPs **A**–**D**, two homoderivatized and two heteroderivatized selectors must be prepared for each family. We present herein the synthesis of eight new CSPs, which differ from the CSPs **A**–**D** because they possess an arylamide moiety and an arylcarbamate group, the evaluation of their enantiodiscrimination properties in the HPLC resolution of selected racemic compounds and the comparison with CSPs **A**–**D**, in order to establish the effect of replacement of a carbamate moiety with an amide group on the enantioselectivity of these chiral selectors.

## 2. Results and discussion

### 2.1. Synthesis of the CSPs A1–D1 and A2–D2

The synthetic route to the selectors having a carbamate group at C(12) and an arylamide moiety at the C(3) of the cholestanic system is summarized in Scheme 1.

The carboxylic function of **1** was firstly converted to its methyl ester.[10] In order to introduce an amino group at C(3) of the cholestanic system with retention of configuration at this stereogenic center, the hydroxyl function was reacted under Mitsunobu conditions[11] to afford the mesylate **3**, followed by nucleophilic displacement with sodium azide[11] and reduction of the azido group by hydrogenation over Pd/C. The less reactive hydroxyl group at C(12) does not react under these experimental conditions[11] and the amino derivative **5** was obtained in 63% overall yield from **2**. The reaction of **5** with 3,5-dimethylbenzoyl chloride and 3,5-dichlorobenzoyl chloride in the presence of triethylamine afforded the amides **6a** and **6b**, respectively. The free carboxylic acids **7a**–**7b**, obtained after hydrolysis of the ester function by means of LiOH,[6a] were treated with tributylamine and ethyl chloroformate and then with *N*-methylallylamine[12] to give the derivatives **8a**–**8b**. The use of *N*-methylallylamine as a reagent bearing a terminal double bond (which serves for linking the selectors to silica gel) represents a slight modification to the procedure used for obtaining CSPs **A**–**D**, where the allylamine was employed.[9b] This choice was made to avoid the formation of a by-product in the reaction of the arylisocyanate with the hydroxyl group at C(12), originating from the attack of the isocyanate on the amide nitrogen of the allylamide.[9b] In fact the reaction of **8a**–**8b** with the aryl isocyanates proceeds much better than in the case of allylamide derivatives,[9b] affording the selectors **9a**–**9d** in yields higher than 80%.

Scheme 2 illustrates the synthetic route to the selectors with an arylamide function at the C(12) and an aryl carbamate group at C(3) of the cholestanic backbone. Deoxycholic acid **1** was treated with methyl acetate in the presence of *p*-toluesulphonic acid and water[13] to afford 3-acetyl methyldeoxycholate **10**. The hydroxyl function of **10** was oxidized with potassium dichromate in acetic acid[14] to afford **11**, which was treated with hydroxylamine hydrochloride to afford the oxime[15] **12**. The hydrogenation of **12** in the presence of $PtO_2$, followed by treatment of the crude product with Zn in

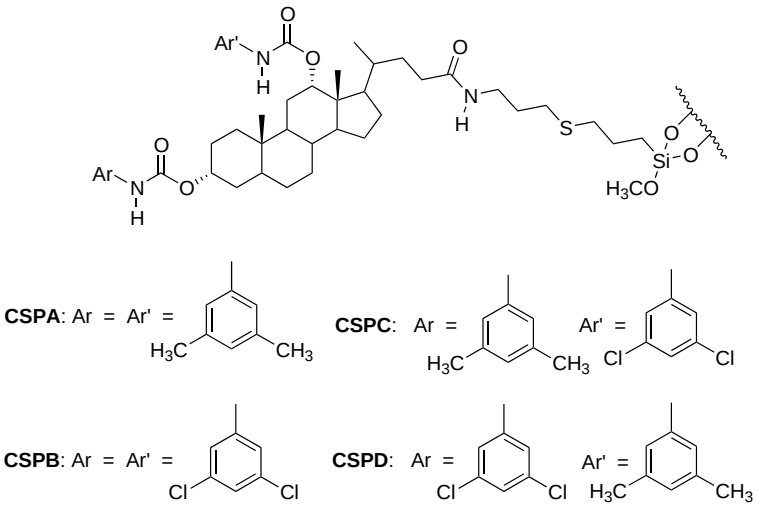
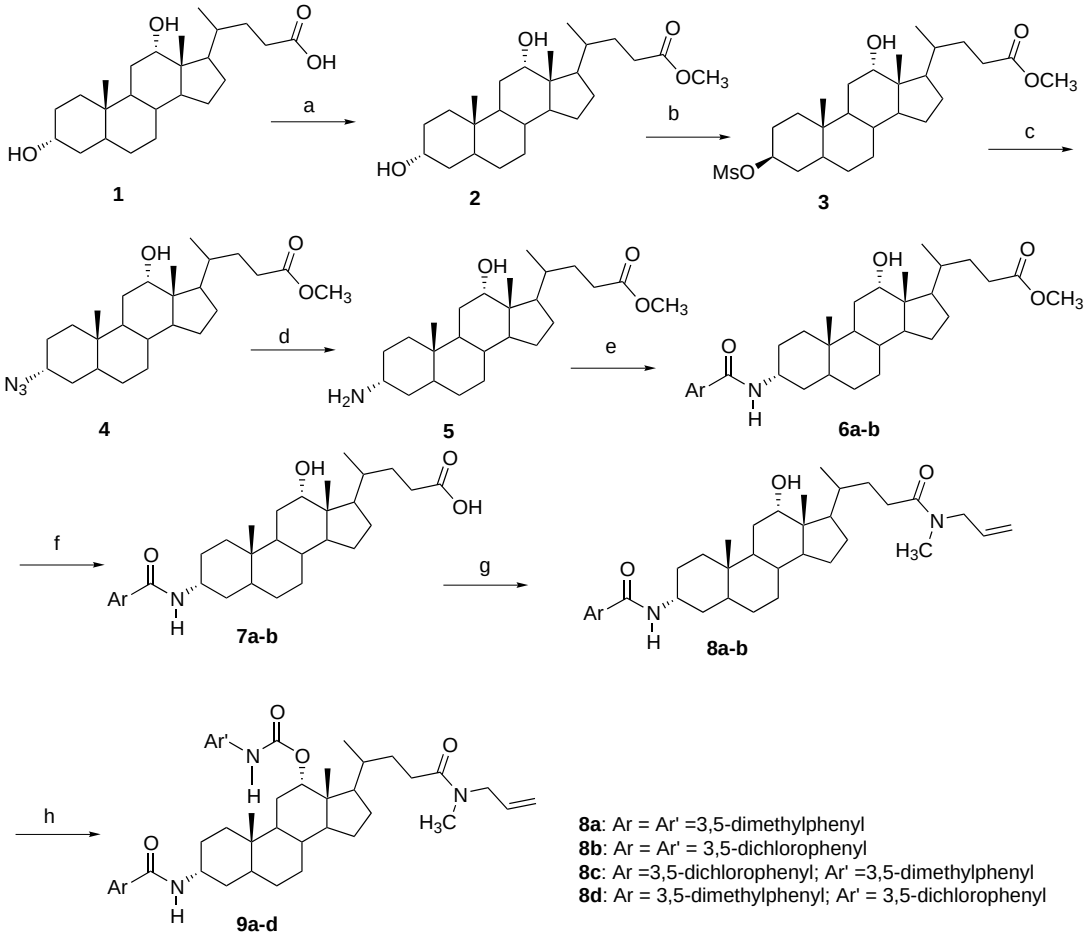



**Figure 2.** Structure of the CSPs **A**–**D**.




**Scheme 1.** *Reagents and conditions*: (a) HCl, $CH_3OH$; (b) $PPh_3$, DEAD, MsOH, THF, 40°C; (c) $NaN_3$, DMF, 40°C; (d) $H_2$, Pd/C AcOEt/$CH_3OH$, rt; (e) ArCOCl, $Et_3N$, TH, rt; (f) LiOH aq., $CH_3OH$, rt; (g) 1. $Bu_3N$, dioxan, 2. EtOCOCl, 10°C, 3. *N*-methylallylamine 10°C to rt; (h) Ar′NCO, toluene, reflux.

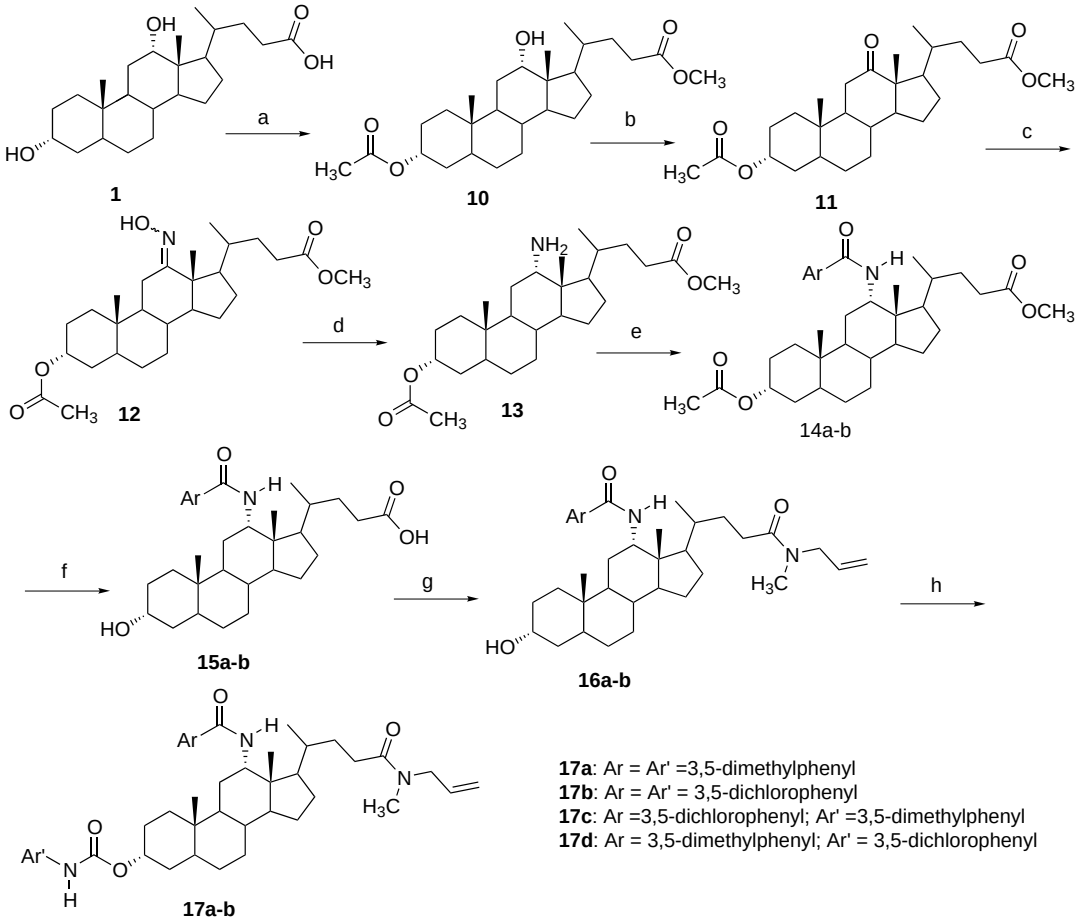
acetic acid[15] gave the diastereoisomerically pure amino derivative **13** in 67% overall yield from **1**. The amide derivatives **14a** and **14b** were obtained by treating **13** with 3,5-dimethylbenzoyl chloride and 3,5-dichlorobenzoyl chloride, respectively. The hydrolysis of the ester functions with LiOH in THF–methanol[6a] afforded the free acids **15a**–**15b**, which were converted to the corresponding *N*-methyl allylamides **16a**–**16b** by means of the mixed anhydride method.[12] Selectors **17a**–**17d** were obtained by reacting **16a**–**16b** with 3,5-dichlorophenyl isocyanate and 3,5-dimethylphenyl isocyanate. Because of the higher reactivity of the C(3) hydroxyl group, this reaction was carried out at room temperature in THF as a solvent, affording derivatives **17a**–**17d** in yields up to 80% after chromatographic purification.

Derivatives **9a**–**9d** and **17a**–**17d** were linked to silica gel as illustrated in Scheme 3. The reaction of the selectors with a five-fold excess of mercaptopropyltrimethoxysilane in the presence of a catalytic amount of AIBN[9b] afforded the corresponding silane derivatives **18a**–**18h** in quantitative yield. In fact, under these experimental conditions the substrate is fully converted to the corresponding silane derivative, which is separated from the excess mercaptopropyltrimethoxysilane simply by washing with pentane.[9b] The grafting to silica gel was carried out in refluxing toluene for 24 h and the derivatized silica, after thoroughly washing and drying, was employed for packing 15 cm stainless steel columns (internal diameter 4.6 mm). The amount of selector bonded to silica gel was determined by means of elemental analysis and was similar for all of the prepared CSPs.

### 2.2. Evaluation of the enantioresolution capability of CSPs A1–D1 and A2–D2 towards benzodiazepin-2-ones

Benzodiazepine derivatives **19a**–**19d** (Fig. 3) were selected as racemic compounds for testing the enantiodiscrimination properties of CSPs **A1**–**D1** and **A2**–**D2**. This choice is mainly due to the consideration that these analytes were well resolved by CSPs **A**–**D**, so that a comparison with this family of selectors can be made and, consequently, the effect of the structural modification on the enantiorecognition capability of the new selectors can be clearly evaluated.

