# Reduction of steroidal ketones with amine—boranes

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Complexes of secondary amines with borane, $R_2NH \cdot BH_3$, surpass sodium borohydride as reducing agents for saturated and unsaturated steroidal 3-, 12-, 17-, and 20-ketones as regards chemo- and regioselectivity and mildness of the reaction conditions. In the case of 12-ketones, stereoselectivity is also improved.

**Key words:** amine—boranes, reduction, hecogenin acetate, dihydroprogesterone, dimethylamine—borane, dicyclohexylamine—borane, diethylamine—borane, ketones, keto steroids, methyltestosterone, morpholine—borane, prednisolone 21-acetate.

Amine—boranes have not yet found extensive use as reducing agents in organic chemistry, despite their stability, ready availability including commercial one, and the possibility to control the reactivity by varying the amine (see reviews, Ref. 1). In recent years, the interest in amine—boranes as reducing or hydroborating reagents has markedly increased. They have been proposed as reagents of choice for reductive amination of carbonyl compounds,[2] reduction of oximes to hydroxylamines,[3] synthesis of higher dialkylboranes (they are used instead of diborane),[4] reductive dehalogenation of aryl halides,[5] and other reductive processes.[6,7] Against this background, the use of amine—boranes for the reduction of carbonyl compounds into alcohols appears inadequately studied. Although this reduction has long been investigated for simple aldehydes and ketones,[8] cases of application of this reaction in the syntheses are few. These include the reduction of several steroidal ketones[9,10] and effective use in the synthesis of the antiviral drug Cyclaradine where stereospecific reduction of the carbonyl group was attained only using the *tert*-butylamine—borane complex.[11]

The purpose of the present study is to evaluate the synthetic potential of these complexes using the reduction of several types of steroidal ketones as examples. The reagents chosen were amine—boranes $R_2NH \cdot BH_3$ derived from dialkylamines, *viz.*, dimethylamine and diethylamine (R = Me and Et, **DMAB** and **DEAB**, respectively), morpholine ($R_2 = O(CH_2CH_2)_2$, **MorB**) and dicyclohexylamine (R = *cyclo*-$C_6H_{11}$, **DCyAB**). The complexes of dialkylamines, unlike derivatives of trialkylamines, are sufficiently reactive to react with carbonyl compounds without activators, and they give no by-products resulting from reductive amination of reactive carbonyl compounds, which was noted in the case of using even more reactive complexes with monoalkylamines.[12] The most important types of steroidal ketones used included saturated 3- (**1**, **13**), 12- (**3**), 17- (**5**), and 20-keto steroids (**15**) and unsaturated 3-keto steroids (**6β**, **7**, **11**) (Scheme 1).

The workup of reaction mixtures after reduction with amine—boranes deserves special mention. The ketone reduction products, *viz.*, the corresponding alcohols, are formed in organic solvents as alkyl borates, which, in addition, bind more or less strongly the amine present in the mixture. If the alcohols formed are acid-stable, they can be easily liberated from the borates by acidification with a mineral acid (method *A*, see Experimental). However, most of allylic alcohols are partially or completely dehydrated under these conditions. Transesterification with methanol and distillation of trimethyl borate, normally used to destroy borates, proved to be inefficient for amine—boranes, and the removal of boron-containing components was unacceptably slow. This is apparently due to the presence of amine and to the low rate of the reaction of the B—H bonds with methanol. The use of carbon-supported palladium to catalyze the reaction with methanol, which has been recommended for similar cases,[13] did accelerate the process but brought about side hydrogenation of double bonds in the products. This can be suppressed by adding excess allyl alcohol, which is easily hydrogenated. Therefore, we have used for some period the following workup procedure: Pd/C + MeOH + + $CH_2$=$CHCH_2OH$, stirring for 2 h, concentration, and extraction. This gave the target reduction products with only minor amounts of boron-containing impurities. Nevertheless, this procedure is not given in the Experimental, because a simpler and a more efficient method has been found. The method is based on the report that the reaction of an aqueous solution of an amine—borane with excess acetone is accompanied by evolution of hydrogen, because the intermediate product of acetone reduction, namely, unstable amine $\cdot BH(Pr^iO)_2$ complex, reacts competitively with water due to the easy dissociation into

