Azepinones. Part 1. Synthesis of 1,2,3,7-Tetrahydroazepin-4-ones and Hexahydroazepin-3-ones

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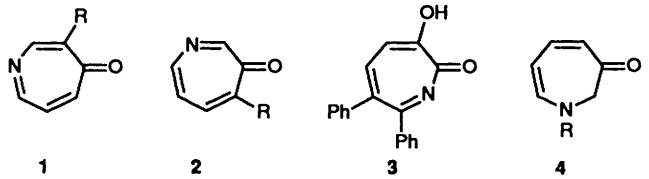
2-Chloro-*N*-tosylprop-2-enylamine (**5**; R = H) was converted into methyl 3-[*N*-(2-chloroprop-2-enyl)-*N*-tosylamino]propanoate (**5**; R = $CH_2CH_2CO_2Me$) and into 3-[*N*-(2-chloroprop-2-enyl)-*N*-tosylamino]propanonitrile (**5**; R = CH_2CH_2CN). These, in turn, were converted into 4-[*N*-(2-chloroprop-2-enyl)-*N*-tosylamino]-1-methylbutan-2-ol [**5**; R = $CH_2CH_2C(OH)Me_2$], 3-[*N*-(2-chloroprop-2-enyl)-*N*-tosylamino]-1-phenylpropan-1-one (**5**; R = CH_2CH_2COPh), 4-[*N*-(2-chloroprop-2-enyl)-*N*-tosylamino]-2-phenylbutan-2-ol [**5**; R = $CH_2CH_2C(OH)(Me)Ph$], 3-[*N*-(2-chloroprop-2-enyl)-*N*-tosylamino]-1-phenylpropan-1-ol [**5**; R = $CH_2CH_2CH(OH)Ph$], 4-[*N*-(2-chloroprop-2-enyl)-*N*-tosylamino]butan-2-ol [**5**; R = $CH_2CH_2CH(OH)Me$] and 3-[*N*-(2-chloroprop-2-enyl)-*N*-tosylamino]propanoic acid (**5**; R = $CH_2CH_2CO_2H$). The alcohols [**5**; R = $CH_2CH_2C(OH)Me_2$] and [**5**; R = $CH_2CH_2CH(OH)Ph$] were cyclised by 90% sulfuric acid to 5,5-dimethyl-*N*-tosylazepan-3-one (**6**; R^1 = R^2 = Me) and 5-phenyl-*N*-tosylazepan-3-one (**6**; R^1 = Ph, R^2 = H), respectively. 6,6-Dichloro-*N*-tosylazepan-4-one **7** was obtained from 3-[*N*-(2-chloroprop-2-enyl)-*N*-tosylamino]propanoic acid (**5**; R = $CH_2CH_2CO_2H$) *via* the acid chloride and was further converted into 6-chloro-1,2,3,7-tetrahydro-*N*-tosylazepin-4-one (**8**, R = Cl) and into the 6-methoxy analogue (**8**; R = OMe).

Substituted azepinones based on structures (**1** and **2**; R = H) have rarely been described,[1-3] nor have their hydroxy derivatives, 'azatropolones' (**1** and **2**; R = OH), been easy targets, although recently, derivatives of the azepin-2-one ring system (*e.g.*, **3**) have been reported.[4,5] The relationship of these molecules to tropones and tropolones make them interesting synthetic targets.

Dihydroazepin-3-ones **4** elegantly made by flash-vacuum pyrolysis (FVP) have been studied by McNab and Monahan.[6] Furthermore, a few examples are known of syntheses leading to tetrahydroazepin-3- and -4-ones: these generally involve ring-expansion procedures.[7-11] To expedite research in these areas, a more direct, productive synthesis of partially reduced azepinones was required. This paper describes such a synthesis which exploits intramolecular Friedel–Crafts cyclisation of easily accessible *N*-tosyl compounds.

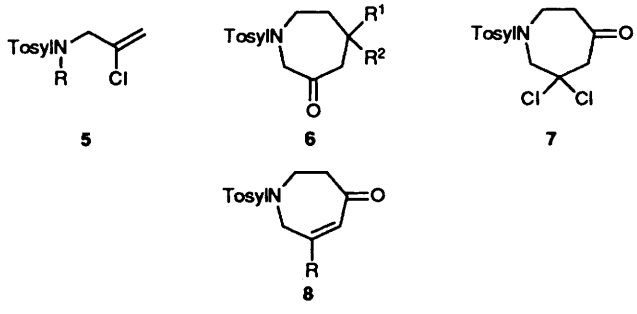


1 **2** **3** **4**

Discussion

The chloroprop-2-enyl group has been shown by Lansbury[12] to be a useful 3-carbon synthon, being resistant to a variety of reagents but capable of undergoing electrophilic substitution at a terminal carbon atom. We have previously adapted such a methodology for the synthesis of 1-benzazepin-3-ones.[13] In the present work the chloroprop-2-enyl group is pivotal.