Table 1 details the chromatographic data obtained using CSPs **A1**–**D1** in comparison with the data related to the use of CSPs **A**–**D**. The comparison is made between CSPs having the same aromatic substituent at



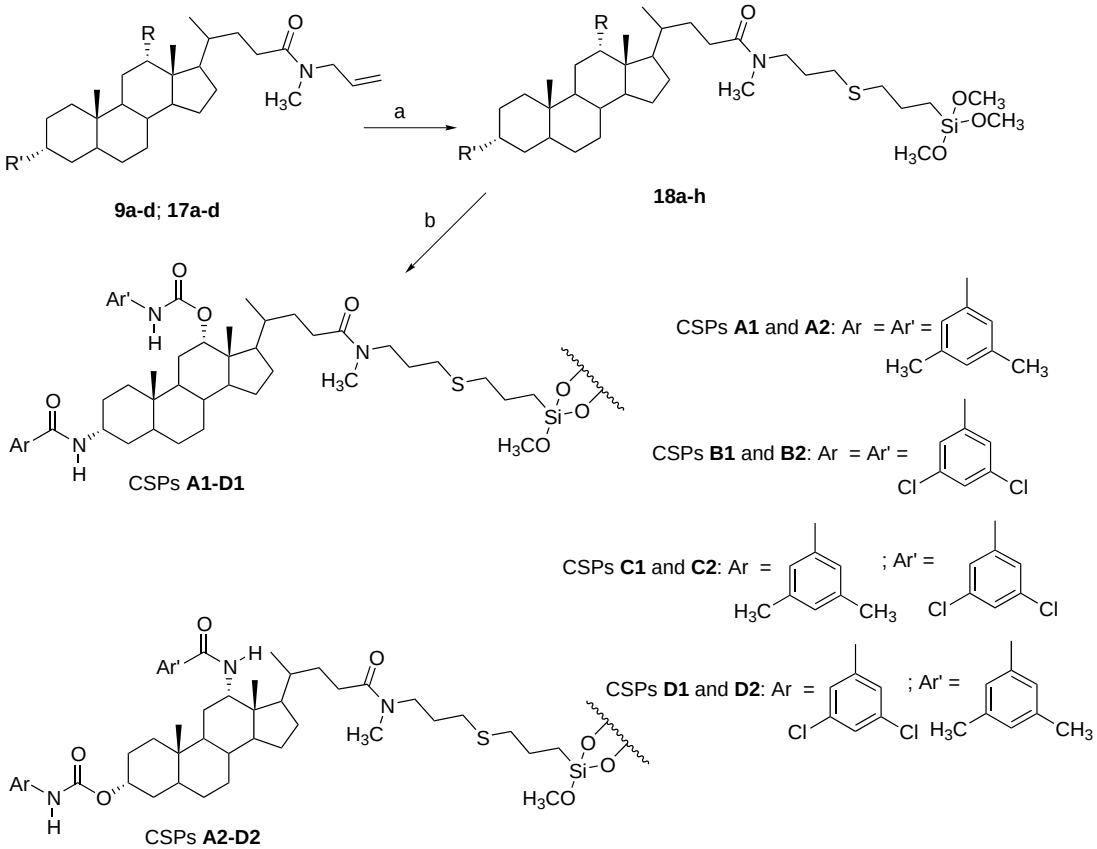

**Scheme 2.** *Reagents and conditions*: (a) AcOMe, TsOH, $H_2O$, reflux; (b) $K_2Cr_2O_7$, AcOH, rt; (c) $NH_2OH$, HCl, AcONa, MeOH, reflux; (d) 1. $H_2$, $PtO_2$, AcOH, 2. Zn, AcOH, rt; (e) Ar′COCl, $Et_3N$, THF; (f) LiOHaq, THF/MeOH; (g) 1. $Bu_3N$, dioxan, 2. EtOCOCl, 10°C, 3. *N*-methylallylamine 10°C to rt; (h) ArNCO, THF, DMAP, rt.

the same position of the cholestanic system. CSPs **A1**–**D1** retain the benzodiazepin-2-ones more than the corresponding CSPs **A**–**D** do: the $k'$ values obtained with this family of CSPs results higher in all the cases (Table 1). This suggests that the substitution of an aryl carbamate group with an aryl amide moiety at C(3) of the cholestanic system gives rise to stronger interactions with the racemic compounds. This property is independent of the nature of the aryl substituent linked to the amide moiety at position 3.

As far as the enantioselectivities are concerned, CSP **A1**, which possesses two 3,5-dimethylphenyl substituents, is capable of resolving only two benzodiazepin-2-ones, **19b** and **19c**, with the same $\alpha$ value as the corresponding CSP **A** in the case of **19c**, or lower in the case of **19b**. CSP **B1**, which has two 3,5-dichlorophenyl groups, behaves rather differently with respect to CSP **A1**. This CSP resolves all the benzodiazepin-2-ones with $\alpha$ values higher not only than those found for CSP **A1**, but also than those obtained using the corresponding CSP **B** in all cases (Table 1). The chromatographic separations obtained with CSP **B1** are very good (Fig. 4), in particular in the case of compound **19b**. CSP **C1**, which bears a 3,5-dimethylphenyl moiety at (C)3 and a 3,5-dichlorophenyl group at C(12), exhibits lower enantioselectivities than those of CSP **B1**. The $\alpha$ values are, however, comparable to those obtained using the corresponding CSP **C**; only in the case of **19a** the chromatographic resolution is worse than that observed on CSP **C**. CSP **D1**, in which the position of the aromatic groups is exchanged with respect to CSP **C1**, exhibits a resolution capability higher than the corresponding CSP **D**, but lower than that shown by CSP **B1**.

Although CSPs **A1**–**D1** show differences in the chromatographic resolution of **9a**–**9d** with respect to the corresponding CSPs **A**–**D**, the trend of the $\alpha$ values is the same in any case. In fact the better resolved benzodiazepin-2-one with all the phases examined is **19b**, whereas **19d** exhibits the lowest $\alpha$ value. The chromatographic data concerning the use of CSPs **A2**–**D2** are reported in Table 2, in comparison with those obtained with CSPs **A**–**D**. Also in this case, the comparison has been performed between analogous CSPs, i.e. those having the same aromatic groups in the same position of the cholestanic backbone.

CSPs **A2**–**D2** retain the benzodiazepin-2-ones more than the corresponding CSPs **A**–**D** (Table 2), thus behaving in the same way as CSPs **A1**–**D1** with respect




**Scheme 3.** *Reagents and conditions*: (a) 3-mercaptopropyltrimethoxysilane, $CHCl_3$, AIBN, reflux; (b) silica gel, toluene, reflux.

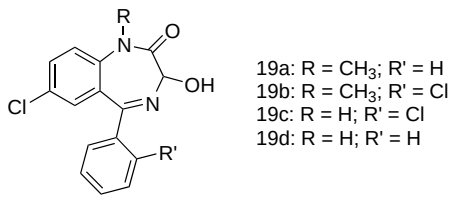



**Figure 3.** Structures of the benzodiazepin-2-ones checked on CSPs **A1**–**D1** and **A2**–**D2**.

to retention times. However, these phases show very different enantiodiscrimination behavior with respect to CSPs **A1**–**D1**. CSP **A2**, which possesses two 3,5-dimethylphenyl moieties, does not resolve any benzodiazepine derivative: this phase, therefore, performs less well than not only the analogous CSP **A**, but also than CSP **A1**, which differs in the position where the amide group is placed. CSP **B2**, having two 3,5-dichlorophenyl moieties, separates the enantiomers of **19a**–**19c**, whereas it does not resolve **19d**. The $\alpha$ values

**Table 1.** Chromatographic resolution[a] of **19a**–**19d** on CSPs **A**–**D** and **A1**–**D1**

| | FSC **A1** *FSC A* | | FSC **B1** *FSC B* | | FSC **C1** *FSC C* | | FSC **D1** *FSC D* | |
|---|---|---|---|---|---|---|---|---|
| Compound | $k'$[b] | $\alpha$[c] (e.o.)[d] | $k'$[b] | $\alpha$[c] (e.o.)[d] | $k'$[b] | $\alpha$[c] (e.o.)[d] | $k'$[b] | $\alpha$[c] (e.o.)[d] |
| **19a** | 2.02 | 1.00 | 3.18 | 2.00 (−) | 1.95 | 1.13 (−) | 1.93 | 1.48 (−) |
| | *1.06* | *1.31 (−)* | *1.99* | *1.40 (−)* | *1.59* | *1.21 (−)* | *1.65* | *1.47 (−)* |
| **19b** | 2.01 | 1.25 (−) | 3.22 | 2.67 (−) | 2.35 | 1.39 (−) | 2.03 | 2.04 (−) |
| | *1.08* | *1.43 (−)* | *1.98* | *1.69 (−)* | *1.65* | *1.37 (−)* | *1.67* | *1.77 (−)* |
| **19c** | 8.51 | 1.16 (−) | 9.25 | 1.71 (−) | 10.58 | 1.12 (−) | 7.69 | 1.57 (−) |
| | *3.84* | *1.16 (−)* | *4.93* | *1.27 (−)* | *5.28* | *1.11 (−)* | *4.89* | *1.30 (−)* |
| **19d** | 8.08 | 1.00 | 8.08 | 1.51 (−) | 10.39 | 1.00 | 7.97 | 1.41 (−) |
| | *4.09* | *1.11 (−)* | *5.25* | *1.17 (−)* | *5.86* | *1.03 (−)* | *5.03* | *1.21 (−)* |

[a] Chromatographic conditions: UV detection ($\lambda$=254 nm), flow 1 mL/min, eluent hexane–dichloromethane–propan-2-ol 70:30:3, $T$=25°C.
[b] Retention factor of the first eluted enantiomer.
[c] Enantioselectivity factor.
[d] Sign of the circular dichroism at 254 nm of the first eluted enantiomer.

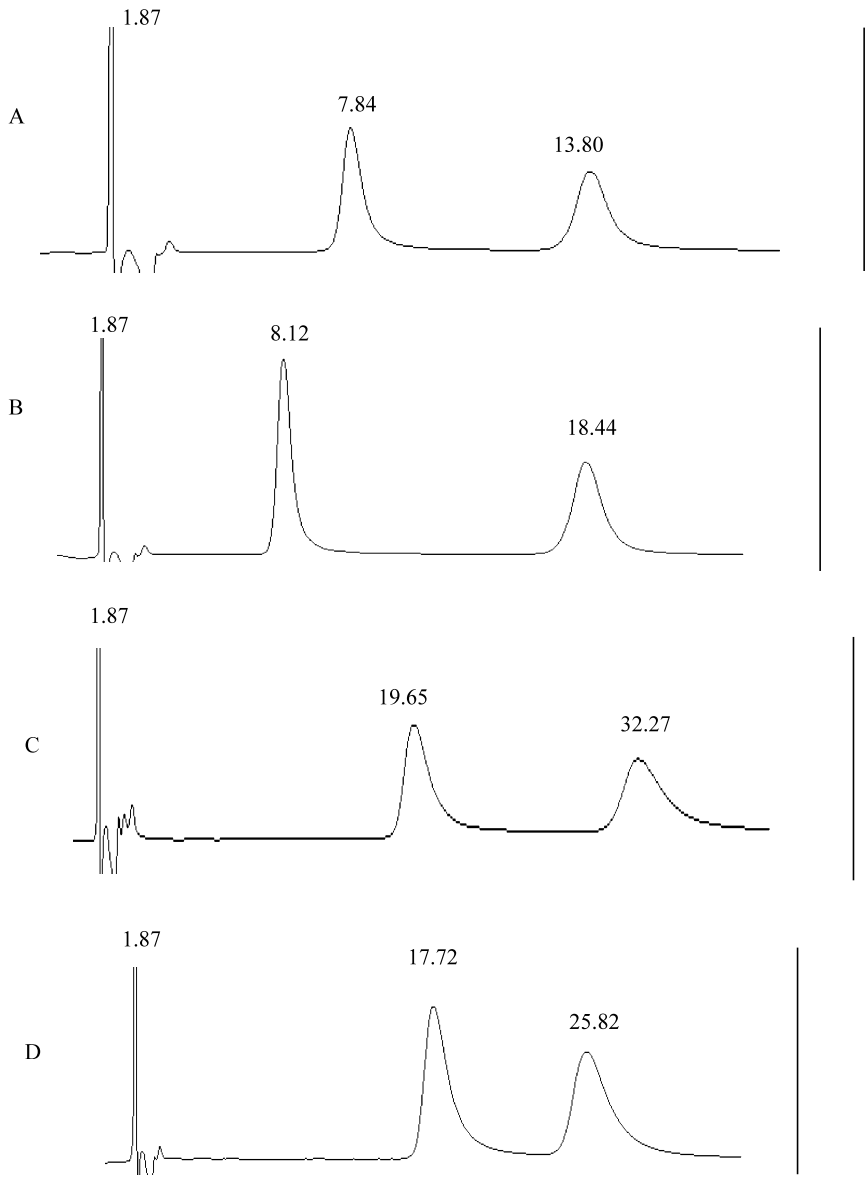



**Figure 4.** Chromatographic separations upon CSP B1 of: (A) **19a**; (B) **19b**; (C) **19c**; (D) **19d**. For chromatographic conditions see Table 1.

