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# SELECTIVE REDUCTION OF THE α-TRICHLOROMETHYL FUNCTION IN PIPERIDINE SULFONAMIDES

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**Abstract**—In a 3-step procedure—overall yield of 30%—the $-CCl_3$ group has been converted into $-CH_2OH$ in a highly selective manner. The steps are (i) selective hydrogenation $CCl_3 \rightarrow CHCl_2$ (ii) 1,5-diazabicyclo-[4,3,0]-nonene-5 catalyzed elimination of HCl to =CHCl and (iii) hydroboration of the vinylchloride. In addition dramatically different results on the hydrogenation of the $CCl_3$ group are reported.

The ready availability of the compounds **1** via ($_\pi 4_s + _\pi 2_s$) cycloaddition[2] initiated a search for selective and efficient conversion routes of the $CCl_3$-moiety into other functional groups, as for instance alcohols and aldehydes, aiming at a wider synthetic scope of the method.

Since the chemical behaviour of **1**[3] strongly invited the use of catalytic methods for its conversion, a series of experiments was conducted with different catalysts and in selected media. The latter variation was brought in because of the known sensitivity of halomethyl derivatives towards variations in base[4] and acid.[5] Selective hydrogenation of **1** ($PtO_2$/EtOH) in presence of solid $K_2CO_3$ ($PtO_2/K_2CO_3$ = 1/10 by weight) gave a high yield of **2**. Upon lowering the concentration of $K_2CO_3$ the unsaturated dichloromethyl derivative **3** is concurrently formed ($PtO_2/K_2CO_3$ = 1/2 by weight) in equal proportion. A further change in reaction pattern is noted if the amount of $K_2CO_3$ is still lowered. Hydrogenation in presence of 2.8 eq. $K_2CO_3$ ($PtO_2/K_2CO_3$ = 1 by weight) leads to a 1:1 mixture of **3** and **5**. Presumably the base is not only involved in the neutralization of the liberated HCl, but also in the dehalogenation step. Moreover the activity of the catalyst seems also dependent upon the quantity of the base added.

A dramatic change in reaction behaviour was noted upon substituting $K_2CO_3$ by triethylamine. Upon hydrogenation of **1** in presence of $NEt_3$ ($PtO_2/NEt_3$ = 1/2 by weight) **3** is formed in quantitative yield. In the absence of base the sole product is **5**. Compound **5** is also formed in high yield upon carrying out the reduction of **1** with Ra–Ni in a 1:1 mixture of HOAc/EtOAc to achieve dechlorination followed by addition of Pd/C (10%) to complete the hydrogenation. This procedure proved eminently suitable for large-scale operation.

While in presence of base dechlorination is the major process observed the hydrogenation of the $C_{1,10b}$ double bond occurs predominantly upon carrying out the $PtO_2$ reduction of **1** in HOAc, yielding **4** as the principal product.

Other dehalogenating agents could also be used in the conversion of **1** albeit with less selectivity. Thus tri-n-butyl-tinhydride[6] gave after 4 hr/60°/xylene a 9:1 mixture of **2** and **7**.

The *cis* B/C stereochemistry for compounds **4** and **5** could be easily deduced from decoupling experiments. For both derivatives $J_{4a,10b}$ proved to be 3.0 Hz, while $J_{4a,5}$ contained a diaxial coupling of 12 Hz. The $C_3$–H position could be inferred from the $W^{1/2}$ values of 8 Hz. These are in agreement with an axial position for the trichloromethylsubstituent and correlate with the stereochemistry deduced for **1**.[2] The relation found by Nagata[7] and Horii[8] for the chemical shift differences between $H_7$ and $H_{10}$ in dependence of the ring B/C stereochemistry did not hold in these systems. In view of the results on amino compounds it can be assumed that the tosyl substituent is mainly responsible for this failure.

The remaining chloromethyl derivative **6** can be obtained in quantitative yield upon Pd/C (10%)/HOAc reduction of **2**. A summary of these results for *quantitative* and selective conversion of **1** is given in Table 1.

