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BASE INDUCED 1,3 N→C TOSYL MIGRATION

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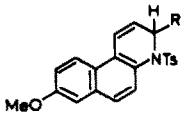
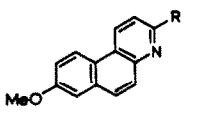
Abstract—A novel type of a 1,3 N→C toluenesulfonyl shift is described. The rearrangement occurs upon treatment with base of α-halomethyl-dehydro piperidine sulfonamides.

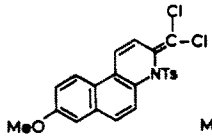
DURING an attempted alkaline hydrolysis of tetrahydropiperidine **1**, containing the N - tosyl - α - trichloro methyl moiety, a crystalline material was formed which on the basis of spectral evidence was assigned the rearranged structure **2**. Although the related N-OR→C-OR rearrangement has been studied extensively in the past years in various α - picoline - N - oxides[2] the observed tosyl shift seems unprecedented. Literature examination revealed the occurrence of 1,3 N→N arylsulfone shifts in some heterocyclic sulfonamides[3] while a formally analogous 1,3 N→C rearrangement is found in the tosyl migration of N-arylsulfonamides.[4] However, the latter reaction is carried out in sulfuric acid and may proceed via a radical mechanism similar to that observed in the aromatic nitramine rearrangement.[5] The latter type of mechanism is also established in the ABIN or peroxide catalyzed 1,3 N→C rearrangement of N - methyl - N - allyl - sulfonamide.[6]



1 R = CCl_3



2 R = $CCl_2SO_2ArCH_3$
3 R = COOEt



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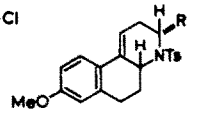
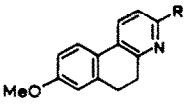
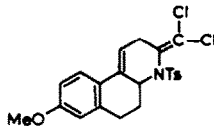


5 R = $-CCl_3$
6 R = $-CHCl_2$



7 R = $CHClSO_2ArCH_3$
8 R = $CH_2SO_2ArCH_3$



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The structure of **2** has been proven via PMR and mass spectral analysis and was confirmed beyond doubt by a comparison of its UV spectrum with that of the corresponding benzo[*f*] quinoline **3**, synthesized by an independent route.[10b] Its formation can be rationalized by assuming a 1,3 N→C tosyl shift in the anhydrobase **4** which is formed after elimination of HCl from **1**. The subsequent or simultaneous aromatization into a pyridine ring might facilitate the rearrangement process.

In order to estimate the importance of the latter factor† the chloromethyl derivatives **5** and **6** were subjected to base treatment. Although no reaction occurred upon use of KOH, reaction of **5** with 1,5 - diaza - bicyclo - [4,4,0] - nonenes - 5[7] in xylene gave two products **7** and **8** in respectively 50% and 15% yield. Similar reaction of **6** afforded **8** in 60% yield. Alternatively **8**-HCl could also be obtained from **7** via PtO_2/H_2 hydrogenation in HCl-ethanol. The structure assignments to **7** and **8** are mainly based on PMR, UV and mass spectral date (cf Experimental). Furthermore the PMR data of **8** (δ-CH_2SO_2 4·79) closely correspond with those of phenyl - 2 - picolyl - sulfone[8] (δ - CH_2SO_2 4·81) in DMSO.

The formation of **8** in the DABCN reaction is most likely to proceed via the anhydrobase **9**, which is regarded as a dihydropyridine precursor. The latter class of compound is extremely sensitive towards disproportionation.[9] The 1,3 tosyl shift then can be visualized Scheme 1.

From these results it may be concluded that α-dichloro- and trichloromethyl-tetrahydro piperidine sulfonamides smoothly rearrange under influence of base and heat.‡ The starting materials can be prepared most conveniently by heterocycloaddition.[11] Whether the actual 1,3 N→C tosyl shift is of anionic or radical type remains to be determined although the former mechanism is more likely in view of the completely different rearrangement[12] in this type of compound under conditions whereby radical formation at the α-methylene substituent is involved.