**Table 2.** Chromatographic resolution[a] of **19a–d** on CSPs **A–D** and **A2–D2**

| | FSC **A2** *FSC A* | | FSC **B2** *FSC B* | | FSC **C2** *FSC C* | | FSC **D2** *FSC D* | |
|---|---|---|---|---|---|---|---|---|
| Compound | $k'^{b}$ | $\alpha^{c}$ (e.o.)[d] | $k'^{b}$ | $\alpha^{c}$ (e.o.)[d] | $k'^{b}$ | $\alpha^{c}$ (e.o.)[d] | $k'^{b}$ | $\alpha^{c}$ (e.o.)[d] |
| **19a** | 2.09 | 1.00 | 2.89 | 1.39 (−) | 2.51 | 1.24 (−) | 2.34 | 1.00 |
| | *1.06* | *1.31 (−)* | *1.99* | *1.40 (−)* | *1.59* | *1.21 (−)* | *1.65* | *1.47 (−)* |
| **19b** | 2.15 | 1.00 | 2.83 | 2.28 (−) | 2.37 | 1.28 (−) | 2.32 | 1.17 (−) |
| | *1.08* | *1.43 (−)* | *1.98* | *1.69 (−)* | *1.65* | *1.37 (−)* | *1.67* | *1.77 (−)* |
| **19c** | 11.73 | 1.00 | 10.13 | 1.33 (−) | 9.41 | 1.00 | 10.41 | 1.00 |
| | *3.84* | *1.16 (−)* | *4.93* | *1.27 (−)* | *5.28* | *1.11 (−)* | *4.89* | *1.30 (−)* |
| **19d** | 13.00 | 1.00 | 11.28 | 1.00 (−) | 10.35 | 1.00 | 10.31 | 1.00 |
| | *4.09* | *1.11 (−)* | *5.25* | *1.17 (−)* | *5.86* | *1.03 (−)* | *5.03* | *1.21 (−)* |

[a] Chromatographic conditions: UV detection ($\lambda = 254$ nm), flow 1 mL/min, eluent hexane–dichloromethane–propan-2-ol 70:30:3, $T = 25$°C.
[b] Retention factor of the first eluted enantiomer.
[c] Enantioselectivity factor.
[d] Sign of the circular dichroism at 254 nm of the first eluted enantiomer.

are comparable to those found using CSP **B**, as far as **19a** and **19c** are concerned. On the contrary, compound **19b** is better resolved by CSP **B2** than by the analogous phase **B**. The heteroderivatized CSP **C2**, which presents a 3,5-dimethylphenyl group at C(12) and a 3,5-dichlorophenyl moiety at C(3) of the cholestanic system, shows similar enantioselectivity to CSP **C** toward **19a**, whereas **19b** is resolved with a slightly lower $\alpha$ value. This phase does not separate the enantiomers of benzodiazepin-2-ones **19c** and **19d**.

The other heteroderivatized phase, CSP **D2**, in which the position of the two different aromatic substituents is exchanged with respect to CSP **C2**, resolves only compound **19b** with enantioselectivity lower than that observed for the separation of the enantiomers of the same derivative upon the corresponding CSP **D**. It is of note that the heteroderivatized CSPs **C2** and **D2** show different behavior with respect the other two pairs of heteroderivatized CSPs **C**–**D** and **C1**–**D1**. In fact, the CSP obtained starting from the selector possessing a 3,5-dichlorophenyl group at C(3) and a 3,5-dimethylphenyl moiety at C(12) of the cholestanic system is the most enantioselective between the two heteroderivatized phases either for the couple **C**–**D** or for the couple **C1**–**D1**. On the contrary, CSP **D2**, possessing the same aromatic groups at the same positions of the cholestanic system as CSPs **D** and **D1**, gave lower enantioselectivity than the other heteroderivatized CSP **C2**. However, in the case of CSPs **A2**–**D2**, the best enantiodiscrimination is still seen with **19b**, as observed with the other CSPs.

In order to establish whether the differences in the enantiodiscrimination properties of CSPs **A1**–**D1** and **A2**–**D2** (with respect to CSPs **A**–**D**) are attributable to a change in the enantiorecognition mechanism due to the replacement of an aryl carbamate moiety with an aryl amide group, the elution orders of **19a**–**19d** on every CSP was determined. If the elution order of a racemic compound is the same on two different CSPs, as for example **A1** and **B1**, then the two CSPs form the most stable diastereoisomeric adsorbate with the same enantiomer of the eluted compound; in other words, the enantiorecognition mechanism exhibited by the two phases should not differ to a large extent. The elution orders were determined by means of a CD detector and are reported in the tables. They are the same for all the compounds upon all the phases, suggesting that the enantiorecognition mechanism responsible of the resolution of these analytes must be similar for all of the deoxycholic based CSPs **A**–**D**, **A1**–**D1**, **A2**–**D2**.

## 3. Conclusions

In summary, the replacement of an aryl carbamate group of deoxycholic-derived CSPs with an aryl amide moiety affords CSPs whose enantiodiscriminating capability depends not only on the position where the aryl amide is on the cholestanic system, but also on the nature of the aryl substituents. The replacement of an aryl carbamate group with an aryl amide moiety at C(3) of the cholestanic system affords CSPs that exhibit higher enantioselectivities when the aryl substituent of the amide is 3,5-dichlorophenyl, independently of the nature of the other aryl substituent. The presence of an aryl amide moiety at C(12) of the cholestanic backbone instead of an aryl carbamate group lowers the enantioresolution capability of this class of chromatographic selectors.

## 4. Experimental

### 4.1. General

$^1$H and $^{13}$C NMR spectra were recorded in $CDCl_3$ on a Varian Gemini-200 200 MHz NMR spectrometer, using TMS as external standard. The following abbreviations are used: s = singlet, d = doublet, dd = double doublet, t = triplet, m = multiplet, br = broad. TLC analysis was performed on silica gel 60 Macherey–Nagel sheets; flash chromatography separations were carried out on adequate dimension columns using silica gel 60 (230–400 mesh). HPLC analyses were performed on a JASCO PU-980 intelligent HPLC pump equipped with a JASCO UV-975 detector. Optical rotations were measured with a JASCO DIP-360 digital polarimeter. Melting points were taken using a Kofler Reichert–Jung apparatus and are uncorrected. IR spectra were recorded on a Perkin–Elmer 1710 spectrophotometer. Toluene, THF and dioxane were refluxed over sodium–benzophenone and distilled directly before the use. *N*-Methylallylamine and tributylamine were distilled over $CaH_2$. Unless otherwise specified the reagents were used without any purification. Methyl deoxycholate[10] **2** and methyl 3α-acetyloxy-12α-hydroxy-5β-cholan-24-oate,[13] **10**, were obtained according to literature procedures.

### 4.2. Methyl 3β-mesyloxy-12α-hydroxy-5β-cholan-24-oate 3

Methanesulphonic acid (2.85 mL, 0.044 mol) was added to a solution of **2** (8.50 g, 0.021 mol) and triphenylphosphine (16.40 g, 0.063 mol) in dry THF (70 mL). The solution was warmed to 40°C and DEAD (9.75 mL, 0.063 mol) was added dropwise with stirring. The reaction mixture was stirred at 40°C for 24 h. After the solvent was removed under vacuum, the crude product was purified by flash chromatography ($SiO_2$, $CH_2Cl_2$:acetone 92:8) affording **3** (9.3 g, impurities are also detectable). $^1$H NMR (200 MHz, $CDCl_3$, $\delta$): 0.70 (s, 3H, $CH_3$); 0.90 (s, 3H, $CH_3$); 0.95 (d, 3H, 21-$CH_3$); 1.00–2.00 (m, 23H, steroidal CH and $CH_2$, 12-OH); 2.00–2.50 (m, 4H); 3.00 (s, 3H, $CH_3SO_3$); 3.65 (s, 3H, $CH_3OCO$); 4.00 (m, 1H, 12-CH); 5.05 (m, 1H, 3-CH).

### 4.3. Methyl 3α-azido-12α-hydroxy-5β-cholan-24-oate 4

$NaN_3$ (8.96 g, 0.140 mol) was added to a solution of **3** (9.2 g, 0.019 mol) in dry DMF and the mixture was stirred at 40°C for 48 h. The reaction mixture was then poured into water, the organic product extracted with diethyl ether (4×80 mL) and the organic solution dried over anhydrous $NaS_2O_4$. The solvent was removed at reduced pressure and the crude product was purified by flash chromatography ($SiO_2$, $CH_2Cl_2$:acetone 93:7) affording **4** (5.8 g, 0.014 mol) in 64% yield from **2**. $[\alpha]_D^{21}$

+55.5 ($c=1.00$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.70 (s, 3H, $CH_3$); 0.90 (s, 3H, $CH_3$); 1.00 (d, 3H, 21-$CH_3$); 1.00–2.00 (m, 25H, steroidal CH and $CH_2$, 12-OH); 2.15–2.50 (m, 2H); 3.35 (m, 1H, 3-CH); 3.65 (s, 3H, $CH_3OCO$); 4.0 (m, 1H, 12-CH). $^{13}C$ NMR (50 MHz, $CDCl_3$, $\delta$): 12.7, 17.3, 23.2, 23.6, 26.0, 26.7, 27.0, 27.4, 28.7, 30.7, 31.0, 32.4, 33.7, 35.0, 35.4, 36.0, 42.4, 46.5, 47.3, 48.2, 51.5 ($OCH_3$), 61.2 (C3), 73.0 (C12), 174.0 (C=O). IR (KBr, $cm^{-1}$): 3513, 3913, 2940, 2899, 2861, 2027, 1719, 1445, 1380, 1362, 1260, 1241, 1212, 1049, 986, 970, 908.

### 4.4. Methyl 3α-amino-12α-hydroxy-5β-cholan-24-oate 5

A solution of **4** (5.70 g, 0.013 mol) in a 1:2 mixture of ethyl acetate:methanol (60 mL) containing Pd/C (0.57 g) was stirred under hydrogen pressure ($P$ 8.5 atm) at room temperature for 24 h at room temperature. After removing the catalyst by filtration and the solvent by evaporation under vacuum, chemically pure **5** (5.25 g, 0.013 mol) was obtained in quantitative yield. Mp 48–51°C. $[\alpha]_D^{22}$ +40.3 ($c=1.00$, EtOH). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.65 (s, 3H, $CH_3$); 0.90 (s, 3H, $CH_3$); 0.95 (d, 3H, 21-$CH_3$); 1.00–2.00 (m, 27H, steroidal CH and $CH_2$, 12-OH and $NH_2$); 2.00–2.50 (m, 2H); 2.65 (m, 1H, 3-CH); 3.65 (s, 3H, $CH_3OCO$); 3.95 (m, 1H, 12-CH). $^{13}C$ NMR (50 MHz, $CDCl_3$, $\delta$): 12.7, 17.3, 21.2, 23.4, 23.6, 26.1, 27.1, 27.2, 27.4, 28.7, 30.8, 31.0, 33.7, 34.1, 35.1, 36.1, 37.4, 37.5, 42.5, 46.5, 47.3, 48.2, 51.4 ($OCH_3$), 58.4 (C3), 73.1 (C12), 174.7 (C=O). IR (KBr, $cm^{-1}$): 3420, 2934, 2862, 2362, 2170, 1740, 1653, 1590, 1448, 1376, 1256, 1169, 1097, 1037, 942, 854, 801, 582.

### 4.5. Methyl 3α-*N*-aroylamino-12α-hydroxy-5β-cholan-24-oate: general procedure

Triethylamine (8.13 mmol) and **5** (7.39 mmol) were dissolved in dry THF (40 mL). The solution was cooled to 0°C and the aroyl chloride (8.13 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 4 h. The solvent was removed at reduced pressure, the residue was dissolved in $CH_2Cl_2$ and the organic phase washed with 10% HCl (1×20 mL), 10% $NaHCO_3$ (2×20 mL) and water (2×20 mL), then dried ($Na_2SO_4$). The solvent was evaporated in vacuo and the crude product was purified by flash chromatography ($SiO_2$, $CH_2Cl_2$:acetone 95:5).

**4.5.1. Methyl 3α-*N*-3,5-dimethylbenzoyl)amino-12α-hydroxy-5β-cholan-24-oate 6a**. Yield 2.70 g, 68%. Mp 156–158°C. $[\alpha]_D^{22}$ +61.8 ($c=1.01$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.70 (s, 3H, $CH_3$); 0.95 (s, 3H, $CH_3$); 1.00 (d, 3H, 21-$CH_3$); 1.00–2.00 (m, 24H, steroidal CH and $CH_2$, OH); 2.20–2.50 (m, 2H); 2.40 (s, 6H, benzylic $CH_3$); 3.70 (s, 3H, $CH_3OCO$); 4.00 (m, 2H, 3-CH and 12-CH); 6.00 (d 1H, NH); 7.10 (s, 1H, $H_a$); 7.40 (s, 2H, $H_b$). $^{13}C$ NMR (200 MHz, $CDCl_3$, $\delta$): 12.8, 17.4, 21.2 (benzylic $CH_3$), 23.3, 23.6, 26.2, 26.9, 27.5, 28.0, 28.7, 31.0, 31.1, 33.7, 34.1, 35.0, 35.8, 36.0, 42.4, 46.6, 47.5, 48.5, 49.6 (C3), 51.5 ($OCH_3$), 73.3 (C12), 124.6, 132.8, 135.0, 138.2 (aromatics), 167.0 (amide C=O), 174.6 (ester C=O). IR (KBr, $cm^{-1}$): 3410, 2938, 2864, 1741, 1630, 1601, 1530, 1466, 1458, 1447, 1438, 1378, 1329, 1301, 1261, 1244, 1193, 1169, 1100, 1066, 1053, 1036, 970, 945, 862, 767, 687.