Toluene-*p*-sulfonamide was alkylated with 2,3-dichloropropene; the mono- (**5**; R = H) and di- [**5**; R = $CH_2C(Cl)=CH_2$] substituted products were separated by a modification of the classical Hinsberg approach. Michael addition of the mono-alkylated product to methyl acrylate or acrylonitrile gave the ester (**5**; R = $CH_2CH_2CO_2Me$) or nitrile (**5**; R = CH_2CH_2CN), respectively, in good yield. From these materials, all of



5 **6** **7** **8**

the required intermediates could be made by established procedures. For example, hydrolysis of the ester (**5**; R = $CH_2CH_2CO_2Me$) gave the acid and hence the acid chloride (**5**; R = CH_2CH_2COCl), whilst reaction of the ester with methylmagnesium iodide gave the tertiary alcohol [**5**; R = $CH_2CH_2C(OH)Me_2$]. The secondary alcohols [**5**; R = $CH_2CH_2CH(OH)Me$] and [**5**; R = $CH_2CH_2CH(OH)Ph$] were obtained from the nitrile (**5**; R = CH_2CH_2CN) (see Experimental section).

The tertiary alcohol [**5**; R = $CH_2CH_2C(OH)Me_2$] could best be cyclised (30%) by treatment with 90% sulfuric acid at 0 °C. The ketone thus produced (**6**; R^1 = R^2 = Me) showed all the spectroscopic features expected. In particular, a carbonyl stretching frequency at 1715 cm^{-1} was observed and the ^1H NMR spectrum included a singlet at δ 1.0 attributed to two identical methyl groups. This method complements those for azepanones reported in the literature.[14] A ketone (**6**; R^1 = Ph, R^2 = H) could also be obtained (57%) from the corresponding secondary benzylic alcohol [**5**; R = $CH_2CH_2CH(OH)Ph$]. However, the alcohols [**5**; R = $CH_2CH_2CH(OH)Me$] and [**5**; R = $CH_2CH_2C(OH)(Ph)Me$] appeared to be dehydrated rather than to cyclise under the above conditions. There is scope for further investigations using other Lewis acids.

Intramolecular acylation was achieved with the acid chloride (**5**; R = CH_2CH_2COCl) and anhydrous aluminium chloride in dichloromethane free from alcohols. Optimisation raised the

yield of dichloro ketone **7** to 56%: a minor product was the chloro enone (**8**; R = Cl) which could also be obtained (95%) when compound **7** was treated with sodium carbonate in aq. tetrahydrofuran (THF). On the other hand, treatment of compound **7** with sodium carbonate in methanol gave the enol ether (**8**; R = OMe). The structure of the dichloro ketone **7** rests on its analyses, mass, ^{1}H NMR, and IR spectra (ν_{max} 1700 cm^{-1}), mode of formation, and the above transformations.

Thus, a satisfactory, novel synthesis of 1,2,3,7-tetrahydroazepin-4-ones has been developed: the overall yield from toluene-*p*-sulfonamide is 18% at present. It will now be possible to explore the chemistry of this series. Furthermore, the relatively rare hexahydroazepin-3-ones (azepan-3-ones) (*e.g.*, **6**) may also be exploited.

Experimental

M.p.s were obtained on a Gallenkamp melting point apparatus in open capillaries and are uncorrected. Mass spectra were determined on an AEIMS9 double-focussing mass spectrometer, modified with solid-state console, using a GEC-05 computer-based data system. ^{1}H NMR spectra were recorded on a Perkin-Elmer R32 spectrometer operating at 90 MHz or on a Bruker SM250 spectrometer operating at 250.13 MHz in Fourier transform mode. All spectra were recorded with deuteriochloroform as solvent with tetramethylsilane as internal reference, unless otherwise stated. *J*-Values are given in Hz.

Chromatographic Materials.—Short-path columns were run on Merck Art. 7747 Kieselgel 60 PF_{254} and the samples were adsorbed onto Merck 7734 silica gel type 60 prior to loading the column. Flash columns were run on Camlab Art. Nr. 81538 MN Kieselgel 60 (0.04–0.063 mm) and samples were applied to the column in solution, or adsorbed onto Merck 7735 silica gel type 60.