EXPERIMENTAL

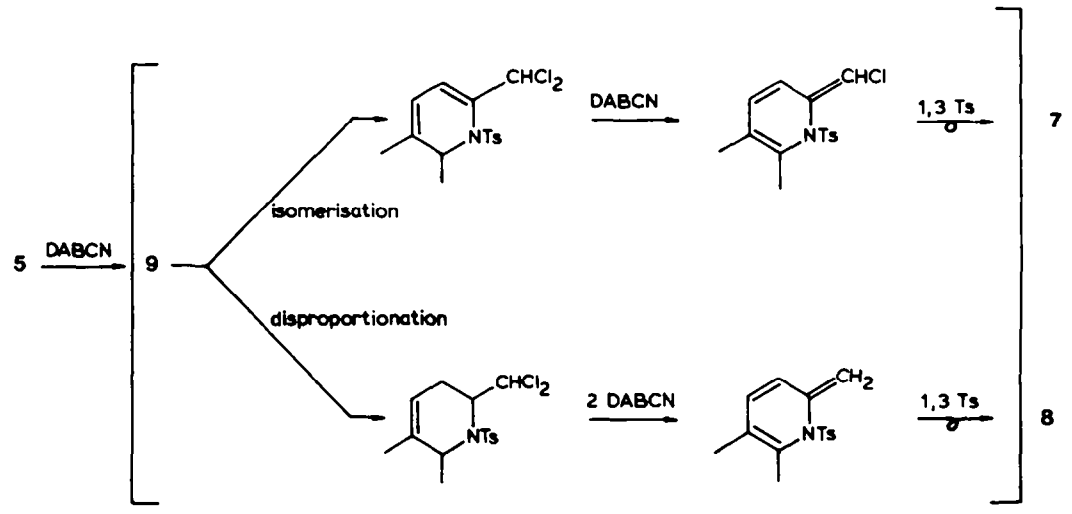
M.ps are not corrected. IR spectra were taken on an Unicam SP-200 as KBr-tablets. The NMR spectra were determined on a Varian HA-100, with TMS as internal standard, δ values are given in ppm. Mass spectra were obtained on an AEI mass-spectrometer type MS 9-H. The UV spectra were measured on a Cary-14 in EtOH.

N - *Tosyl* - 3 - *trichloromethyl* - 8 - *methoxy* - 3,4 - *dihydro* - *benzo(f)quinoline* **1**. Prepared according to the procedure of Loven.[1]

3 - *Dichloro* - p - *toluenesulfonmethyl* - 8 - *methoxy* - *benzo(f)quinoline* **2**. Compound **1** (0·63 mmol) was dissolved in a mixture of 4·5 mmol KOH and 30 ml EtOH. After 65 hr the solvent was evaporated. The residue was shaken with $CHCl_3$ and H_2O. The organic layer was washed with 2N KOH, H_2O, 2N HCl, sat NaCl aq and dried. After evaporation the PMR spectrum indicated a yield of 85% (oil); mp (EtOH): 222–225°. IR ($CHCl_3$): 1620, 1600 (arom), 1330, 1145 (SO_2) cm^{-1}; PMR δ ($CDCl_3$): 2·41 (s)

†Saturated α-halomethylpiperidines do not undergo the rearrangement.

‡A similar process occurred also in simple α-halomethyl-piperidine sulfonamides.[10]



Scheme 1.

$ArCH_3$; 3·97 (s) OCH_3; 7·31 (d) and 7·66 (d) tosyl; 8·28 (d, J = 8·5°/s)H_2; 8·54 (d, J = 8·5 °/s)H_{10}; 8·94 (d, J = 8·5 °/s)H_1. UV λ_{max}^{EtOH}: 273 (31,000), 317 (11,000), 344 (5,500), 362 (5,000) nm. (Found: C, 59·0; H, 4·4; N, 3·6; S, 7·5; Cl, 15·2%). Calc. for $C_{22}H_{17}O_3NSCl_2$ (446·38): C, 59·19; H, 3·84; N, 3·13; S, 7·18; Cl, 15·89).

N - *Tosyl* - 3 - *dichloromethyl* - 8 - *methoxy* - 2,3,4,4a,5,6 - *hexahydro* - *benzo*(f) *quinoline* **5**. Prepared according to the procedure of Loven.[1]

N - *Tosyl* - 3 - *dichloromethyl* - 8 - *methoxy* - 2,3,4,4a,5,6 - *hexahydro* - *benzo*(f)*quinoline* **6**. A mixture of **1** (0·25 mmol) NEt_3 (0·50 mmol) and 25 mg PtO_2 was hydrogenated at atm press. After filtration and evaporation, the residue was dissolved in $CHCl_3$ and H_2O. The organic layer was washed with 2N HCl, sat NaCl aq and dried. After evaporation oily **6** was obtained quantitatively; m.p. (ether): 160–162°. IR ($CHCl_3$): 1355, 1330, 1160 (SO_2) cm^{-1}; PMR δ ($CDCl_3$): 2·39(s) $ArCH_3$; 3·77(s) OCH_3; 4·31 (diff. d, J = 12 °/s)H_{4a}; 4·53(m) H_5; 5·61 (d, J = 9 °/s) $CHCl_2$; 5·97(m) vinylic H; 7·36(d) H_{10}; 7·27(d) and 7·71(d) tosyl. (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%).