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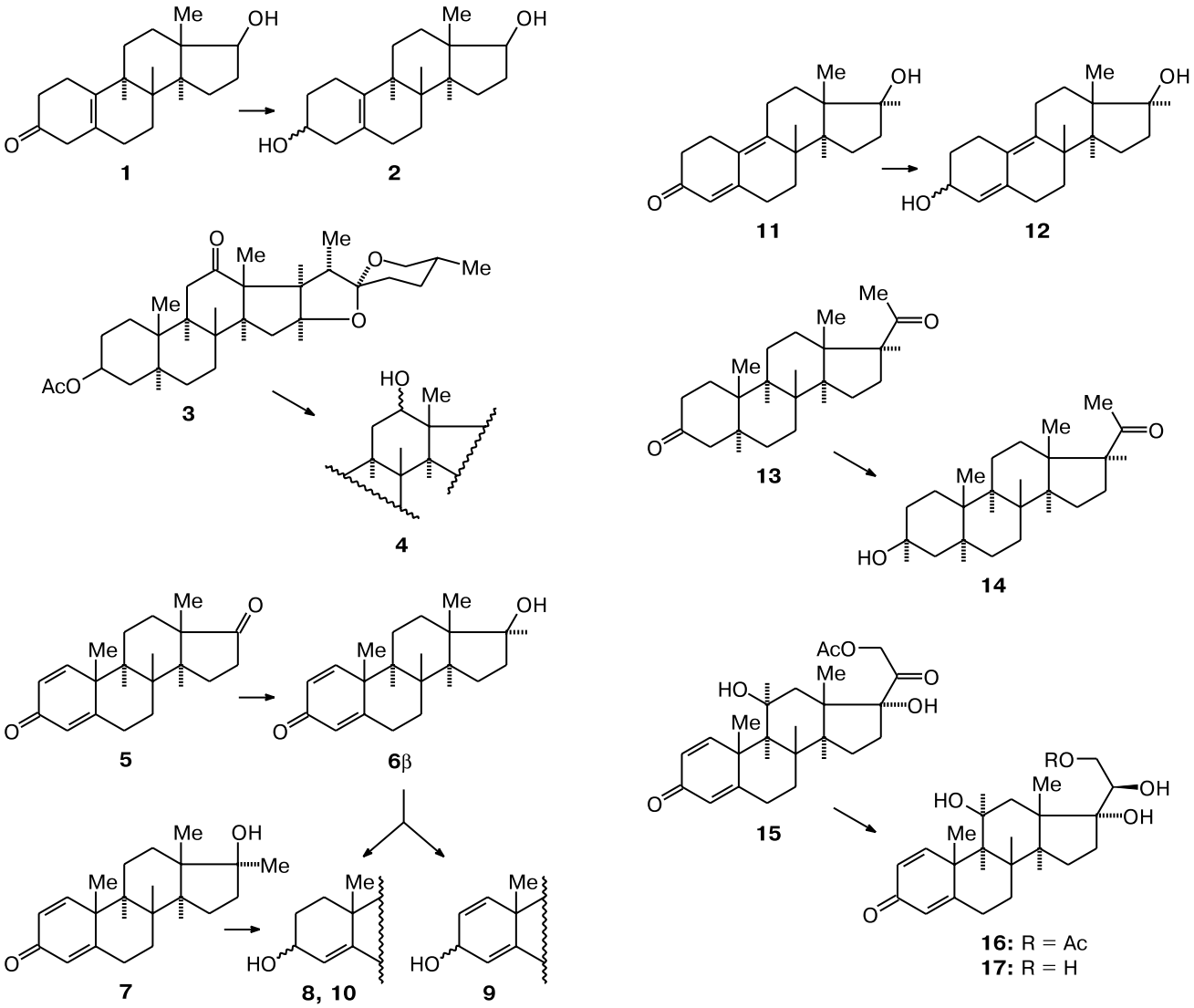
**Scheme 1**




components.[14] The same can be expected in the case of the methanolic medium. Therefore, a novel, nonacidic workup of the reaction mixtures formed after the reduction with amine—boranes (method *B*) consists of decomposition of excess hydride and intermediate borates with an acetone—methanol mixture followed by washing of the extract with an aqueous solution of a weak base. The products obtained with a quantitative balance are free from boron-containing impurities (Table 1). This nonacidic workup of the reaction mixtures can also be recommended for other reactions with amine—boranes.