2-*Chloro*-N-*tosylprop*-2-*enylamine* (**5**; R = H).—A solution of sodium carbonate (12.4 g, 117 mmol) in water (400 cm^3) was added to a stirred solution of toluene-*p*-sulfonamide (40.1 g, 234 mmol) in ethanol (350 cm^3). The whole was then refluxed and stirred while a solution of freshly distilled 2,3-dichloropropene (26 g, 235 mmol) in ethanol (50 cm^3) was added dropwise during 1 h. The mixture was refluxed for a further 18 h, the ethanol was removed under reduced pressure, and the aqueous solution was acidified, and extracted with toluene. Interfacial material and extraction (aq. sodium carbonate) gave recovered toluene-*p*-sulfonamide (8.1 g). Washing of the toluene phase with aq. sodium hydroxide extracted the *title product* (19.8 g, 34.5%), which when recrystallised from toluene had m.p. 62–63 °C (Found: C, 49.1; H, 4.8; N, 5.6; Cl, 14.6. $C_{10}H_{12}Cl_2NO_2S$ requires C, 48.9; H, 4.9; N, 5.7; Cl, 14.4%); ν_{max}(film)/cm^{-1} 3400 (NH) and 1640 (C=C); δ_H 7.25–7.9 (4 H, m, ArH), 5.3 (1 H, s, exch., NH), 5.2 (2 H, s, =CH_2), 3.7 (2 H, s, CH_2) and 2.4 (3 H, s, Me).

Evaporation of the toluene gave the *bis adduct* [**5**; R = $CH_2C(Cl)=CH_2$] (2.2 g) as a yellow oil which slowly solidified, m.p. 36–37 °C (Found: C, 49.1; H, 4.5; N, 4.4; Cl, 22.4. $C_{13}H_{15}Cl_2NO_2S$ requires C, 48.8; H, 4.7; N, 4.4; Cl, 22.1%); ν_{max}/cm^{-1} 1630 (C=C); δ_H 7.3–7.7 (4 H, m, ArH), 5.4 (4 H, s, 2 × CH_2=C), 4.1 (4 H, s, 2 × CH_2) and 2.4 (3 H, s, Me).

Methyl 3-[*N*-(2-*Chloroprop*-2-*enyl*)-N-*tosylamino*]*propanoate*(**5**;R = $CH_2CH_2CO_2Me$).—2-Chloro-*N*-tosylprop-2-enylamine (10 g, 41.2 mmol) and methyl acrylate (4.01 g, 42 mmol) were stirred together at room temperature under nitrogen for 1 h, when sodium hydride (60%; 0.06 g, 2.5 mmol) was added. After the mixture had been stirred for a further 18 h, chloroform (600 cm^3) was added and the whole was washed with aq. hydrogen chloride (2 mol dm^{-3}; 3 × 150 cm^3), dried, and evaporated. Chromatography gave the *title product* as an oil (11.2 g, 81.5%) (Found: C, 50.6; H, 5.5; N, 4.2. $C_{14}H_{18}ClNO_2S$ requires C, 50.7; H, 5.5; N, 4.2%); ν_{max}(film)/cm^{-1} 1730 (C=O) and 1600 (C=C + arom); δ_H 7.25–7.85 (4 H, m, ArH), 5.45 (2 H, s, =CH_2), 4.05 (2 H, s, CH_2), 3.7 (3 H, s, OMe), 3.45–3.65 (2 H, t, CH_2), 2.6–2.8 (2 H, t, CH_2) and 2.5 (3 H, s, Me).

4-[N-(2-*Chloroprop*-2-*enyl*)-N-*tosylamino*]-2-*methylbutan*-2-*ol* [**5**; R = $CH_2CH_2C(OH)Me_2$].—Iodomethane (910 mg, 6.3 mmol) and magnesium turnings (150 mg, 6.3 mmol) were allowed to react under nitrogen in dry diethyl ether (50 cm^3); a solution of the ester (**5**; R = $CH_2CH_2CO_2Me$) (1.0 g, 3 mmol) in dry diethyl ether (25 cm^3) was added. After 1 h, the usual work-up gave a yellow oil (1.105 g), purified by flash chromatography [toluene–ethyl acetate (4:1)]. The *title product* was a solid (0.39 g, 40%), m.p. 46–48 °C (Found: C, 54.8; H, 6.9; N, 3.9%; M$^+$, 267.137 42. $C_{15}H_{22}ClNO_3S$ requires C, 54.3; H, 6.7; N, 3.7%; M, 267.138 99); ν_{max}($CHCl_3$)/cm^{-1} 3500 (OH); δ_H 7.3 (4 H, m, ArH), 5.4 (2 H, d, =CH_2), 3.9 (2 H, s, CH_2), 3.4 (2 H, t, CH_2), 2.4 (3 H, s, Me), 1.7 (2 H, t, CH_2), 1.5 (1 H, s, exch., OH) and 1.2 (6 H, s, 2 × Me).