### *Chemical conversion of* 5 *and* 6

Presumably as a consequence of the steric influence of the large tosyl substituent the chloromethyl moiety in **2** is rather inert in a variety of nucleophilic displacements. Even under rather forcing conditions (AgOAc/MeCN, 30 hr, 130°) no reaction took place. In view of the lability

Table 1. Catalytic reduction of **1**

| Exp | Conditions | Ratio† C:B | Products | Yield % | Product ratio |
|---|---|---|---|---|---|
| 1 | $PtO_2$/EtOH/$K_2CO_3$ | 1:10 | **2** | 80 | |
| 2 | $PtO_2$/EtOH/$K_2CO_3$ | 1:2 | **2**+**3** | >90‡ | 1:1 |
| 3 | $PtO_2$/EtOH/$K_2CO_3$ | 1:1 | **3**+**5** | >95‡ | 1:1 |
| 4 | $PtO_2$/EtOH/$K_2CO_3$ | 1:2 | **3** | 98 | |
| 5 | $PtO_2$/EtOH | — | **5** | 83 | |
| 6 | Ra–Ni/EtOAc/HOAc Pd/C (10%) | — | **5** | 81 | |
| 7 | $PtO_2$/HOAc | — | **4**+**2** | 85 | 3:1 |
| 8 | $SnBu_3$/xylene§ | — | **2**+**7** | >90‡ | 9:1 |

†Weight proportions of catalyst C and added base B.
‡Determined by PMR spectroscopy.
§Temperature 60°C, reaction time 4 hr.

of this type of tetrahydropyridine structure in alkaline medium[3] further experiments were conducted with the saturated analogue **6**. The latter compound was inert in various substitution reactions and only at 160° HCl-elimination occurred upon treatment with 1,5 diazabicyclo[4,3,0]nonene-5 DABCN.[9] Under these circumstances, however, a mixture of **8** and **11** was obtained which could be characterized on the basis of its PMR spectral data and also by independent synthesis of **11** as indicated in the experimental. Acid treatment ($HCl_{aq}$/dioxane) of the mixture of **8** and **11** to complete isomerisation led to ring cleavage under formation of **13**. While several examples have been described in which an N-acylenamine is hydrolysed[10] the solvolytic behaviour of a N-tosylenamine is of interest in view of the virtually non-basic character of the N atom. Thus it appeared impossible to prepare a stable N–Ts immonium-salt. Other methods for the preparation of acyclic N-vinyl-sulfonamides have been described[11] but no results of the solvolysis of this compound class are reported.

Reaction of the dichloride **5** with base afforded a mixture of *endo*- and *exo*-vinylchlorides **9** and **10** as indicated in Table 2.

Depending on the conditions it appeared possible to influence the ratio **9** and **10** greatly. This fact proved to be of synthetic significance since **9** was found to be a reactive starting material for further conversion while **10** remained almost inert. Structure assignment of **9** and **10** is based upon the difference in $\delta$-values of the *endo*- and *exo*-vinylic hydrogen the lower field absorption at 6.40 ppm being ascribed to the *endo*-hydrogen, due to the anisotropy effect of the N-sulfonylgroup.[13] Support for this assumption can be derived from the experiments described in the Table: the mode of action of the azabicyclic bases is suggested to proceed preferably in a *cis*-elimination while the inorganic base may well follow a *trans*-elimination pathway. From simple model studies it can be inferred that the former reaction favors the formation of the *endo*-isomer while the latter mainly leads to the *exo*-isomer. Definite proof, however, is still lacking.

$CF_3COOH$ isomerisation of **9** proceeds instantaneously at 0° to produce **12**. A similar reaction of **10** at r.t. during 168 hr is still incomplete, although the presence of **12** can be demonstrated. These results clearly indicate the difference in reactivity between **9** and **10**. As described for **8**+**11** hydrolysis of **9** in $HCl_{aq}$/dioxane also gave ringopening to **14**, **10** being unreactive. A likely explanation for the difference in behaviour between **9** and **10** is seen in the position of the chloroatom, which is locked up between the sulfonyl oxygens in isomer **10**. Additional evidence for this steric interaction can be derived from temperature dependent $^1H$ NMR studies of a series of compounds of type **9** and **12**.[14]

Functionalization of the vinylchloride **9** was realized via diborane addition and oxidation with $H_2O_2$/NaOAc to yield alcohol **15**. Interestingly, none of the corresponding aldehyde **18** could be detected, which normally[15] is found as the principal product. Since traces of $BF_3$ are known[16] to catalyze the H⟷Cl exchange in the intermediate $\alpha$-chloro-alkylborane **19**, the reaction was repeated with rigourously purified diborane solution. Results were, however, the same and none of the desired **18** could be obtained. Again a steric compression of the tosyl substituent might be responsible since the stability of **19** in which the $\alpha$-substituent presumably occupies the equatorial position is expected to be diminished as a result of non-bonding interactions of the two large coplanar groups.