The results of reduction of the ketones are summarized in Table 1; for comparison, the Table also gives the results of reduction of the same ketones with sodium borohydride carried out in parallel. The ratio of the α- to β-epimers of the alcohols **2**, **4**, **6**, **8—10**, **12**, **14**, and **16** was determined using $^1$H NMR spectroscopy by analyzing either the alcohols themselves and/or their acetates. The reporter signals used for this purpose and characteristics of the alcohols are listed in Tables 2 and 3.

The influence of the conditions and structures of amine—boranes on the results of reduction were studied taking 12-ketone **3** as an example. Strange as it may seem, the effect of the amine structure on the reduction rate and stereochemistry was insignificant (runs *5—7*, *9*), nor was the effect of the solvent (run *8*). Therefore, all the subsequent reduction experiments were carried out with morpholine—borane (**MorB**) in toluene (with addition of ethanol if this was required by the solubility of the starting ketone). The fact that the amine structure does not influence the reaction selectivity, even in the case of sterically most hindered amine—borane complex (**DCyAB**), is consistent with the mechanism of reduction, which includes displacement of the amine from the complex during the

**Table 1.** Reduction of steroidal ketones with amine—boranes

| Entry | Ketone | Hydride (mol.-equiv.) | Reaction conditions | | | | Yield of alcohols (%) | Ratio of α : β epimers* |
|---|---|---|---|---|---|---|---|---|
| | | | Solvent | *T*/°C | τ/h | Method | | |
| *1* | **1** | $NaBH_4$ (3.6) | $CH_2Cl_2$—EtOH—$H_2O$ (32 : 62 : 6) | 20 | 1.5 | *C* | **2** (96) | 29 : 71 |
| *2* | | **MorB** (2.9—3.4) | PhMe | 20 | 1.5 | *A* | **2** (100) | 25 : 75 |
| *3* | | **DCyAB** (2.9) | PhMe | 20 | 1.5 | *A* | **2** (100) | 27 : 73 |
| *4* | **3** | $NaBH_4$ (2.0) | $CH_2Cl_2$—EtOH—$H_2O$ (32 : 62 : 6) | 25 | 72 | *C* | **4** (95) | 25 : 75 |
| *5* | | **DMAB** (3.3) | PhMe | 19 | 2 | *A* | **4** (94) | 6.5 : 93.5 |
| *6* | | **DEAB** (2.9) | PhMe | 17 | 3 | *A* | **4** (98) | 4.5 : 95.5 |
| *7* | | **MorB** (2.4) | PhMe | 26 | 2 | *A* | **4** (98) | 5 : 95 |
| *8* | | **MorB** (2.5) | EtOH | 26 | 1 | *A* | **4** (~100) | |
| *9* | | **DCyAB** (1.6) | PhMe | 27 | 1 | *A* | **4** (97) | 7 : 93 |
| *10* | **5** | $NaBH_4$ (0.4) | EtOH—$H_2O$ (81 : 19) | 22 | 0.25 | *C* | **6** (100) | 2 : 98 |
| *11* | | **MorB** (3.0) | PhMe—EtOH (93 : 7) | 20 | 20 | *A* | **6** (96) | 8 : 92 |
| *12* | **6b** | $NaBH_4$ (1.9) | EtOH—$H_2O$ (94 : 6) | 25 | 3 | *D* | **8** (43)<br>**9** (47) | 5 : 95<br>50 : 50 |
| *13* | | **MorB** (3.0) | PhMe—EtOH (93 : 7) | 70—110 | 3 | *B* | **8** (44)<br>**9** (44) | 6 : 94<br>55 : 45 |
| *14* | **7** | $NaBH_4$ (3.6) | EtOH | 20 | 2 | *D* | **10** (97) | 4.5 : 95.5 |
| *15* | | **MorB** (3.5) | PhMe—MeOH (96 : 4) | 65—75 | 70 | *B* | **10** (95) | 12 : 88 |
| *16* | **11** | $NaBH_4$ (10.8) | EtOH—$H_2O$ (94 : 6) | 22 | 0.5 | *D* | **12** (99) | 23 : 77 |
| *17* | | **MorB** (3.1) | PhMe—EtOH (96 : 4) | 65—70 | 12 | *B* | **12** (92) | 31 : 69 |
| *18* | **13** | $NaBH_4$ (0.34) | EtOH—PhMe—$H_2O$ (73 : 26 : 1) | 21 | 0.5 | *C* | **14** (100) | 10 : 90 |
| *19* | | **MorB** (1.3) | PhMe | 23 | 1.5 | *A* | **14** (100) | 6.5 : 93.5 |
| *20* | **15** | $NaBH_4$ (0.65) | EtOH—PhMe—$H_2O$ (83 : 14 : 3) | 19 | 1.0 | *D* | **16** + **17** (85) | 22 : 78 |
| *21* | | **MorB** (3.6) | PhMe—EtOH (87 : 13) | 18 | 20 | *B* | **16** (90) | 28 : 72 |