3 - *Chloro* - p - *toluenesulfonmethyl* - 8 - *methoxy* - 5,6 - *dihydro* - *benzo*(f)*quinoline* **7** *and* 3 - p - *toluenesulfonmethyl* - 8 - *methoxy* - 5,6 - *dihydro* - *benzo*(f)*quinoline* **8**. A mixture of **5** (1·65 mmol) 1,5 - diaza - bicyclo - [4,3,0]nonene - 5 (DABCN) (5·75 mmol) was heated in 0·5 ml xylene during 70 min at 100°. The product was dissolved in $CHCl_3$ and H_2O. The organic layer was washed with 2N HCl (5 times) and chromatographated on thick layer (silicagel F254, Merck) with $CHCl_3$/EtOAc = 94/6. **7** Was isolated in 50% yield (oil), yield: 23% (cryst.); m.p. (EtOH): 145–147°. IR ($CHCl_3$): 1328, 1150 (SO_2) cm^{-1}; PMR δ ($CDCl_3$): 2·41 (s) $ArCH_3$; 2·88 (s) H_5,H_6; 3·81 (s) OCH_3; 5·82(s) CHCl tosyl; 7·27(d) and 7·70(d) tosyl; 7·51 (d, J = 8·5 °/s)H_2; 7·93 (d, J = 8·5 °/s)H_1. (Found: C, 63·8; H, 4·9; N, 3·2, S, 7·8, Cl, 8·6. Calc. for $C_{22}H_{20}O_3$ NSCl (413·92): C, 63·83; H, 4·87; N, 3·38; S, 7·75; Cl, 8·57%). **8** Was isolated in 15% yield (oil). Yield: 8% (cryst.); m.p. (EtOH): 154–155·5°. IR ($CHCl_3$): 1317, 1148 (SO_2) cm^{-1}. PMR δ ($CDCl_3$): 2·39(s) $ArCH_3$; 2·84(s) H_5, H_6; 3·81(s) OCH_3; 4·50(s) CH_2 tosyl; 7·21(d) and 7·57(d) tosyl; 7·86 (d, J = 8·5 °/s) H_1. (Found: C, 69·6; H, 5·6; N, 3·8; S, 8·4. Calc. for $C_{22}H_{21}O_3$ NS (379·47): C, 69·63; H, 5·58; N, 3·69; S, 8·45%). The HCl-salt of **7** could be prepared by dissolving **7** in boiling conc HCl and cooling, yield: 90%; m.p. 110–120°; PMR δ ($CDCl_3$): 2·47(s) $ArCH_3$; 3·86(s) OCH_3; 7·33(s) CHCl tosyl; 7·42(d) and 8·07(d) tosyl; 7·72(d) H_{10}; 8·09 (d, J = 8 °/s) H_2; 8·48 (d, J = 8 °/s) H_1. (Found: C, 58·6; H, 4·6; N, 3·2; S, 7·1; Cl, 8·0; $Cl^{\ominus}$, 7·7. Calc. for $C_{22}H_{20}O_3$ NSCl. HCl (450·39): C, 58·66; H, 4·70; N, 3·11; S, 7·12; Cl, 7·87; $Cl^{\ominus}$, 7·87%). The $HClO_4$-salt of **7** was prepared by adding a few drops of 60% $HClO_4$ to a soln of **7** in EtOAc, yield: 80%; m.p. 221–225°; PMR δ ($CDCl_3$): 2·49(s) $ArCH_3$; 3·89(s) OCH_3; 6·54(s) CHCl tosyl; 7·46(d) and 8·04(d) tosyl; 7·73(d) H_{10}; 8·20 (d) H_2; 8·57 (d) H_1. The HCl-salt of **8** was prepared by dissolving **8** in 2N HCl and cooling, yield: 40%; m.p. 165–169°; PMR δ ($CDCl_3$): 2·43(s) $ArCH_3$; 3·86(s) OCH_3; 5·22(s) CH_2 tosyl; 7·37(d) and 7·95(d) tosyl; 7·70 (d, J = 8 °/s) H_{10}; 7·93 (d, J = 8 °/s) H_2; 8·42(d) H_1. (Found: C, 63·4; H, 5·4; N, 3·5; S, 7·7 $Cl^{\ominus}$, 8·4. Calc. for $C_{22}H_{21}O_3$ NS . HCl (415·94): C, 63·52; H, 5·33; N, 3·37; S, 7·71; $Cl^{\ominus}$, 8·53%).

Conversion of **7** to **8**-HCl. To a mixture of **7** (0·48 mmol) 200 mg PtO_2 and 125 ml EtOH, 3 drops of conc HCl were added. After 17 hr hydrogenation at 1 atm the product was filtered, evaporated and crystallized from CH_2Cl_2/EtOAc yielding 78% pure **8**-HCl.

Reaction of **6** *with DABCN.* Compound **6** (0·09 mmol) was dissolved in 0·3 ml DABCN and 0·7 ml xylene and heated at 110° for 2 hr. After work-up **8** was isolated in 60% yield.

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