Apart from a catalytic hydrogenation ($PtO_2$/EtOH) resulting in a mixture of methyl epimers **17** and **20** (ratio 3:7) other reactions KOH/HMTP 20 hr/95°[17] or NaOMe/xylene 24 hr/60°[18] starting with **9** failed. Determination of the stereochemistry of alcohol **15** proved straightforward since the structure of **1** had been established previously via X-ray analysis.[19] $SOCl_2$ conversion of **15** gave the monochloride **16**, which was different in all respects from the monochloride **6** obtained via dechlorination-hydrogenation of **1**. As the stereochemistry of the *cis* ring junction remains unaltered the only change is the spatial orientation of the $C_3$-substituent.

The $^1H$ NMR data supported the above conclusion. From the analysis of the spectra of **15** and the corresponding acetate the following J values for $H_{4a}$ ($\delta$ 4.49) were found: $J_{4a-5} = 12.0$ and 3.0 Hz, $J_{4a-10b} = 5.5$ Hz indicating an equatorial position for $H_{4a}$ with respect to the heterocyclic ring. In view of the axial position of $H_3$ a relation $\Delta = \delta H_{4a} - \delta H_3$ can be formulated in the series **15–17**. The observed $\Delta$ of 0.5–1.2 ppm correlates remarkably well with earlier values of $\delta H_{ax} - \delta H_{eq}$ in N-tosyl bicyclo[3,3,1]nonanes.[13] As could be expected a similar calculation of $\delta H_{4a} - \delta H_3$ in the axial series (cf compounds **6** and **7**) shows a value of nearly zero, since both hydrogens occupy equatorial positions.

It should be emphasized that during the transformation of the $CCl_3$ moiety complete inversion has occurred at $C_3$. From a synthetic viewpoint the presently described method constitutes an attractive procedure for the preparation of various $\alpha$-substituted piperidines bearing additional functionality.[20]

Table 2. Formation of chlorides **9** and **10** upon alkaline treatment of **5**

| Exp | Base | Condition | Ratio 9/10†‡ |
|---|---|---|---|
| 1 | DABCN§ | xylene, 7 hr 130°C | 2.0 |
| 2 | DABCN | pure, 65 hr 90°C | 2.5 |
| 3 | DABCU¶ | pure, 120 hr 75°C | 1.2 |
| 4 | KOH | EtOH, 65 hr 80°C | 0.5 |
| 5 | KOtBu | tBuOH, 65 hr 45°C | 0.3 |
| 6 | KOtBu | xylene, 65 hr 45°C | 0.2 |

†Combined yield >85%.
‡Determined via PMR-analysis.
§Ref. 9.
¶Ref. 12.

## EXPERIMENTAL

All m.ps are uncorrected. Analyses were carried out by Messr H. Pieters of the Micro-analytical Department of this laboratory. IR spectra were taken on an Unicam SP-200 as KBr-tablets. The NMR spectra were determined on a Varian H-100 in $CDCl_3$, unless otherwise stated, with TMS as internal standard, $\delta$ values are given in ppm. Mass spectra were obtained on an AEI spectrometer type MS 9-H. The UV spectra were measured on a Cary-14 in ethanol.