* Epimer ratio in the crude product was determined from the reporter signals in the $^1$H NMR spectrum (see Table 2).

process.[15] This hypothesis accounts for the parallel variation of the reactivity and the ease of dissociation of the amine complexes with borane (primary > secondary > > tertiary), but it is at variance with the known substantial difference between the stereoselectivities of reduction with diborane and amine—boranes.[16]

### Chemoselectivity of reduction

Morpholine—borane (**MorB**) reduces saturated ketones **1**, **3**, and **13** (entries *2*, *7*, and *19*) and nonconjugated keto groups in steroids **5** and **15** (entries *11* and *21*) an order of magnitude faster than conjugated enones and dienones **6β**, **7**, and **11** (entries *13*, *15*, and *17*). Whereas the reduction of saturated ketones occurs rapidly at room temperature, the reduction of unsaturated ketones starts only at 65 °C and requires many hours for completion. This chemoselectivity allows one to carry out totally selective reduction of saturated ketones (the 17-keto group in diketone **5** (entry *11*) and the 20-keto group in prednisolone acetate **15** (entry *21*)) in the presence of unsaturated ketones (the 3-keto group) using an excess of **MorB**, whereas similar reduction with $NaBH_4$ requires dosage of the reducing agent (entries *10* and *20*), while with its excess, the 3-keto group is also rapidly reduced (entry *12*).

It should be noted that neither double bond hydroboration nor reductive amination was observed even under drastic conditions used for the reduction of unsaturated keto groups. Yet another positive feature of the reduction with amine—boranes is that low-polar aprotic solvents (toluene, dichloromethane) can be employed. The reaction media are weakly basic, which is due to the amine, this, in addition, being complexed with boron-containing compounds. Therefore, the acetoxy groups in hecogenin acetate **3** and prednisolone acetate **15** are completely stable during the reduction with amine-boranes, even in the presence of ethanol (entries *8*, *21*), whereas in the reduction with sodium borohydride, which produces a highly basic medium, partial deacetylation always takes place (entries *4*, *20*).

### The selectivity of reduction of saturated carbonyl compounds

Even in an early publication,[12] considerable (up to a 25-fold) difference was noted between the rates of reduction of different saturated ketones with $Bu^tNH_2 \cdot BH_3$,