**4.5.2. Methyl 3α-*N*-3,5-dichlorobenzoyl)amino-12β-hydroxy-5β-cholan-24-oate 6b**. Yield 3.30 g, 5.70 mmol. Mp 173–175°C. $[\alpha]_D^{22}$ +46.7 ($c=0.54$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.70 (s, 3H, 18-$CH_3$); 0.90 (s+d, 6H, 19-$CH_3$ and 21-$CH_3$); 1.00–2.00 (m, 24H, steroidal CH and $CH_2$, 12-OH); 2.10–2.40 (m, 4H); 3.60 (s, 3H, $CH_3OCO$); 4.00 (m, 2H, 3-CH and 12-CH); 6.85 (d, 1H, amide NH); 7.40 (t, 1H, $H_a$); 7.75 (d, 2H, $H_b$). $^{13}C$ NMR (50 MHz, $CDCl_3$, $\delta$): 12.5, 17.2, 23.0, 23.5, 25.9, 26.8, 27.3, 28.3, 30.7, 31.0, 33.1, 33.5, 33.9, 34.9, 35.6, 35.7, 42.2, 43.5, 47.0, 47.2, 48.2, 50.1 (C3), 51.4 ($OCH_3$), 73.1 (C12), 125.8, 130.8, 135.1, 137.7 (aromatics), 164.1 (amide C=O), 174.5 (ester C=O). IR (KBr, $cm^{-1}$): 3510, 3328, 3068, 2938, 2862, 1741, 1640, 1566, 1541, 1472, 1465, 1458, 1448, 1437, 1378, 1327, 1290, 1252, 1192, 1169, 1098, 1033, 867.

### 4.6. Methyl 3α-acetyloxy-12-keto-5β-cholan-24-oate 11

A solution of $K_2Cr_2O_7$ (11.91 g, 0.040 mol) in water (22 mL) was added to a solution of **10** (17 g, 0.038 mol) in acetic acid (280 mL). The mixture was stirred at room temperature for 20 h, then poured into water (500 mL): the solid was filtered, washed with water then dried under vacuum affording chemically pure **11** (16.08 g, 0.036 mol) in 95% yield. Mp 150–152°C. $[\alpha]_D^{25}$ +54.8 ($c=1.00$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.80 (d, 3H, 21-$CH_3$); 1.00 (s, 6H, $CH_3$); 1.00–1.90 (m, 22H, steroidal CH and $CH_2$); 1.98 (s, 3H, $CH_3CO$); 2.30 (m, 4H); 3.60 (s, 3H, $CH_3OCO$); 4.65 (m, 1H, 3-CH). $^{13}C$ NMR (50 MHz, $CDCl_3$, $\delta$): 11.6, 15.5, 21.3 ($CH_3CO$), 22.7, 24.3, 26.0, 26.3, 26.9, 27.4, 30.4, 31.2, 32.1, 35.0, 35.3, 35.6, 38.0, 41.3, 44.0, 46.4, 52.0, 51.4 ($CH_3O$), 57.4, 58.6, 73.6 (C3), 170.5 (acetate C=O), 174.6 (24 C=O), 214.6 (carbonyl C=O). IR (KBr, $cm^{-1}$): 2953, 2869, 1733, 1699, 1466, 1448, 1437, 1382, 1361, 1330, 1317, 1244, 1210, 1030, 984, 881, 872, 629.

### 4.7. Methyl 3α-acetyloxy-12-oxime-5β-cholan-24-oate 12

Sodium acetate (15.43 g, 0.188 mol) and hydroxylamine hydrochloride (4.32 g, 0.062 mol) were added to a solution of **11** (15.00 g, 0.035 mol) in methanol (300 mL). The reaction mixture was stirred under reflux for 4.5 h. The solvent was removed under vacuum and the residue dissolved in $CH_2Cl_2$ (300 mL). The organic solution was washed with water (3×70 mL) then dried ($Na_2SO_4$). The solvent was evaporated under reduced pressure affording chemically pure **12** (15.0 g, 0.033 mol) in 94% yield. Mp 170–172°C. $[\alpha]_D^{25}$ +54.8 ($c=1.00$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.80 (s, 3H, $CH_3$); 0.85 (d, 3H, 21-$CH_3$); 1.00 (s, 3H, $CH_3$); 1.00–2.00 (m, 24H, steroidal CH and $CH_2$); 2.00 (s, 3H, $CH_3CO$); 2.25 (m, 2H); 3.60 (s, 3H, $CH_3OCO$); 4.65 (m, 1H, 3-CH). $^{13}C$ NMR (50 MHz, $CDCl_3$, $\delta$): 12.1, 19.1, 20.0, 21.4 ($CH_3CO$), 22.7, 24.1, 26.1, 26.34, 26.9, 27.9, 30.6, 31.5, 32.2, 35.1, 35.2, 35.6, 41.5, 47.0, 49.8, 51.4 ($CH_3O$), 59.2, 74.0 (C3), 167.0 (C=NOH), 170.6

($CH_3\underline{C}$=O); 174.8 (24 C=O). IR (KBr, $cm^{-1}$): 3460, 2960, 2880, 1737, 1718, 1646, 1450, 1380, 1360, 1245, 1190, 1170, 1105, 1070, 1030, 980, 940, 920, 890, 860, 800, 735, 670, 620, 610.

### 4.8. Methyl 3α-acetyloxy-12α-amino-5β-cholan-24-oate 13

Hydrated $PtO_2$ (0.924 g, 4.0 mmol) was added to a solution of **12** (14.8 g, 32.0 mmol) in acetic acid (35 mL) and the mixture was stirred under $H_2$ at room temperature for six days. The solid was filtered off and powdered Zn (17.1 g, 26.2 mmol) was added to the solution, concentrated under vacuum to 25 mL. The mixture was stirred at room temperature for 12 h, then the solid was filtered and washed with acetic acid. After evaporation of the solvent at reduced pressure, water (200 mL) was added and the aqueous solution made basic with KOH pellets. The organic product was extracted with ethyl acetate (4×70 mL) and the organic extracts dried ($Na_2SO_4$). The solvent was evaporated under vacuum affording **13** (12.9 g, 28.8 mmol) in 90% yield. Mp 132–135°C. $[\alpha]_D^{25}$ +59.16 ($c=1.00$, $CH_2Cl_2$). $^1$H NMR (200 MHz, $CDCl_3$, $\delta$): 0.60 (s, 3H, $CH_3$); 0.90 (s, 3H, $CH_3$); 1.00 (d, 3H, 21-$CH_3$); 1.05–1.09 (m, 26H, steroidal CH and $CH_2$, $NH_2$); 1.98 (s, 3H, $CH_3CO$); 2.25 (m, 2H); 3.10 (m, 1H, 12-CH); 3.60 (s, 3H, $CH_3OCO$); 4.70 (m, 1H, 3-CH). $^{13}$C NMR (50 MHz, $CDCl_3$, $\delta$): 13.8, 17.2, 21.5 ($CH_3CO$), 23.1, 23.8, 26.1, 26.6, 27.0, 27.7, 28.8, 31.0, 31.1, 32.2, 33.6, 34.2, 35.0, 35.2, 36.4, 41.9, 46.2, 47.9, 48.0, 51.5 ($CH_3O$), 54.1 (C12), 74.3 (C3), 170.4 (acetate C=O), 170.8 (24 C=O). IR (KBr, $cm^{-1}$): 2951, 2916, 2863, 1740, 1731, 1609, 1467, 1452, 1439, 1383, 1362, 1262, 1214, 1163, 1032.

### 4.9. Methyl 3α-acetyloxy-12α-*N*-aroylamino-5β-cholan-24-oate: general procedure

Triethylamine (19 mmol) and **13** (17.2 mmol) were dissolved in dry THF (50 mL). The solution was cooled to 0°C and the aroyl chloride (19 mmol) dissolved in dry THF (4 mL) was dropwise added, then the reaction mixture was stirred at room temperature for 4 h. The solvent was removed at reduced pressure, the residue dissolved in $CH_2Cl_2$ (300 mL) and the organic phase washed with 10% HCl (1×20 mL), 10% $NaHCO_3$ (2×20 mL) and water (2×20 mL), then dried ($Na_2SO_4$). The solvent was evaporated in vacuo and the crude product was purified by flash chromatography ($SiO_2$, $CH_2Cl_2$:acetone 97:3).

**4.9.1. Methyl 3α-acetyloxy-12α-*N*-(3,5-dimethylbenzoyl)amino-5β-cholan-24-oate 14a**. Yield 9.2 g, 92%. Mp 65–68°C. $[\alpha]_D^{25}$ +75.76 ($c=1.13$, $CH_2Cl_2$). $^1$H NMR (200 MHz, $CDCl_3$, $\delta$): 0.85 (s, 3H, $CH_3$); 0.88 (d, 3H, 21-$CH_3$); 0.95 (s, 3H, $CH_3$); 1.00–2.50 (m, 24H, steroidal CH and $CH_2$); 1.95 (s, 3H, $CH_3CO$); 2.45 (s, 6H, benzylic $CH_3$); 3.60 (s, 3H, $CH_3OCO$); 4.45 (dt, 1H, 12-CH); 4.7 (m, 1H, 3-CH); 6.3 (d, 1H, amide NH); 7.10 (s, 1H, $H_a$); 7.3 (s, 2H, $H_b$). $^{13}$C NMR (50 MHz, $CDCl_3$, $\delta$): 13.9, 17.3, 21.3 ($\underline{C}H_3CO$), 21.4 (benzylic $CH_3$), 23.3, 23.8, 26.2, 26.6, 26.8, 27.4. 30.9, 31.0, 33.0, 34.2, 34.7, 34.9, 35.3, 36.0, 41.7, 44.8, 49.2, 51.4 ($CH_3O$), 52.4 (C3), 74.10 (C12), 124.5, 132.9, 138.5 (aromatics), 167.4 amide (C=O), 170.6 (acetate C=O), 174.6 (24 C=O). IR (KBr, $cm^{-1}$): 3380, 2951, 2868, 1736, 1718, 1662, 1654, 1641, 1604, 1508, 1448, 1382, 1362, 1260, 1242, 1167, 1096, 1026, 859, 801.

**4.9.2. Methyl 3α-acetyloxy-12α-*N*-(3,5-dichlorobenzoyl)amino-5β-cholan-24-oate 14b**. Yield 9.70 g, 91%. Mp 99–101°C. $[\alpha]_D^{22}$ +67.2 ($c=1.02$, $CH_2Cl_2$). $^1$H NMR (200 MHz, $CDCl_3$, $\delta$): 0.88 (d, 3H, 21-$CH_3$); 0.90 (s, 3H, $CH_3$); 0.95 (s, 3H, $CH_3$); 1.00–1.90 (m, 23H; steroidal CH and $CH_2$); 1.95 (s, 3H, $CH_3CO$); 2.10–2.40 (m, 2H); 3.60 (s, 3H, $CH_3OCO$); 4.45 (dt, $J=6$ Hz, 1H, 12-CH); 4.70 (m, 1H, 3-CH); 6.40 (d, $J=6$ Hz, 1H, amide NH); 7.40 (t, $J=2$ Hz, 1H, $H_a$); 7.60 (d, $J=2$ Hz, 2H, $H_b$). $^{13}$C NMR (50 MHz, $CDCl_3$, $\delta$): 13.9, 17.3, 21.3 ($\underline{C}H_3CO$), 21.4 23.2, 23.7, 25.9, 26.4, 26.6, 26.7, 27.3, 30.8, 31.0, 32.2, 34.1, 34.6, 34.9, 35.1, 35.9, 41.6, 44.7, 51.3 ($OCH_3$), 53.0 (C12), 73.8 (C3), 125.4, 131.2, 135.5, 138.4 (aromatics), 164.1 (CONH), 170.4 (acetate C=O), 174.3 (24 C=O). IR ( KBr, $cm^{-1}$): 3345, 3076, 2950, 2868, 1738, 1713, 1665, 1640, 1567, 1520, 1448, 1382, 1362, 1261, 1243, 1098, 1026, 864, 805, 760, 711, 667, 618.

### 4.10. Hydrolysis of the ester functions: general procedure

A 1.25 M solution of aqueous LiOH was added to a solution of **6** or **14** (1.45 mmol) in THF–methanol 1:2 (20 mL) and the mixture was stirred at room temperature for 5 h, then acidified with 10% aqueous HCl. The solvents were removed at reduced pressure and ethyl acetate (200 mL was added. The organic solution was washed with brine then dried ($Na_2SO_4$). The chemically pure products were obtained after evaporation of the solvent at reduced pressure.

**4.10.1. 3α-*N*-(3,5-Dimethylbenzoyl)amino-12α-hydroxy-5β-cholan-24-oic acid 7a**. Yield 740 mg, 98%. Mp 142–144°C. $[\alpha]_D^{24}$ +68.8 ($c=0.80$, acetone). $^1$H NMR (200 MHz, DMSO-$d_6$, $\delta$): 0.60 (s, 3H, $CH_3$); 0.90 (s, 3H, $CH_3$); 1.00 (d, 3H, 21-$CH_3$); 1.00–2.00 (m, 24H, steroidal CH and $CH_2$); 2.00–2.30 (m, 2H); 2.30 (s, 6H, benzylic $CH_3$);3.75 (m, 2H, 3-CH and 12-CH); 4.20 (br s, 1H, 12-OH); 7.10 (s, 1H, $H_a$); 7.50 (s, 2H, $H_b$); 8.20 (d, 1H, CONH). $^{13}$C NMR (50 MHz, DMSO-$d_6$, $\delta$): 12.5, 17.0, 20.9 (benzylic $CH_3$), 23.3, 23.6, 26.1, 27.0, 27.2, 27.3, 28.8, 30.6, 31.0, 32.7, 33.1, 34.0, 35.1, 35.8, 35.9, 42.3, 46.0, 46.2, 47.6, 49.2 (C3), 71.0 (C12), 125.0, 132.1, 134.8, 137.2 (aromatics), 165.5 (amide C=O), 174.4 (24 C=O). IR (KBr, $cm^{-1}$): 3379, 2937, 2864, 1709, 1636, 1601, 1534, 1466, 1458, 1448, 1377, 1333, 1299, 1262, 1241, 1243, 1182, 1047, 969, 945, 862, 804, 764, 685.