*N - Tosyl - 3α - chloromethyl - 8 - methoxy - 2,3,4,4a,5,6 - hexahydro - benzo(f)quinoline* **2**

A mixture of 500 mg $PtO_2$, 5300 g $K_2CO_3$, 1270 g (2.6 mmol) of **1** and 200 ml EtOH was hydrogenated for 18 hr. After filtration and evaporation of the solvent, the residue was triturated with $Et_2O$, yield: 80%; m.p. ($Et_2O$): 126–128°; PMR $\delta$ ($CDCl_3$): 2.37 (s)

$ArCH_3$; 3.5 (m) $CH_2Cl$; 3.75 (s) $OCH_3$; 4.1–4.5 (m) $H_3$, $H_{4a}$; 5.95 (m) = CH; 7.25 (d), 7.69 (d) tosyl; 7.37 (d) $H_{10}$. Mass: 417 (M) 6%; 262 (M-Ts) 20%; 186 (retro Diels–Alder fragment) 100%. (Found: C, 63.2; H, 5.9; N, 3.5; S, 7.7; Cl, 8.1. Calc. for $C_{22}H_{24}O_3NSCl$ (417.95): C, 63.22; H, 5.79; N, 3.35; S, 7.67; Cl, 8.48%).

N - *Tosyl* - 3α - *dichloromethyl* - 8 - *methoxy* - 2,3,4,4a,5,6 - *hexahydro* - *benzo(f)quinoline* **3**

A mixture of 35 mg $PtO_2$, 51 mg $NEt_3$, 0.26 mmol **1** and 10 ml EtOH was hydrogenated for 45 hr. After work-up the obtained oil was pure, m.p. ($Et_2O$): 160–162°; PMR δ ($CDCl_3$): 2.39 (s) $ArCH_3$; 4.31 (diff. doublet, J = 13 Hz) $H_{4a}$; 4.53 (m) $H_3$; 5.61 (d, J = 9 c/s) $CHCl_2$; 5.97 (m) = CH; 7.36 (d) $H_{10}$; 7.27 (d), 7.71 (d) tosyl. Mass: 451 (M) 24%; 368 (M-C $Cl_2$) 13%; 296 (M-Ts) 39%; 212, 70%; 186 (retro Diels–Alder fragment) 100%; 91 ($C_7H_7$) 48%. (Found: C, 58.4; H, 5.3; N, 3.1; S, 7.2; Cl, 15.5. Calc. for $C_{22}H_{23}O_3NSCl_2$ (452.39): C, 58.41; H, 5.12; N, 3.10; S, 7.09; Cl, 15.67%).

N - *Tosyl* - 3α - *trichloromethyl* - 8 - *methoxy* - 1,2,3,4,4a,5,6,10b - *octahydrobenzo(f)quinoline* **4**

A mixture of 100 mg $PtO_2$, 0.51 mmol **1** and 40 ml HOAc was hydrogenated for 18 hr and worked up. PMR indicated a mixture of 65% **4** and 20% **5**; **4** was obtained as a crystalline product after thick layer chromatography (silicagel F254 Merck, eluant $C_6H_6/CHCl_3$ = 2/3), yield: 33%; m.p. (EtOH): 193–196°; PMR δ ($CDCl_3$): 2.41(s) $ArCH_3$; 3.73 (s) $OCH_3$; 3.94 (m) $H_{4a}$; 5.07 (d, J = 7.5 Hz) $H_3$; 6.80 (d) $H_{10}$; 7.28 (d) and 7.74 (d) tosyl. UV $\lambda_{max}^{EtOH}$: 229 (16,500); 265 (1850); 271 (1850); 275 (2100); 286 (1800). Mass: 487 (M) 1%, 91 100%. (Found: C, 54.3; H, 5.2; N, 2.8; S, 6.8; Cl, 21.7. Calc. for $C_{23}H_{24}O_3NSCl_3$ (488.86): C, 54.05; H, 4.95; N, 2.87; S, 6.56; Cl, 21.76%).

N - *Tosyl* - 3α - *dichloromethyl* - 8 - *methoxy* - 1,2,3,4,4a,5,6,10b - *octahydro* - *benzo(f)quinoline* **5**

(a) via $PtO_2$–$H_2$–EtOH *Hydrogenation.* A mixture of 500 mg $PtO_2$, 2.56 mmol **1** and 200 ml EtOH was hydrogenated for 16 hr. After reaction the pH was 4. After filtration and evaporation of the solvent the residue was triturated with EtOH, yield: 83%; m.p. (EtOH): 158–160°; PMR δ ($CDCl_3$): 2.40 (s) $ArCH_3$; 2.81 (m) $H_{10b}$; 3.75 (s) $OCH_3$; 4.05 (m) $H_{4a}$; 4.57 (m) $H_3$; 5.89 (d, J = 8 Hz) $CHCl_2$; 7.26 (d) and 7.70 (d) tosyl. (Found: C, 58.0; H, 5.6; N, 3.0; S, 7.2; Cl, 15.5. Calc. for $C_{22}H_{25}O_3NSCl_2$ (454.41): C, 58.14; H, 5.55; N, 3.08; S, 7.06; Cl, 15.61%).