**Table 2.** Characteristics of the reduction products of steroidal ketones with amine—boranes

| Entry[a] | Alcohol (its acetate) | Yield[b] (%) | Epimer ratio α : β[b] | M.p./°C (solvent) [lit. data][c] | TLC, $R_f$, α/β |
|---|---|---|---|---|---|
| *2* | **2** | 80 | 25 : 75[d] | 201—202 (EtOH) [208—209][17] | 0.22[e] |
| | 3,17-*O*-$Ac_2$-**2**[f] | | 25 : 75 | | 0.73[e] |
| *7* | **4** | 83 | β[d] (100) | 225—226 (MeOH) [218—220][18] | 0.28[g] |
| | 12-*O*-Ac-**4**[f] | | β (100) | 212—213 (MeOH) [204—206][18] | 0.56[g] |
| *11* | **6** | 74 | 4 : 96 | 170—171 (EtOH) [168—169][19] | 0.28[e] |
| *13* | **8** | —[h] | 6 : 94 | | |
| | **9** | —[h] | 55 : 45 | see Ref. 20 | 0.44/ −0.30[e] |
| *15* | **10** | 90 | β (100) | 172—173 (MeOH) [166—170][21] | 0.19[i] |
| *17* | **12** | 82 | 22 : 78 | 182—192 (PhMe—MeOH) [125—127.5 (**12α**), 156—158 (**12β**)][22]; [183—184 (**12α**+**12β**)][23] | 0.30/ −0.24[j] |
| *19* | **14** | 91 | β (100) | 194 (EtOH—hexane) [194][24] | 0.38/ −0.34[k] |
| *21* | **16** | 58 | <5 : >95[d] | 211—213 ($H_2O$) | 0.27[l] |
| | 20,21-*O*-$Ac_2$-**16** | | <5 : >95 | 243—244 ($H_2O$) [241.5—243][25] | 0.40[l] |

[a] The numbering of the entries is the same as in Table 1.
[b] After recrystallization.
[c] The best published data for the individual major epimers.
[d] Analyzed as the acetate.
[e] Silufol, EtOAc—hexane (3 : 2, two runs).
[f] Prepared by standard acetylation ($Ac_2O$—Py).
[g] Silufol, EtOAc—PhMe (1 : 9).
[h] Recrystallization was not carried out due to instability of the compounds.
[i] Alufol, EtOAc—hexane (2 : 3, two runs).
[j] Silufol, EtOAc—hexane (4 : 1, three runs).
[k] Silufol, EtOAc—hexane (2 : 3, two runs).
[l] Silufol, EtOAc (two runs).

which was the highest for cyclohexanone and the lowest for heptan-4-one. A similar selectivity is also observed in the reduction of steroidal ketones with **MorB**. Competitive reduction experiments have revealed the following sequence for the ease of reduction of saturated steroidal ketones: 12-keto ≈ 3-keto > 17-keto ≫ 20-keto (for the ketones used in this study). This allowed us to conduct highly regioselective reduction of the 3-keto group in 3,20-diketone **13** (entry *19*).

### The 1,2 and 1,4 (or 1,6) addition to unsaturated ketones

In this respect, **MorB** proved to be analogous to $NaBH_4$. In particular, in ketones **7** and **11**, which are not prone to conjugate addition, only the carbonyl groups are reduced (entries *15* and *17*), whereas in the case of cross-conjugated dienone **6β**, highly susceptible to 1,4-addition, both reducing agents produced equal amounts of 1,2- and 1,4-addition products. In the latter, it is the less substituted double bond that is involved (entries *12* and *13*).

### Stereochemistry of reduction

This aspect shows some ambiguity of the results. The stereoselectivities of reduction of the 3-keto groups of ketones **1**, **6β**, **7**, **11**, and **13**, the 17-keto group in diketone **5**, and the 20-keto group in diketone **15** with **MorB** were somewhat higher (entries *2* and *19*), or approximately the same (entries *13* and *21*), or markedly lower (entries *11*, *15*, and *17*) than those for the reduction with $NaBH_4$, and the use of much more bulky **DCyAB** did not enhance the stereoselectivity (entry *3*). However, the reduction of the 12-keto group in ketone **3** with the amine—borane studied was much more stereoselective (**4α** : **4β** = (5—7) : (93—95)) than the reduction with $NaBH_4$ (25 : 75) (entries *4—7* and *9*). The reduction of other 12-keto steroids with $Bu^tNH_2 \cdot BH_3$ has been studied previously, and the stereoselectivity was found to vary from 17 : 83 to 40 : 60, depending on the substrate.[10] Thus, the reduction with secondary amine—boranes, at least, for hecogenin acetate **3**, is the most stereoselective method for the synthesis of rockogenin acetate **4β**.

To summarize, we can conclude that the reduction with commercially available amine—boranes can serve as a convenient alternative to the reduction with sodium borohydride, being superior as regards the chemo- and regioselectivity, mildness of the reaction conditions, and, in some cases, stereoselectivity.