**4.10.2. 3α-*N*-(3,5-Dichlorobenzoyl)amino-12α-hydroxy-5β-cholan-24-oic acid 7b**. Yield 770 mg, 94%. Mp 163–166°C. $[\alpha]_D^{27}$ +96.2 ($c=1.01$, EtOH). $^1$H NMR (200 MHz, DMSO-$d_6$, $\delta$): 0.70 (d, 3H, 21-$CH_3$); 0.80 (s, 3H, $CH_3$); 0.90 (s, 3 H, $CH_3$); 1.00–2.00 (m, 24H, steroidal CH and $CH_2$); 2.10 (m, 2H); 3.40 (m, 1H, 3-CH); 4.25 (dt, 1H, 12-CH); 4.50 (br s, 1H, 12-OH); 7.80 (m, 3H,

aromatics); 8.30 (d, 1H, amide NH); 12.00 (br s, 1H, COOH). $^{13}$C NMR (50 MHz, DMSO-$d_6$, $\delta$): 13.6, 17.1, 23.1, 23.5, 25.7, 26.5, 27.0, 27.2, 30.1, 30.6, 30.8, 33.7, 33.9, 34.2, 34.3, 35.0, 36.1, 44.3, 48.0, 48.1, 53.2 (C12), 70.0 (C3), 125.1, 130.3, 134.2, 137.9 (aromatics), 162.3 (amide C=O), 174.9 (24 C=O). IR (KBr, cm$^{-1}$): 3448, 3358, 3078, 2948, 2868, 2661, 1741, 1705, 1634, 1567, 1516, 1448, 1364, 1262, 1202, 1167, 1099, 1046, 1031, 937, 909, 862, 807, 759, 710, 663, 620.

**4.10.3. 3α-Hydroxy-12α-*N*-(3,5-dimethylbenzoyl)amino-5β-cholan-24-oic acid 15a**. Yield 740 mg, 97%. Mp 173–175°C. $[\alpha]_D^{24}$ +70.5 ($c$=1.00, acetone). $^1$H NMR (200 MHz, DMSO-$d_6$, $\delta$): 0.75 (d, 3H, 21-$CH_3$); 0.80 (s, 3H, $CH_3$); 0.85 (s, 3H, $CH_3$); 0.80–2.10 (m, 24H, steroidal CH and $CH_2$); 2.10–2.6 (m, 2H); 2.30 (s, 6H, benzylic $CH_3$); 3.40 (m, 1H, 3-CH); 4.25 (dt, 1H, 12-CH); 4.50 (br s, 1H, 3-OH); 7.30 (s, 1H, $H_a$); 7.60 (s, 2H, $H_b$); 7.95 (d, 1H, amide NH); 12.00 (br s, 1H, COOH). $^{13}$C NMR (50 MHz, DMSO-$d_6$, $\delta$): 13.5, 17.0, 20.9 (benzylic $CH_3$), 23.0, 23.5, 25.6, 26.5, 27.0, 27.2, 30.0, 30.4, 30.6, 33.6, 33.8, 34.4, 35.6, 36.0, 41.7, 41.2, 47.7, 48.0, 49.7, 52.4 (C12), 70.9 (C12), 125.1, 130.3, 134.2, 137.9 (aromatics), 162.3 (amide C=O), 174.9 (24 C=O). IR (KBr, cm$^{-1}$): 3330, 2934, 2869, 1706, 1640, 1602, 1533, 1449, 1384, 1307, 1252, 1207, 1168, 1094, 1015, 939, 908, 855, 801, 680.

**4.10.4. 3α-Hydroxy-12α-*N*-(3,5-dichlorobenzoyl)amino-5β-cholan-24-oic acid 15b**. Yield 770 mg, 94%. Mp 163–166°C. $[\alpha]_D^{27}$ +96.2 ($c$=1.01, EtOH). $^1$H NMR (200 MHz, DMSO-$d_6$, $\delta$): o.70 (d, 3H, 21-$CH_3$); 0.80 (s, 3H, $CH_3$); 0.90 (s, 3H, $CH_3$); 1.00–2.00 (m, 24H, steroidal CH and $CH_2$); 2.10 (m, 2H); 3.40 (m, 1H, 3-CH); 4.25 (dt, 1H, 12-CH); 4.50 (br s, 1H, 3-OH); 7.80 (m, 3H, H aromatics); 8.30 (d, 1H, amide NH); 12.00 (br s, 1H, COOH). $^{13}$C NMR (200 MHz, DMSO-$d_6$, $\delta$): 13.6, 17.1, 23.1, 23.5, 25.7, 26.5, 27.0, 27.2, 30.1, 30.6, 30.8, 33.7, 33.9, 34.2, 34.3, 35.0, 36.1, 44.3, 48.0, 48.1, 53.2 (C12), 70.0 (C3), 125.1, 130.3, 134.), 137.9 (aromatics), 162.3 (amide C=O), 174.9 (24 C=O). IR (KBr, cm$^{-1}$): 3448, 3358, 3078, 2948, 2868, 2661, 1741, 1705, 1634, 1567, 1516, 1448, 1364, 1262, 1202, 1167, 1099, 1046, 1031, 937, 909, 862, 807, 759, 710, 663, 620.

### 4.11. *N*-Allyl-*N*′-methyl-5β-cholan-24-amides: general procedure

Dry tri-*n*-butyl amine (0.96 mL, 4.02 mmol) was added to a solution of cholan-24-oic acid (4.02 mmol) in dry dioxane (60 mL) and the mixture was cooled to 10°C. Ethyl chloroformate (0.39 mL, 4.02 mmol) in dry dioxane (6 mL) was added and, after 10 min, *N*-methyl allylamine (0.96 mL, 10.05 mmol) were added dropwise at the same temperature under stirring. The mixture was stirred at the same temperature for 30 min, then at room temperature for 2.5 h. The reaction mixture was poured into water (150 mL) then extracted with ethyl acetate (4×50 mL). The collected organic extracts were washed with 10% HCl (1×20 mL), 10% $NaHCO_3$ (2×20 mL) and water (2×20 mL), then dried ($Na_2SO_4$). The solvent was evaporated at reduced pressure and the crude product purified by flash chromatography.

**4.11.1. *N*-Allyl-*N*′-methyl-3α-3,5-dimethylbenzoyl)-amino-12α-hydroxy-5β-cholan-24-amide 8a**. Yield 1.89 g, 82% after flash chromatography ($SiO_2$, $CH_2Cl_2$: acetone 88:12). Mp 96–98°C. $[\alpha]_D^{25}$ +53.8 ($c$=0.92, $CH_2Cl_2$). $^1$H NMR (200 MHz, $CDCl_3$, $\delta$): 0.70 (s, 3H, $CH_3$); 0.95 (s, 3H, $CH_3$); 1.00 (d, 3H, 21-$CH_3$); 1.00–2.00 (m, 25H, steroidal CH and $CH_2$, 12-OH); 2.15–2.50 (m, 2H); 2.40 (s, 6H, benzylic $CH_3$); 2.90 and 2.92 (s, 3H, $CONCH_3$); 3.95 (m, 4H, C$\underline{H}_2$CH=$CH_2$, 3-CH and 12-CH); 5.20 (m, 2H, C$\underline{H}_2$=CH); 5.70 (m, 1H, C$\underline{H}$=$CH_2$); 6.00 (d, 1H, amide NH); 7.10 (s, 1H, $H_a$); 7.35 (s, 2H, $H_b$). $^{13}$C NMR (50 MHz, $CDCl_3$, $\delta$): 12.8, 17.7, 21.1 (benzylic $CH_3$), 23.2, 23.6, 26.1, 26.9, 27.4, 27.9, 28.6, 29.8 and 30.4 ($NCH_3$), 31.1, 31.4, 33.7, 33.8, 34.1, 35.2, 35.8, 36.0, 42.4, 46.6, 47.6, 48.5, 49.6 (C3), 50.0 and 52.2 ($NCH_2$), 73.3 (C12), 116.6 and 117.0 ($CH_2$=), 124.6, 132.7 (aromatics), 132.8 and 133.3 (CH=), 135.1, 138.0 (aromatics), 167.0 (CONH), 173.8 and 173.3 (24 C=O). IR (KBr, cm$^{-1}$): 3407, 3342, 3082, 2945, 2869, 1630, 1541, 1461, 1448, 1400, 1378, 1334, 1301, 1287, 1276, 1261, 1239, 1196, 1162, 1099, 1089, 1064, 1052, 988, 970, 945, 931, 865, 803, 762, 686, 641, 624.

**4.11.2. *N*-Allyl-*N*′-methyl-3α-(3,5-dichlorobenzoyl)-amino-12α-hydroxy-5β-cholan-24-amide 8b**. Yield 1.23 g, 50% after flash chromatography ($SiO_2$, $CH_2Cl_2$:acetone 90:10). Mp 90–93°C. $[\alpha]_D^{24}$ +58.2 ($c$=1.00, $CH_2Cl_2$). $^1$H NMR (200 MHz, $CDCl_3$, $\delta$): 0.70 (s, 3H, $CH_3$); 0.90 (s, 3H, $CH_3$); 1.00 (d, 3H, 21-$CH_3$); 1.00–2.00 (m, 25H, steroidal CH and $CH_2$, 12-OH); 2.15–2.50 (m, 2H); 2.90 and 2.92 (s, 3H, $CONCH_3$); 3.95 (m, 4H, C$\underline{H}_2$CH=$CH_2$, 3-CH and 12-CH); 5.20 (m, 2H, C$\underline{H}_2$=CH); 5.75 (m, 1H, C$\underline{H}$=$CH_2$); 6.20 (d, 1H, CONH); 7.4 (t, 1H, $H_a$); 7.60 (d, 2H, $H_b$). $^{13}$C NMR (50 MHz, $CDCl_3$, $\delta$): 12.8, 17.7, 23.2, 23.6, 26.1, 26.7, 27.5, 27.8, 28.5, 29.7 and 30.5 ($NCH_3$), 31.1, 31.4, 33.4, 33.7, 35.3, 35.7, 36.0, 42.3, 46.6, 47.6, 48.5, 50.0 (C3), 50.1 and 52.2 ($NCH_2$), 73.2 (C12), 116.6 and 117.0 (=$CH_2$), 125.6, 131.04 (aromatics), 132.7 and 133.2 (CH=), 135.4, 138.0 (aromatics, 164.0 (CONH), 173.8 and 173.3 (24 C=O). IR (KBr, cm$^{-1}$): 3448, 3328, 3078, 2935, 2863, 1654, 1646, 1636, 1628, 1566, 1542, 1466, 1458, 1448, 1414, 1405, 1399, 1377, 1325, 1289, 1242, 1098, 1049, 920, 866, 802, 760, 732, 670.

**4.11.3. *N*-Allyl-*N*′-methyl-3α-hydroxy-12α-(3,5-dimethylbenzoyl)amino-5β-cholan-24-amide 16a**. Yield 1.5 g 65% after flash chromatography ($SiO_2$, $CH_2Cl_2$: acetone 85:15). Mp 88–90°C. $[\alpha]_D^{25}$ +69.4 ($c$=1.00, $CH_2Cl_2$). $^1$H NMR (200 MHz, $CDCl_3$, $\delta$): 0.88 (s, 3H, $CH_3$); 0.90 (d, 3H, 21-$CH_3$); 0.92 (s, 3H, $CH_3$); 1.00–2.10 (m, 25H, steroidal CH and $CH_2$, 3-OH); 2.10–2.40 (m, 2H); 2.40 (s, 6H, benzylic $CH_3$); 2.80 and 2.83 (s, 3H, $NCH_3$); 3.60 (m, 1H, 3-CH); 3.90 (dd, 2H, C$\underline{H}_2$CH=$CH_2$); 4.50 (dt, $J$=7 Hz, 1H, CH12); 5.10 (m, 2H, C$\underline{H}_2$=CH); 5.70 (m, 1H, C$\underline{H}$=$CH_2$); 6.30 (d, $J$=7 Hz, 1H, CONH); 7.10 (s, 1H, $H_a$); 7.30 (s, 2H, $H_b$); $^{13}$C NMR (50 MHz, $CDCl_3$, $\delta$): 13.9, 17.5, 21.3 (benzylic $CH_3$), 23.3, 23.7, 26.1, 26.6, 27.0, 27.4, 29.7, 30.5, 30.9 and 31.2 ($NCH_3$), 34.2, 35.1, 35.2, 36.0, 36.2, 41.9, 44.6, 49.4, 49.9, 51.3 and 52.2 (C$\underline{H}_2$CH=$CH_2$), 52.4 (C12), 71.6 (C3), 116.5 and 117.0 (C$\underline{H}_2$=CH), 124.5, 133.0,

136.4 (aromatics), 133.1 (C<u>H</u>=$CH_2$), 167.08 (amide C=O), 173.0 (24 C=O). IR (KBr, $cm^{-1}$): 3447, 2934, 2863, 2365, 2344, 1708, 1636, 1603, 1522, 1448, 1400, 1383, 1363, 1303, 1240, 1166, 1093, 1049, 1034, 938, 858, 800.