5,5-*Dimethyl*-N-*tosylazepan*-3-*one* (**6**; R^1 = R^2 = Me).—A solution of the above alcohol (2.0 g, 6.0 mmol) in diethyl ether (10 cm^3) was added to stirred 90% sulfuric acid (50 cm^3) at −15 °C. After 30 min the mixture was poured into ice–water (400 cm^3) and extracted with dichloromethane, which was then dried and evaporated. The crude oil was chromatographed [toluene–ethyl acetate (12:1)] and recrystallised from light petroleum (b.p. range 40–60 °C) to give the *title product* as a solid, m.p. 100–102 °C (524 mg, 30%) (Found: C, 61.0; H, 7.1; N, 4.7%; M$^+$, 295.1235. $C_{15}H_{21}NO_3S$ requires C, 60.7; H, 6.95; N, 4.6%; M, 295.1242); ν_{max}($CHCl_3$)/cm^{-1} 1705 (C=O); δ_H 7.2–7.7 (4 H, m, ArH), 3.8 (2 H, s, CH_2), 3.2 (2 H, t, CH_2), 2.7 (2 H, s, CH_2), 2.4 (3 H, s, Me), 1.7 (2 H, t, CH_2) and 1.0 (6 H, s, 2 × Me).

3-[N-(2-*Chloroprop*-2-*enyl*)-N-*tosylamino*]*propanonitrile* (**5**; R = CH_2CH_2CN).—2-Chloro-*N*-tosylprop-2-enylamine (**5**; R = H) (1.0 g, 4.13 mmol), acrylonitrile (2.0 g, 4.1 mmol), sodium hydride (60%; 6 mg), and THF (1 cm^3) were stirred under N_2 at ambient temperature for 8 h. After addition of chloroform (100 cm^3) and aq. hydrogen chloride (2 mol dm^{-3}; 100 cm^3), the organic layer was separated and worked up to give the *title product* (0.98 g, 86%) as a solid, m.p. 60–62 °C, on evaporation (Found: C, 52.45; H, 5.1; N, 9.8; Cl, 11.7. $C_{13}H_{15}ClN_2OS$ requires C, 52.4; H, 5.1; N, 9.8; Cl, 11.9%); ν_{max}($CHCl_3$)/cm^{-1} 2250 (C≡N), 1660 (C=C) and 1600 (C=C aryl); δ_H 7.3 (4 H, m, ArH), 5.4 (2 H, s, =CH_2), 4.1 (2 H, s, CH_2), 3.4 (2 H, t, CH_2), 2.7 (2 H, t, CH_2) and 2.4 (3 H, s, Me).

3-[N-(2-*Chloroprop*-2-*enyl*)-N-*tosylamino*]-1-*phenylpropan*-1-*one* (**5**; R = CH_2CH_2COPh).—Phenylmagnesium bromide was made from bromobenzene (23.64 g, 150 mmol) and magnesium turnings (3.66 g, 150 mmol) in dry diethyl ether (250 cm^3) under N_2, and a solution of the above nitrile (15.0 g, 50 mmol) in toluene–diethyl ether (1:1; 100 cm^3) was added dropwise. After 18 h at ambient temperature, the usual work-up gave the crude waxy title product (15.89 g, 84%), which crystallised from diisopropyl ether as a solid, m.p. 64–66 °C (Found: C, 60.1; H, 5.2; N, 3.6; Cl, 9.3. $C_{19}H_{20}ClNO_3S$ requires C, 60.4; H, 5.3; N, 3.7; Cl, 9.4%); ν_{max}(film)/cm^{-1} 1680 (C=O); δ_H 7.2–7.8 (9 H, m, ArH), 5.5 (2 H, d, =CH_2), 4.0 (2 H, s, CH_2), 3.5 (4 H, m, CH_2) and 2.4 (3 H, s, Me).