### Experimental

$^1H$ NMR spectra were recorded in $CDCl_3$ on Bruker WM-250 (250.13 MHz) and Bruker AM-300 (300.13 MHz) spectrometers, the chemical shifts being referred to internal $Me_4Si$ (δ 0.00). The melting points were determined on a Koefler (Boetius) hot stage and were not corrected. Analytical TLC was performed on Silufol and Alufol plates (Czechia) in the indicated solvent systems, the spots being visualized with a 5% solution of phosphomolybdic acid in ethanol or a solution of $Ce(SO_4)_2$ in 10% $H_2SO_4$ with subsequent heating. The extracts were concentrated *in vacuo* (water-jet pump) at 30 °C, and the residues were dried to a constant weight *in vacuo* (2 Torr).

All steroids with >98% purity were taken from the laboratory collection. Amine—boranes, **DMAB** (m.p. 37 °C, b.p. 63 °C (1 Torr)),[26] **DEAB** (b.p. 98—100 °C (12 Torr)),[27] **MorB** (m.p. 95 °C),[28] and **DCyAB** were synthesized according to a general procedure,[26,29] *i.e.*, by the reaction of the corresponding amine hydrochlorides with sodium borohydride in DME. The complexes were >95% pure (according to NMR).

**Dicyclohexylamine—borane complex (DCyAB).** A 12% solution of HCl (18 mL, 60 mmol) was added with shaking to

**Table 3.** $^1$H NMR spectra of the reduction products of steroid ketones with amine—borane complexes

| Alcohol (its acetate) | $^1$H NMR ($CDCl_3$, δ, *J*/Hz) | |
|---|---|---|
| | Mixture of α/β epimers[a] | Major epimer |
| **2** | 4.07/3.85 | **2β:** 0.80 (s, 3 H, C(18)$H_3$); 3.70 (t, 1 H, H(17), *J* = 8.2); 3.85 (m, 1 H, H(3)) |
| 3,17-*O*-$Ac_2$-**2** | 5.06/4.86<br>0.83/0.81 | **3,17-*O*-$Ac_2$-2β:** 0.81 (s, 3 H, C(18)$H_3$); 2.04 (s, 6 H, 2 OAc); 4.63 (dd, 1 H, H(17), *J* = 7.8, *J* = 8.9); 4.86 (s, 1H, H(3)) |
| **4** | 3.69/3.33 | **4β:** 0.76 (s, 3 H, C(18)$H_3$); 0.80 (d, 3 H, C(27)$H_3$, *J* = 6.2); 0.86 (s, 3 H, C(19)$H_3$); 1.04 (d, 3 H, C(21)$H_3$, *J* = 7.0); 2.03 (s, 3 H, OAc); 3.33 (dd, 1 H, H(12), *J* = 4.6, *J* = 11.2); 3.37 (t, 1 H, H(26α), *J* = 10.8); 3.46 (dd, 1 H, H(26β), *J* = 4.2, *J* = 10.8); 4.41 (q, 1 H, H(16), *J* = 7.1); 4.68 (tt, 1 H, H(3), *J* = 5.3, *J* = 10.6) |
| 12-*O*-Ac-**4** | 4.92/4.55<br>2.06/2.03 | **12-*O*-Ac-4β:** 0.86 (s, 3 H, C(18)$H_3$); 0.79 (d, 3 H, C(27)$H_3$, *J* = 6.0); 0.85 (s, 3 H, C(19)$H_3$); 0.91 (d, 3 H, C(21)$H_3$, *J* = 6.5); 2.01 (s, 3 H, 3-*O*Ac); 2.03 (s, 3 H, 12-*O*Ac); 3.36 (t, 1 H, H(26α), *J* = 10.8); 3.45 (dd, 1 H, H(26β), *J* = 4.2, *J* = 10.8); 4.40 (q, 1 H, H(16), *J* = 7.4); 4.55 (dd, 1 H, H(12), *J* = 4.8, *J* = 11.4); 4.68 (tt, 1 H, H(3), *J* = 5.3, *J* = 10.6) |