**4.11.4. *N*-Allyl-*N*′-methyl-3αhydroxy-12α-(3,5-dichlorobenzoyl)amino-5β-cholan-24-amide 16b**. Yield 1.25 g, 42% after flash chromatography ($SiO_2$, $CH_2Cl_2$:acetone 90:10). Mp 65–68°C. $[\alpha]_D^{26}$ +64.7 ($c=1.00$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.85 (d, 3H, 21-$CH_3$); 0.90 (s, 3H, $CH_3$); 0.95 (s, 3H, $CH_3$); 1.00–2.00 (m, 25H, steroidal CH and $CH_2$, 3OH); 2.00–2.40 (m, 2H); 2.90 and 2.93 (s, 3H, $NCH_3$); 3.60 (m, 1H, 3CH); 3.90 (dd, 2H, C<u>H</u>$_2$CH=$CH_2$); 4.45 (dt, $J=7$ Hz, 1H, 12-CH); 5.10 (m, 2H, C<u>H</u>$_2$=CH); 5.70 (m, 1H, C<u>H</u>=$CH_2$); 6.45 (d, $J=7$ Hz, 1H, CONH); 7.50 (m, 1H, $H_a$); 7.60 (m, 2H, $H_b$); $^{13}C$ NMR (50 MHz, $CDCl_3$, $\delta$): 13.7, 17.5, 23.3, 26.4, 26.9, 27.3, 29.7, 30.5, 30.7 and 31.2 ($NCH_3$), 33.6, 34.6, 34.7, 35.0, 36.0, 36.2, 41.9, 44.8, 49.6, 49.9, 51.2 and 52.2 (C<u>H</u>$_2$CH=$CH_2$), 53.0 (C12), 71.5 (C3), 116.5 and 117.0 (C<u>H</u>$_2$=CH), 125.5, 131.3 (aromatics), 132.5 and 133.1 (C<u>H</u>=$CH_2$); 135.6, 138.0 (aromatics), 166.9 (amide C=O), 173.0 (24 C=O). IR (KBr, $cm^{-1}$): 3447, 3310, 3078, 2934, 2863, 1654, 1628, 1566, 1540, 1533, 1508, 1468, 1419, 1272, 1098, 1048, 936, 864, 805, 761, 669.

### 4.12. *N*-Allyl-*N*′-methyl-3α-*N*-aroylamino-12α-arylcarbamoyloxy-5β-cholan-24-amide 9: general procedure

Aryl isocyanate (1.56 mmol) was added to a solution of 8 in dry toluene (20 mL) and the solution was stirred under reflux for 20 h. The solvent was evaporated at reduced pressure and the crude product purified by flash chromatography.

**4.12.1. *N*-Allyl-*N*′-methyl-3α-*N*-3,5-dimethylbenzoyl)-amino-12α-(3,5-dimethylphenyl)carbamoyloxy-5β-cholan-24-amide 9a**. Yield 960 mg, 85% after flash chromatography ($SiO_2$, $CH_2Cl_2$:acetone 93:7). Mp 105–107°C. $[\alpha]_D^{29}$ +113.8 ($c=0.84$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.75 (d, 3H, 21-$CH_3$); 0.80 (s, 6H, $CH_3$); 0.80–2.00 (m, 22H, steroidal CH and $CH_2$); 2.10–2.40 (m, 4H); 2.25 (s, 6H, benzylic $CH_3$); 2.35 (s, 6H, benzylic $CH_3$); 2.90 (s, 3H, $NCH_3$); 3.90 (m, 3H, C<u>H</u>$_2$CH=$CH_2$ and 3-CH); 5.10 (m, 3H, C<u>H</u>$_2$=CH and 12-CH); 5.90 (m, 1H, C<u>H</u>=$CH_2$); 6.20 (br s, 1H, amide NH); 6.65 (s, 1H, $H_{a'}$); 7.10 (s, 4H, $H_{a'}$, $H_{b'}$ and carbamate NH); 7.40 (s, 2H, $H_b$). $^{13}C$ NMR (50 MHz, $CDCl_3$, $\delta$):12.5, 17.7, 21.2 and 21.3 (benzylic $CH_3$), 23.2, 23.4, 25.8, 26.1, 26.7, 27.5, 27.6, 30.0 and 30.6 ($NCH_3$), 31.0, 31.3, 33.5, 33.8, 34.0, 34.4, 35.2, 35.7, 42.2, 45.3, 47.8, 48.0, 49.8, 50.0 (C3), 50.1 and 52.2 ($NCH_2$), 76.8 (C12), 116.3 (aromatic), 116.8 and 117.0 (C<u>H</u>$_2$=CH), 124.6, 124.8 (aromatics), 132.6 and 132.8 (C<u>H</u>=$CH_2$), 133.1, 135.0, 138.1, 138.7 (aromatics), 153.3 (carbamate C=O), 167.4 (amide C=O), 173.3 and 173.8 (24-C=O). IR (KBr, $cm^{-1}$): 3441, 3336, 3082, 2922, 2865, 1725, 1653, 1646, 1636, 1616, 1603, 1541, 1472, 1466, 1458, 1448, 1438, 1419, 1401, 1377, 1328, 1303, 1270, 1222, 1192, 1162, 1079, 1010, 969, 947, 937, 919, 860, 840, 734, 688. Anal. calcd for $C_{46}H_{65}N_3O_4$: C, 76.31; H, 9.05; N, 5.80. Found: C, 76.35; H, 9.08; N, 5.81%.

**4.12.2. *N*-Allyl-*N*′-methyl-3α-*N*-3,5-dichlorobenzoyl)-amino-12α-(3,5-dichlorophenyl)carbamoyloxy-5β-cholan-24-amide 9b**. Yield 800 mg, 76% after flash chromatography ($SiO_2$, $CH_2Cl_2$:acetone 96:4). Mp 119–121°C. $[\alpha]_D^{27}$ +119.2 ($c=1.00$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.70 (d, 3H, 21-$CH_3$); 0.90 (s, 6H, $CH_3$); 0.90–2.00 (m, 24H, steroidal CH and $CH_2$); 2.00 (s, 1H); 2.20–2.50 (m, 2H); 2.95 and 2.98 (s, 3H, $CONCH_3$); 3.90 (m, 3H, $CONCH_2$ and 3-CH); 5.20 (m, 3H, C<u>H</u>$_2$=CH and 12-CH); 5.75 (m, 1H, C<u>H</u>=$CH_2$); 6.40 (br s, 1H, CONH); 7.00 (t, 1H, $H_{a'}$); 7.50 (m, 3H, $H_a$ and $H_{b'}$); 7.70 (d, 2H, $H_b$); 8.10 (ss, 1H, carbamate NH). $^{13}C$ NMR (50 MHz, $CDCl_3$, $\delta$): 12.4, 17.6, 17.7, 23.0, 23.4, 25.8, 26.0, 26.7, 27.0, 27.5, 30.2, 30.8, 31.0, 31.4, 33.1, 33.7, 34.4, 34.7, 35.3, 35.5, 35.6, 45.2, 47.7, 47.9, 49.9, 50.1 (C3), 50.7 and 52.3 ($NCH_2$), 77.8 (C12), 116.7 and 117.2 (C<u>H</u>$_2$=CH), 122.8, 125.5, 125.6, 131.1 (aromatics), 132.5 and 132.7 (C<u>H</u>=$CH_2$), 135.2, 135.5, 137.8, 140.7 (aromatics), 153.0 (carbamate C=O), 164.3 (CONH), 174.5 and 174.7 (24 C=O). IR (KBr, $cm^{-1}$): 3420, 3288, 3174, 3080, 2930, 2865, 1734, 1709, 1701, 1685, 1654, 1647, 1636, 1628, 1618, 1594, 1566, 1534, 1449, 1410, 1322, 1306, 1291, 1243, 1216, 1192, 1114, 1096, 1059, 993, 967, 947, 916, 866, 838, 803, 762, 669. Anal. calcd for: $C_{42}H_{53}Cl_4N_3O_4$: C, 62.61; H, 6.63; Cl, 17.60; N, 5.22. Found: C, 62.73; H, 6.60; Cl, 17.56;N, 5.19%.

**4.12.3. *N*-Allyl-*N*′-methyl-3α-*N*-3,5-dimethylbenzoyl)-amino-12α-(3,5-dichlorophenyl)carbamoyloxy-5β-cholan-24-amide 9c**. Yield 820 mg, 82% after flash chromatography ($SiO_2$, $CH_2Cl_2$:acetone 93:7). Mp 123–125°C. $[\alpha]_D^{28}$ +124.0 ($c=0.89$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.75 (d, 3H, 21-$CH_3$); 0.80 (s, 6H, $CH_3$); 0.80–2.00 (m, 24H, steroidal CH and $CH_2$); 2.10–2.50 (m, 2H); 2.45 (s, 6H, benzylic $CH_3$); 2.90 and 2.93 (s, 3H, $NCH_3$); 3.70–4.10 (m, 3H, C<u>H</u>$_2$CH=$CH_2$ and 3-CH); 5.10 (m, 3H, C<u>H</u>$_2$=CH and 12-CH); 5.70 (m, 1H, C<u>H</u>=$CH_2$); 6.20 (d, 1H, amide NH); 7.00 (t, 1H, $H_{a'}$); 7.10 (s, 1H, $H_a$); 7.40 (s, 2H, $H_b$); 7.50 (dd, 2H, $H_{b'}$); 8.20 (br s, 1H, carbamate NH). $^{13}C$ NMR (50 MHz, $CDCl_3$, $\delta$): 12.4, 17.6, 17.7, 21.2, 23.0, 23.4, 25.8, 26.0, 26.7, 27.2, 27.5, 30.3, 30.6, 31.3, 33.2, 33.7, 33.9, 34.3, 34.7, 35.3, 35.4, 35.5, 35.8, 42.2, 45.2, 47.7, 47.8, 49.6, 50.1, 50.5, 52.3, 116.7 and 117.1 (C<u>H</u>$_2$=CH), 122.7 (aromatic C), 124.5 (aromatic C), 124.6 (aromatico C), 132.5 and 132.9 (C<u>H</u>=$CH_2$), 134.8, 135.1, 136.2, 140.8 (aromatics), 153.0 (carbamate C=O), 167.4 (amide C=O), 184.2 (24 C=O). IR (KBr, $cm^{-1}$): 3421, 3107, 3079, 2935, 2864, 1734, 1728, 1718, 1684, 1654, 1636, 1590, 1540, 1534, 1528, 1522, 1508, 1499, 1490, 1474, 1465, 1458, 1448, 1406, 1376, 1329, 1305, 1243, 1217, 1192, 1162, 1113, 1095, 1056, 990, 945, 915, 861, 837, 800, 783, 763, 669. Anal. calcd for: $C_{44}H_{59}Cl_2N_3O_4$: C, 69.09; H, 7.78; Cl, 9.27; N, 5.49. Found: C, 68.97; H, 7.79; Cl, 9.31;N, 5.47%.

**4.12.4. *N*-Allyl-*N*′-methyl-3α-*N*-3,5-dichlorobenzoyl)-amino-12α-(3,5-dimethylphenyl)carbamoyloxy-5β-cholan-24-amide 9d**. Yield 820 mg, 82% after flash chromatography ($SiO_2$, $CH_2Cl_2$:acetone 95:5). Mp 111–113°C. $[\alpha]_D^{24}$ +115.1 ($c=0.98$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.70 (d, 3H, 21-$CH_3$); 0.90 (s, 6H, $CH_3$); 0.90–2.00 (m, 24H, steroidal CH and $CH_2$); 2.10–2.40 (m, 2H); 2.20 (s, 6H, benzylic $CH_3$); 2.90 (s, 3H, $CONCH_3$); 3.90 (m, 3H, $CONCH_2$ and 3-CH); 5.10 (m, 3H, C$\underline{H}_2$=CH and 12-CH); 5.90 (m, 1H, C$\underline{H}$=$CH_2$); 6.30 (br s, 1H, CONH); 6.70 (s, 1H, $H_{a'}$); 7.10 (s, 3H, $H_{b'}$ and carbamate NH); 7.40 (t, 1H, $H_a$); 7.60 (d, 2H, $H_b$). $^{13}C$ NMR (50 MHz, $CDCl_3$, $\delta$): 12.5, 17.7, 17.8, 21.3 (benzylic $CH_3$), 23.1, 23.5, 25.7, 26.0, 26.8, 27.4, 30.1 and 31.0 ($NCH_3$), 31.4, 33.3, 34.0, 34.4, 35.2, 42.2, 45.3, 47.8, 47.9, 49.9, 50.0 (C3), 50.5 and 52.2 ($NCH_2$), 116.1, 116.2 (aromatics), 116.5 and 117.0 (C$\underline{H}_2$=CH), 124.8, 125.0, 125.6, 131.0 (aromatics), 132.6 and 133.1 (C$\underline{H}$=$CH_2$), 135.3, 137.9, 138.2, 138.8 (aromatics), 153.2 (carbamate C=O), 164.1 (CONH), 174.6 and 174.8 (24 C=O). IR (KBr, $cm^{-1}$): 3426, 3311, 3078, 2926, 2864, 1725, 1654, 1647, 1636, 1618, 1566, 1542, 1534, 1528, 1508, 1498, 1489, 1474, 1466, 1459, 1447, 1417, 1377, 1323, 1271, 1221, 1192, 1079, 1010, 920, 866, 840, 804, 762, 688. Anal. calcd for: $C_{44}H_{59}Cl_2N_3O_4$: C, 69.09; H, 7.78; Cl, 9.27; N, 5.49. Found: C, 68.95; H, 7.80; Cl, 9.24;N, 5.50%.