(b) via RaNi–Pd/C *Hydrogenation.* A soln of 70.0 g (0.144 mmol) of **1** in a mixture of 1.4 l HOAc and 1.4 l of EtOAc was cooled at 0°. In a $N_2$-atmosphere, 250 ml of RaNi soln was added. After stirring for 3 hr at 0° 50 g of Pd/C 10% was added and the cooling was stopped. The mixture was filtered after 2 hr and worked up, yield: 52.8 g 81%.

N - *Tosyl* - 3α - *trichloromethyl* - 8 - *methoxy* - 1,2,3,4,4a,5,6,10b - *octahydrobenzo(f)quinoline* **6**

Compound **2** (0.7 g) was converted to **6** (60%) after 18 hr using $PtO_2$ (0.42 g) EtOH (120 ml). The catalytic hydrogenation of **2** was complete in 2.5 hr when Pd/C (10%) HOAc was used, yield: 83%; m.p. (EtOH): 113–116.5°; PMR δ ($CDCl_3$): 2.41 (s) $ArCH_3$; 3.7 (m) $CH_2Cl$; 3.7 (m) $H_3$, $H_{4a}$; 6.90 (d) $H_{10}$; 7.27 (d) and 7.72 (d) tosyl. UV $\lambda_{max}^{EtOH}$: 229 (16,000); 265 (sh, 2100); 272 (sh, 2000); 276 (2300); 286 (1900). Mass: 419 (M) 1%; 264 (M-Ts) 23%; 91 67%. Calc. exact mass: 419.1331. (Found: 419.1295). (Found: C, 62.8; H, 6.3; N, 3.5; S, 7.7; Cl, 8.0. Calc. for $C_{22}H_{26}O_3NSCl$: C, 62.91; H, 6.24; N, 3.33; S, 7.64; Cl, 8.45%).

N - *Tosyl* - 3α - *methyl* - 8 - *methoxy* - 2,3,4,4a,5,6 - *hexahydro* - *benzo(f)quinoline* **7**

To a soln of 1.44 mmol **1** in xylene (15 ml) 5.85 mmol $nBu_3SnH$ was added. The reaction was started with a catalytic amount of azobisisobutyronitrile. After stirring for 3.5 hr at 50°GLC indicated a mixture of 90% **2** and 10% **4**. After 160 hr at 85° **7** was worked up, yield: 70%; m.p. (ether): 122–124°; IR ($CHCl_3$): 1330 (m); 1160 (s) $SO_2$. PMR δ ($CDCl_3$): 1.25 (d, J = 7 Hz) $CH_3$; 2.37 (s) $ArCH_3$; 3.77 (s) $OCH_3$; 5.98 (m) = CH; 7.40 (d) and 7.23 (d) tosyl. Mass: 383 (M) 100%; 228 (M-Ts) 3%; 186 (retro Diels–Alder) 36%. (Found: C, 68.8; H, 6.6; N, 3.5; S, 8.3. Calc. for $C_{22}H_{25}O_3NS$ (383.50): C, 68.90; H, 6.57; N, 3.65; S, 8.36%).

N - *Tosyl* - 3 - *chloromethylene* - 8 - *methoxy* - 1,2,3,4,4a,5,6,10b - *octahydro* - *benzo(f)quinolines* **9** *and* **10**

A mixture of 7.27 mmol **5**, 20 mmol DABCN (0.7 ml) and 2 ml xylene was heated at 130° for 7 hr. The mixture was dissolved in $CHCl_3$, the soln extracted with 2N HCl (4 × 20 ml) and worked up. After trituration of the residue a crystalline mixture of vinyl-chlorides **9** and **10** was obtained, which could be separated by thick layer chromatography (silica gel F254 eluent: p.a. 60–80: EtOAc = 4/1).