| **6** | 3.77[b]/3.65;<br>0.74/0.83 | **6β:** 0.83 (s, 3 H, C(18)$H_3$); 1.25 (s, 3 H, C(19)$H_3$); 3.65 (t, 1 H, H(17), *J* = 8.2); 6.08 (br.s, 1 H, H(4)); 6.24 (dd, 1 H, H(2), *J* = 1.7, *J* = 10.3); 7.05 (d, 1 H, H(1), *J* = 10.3) |
| **8** | 5.46/5.28 | **8β:** 0.76 (s, 3 H, C(18)$H_3$); 1.06 (s, 3 H, C(19)$H_3$); 3.62 (t, 1 H, H(17), *J* = 8.3); 4.14 (m, 1 H, H(3)); 5.28 (d, 1 H, H(4), *J* = 1.5) |
| **9** | 5.53/5.50 | **9α:** 0.78 (s, 3 H, C(18)$H_3$); 1.12 (s, 3 H, C(19)$H_3$); 3.62 (t, 1 H, H(17), *J* = 8.3); 4.48 (m, 1 H, H(3)); 5.53 (m, 1 H, H(4)); 5.77 (d, 1 H, H(2), *J* = 10.7); 5.96 (d, 1 H, H(1), *J* = 10.7) |
| **10** | 5.47[c]/5.29 | **10β:** 0.88 (s, 3 H, C(18)$H_3$); 1.07 (s, 3 H, C(17)$H_3$); 1.19 (s, 3 H, C(19)$H_3$); 4.14 (m, 1 H, H(3)); 5.28 (q, 1 H, H(4), *J* = 1.7) |
| **12** | 5.42[b]/5.36<br>4.22/4.32 | **12β:** 0.86 (s, 3 H, C(18)$H_3$); 3.63 (t, 1 H, H(17), *J* = 8.2); 4.32 (m, 1 H, H(3)); 5.36 (br.s, 1 H, H(4)) |
| **14** | 4.04[d]/3.59 | **14β:** 0.60 (s, 3 H, C(18)$H_3$); 0.81 (s, 3 H, C(19)$H_3$); 2.10 (s, 3H, C(20)$H_3$); 2.52 (t, 1 H, H(17), *J* = 8.5); 3.59 (tt, 1 H, H(3), *J* = 5.0, *J* = 11.0) |
| **16** | | **16β:** 1.11 (s, 3 H, C(18)$H_3$); 1.46 (s, 3 H, C(19)$H_3$); 2.10 (s, 3 H, 21-OAc); 4.02 (dd, 1 H, H(20), *J* = 3.0, *J* = 7.7); 4.08—4.28 (m, 2 H, $H_2$(21)); 4.41 (q, 1 H, H(11), *J* = 2.8); 6.01 (br.s, 1 H, H(4)); 6.26 (dd, 1 H, H(2), *J* = 1.8, *J* = 10.1); 7.28 (d, 1 H, H(1), *J* = 10.1) |
| 20,21-*O*-$Ac_2$-**16** | 5.35/5.38 | **20,21-*O*-$Ac_2$-16β**: 1.04 (s, 3 H, C(18)$H_3$); 1.45 (s, 3 H, C(19)$H_3$); 2.02 (s, 3 H, 20-OAc); 2.12 (s, 3 H, 21-OAc); 4.14 (dd, 1 H, H(21A), *J* = 8.2, *J* = 12.3); 4.40—4.48 (m, 2 H, H(11) + H(21B)); 5.38 (dd, 1 H, H(20), *J* = 2.3, *J* = 8.2); 6.01 (br.s, 1 H, H(4)); 6.26 (dd, 1 H, H(2), *J* = 1.3, *J* = 10.3); 7.23 (d, 1 H, H(1), *J* = 10.3) |

[a] The reporter signals in the epimer mixture.
[b] Unlike the corresponding triplet signal of the epimer, this signal is a doublet with *J* = 4.4 Hz.
[c] Unlike the corresponding signal of the epimer, this signal is a doublet with *J* = 5.0 Hz.
[d] Unlike the corresponding signal of the epimer, this signal is a quintet with *J* = 2.5 Hz.