### 4.13. *N*-Allyl-*N*′-methyl-3α-arylcarbamoyloxy-12α-*N*-aroylamino-5β-cholan-24-amide 17: general procedure

Arylisocyanate (1.48 mmol) and DMAP (80 mg, 0.065 mmol) were added to a solution of **16** (1.21 mmol) in dry THF (30 mL) and the mixture was stirred at room temperature for 15 h. The solvent was evaporated under reduced pressure and the crude product was purified by flash chromatography.

**4.13.1. *N*-Allyl-*N*′-methyl-3α-(3,5-dimethylphenyl)carbamoyloxy - 12α - *N* - (3,5 - dimethylbenzoyl)amino - 5β-cholan-24-amide 17a**. Yield 760 mg, 86% after flash chromatography ($SiO_2$, $CH_2Cl_2$:acetone 90:10). Mp 124–126°C. $[\alpha]_D^{26}$ +98.7 ($c=1.01$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.88 (s, 3 H, $CH_3$); 0.90 (d, 3H, 21-$CH_3$); 0.98 (s, 3H, $CH_3$); 1.00–2.10 (m, 24H, steroidal CH and $CH_2$); 2.10–2.30 (m, 2H); 2.30 (s, 6H, benzylic $CH_3$); 2.40 (s, 6H, benzylic $CH_3$); 2.88 and 2.90 (s, 3H, $NCH_3$); 3.90 (dd, 2H, C$\underline{H}_2$CH=$CH_2$); 4.50 (dt, 1H, 12-CH); 4.65 (m, 1H, 3-CH); 5.10 (m, 2H, C$\underline{H}_2$=CH); 5.70 (m, 1H, C$\underline{H}$=$CH_2$); 6.30 (s+d, 2H, carbamate NH and amide NH); 6.70 (s, 1H, $H_{a'}$); 6.90 (s, 2H, $H_{b'}$); 7.10 (s, 1H, $H_a$); 7.3 (s, 2H, $H_b$). $^{13}C$ NMR (50 MHz, $CDCl_3$, $\delta$): 13.9, 17.5, 21.3 (benzylic $CH_3$), 23.2, 23.8, 26.1, 26.5, 26.8, 27.4, 29.9, 30.5, 31.0 and 31.3 ($NCH_3$), 32.6, 33.5, 34.2, 34.7, 35.2, 36.0, 41.8, 44.8, 49.5, 50.0, 51.3 and 52.1 (C$\underline{H}_2$CH=$CH_2$), 52.4 (C12), 75.0 (C3), 116.2 (aromatic C), 116.5 and 117.0 (C$\underline{H}_2$=CH), 124.7, 125.0 (aromatics), 132.5 and 133.1 (C$\underline{H}$=$CH_2$), 132.8, 137.7, 138.3, 138.7 (aromatics), 153.0 (carbamate C=O), 167.0 (amide C=O), 173.0 (24 C=O). IR (KBr, $cm^{-1}$): 3630, 3298, 2945, 2866, 1734, 1654, 1636, 1603, 1560, 1508, 1465, 1458, 1449, 1420, 1384, 1270, 1220, 1082, 1018, 936, 839, 802, 764, 687. Anal. calcd for $C_{46}H_{65}N_3O_4$: C, 76.31; H, 9.05; N, 5.80. Found: C, 76.26; H, 9.07; N, 5.78%.

**4.13.2. *N*-Allyl-*N*′-methyl-3α-(3,5-dichlorolphenyl)carbamoyloxy - 12α - (3,5 - dichlorobenzoyl)amino - 5β - cholan-24-amide 17b**. Yield 690 mg, 71% after flash chromatography ($SiO_2$, $CH_2Cl_2$:acetone 94:6). Mp 140–142°C. $[\alpha]_D^{23}$ +123.5 ($c=1.01$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.85 (s, 3H, $CH_3$); 0.90 (d, 3H, 21-$CH_3$); 0.95 (s, 3H, $CH_3$); 1.00–2.10 (m, 24H, steroidal CH and $CH_2$); 2.10–2.40 (m, 2H); 2.90 and 2.92 (s, 3H, $NCH_3$); 3.90 (dd, 2H, C$\underline{H}_2$CH=$CH_2$); 4.45 (dt, 1H, CH12); 4.65 (m, 1H, CH3); 5.20 (m, 2H, C$\underline{H}_2$=CH); 5.75 (m, 1H, C$\underline{H}$=$CH_2$); 6.30 (d, 1H, amide NH); 7.00 (t, $J=1.8$ Hz, 1H, $H_{a'}$); 7.30 (d $J=1.8$ Hz, 2H, $H_{b'}$); 7.40 (s, 1H, carbamate NH); 7.46 (t, $J=1.9$ Hz, 1H, $H_a$); 7.60 (t, $J=1.9$ Hz, 2H, $H_b$). $^{13}C$ NMR (200 MHz, $CDCl_3$, $\delta$): 13.6, 17.5, 23.1, 23.8, 26.0, 26.2, 26.7, 26.8, 27.4, 29.8, 30.4, 31.0 and 31.4 ($NCH_3$), 32.6, 33.7, 34.3, 34.8, 35.1, 35.9, 41.7, 44.7, 49.8, 49.9, 51.3 and 52.2 (C$\underline{H}_2$CH=$CH_2$), 53.5 (C12), 75.7 (C3), 116.5 and 117.0 (C$\underline{H}_2$=CH), 116.6, 122.7, 125.4, 131.1 (aromatics), 132.6 and 133.1 (C$\underline{H}$=$CH_2$), 135.0, 135.3, 138.7, 140.5 (aromatics), 152.8 (carbamate C=O), 164.7 (amide C=O 12), 173.0 (24 C=O). IR (KBr, $cm^{-1}$): 3427, 3283, 3172, 3107, 3080, 2944, 2867, 1734, 1653, 1646, 1628, 1591, 1566, 1522, 1449, 1410, 1242, 1214, 1114, 1094, 1063, 982, 923, 865, 837, 806, 758, 711, 668. Anal. calcd for: $C_{42}H_{53}Cl_4N_3O_4$: C, 62.61; H, 6.63; Cl, 17.60; N, 5.22. Found: C, 62.68; H, 6.65; Cl, 17.58; N, 5.25%.

**4.13.3. *N*-Allyl-*N*′-methyl-3α-(3,5-dimethylphenyl)carbamoyloxy - 12α - *N* - (3,5 - dichlorobenzoyl)amino - 5β - cholan-24-amide 17c**. Yield 670 mg, 72% after flash chromatography ($SiO_2$, $CH_2Cl_2$:acetone 95:5). Mp 131–133°C. $[\alpha]_D^{25}$ +90.4 ($c=1.00$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.88 (s, 3H, $CH_3$); 0.90 (d, 3H, 21-$CH_3$); 1.00 (s, 3H, $CH_3$); 1.00–2.10 (m, 24H, steroidal CH and $CH_2$); 2.10–2.40 (m, 2H); 2.40 (s, 6H, benzylic $CH_3$); 2.87 and 2.90 (s, 3H, $NCH_3$); 3.90 (dd, 2H, C$\underline{H}_2$CH=$CH_2$); 4.45 (dt, 1H, 12-CH); 4.55 (m, 1H, 3-CH); 5.15 (m, 2H, C$\underline{H}_2$=CH); 5.70 (m, 1H, C$\underline{H}$=$CH_2$); 6.40 (d+s, 2H, amide NH and carbamate NH); 6.60 (s, 1H, $H_{a'}$); 6.90 (s, 2H, $H_{b'}$); 7.50 (m, 1H, $H_a$); 7.60 (m, 2H, $H_b$). $^{13}C$ NMR (200 MHz, $CDCl_3$, $\delta$): 13.9, 17.5, 21.3 (benzylic $CH_3$), 23.1, 23.7, 26.0, 26.3, 26.7, 26.8, 27.4, 29.8, 30.4, 30.9 and 31.2 ($NCH_3$), 32.5, 33.6, 34.2, 34.6, 35.1, 35.2, 35.9, 41.6, 44.7, 49.7, 50.0, 51.3 and 52.2 (C$\underline{H}_2$CH=$CH_2$), 53.1 (C12), 74.7 (C3), 116.2 (aromatico), 116.5 and 117.0 (C$\underline{H}_2$=CH), 125.0, 125.5, 131.2 (aromatics), 132.6 and 133.1 (C$\underline{H}$=$CH_2$); 135.5, 137.8, 138.4, 138.7 (aromatics), 153.1 (carbamate C=O), 164.1 (amide C=O), 172.9 and 173.4 (24 C=O). IR (KBr, $cm^{-1}$): 3427, 3314, 3078, 2946, 2866, 1735, 1719, 1708, 1701, 1686, 1654, 1628, 1566, 1540, 1458, 1271, 1211, 1082, 1018, 933, 865, 839, 805, 763, 687, 668. Anal. calcd for: $C_{44}H_{59}Cl_2N_3O_4$: C, 69.09; H, 7.78; Cl, 9.27; N, 5.49. Found: C, 69.15; H, 7.76; Cl, 9.23; N, 5.52%.

**4.13.4. *N*-Allyl-*N*′-methyl-3α-(3,5-dichlorophenyl)carbamoyloxy-12α-*N*-(3,5-dimethylbenzoyl)amino-5β-cholan-24-amide 17d**. Yield 1.26 g, 77%) after flash chromatography ($SiO_2$, $CH_2Cl_2$:acetone 90:10). Mp 118–120°C. $[\alpha]_D^{25}$ +99.0 ($c=1.00$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.88 (s, 3 H, $CH_3$); 0.90 (d, 3H, 21-$CH_3$); 1.10 (s, 3H, $CH_3$); 1.10–2.10 (m, 24H, steroidal CH and $CH_2$); 2.10–2.30 (m, 2H); 2.3 (s, 6H, benzylic $CH_3$); 2.90 and 2.93 (s, 3H, $NCH_3$); 3.90 (dd, 2H, $C\underline{H}_2CH{=}CH_2$); 4.50 (dt, 1H, CH12); 4.65 (m, 1H, 3-CH); 5.10 (m, 2H, $C\underline{H}_2{=}CH$); 5.70 (m, 1H, $C\underline{H}{=}CH_2$); 6.30 (d, 1H, amide NH); 6.60 (s, 1H, carbamate NH); 7.00 (t, 1H, $H_{a'}$); 7.10 (s, 1H, $H_a$); 7.20 (d, 2H, $H_{b'}$); 7.30 (s, 2H, $H_b$); $^{13}C$ NMR (50 MHz, $CDCl_3$, $\delta$): 13.9, 17.4, 21.4 (benzylic $CH_3$), 23.3, 23.8, 26.1, 26.5, 26.8, 27.4, 29.7, 29.9, 30.5, 31.0 and 31.3 ($NCH_3$), 32.5, 33.6, 34.2, 34.6, 35.2, 36.0, 41.7, 44.6, 49.6, 50.0, 51.3 and 52.2 ($C\underline{H}_2CH{=}CH_2$), 52.5 (C12), 75.9 (C3), 116.5 and 117.0 ($C\underline{H}_2{=}CH$), 116.6, 123.1, 124.6 (aromatics), 132.5 and 133.1 ($C\underline{H}{=}CH_2$), 132.9, 135.2, 135.5, 138.4, 140.0 (aromatics), 152.5 (carbamate C=O), 167.0 (amide C=O), 173.0 and 173.6 (24 C=O). IR (KBr, $cm^{-1}$): 3272, 3080, 2944, 2867, 1731, 1632, 1591, 1516, 1505, 1449, 1409, 1304, 1242, 1215, 1115, 1094, 1063, 992, 923, 859, 836, 806, 761, 670, 617. Anal. calcd for: $C_{44}H_{59}Cl_2N_3O_4$: C, 69.09; H, 7.78; Cl, 9.27; N, 5.49. Found: C, 68.99; H, 7.75; Cl, 9.29; N, 5.47%.

## 4.14. Mercaptopropyltrimethoxysilyl derivative 18: general procedure

3-Mercaptopropyl trimethoxysilane (0.76 mL, 4.1 mmol) and AIBN (30 mg, 0.18 mmol) were added to a solution of **9** or **17** (0.82 mmol) in $CHCl_3$ (10 mL) and the mixture was stirred under reflux for 20 h. The solvent was removed under vacuum and the oily residue dispersed in pentane (30 mL). The precipitated solid was collected by filtration and washed with pentane (5×30 mL) the dried, affording the pure product in quantitative yield.

**4.14.1. *N*-Methyl-*N*′-[(3-trimethoxysilylpropylthio)propyl]-3α-*N*-3,5-dimethylbenzoyl)amino-12α-(3,5-dimethylphenyl)carbamoyloxy-5β-cholan-24-amide 18a**. 690 mg. Mp 75–76°C. $[\alpha]_D^{26}$ +85.0 ($c=0.78$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.70 (m, 2H, $CH_2Si$); 0.75 (s, 3H, $CH_3$); 0.90 (d, 3H, 21-$CH_3$); 0.95 (s, 3H, $CH_3$); 1.00–2.10 (m, 28H, steroidal CH and $CH_2$, chain $CH_2$); 2.10–2.40 (m, 4H); 2.25 (s, 6H, benzylic $CH_3$); 2.35 (s, 6H, benzylic $CH_3$); 2.50 (m, 4H, $CH_2SCH_2$); 2.90 (s, 3H, $NCH_3$); 3.40 (m, 2H, $NCH_2$); 3.55 (s, 9H, $Si(OCH_3)_3$); 3.80 (m, 1H, 3-CH); 5.10 (m, 1H, 12-CH); 5.90 (br s, 1H, amide NH); 6.65 (s, 1H, $H_{a'}$); 6.90 (s, 1H, carbamate NH); 7.10 (s, 3H, $H_a$ and $H_{b'}$); 7.35 (s, 2H, $H_b$). IR (KBr, $cm^{-1}$): 3309, 3161, 2940, 2864, 1733, 1725, 1702, 1685, 1654, 1647, 1636, 1628, 1617, 1602, 1560, 1542, 1534, 1528, 1508, 1499, 1490, 1474, 1466, 1458, 1449, 1376, 1329, 1270, 1222, 1191, 1083, 1011, 969, 947, 919, 808, 763, 688, 617.