Compound **9**: yield: 45% (PMR, crude reaction mixture), 14% (pure); m.p. (ether): 159–161.5°. PMR δ ($CDCl_3$): 2.42 (s) $ArCH_3$; 3.73 (s) $OCH_3$; 4.50 (m) $H_{4a}$; 6.40 (s) = CH; 6.85 (d) $H_{10}$; 7.29 (d) and 7.72 (d) tosyl. UV $\lambda_{max}^{CH_2Cl_2}$: 278 (3000); 287 (1900). Mass: 417 (M) 0.4%; 353 (M-$SO_2$) 8%; 262 (M-Ts) 18%; 91,100%. (Found: C, 63.1; H, 5.7; N, 3.3; S, 7.8; Cl, 8.4. Calc. for $C_{22}H_{24}O_3NSCl$ (417.95): C, 63.22; H, 5.79; N, 3.35; S, 7.81; Cl, 8.48%).

Compound **10**: yield: 20% (PMR, crude reaction mixture), (5% pure); m.p. (ether): 201.5–204°. PMR δ ($CDCl_3$): 2.42 (s) $ArCH_3$; 3.72 (s) $OCH_3$; 4.13 (m) $H_{4a}$; 6.21 (s) = CH; 6.86 (d) $H_{10}$; 7.28 (d) and 7.78 (d) tosyl. UV $\lambda_{max}^{CH_2Cl_2}$: 277 (2200); 287 (1800). Mass: 417 (M) 2%; 353 (M-$SO_2$) 10%; 262 (M-Ts) 10%; 91,100%. (Found for $C_{22}H_{24}O_3NSCl$: C, 63.1; H, 5.7; N, 3.3; S, 7.5; Cl, 8.4%).

N - *Tosyl* - 3 - *methyl* - 8 - *methoxy* - 1,4,4a,5,6,10b - *hexahydro* - *benzo(f)quinoline* **11**

A mixture of 0.39 mmol **12**, 0.75 mmol $nBu_3SnH$ 10 ml $C_6H_6$ and a small amount of azobisisobutyronitrile was boiled for 20 hr. After the reaction, the product was passed through a column (silica gel; eluent: $C_6H_6$), and 0.17 mmol (44%) of **11** (oil) was obtained, yield: 28% (cryst); m.p. (MeOH): 123–125°; IR ($CHCl_3$): 1650 (w) C=C; 1340 (s); 1160 (s) $SO_2$. PMR δ ($CDCl_3$): 2.17 (broad singlet $W_{1/2}$ = 5 Hz) =C–$CH_3$; 2.42 (s) $ArCH_3$; 3.73 (s) $OCH_3$; 4.38 (m) $H_{4a}$; 4.97 (t, J = 3 Hz) =CH; 7.28 (d) and 7.69 (d) tosyl. Mass: 383 (M) 18%, 228 (M-Ts) 26% 160 (retro Diels–Alder fragment) 100%, 91 19%. (Found: C, 68.8; H, 6.6; N, 3.5; S, 8.2. Calc. for $C_{22}H_{25}O_3NS$ (383.50): C, 68.90; H, 6.57; N, 3.65; S, 8.36%).

N - *Tosyl* - 3 - *chloromethyl* - 8 - *methoxy* - 1,4,4a,5,6,10b - *hexahydro* - *benzo(f)quinoline* **12**

To a soln of 0.96 mmol **9** in 20 ml $C_6H_6$ a catalytic amount of $BF_3$-etherate was added at r.t. After 2 hr $K_2CO_3$ was added. After filtration and evaporation of the solvent the residue was triturated with EtOH, yield: 96%; m.p. (MeOH): 170–173°; PMR δ ($CDCl_3$): 2.43 (s) $ArCH_3$; 3.71 (s) $OCH_3$; 4.19 (d, J = 12.0 Hz) =C–$CHaHbCl$; 5.02 (d, J = 12.0 Hz) =C–$CHaHbCl$; 5.61 (t) =CH; 7.27 (d) and 7.77 (d) tosyl. UV $\lambda_{max}^{EtOH}$: 222 (21,700); 276 (3300); 287 (2100). Mass: 417 (M) 15%, 262 (M-Ts) 18%; 160 (retro Diels–Alder fragment) 100%. (Found for $C_{22}H_{24}O_3NSCl$: C, 63.1; H, 5.9; N, 3.3; S, 7.7; Cl, 8.3%). Isomerisations of **9** in boiling HCl/EtOH or $CF_3COOH$ at 0° were also successful. Isomerisation of **10** in $BF_3$-etherate/ether r.t. and boiling HCl/EtOH did not occur. The isomerisation in $CF_3COOH$ was very slow: after 1 week, r.t. the ratio **10**/**12** was 1/2.