dicyclohexylamine (5.0 g, 27.6 mmol). After cooling, the white crystalline precipitate was filtered off and dried in a vacuum desiccator to give 6.0 g (100%) of the corresponding hydrochloride. Sodium borohydride (400 mg, 10.6 mmol) was added in portions with stirring at 20 °C to a suspension of this hydrochloride (4.3 g, 19.7 mmol) in 30 mL of DME. The suspension was stirred for 1 h and the precipitate was filtered off and washed with hexane. The filtrate was concentrated *in vacuo* to dryness, and the residue was recrystallized from hexane to give 2.41 g (63%) of **DCyAB** as a white crystalline solid stable in air and during storage, m.p. 121—122 °C. Found (%): C, 73.73, 73.87; H, 13.62, 13.62; B, 5.66, 5.62; N, 7.01, 7.15. $C_{12}H_{26}BN$. Calculated (%): C, 73.86; H, 13.43; B, 5.54; N, 7.18. IR, ν/$cm^{-1}$: 1280 (B—N); 2288, 2328, 2344, 2368, 2396 (B—H); 3224 (N—H). $^1$H NMR, δ: 0.70—1.45 (m, 7 H, 3 BH + 2 $CH_2$); 1.45—2.00 (m, 16 H, 8 $CH_2$); 2.85 (m, 3 H, NH + 2 HCN).

**Reduction of ketones with amine—boranes (general procedures).** *Method A*. A solution of a steroidal ketone and an amine—borane in toluene or in another solvent (depending on the steroid solubility, 15—30 mL per mmol of the steroid) was stirred at the temperature indicated in Table 1 to complete transformation of the starting compound (TLC). The reaction mixture was diluted with EtOAc, and 7% aqueous HCl was added until the mixture became acidic and hydrogen evolution ceased. The organic layer was separated and washed with a saturated aqueous solution of $NaHCO_3$ and water to a neutral pH. The solution was dried by filtering through a microcolumn with $MgSO_4$ and concentrated. The crystalline precipitate was analyzed (NMR) before and after recrystallization. When indicated in Table 2, the sample was acetylated before analysis (excess $Ac_2O$—Py, 15 h, concentration to dryness).

*Method B*. The reduction was carried out as described in method *A*, but the workup was performed in the following way: the reaction mixture was diluted with a mixture of acetone with methanol (10 mol.-equiv. each per mole of the amine—borane) and kept until hydrogen evolution ceased (2 h), $CH_2Cl_2$ (up to 35% of the total volume) and a saturated aqueous solution of $NaHCO_3$ were added, and the organic layer was washed to a

neutral pH, dried by filtering through a microcolumn with $Al_2O_3$, and concentrated. Subsequent analysis of the residue was carried out as in procedure *A*.

**The reduction of ketones with sodium borohydride (general procedures).** *Method C*. An aqueous solution of $NaBH_4$ (1—2 mL per mmol of the steroid) was added to a solution of the steroidal ketone in the mixture of organic solvents indicated in Table 1 (determined by the steroid solubility, 15—30 mL per mmol of the steroid) and the solution was stirred at 19—25 °C to complete transformation of the starting compound (TLC). The workup of the reaction mixture and analysis were carried out as described in method *A*.

*Method D*. The reduction and analysis were carried out as described in method *C* but the phosphate buffer (pH 5) was used instead of hydrochloric acid.

**Competitive reduction of ketones with amine—boranes.** A mixture of equal amounts of 12-keto steroid **3** and keto steroid **5**, **13**, or **15** was reduced at ~20 °C according to methods *A* or *B* (depending on the structure) using 1.2 mol of **MorB** per mole of both ketones. During the period from 3 to 120 min, aliquots of the reaction mixtures were withdrawn and the product ratio was determined by TLC after the appropriate workup. In aliquots with ≥95% reduction of ketone **3**, the degree of reduction of the second ketone was 90, 70, and 20% for ketones **13**, **5**, and **15**, respectively.

The conditions and results of preparative reduction are summarized in Table 1, while characteristics of the products are given in Table 2. All the obtained steroidal alcohols (except for **16**) had been described in the literature and were identified, in addition to other methods, by direct comparison with authentic samples either from the laboratory collection of steroids or specially prepared by reported procedures. Alcohols **16** obtained by reduction with **MorB** were identified by comparison with the sample prepared by reduction with $NaBH_4$, for which the 20β-configuration for the major isomer was accepted on the basis of the well-known stereochemistry of the reduction of the 20-keto group in the dihydroxyacetone side chain of steroids.[30]

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