**4.14.2. *N*-Methyl-*N*′-[(3-trimethoxysilylpropylthio)propyl]-3α-*N*-3,5-dichlorobenzoyl)amino-12α-(3,5-dichlorophenyl)carbamoyloxy-5β-cholan-24-amide 18b**. 800 mg. Mp 38–40°C. $[\alpha]_D^{29}$ +84.5 ($c=0.56$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.75 (m, 2H, $CH_2Si$); 0.80 (s, 3H, $CH_3$); 0.90 (d, 3H, 21-$CH_3$); 0.95 (s, 3H, $CH_3$); 1.00–2.10 (m, 28H, steroidal CH and $CH_2$, chain $CH_2$); 2.10–2.40 (m, 4H); 2.50 (m, 4H, $CH_2SCH_2$); 2.90 (s, 3H, $NCH_3$); 3.40 (m, 2H, $NCH_2$); 3.60 (s, 9H, $Si(OCH_3)_3$); 3.80 (m, 1H, 3-CH); 5.10 (m, 1H, 12-CH); 6.00 (br s, 1H, amide NH); 7.00 (s, 1H, $H_{a'}$); 7.40 (m, 3H, $H_a$ and $H_{b'}$); 7.60 (s, 2H, $H_b$); 8.20 (s, 1H, carbamate NH). IR (KBr, $cm^{-1}$): 3315, 3077, 2937, 2864, 1727, 1617, 1566, 1541, 1449, 1377, 1323, 1271, 1221, 1192, 1162, 1082, 918, 866, 840, 804, 761, 732, 688, 669, 617.

**4.14.3. *N*-Methyl-*N*′-[(3-trimethoxysilylpropylthio)propyl]-3α-*N*-3,5-dimethylbenzoyl)amino-12α-(3,5-dichlorophenyl)carbamoyloxy-5β-cholan-24-amide 18c**. 730 mg. Mp 82–83°C. $[\alpha]_D^{27}$ +92.8 ($c=0.90$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.75 (m+s, 5H, $CH_2Si$ and $CH_3$); 0.90 (s+d, 6H, $CH_3$ and 21-$CH_3$); 1.00–2.10 (m, 28H, steroidal CH and $CH_2$, chain $CH_2$); 2.10–2.40 (m, 4H); 2.25 (s, 6H, benzylic $CH_3$); 2.50 (m, 4H, $CH_2SCH_2$); 2.90 (s, 3H, $NCH_3$); 3.40 (m, 2H, $NCH_2$); 3.55 (s, 9H, $Si(OCH_3)_3$); 3.80 (m, 1H, 3-CH); 5.10 (m, 1H, CH12); 6.20 (br s, 1H, amide NH); 7.00 (s, 1H, $H_{a'}$); 7.10 (s, 1H, $H_a$); 7.35 (s, 2H, $H_b$); 7.50 (d, 2H, $H_{b'}$); 8.00 (s, 1H, carbamate NH). IR (KBr, $cm^{-1}$): 3428, 3275, 3172, 3108, 3078, 3050, 2939, 2864, 2839, 1734, 1701, 1684, 1646, 1637, 1629, 1618, 1590, 1560, 1449, 1409, 1376, 1328, 1306, 1244, 1218, 1191, 1161, 1085, 967, 946, 915, 860, 811, 800, 762, 669, 617, 578.

**4.14.4. *N*-Methyl-*N*′-[(3-trimethoxysilylpropylthio)propyl]-3α-*N*-3,5-dichlorobenzoyl)amino-12α-(3,5-dimethylphenyl)carbamoyloxy-5β-cholan-24-amide 18d**. 720 mg. Mp 85–86°C. $[\alpha]_D^{30}$ +83.6 ($c=0.61$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.75 (m+s, 5H, $CH_2Si$ and $CH_3$); 0.90 (d, 3H, 21-$CH_3$); 0.95 (s, 3H, $CH_3$); 0.90–2.00 (m, 28H, steroidal CH and $CH_2$, chain $CH_2$); 2.10–2.40 (m, 4H); 2.25 (s, 6H, benzylic $CH_3$); 2.50 (m, 4H, $CH_2SCH_2$); 2.90 (s, 3H, $NCH_3$); 3.40 (m, 2H, $NC\underline{H}_2$); 3.6 (s, 9H, $Si(OCH_3)_3$); 3.90 (m, 1H, 3-CH); 5.10 (m, 1H, 12-CH); 6.00 (br s, 1H, amide NH); 6.70 (s, 1H, $H_{a'}$); 6.90 (s, 1H, carbamate NH); 7.10 (s, 2H, $H_{b'}$); 7.40 (t, 1H, $H_a$); 7.60 (s, 2H, $H_b$). IR (KBr, $cm^{-1}$): 3315, 3077, 2937, 2864, 1727, 1617, 1566, 1541, 1449, 1377, 1271, 1221, 1192, 1162, 1082, 918, 866, 840, 804, 761, 732, 688, 669, 617.

**4.14.5. *N*-Methyl-*N*′-[(3-trimethoxysilylpropylthio)propyl]-3α-(3,5-dimethylphenyl)carbamoyloxy-12α-*N*-(3,5-dimethylbenzoyl)amino-5β-cholan-24-amide 18e**. 670 mg. Mp 90–92°C. $[\alpha]_D^{23}$ +82.2 ($c=1.03$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.70 (m, 2H, $CH_2Si$); 0.85 (s, 3H, $CH_3$); 0.90 (d, 3H, 21-$CH_3$); 0.92 (s, 3H, $CH_3$); 1.00–2.10 (m, 30H, steroidal CH and $CH_2$, chain $CH_2$); 2.10–2.40 (m, 2H); 2.20 (s, 6H, benzylic $CH_3$); 2.30 (s, 6H, benzylic $CH_3$); 2.50 (m, 4H, $CH_2SCH_2$); 2.90 (s, 3H, $NCH_3$); 3.45 (m, 2H, $NCH_2$); 3.55 (s, 9H,

$Si(OCH_3)_3$); 4.45 (dt, 1H, 12-CH); 4.55 (m, 1H, 3-CH); 6.30 (d, 1H, amide NH and s, 1H, carbamate NH); 6.70 (s, 1H, $H_{a'}$); 6.90 (s, 2H, $H_{b'}$); 7.15 (s, 1H, $H_a$); 7.40 (s, 2H, $H_b$). IR (KBr, $cm^{-1}$): 3446, 3400, 2943, 2867, 2840, 1728, 1636, 1618, 1540, 1508, 1458, 1270, 1222, 1084, 1020, 936, 815, 765, 688.

**4.14.6. *N*-Methyl-*N*′-[(3-trimethoxysilylpropylthio)propyl]-3α-(3,5-dichlorolphenyl)carbamoyloxy-12α-N-(3,5-dichlorobenzoyl)amino-5β-cholan-24-amide 18f**. 740 mg. Mp 97–99°C. $[\alpha]_D^{26}$ +95.2 ($c=0.90$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.75 (m, 2H, $CH_2Si$); 0.90 (s+d, 6H, $CH_3$ and 21-$CH_3$); 0.92 (s, 3H, $CH_3$); 1.00–2.10 (m, 30H, steroidal CH and $CH_2$, chain $CH_2$); 2.10–2.40 (m, 2H); 2.50 (m, 4H, $CH_2SCH_2$); 2.90 (s, 3H, $NCH_3$); 3.40 (m, 2H, $NCH_2$); 3.60 (s, 9H, $Si(OCH_3)_3$); 4.40 (dt, 1H, 12-CH); 4.65 (m, 1H, 3-CH); 6.35 (d, 1H, amide NH); 7.00 (t, 1H, $H_{a'}$); 7.30 (dd, 2H, $H_{b'}$); 7.50 (t, 1H, $H_a$); 7.60 (dd, 2H, $H_b$). IR (KBr, $cm^{-1}$): 3422, 3289, 3078, 2942, 2866, 2840, 1734, 1708, 1701, 1685, 1654, 1625, 1591, 1566, 1522, 1449, 1411, 1243, 1215, 1090, 924, 807, 670.

**4.14.7. *N*-Methyl-*N*′-[(3-trimethoxysilylpropylthio)propyl]-3α-(3,5-dimethylphenyl)carbamoyloxy-12α-*N*-(3,5-dichlorobenzoyl)amino-5β-cholan-24-amide 18g**. 0.84 g. Mp 87–89°C. $[\alpha]_D^{25}$ +76.7 ($c=0.42$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.75 (m, 2H, $CH_2Si$); 0.90 (s+d, 9H, 18-$CH_3$, 19-$CH_3$ and 21-$CH_3$); 1.00–2.10 (m, 30H, steroidal CH and $CH_2$, chain $CH_2$); 2.10–2.40 (m, 2H); 2.30 (s, 6H, benzylic $CH_3$); 2.50 (m, 4H, $CH_2SCH_2$); 2.90 (s, 3H, $NCH_3$); 3.40 (m, 2H, $NCH_2$); 3.60 (s, 9H, $Si(OCH_3)_3$); 4.45 (dt, 1H, 12-CH); 4.70 (m, 1H, 3-CH); 6.30 (d, 1H, amide NH); 6.40 (d, 1H, carbamate NH); 6.70 (s, 1H, $H_{a'}$); 7.00 (s, 2H, $H_{b'}$); 7.50 (t, 1H, $H_a$); 7.60 (dd, 2H, $H_b$). IR (KBr, $cm^{-1}$): 3430, 2942, 2866, 1734, 1718, 1685, 1654, 1624, 1560, 1540, 1534, 1527, 1522, 1516, 1508, 1458, 1449, 1437, 1430, 1420, 1271, 1215.

**4.14.8. *N*-Methyl-*N*′-[(3-trimethoxysilylpropylthio)propyl]-3α-(3,5-dichlorophenyl)carbamoyloxy-12α-*N*-(3,5-dimethylbenzoyl)amino-5β-cholan-24-amide 18h**. 720 mg. Mp 90–92°C. $[\alpha]_D^{24}$ +83.2 ($c=0.97$, $CH_2Cl_2$). $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$): 0.75 (m, 2H, $CH_2Si$); 0.88 (s, 3H, $CH_3$); 0.90 (d, 3H, 21-$CH_3$); 0.95 (s, 3H, $CH_3$); 1.00–2.10 (m, 30H, steroidal CH and $CH_2$, chain $CH_2$); 2.10–2.40 (m, 2H); 2.30 (s, 6H, benzylic $CH_3$); 2.50 (m, 4H, $CH_2SCH_2$); 2.90 (s, 3H, $NCH_3$); 3.40 (m, 2H, $NCH_2$); 3.60 (s, 9H, $Si(OCH_3)_3$); 4.45 (dt, 1H, 12-CH); 4.65 (m, 1H, 3-CH); 6.40 (d, 1H, amide NH); 6.65 (s, 1H, carbamate NH); 7.00 (t, 1H, $H_{a'}$); 7.35 (d, 2H, $H_{b'}$); 7.50 (t, 1H, $H_a$); 7.60 (dd, 2H, $H_b$). IR (KBr, $cm^{-1}$): 3439, 3281, 2942, 2868, 1734, 1653, 1647, 1636, 1626, 1591, 1560, 1534, 1508, 1500, 1410, 1305, 1243, 1216, 1086, 993, 923, 859, 808, 763, 671.

### 4.15. CSPs A1–D1 and A2–D2: general procedure

A solution of **18** (0.82 mmol) in 15 mL of dry toluene was dropwise added to 2.5 g of spherical silica gel (100 Å, 5 μm), previously dried at 180°C at 0.1 mmHg for 15 h, slurried in 15 mL of dry toluene and the mixture was gently stirred at reflux for 24 h. The mixture, cooled to room temperature was filtered and washed with toluene (3×30 mL), dichloromethane (3×30 mL), methanol (3×30 mL), THF (3×30 mL) and pentane (3×30 mL), then dried at 50°C at 0.1 mmHg.

The amount of chiral selector linked to silica gel was determined by elemental analysis.
FSC **A1**: C% 14.92; H% 2.21; N% 1.00; S% 0.79 corresponding to 0.254 mmol/g.
FSC **B1**: C% 11.87; H% 1.63; N% 0.87; S% 0.65 corresponding to 0.217 mmol/g.
FSC **C1**: C% 14.53; H% 1.95; N% 1.02; S% 0.82 corresponding to 0.250 mmol/g.
FSC **D1**: C% 13.51; H% 1.32; N% 0.95; S% 0.74 corresponding to 0.214 mmol/g.
FSC **A2**: C% 10.70; H% 1.57; N% 0.73; S% 0.52 corresponding to 0.174 mmol/g.
FSC **B2**: C% 11.98; H% 1.71; N% 0.88; S% 0.67 corresponding to 0.217 mmol/g.
FSC **C2**: C% 12.78; H% 1.56; N% 0.90; S% 0.68 corresponding to 0.211 mmol/g.
FSC **D2**: C% 13.36; H% 1.97; N% 0.93; S% 0.71 corresponding to 0.231 mmol/g

The derivatized silica gels were slurried in dichloromethane and packed into 15 cm stainless steel columns at 400 bar using acetone

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