4 - (2' - N - *Tosylamino* - 6' - *methoxy* - 1',2',3',4' - *tetrahydro* - *naphthyl* - 1') - *butanone* - 2 **13**

Compound **6** (0.5 g) and 2.5 ml of DABCN were heated at 165° for 20 hr. The mixture was dissolved in $CHCl_3$ (80 ml) and extracted four times with 0.2 M HCl (20 ml). After addition of ether (200 ml) and work-up the residue was shown to contain **8** (20%) and **11** (55%) by PMR analysis. The residue was refluxed for 24 hr in dioxane (10 ml) to which 2 drops of 12 M HCl were added. After work-up and chromatography $SiO_2$/cyclohexane-EtOAc 3:2) **13** was obtained as an oil in 40% yield (based on **6**); m.p. (ether): 114–115°. IR ($CHCl_3$): 3300 (m) NH; 1700 (s) C=O; 1320 (m) and 1150 (s) $SO_2$; PMR δ ($CDCl_3$): 2.07 (s) ($COCH_3$); 2.40 (s) $ArCH_3$; 3.6 (m) $H_2$; 3.72 (s) $OCH_3$; 5.70 (d, J = 7.5 Hz exchangeable) NHTs; 6.97 $H_8$; 7.27 (d) and 7.76 (d) tosyl. Mass: 246 (M = Ts) 3%; 230 (M-$H_2$NTs) 100%; 91 26%. (Found: C, 65.7; H, 6.7; N, 3.5; S, 8.0. Calc. for $C_{22}H_{27}O_4NS$ (401.52): C, 65.80; H, 6.78; N, 3.49; S, 7.99%).

4 - (2' - N - *Tosylamino* - 6' - *methoxy* - 1',2',3',4' - *tetrahydro* - *naphtyl* - 1') - 1 - *chloro* - *butanon* - 2 **14**

A 2/1 mixture of **9** and **10** (0.5 g) was boiled in a mixture of 10 ml dioxane and 2 ml 0.3 N HCl for 19 hr. After addition of $CHCl_3$ the mixture was washed with $H_2O$. **15** was separated from unreacted **11** by crystallization from acetone, yield: 50%; m.p. (EtOH): 131–133°. IR ($CHCl_3$) 3300 (m) NH; 1725 (m) C=O; 1325 (m); 1160 (s) $SO_2$. PMR $\delta$ ($CDCl_3$): 2.42 (s) $ArCH_3$; 3.6 (m) $H_2$; 3.73 (s) $OCH_3$; 4.04 (s) $CH_2Cl$; 5.06 (d, $J = 7.5$ NH; 6.99 (d) $H_6$; 7.29 (d) and 7.77 (d) tosyl; Mass: 435 (M) 1%; 280 (M-Ts) 8%; 91 100%. (Found: C, 60.7; H, 6.0; N, 3.3; S, 7.4; Cl, 8.1. Calc. for $C_{22}H_{26}O_4NSCl$ (435.97): C, 60.61; H, 6.01; N, 3.21; S, 7.35; Cl, 8.13%).

N - *Tosyl* - 3$\beta$ - *hydroxymethyl* - 8 - *methoxy* - 1,2,3,4,4a,5,6,10b - *octahydro* - *benzo(f)quinoline* **15**

To a mixture of 5.02 mmol **9** and 2.17 mmol **10** in 30 ml THF was added 15 ml $B_2H_6$/THF-solution (5.8 molar) and the mixture was stirred at r.t. for 7 hr. To the cooled soln (0°) was added 7.5 ml $H_2O$, 7.5 ml 2N NaOAc soln and 1.5 ml 30% $H_2O_2$. Unreacted **10** crystallized quantitatively. After work-up **15** was triturated with ether, yield: 57%; m.p. (ether): 121–123°; PMR $\delta$ ($C_6D_6$): 3.25 (m) $H_3$; 3.35 (s) $OCH_3$; 3.95 (m) $CH_2OH$; 4.49 (m) $H_{4a}$. Mass: 401 (M) 0.6%; 246 (M-Ts) 10%; 91.92%. (Found: C, 65.7; H, 6.8; N, 3.6; S, 8.0. Calc. for $C_{22}H_{27}O_4NS$ (401.52): C, 65.80; H, 6.78; N, 3.49; S, 7.99%).

N - *Tosyl* - 3$\beta$ - *chloromethyl* - 8 - *methoxy* - 1,2,3,4,4a,5,6,10b - *octahydro* - *benzo(v)quinoline* **16**

A mixture of 0.80 mmol **15**, 2.5 mmol pyridine, 5.5 mmol $SOCl_2$ and 10 ml $C_6H_6$ was boiled for 1 hr. After work-up the residue was passed through a column (silanized silica gel, eluant: $C_6H_{12}/C_6H_6 = 3/1$. Yield: 100%; m.p. (ether): 126.5–129.5°. PMR $\delta$ ($CDCl_3$): 2.40 (s) $ArCH_3$; 3.73 (s) $OCH_3$; 3.9 (m) $H_3$ and $CH_2Cl$; 4.29 (m) $H_{4a}$; 6.93 (d) $H_{10}$; 7.26 (d) and 7.74 (d) tosyl. UV $\lambda_{max}^{EtOH}$: 226 (16,500); 277 (2500); 287 (2200). Mass: 419 (M) 16%; 264 (M-Ts) 23%; 91 30%. (Found: C, 63.0; H, 6.4; N, 3.4; S, 7.7; Cl, 8.5. Calc. for $C_{22}H_{26}O_3NSCl$ (419.97): C, 62.91; H, 6.24; N, 3.33; S, 7.64; Cl, 8.45%).

N - *Tosyl* - 3$\beta$ - *methyl* - 8 - *methoxy* - 1,2,3,4,4a,5,6,10b - *octahydro* - *benzo(f)quinoline* **17**

A mixture of 0.15 mmol **9**, 40 mg $PtO_2$ and 10 ml EtOH was hydrogenated at 3.5 atm. From PMR the ratio **17**/**20** = 7/3 was deduced. From this mixture **17** was isolated by crystallization, yield: 20%; m.p. (MeOH): 144–147°. PMR $\delta$ ($CDCl_3$): 1.24 (d, $J = 7$ Hz) $CH_3$; 2.40 (s) $ArCH_3$; 3.5 (m) $H_3$; 3.75 (s) $OCH_3$; 4.65 (m) $H_{4a}$; 6.97 (d) $H_{10}$; 7.26 and 7.75 tosyl. Mass: 385 (M) 20%; 230 (M-Ts) 95%; 91 100%. (Found: C, 68.3; H, 7.1; N, 3.7; S, 8.3. Calc. for $C_{22}H_{27}O_3NS$ (385.52): C, 68.54; H, 7.06; N, 3.65; S, 8.32%).

N - *Tosyl* - 3$\alpha$ - *methyl* - 8 - *methoxy* - 1,2,3,4,4a,5,6,10b - *octahydro* - *benzo(f)quinoline* **20**

A mixture of 120 mg $PtO_2$, 0.52 mmol **7** and 36 ml EtOH was hydrogenated at 4.0 atm for 20 hr. After work-up the oil (90% pure) was crystallized, yield: 20%; m.p. (diisopropylether): 93–96.5°. PMR $\delta$ ($CDCl_3$): 1.32 (d, $J = 7$ Hz) $CH_3$; 2.41 (s) $ArCH_3$; 3.75 (s) $OCH_3$; 4.5 (m) $H_3$, $H_{4a}$; 6.93 (s) $H_{10}$; 7.25 (d) and 7.73 (d) tosyl. Mass: 385 (M) 54%; 230 (M-Ts) 100%; 91.45%. (Found: C, 68.5; H, 6.9; N, 3.8; S, 8.2. Calc. for $C_{22}H_{27}O_3NS$ (385.52): C, 68.54; H, 7.06; N, 3.65; S, 8.33%).

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