4-[N-(2-*Chloroprop*-2-*enyl*)-N-*tosylamino*]-2-*phenylbutan*-2-*ol* [**5**; R = $CH_2CH_2C(OH)(Me)Ph$].—Methylmagnesium

iodide was made from iodomethane (5.71 g, 4.0 mmol) and magnesium turnings (0.95 g, 40 mmol) in dry diethyl ether (100 cm^3) under N_2 at 0 °C. After 1 h a solution of the above ketone (5.0 g, 13.23 mmol) in anhydrous toluene–diethyl ether (1:1; 100 cm^3) was added dropwise and the mixture was then stirred for 90 min. On work-up, the *title product* was obtained as a yellow oil, which was purified by chromatography [toluene–ethyl acetate (4:1)] (2.53 g, 49%) (Found: C, 61.2; H, 6.1; N, 3.7; Cl, 9.0. $C_{20}H_{24}ClNO_3S$ requires C, 61.0; H, 6.1; N, 3.55; Cl, 9.0%); ν_{max}(film)/cm^{-1} 3500 (OH); δ_H 7.1–7.8 (9 H, m, ArH), 5.2 (2 H, s, $=CH_2$), 3.8 (2 H, s, CH_2), 3.0 (2 H, m, CH_2), 2.4 (3 H, s, Me), 2.1 (1 H, s, exch., OH), 1.8 (2 H, m, CH_2) and 1.5 (3 H, s, Me).

3-[N-(2-*Chloroprop*-2-*enyl*)-N-*tosylamino*]-1-*phenylpropan*-1-*ol* [**5**; R = $CH_2CH_2CH(OH)Ph$].—3-[*N*-(2-Chloroprop-2-enyl)-*N*-tosylamino]-1-phenylpropan-1-one (5.09 g, 13.23 mmol), sodium borohydride (123 mg, 3.3 mmol) and ethanol (50 cm^3) were stirred under N_2 at −15 °C for 1 h and then at room temperature for 18 h with a few more mg of sodium borohydride. The usual work-up led to an orange oil (4.78 g), which was purified by chromatography as in the previous case. The *title product*, initially a yellow oil, crystallised from diisopropyl ether as a solid, m.p. 68–70 °C (2.16 g, 43%) (Found: C, 60.2; H, 5.9; N, 3.5; Cl, 9.7. $C_{19}H_{22}ClNO_3S$ requires C, 60.1; H, 5.8; N, 3.7; Cl, 9.3%); ν_{max}(film)/cm^{-1} 3350 (OH); δ_H 7.2–7.8 (9 H, m, ArH), 5.4 (2 H, s, $=CH_2$), 4.8 (1 H, m, CH), 3.9 (2 H, s, CH_2), 3.0–3.8 (2 H, m, CH_2), 2.7 (1 H, s, exch., OH), 2.5 (3 H, s, Me) and 1.8 (2 H, m, CH_2).

5-*Phenyl*-N-*tosylazepan*-3-*one* (**6**; R^1 = Ph, R^2 = H).—A solution of the above alcohol [**5**; R = $CH_2CH_2CH(OH)Ph$] (500 mg) in diethyl ether (1 cm^3) was added to stirred 90% sulfuric acid (10 cm^3) at 0 °C. After 5 min, diethyl ether (100 cm^3) and water (100 cm^3) were added and the organic layer was separated. The usual work-up gave a solid (460 mg). Crystallisation from diisopropyl ether gave the *title product* (256 mg, 57%) as a solid, m.p. 115–117 °C (Found: C, 66.2; H, 6.0; N, 3.8%; M^+, 343.1240. $C_{19}H_{21}NO_3S$ requires C, 66.4; H, 6.2; N, 4.1%; *M*, 343.1243); ν_{max}($CHCl_3$)/cm^{-1} 2900 (CH), 1710 (C=O) and 1600 (C=C, aryl); δ_H 7.1–7.8 (9 H, m, ArH), 4.3–4.5 (2 H, d, CH_2CH), 3.35 (2 H, s, CH_2), 2.5–2.8 (3 H, m, 2 H + 1 H), 2.4 (3 H, s, Me) and 2.0–2.2 (2 H, m, CH_2).

Dehydration of Alcohols.—(*a*) 97% Sulfuric acid (5 drops) was added to a solution of the alcohol [**5**; R = $CH_2CH_2C(Me)(OH)Ph$] (500 mg) in diethyl ether (25 cm^3) at 0 °C and the mixture then left for 18 h. Further sulfuric acid (5 drops) was added and the whole mixture was stirred for 3 days. The usual work-up gave a mixture of isomeric alkenes (308 mg, 71%) (Found: C, 63.7; H, 6.1; N, 4.1; Cl, 9.9%; M^+, 375.1060. $C_{20}H_{22}ClNO_2S$ requires C, 63.9; H, 5.9; N, 3.7; Cl, 9.4%; *M*, 375.1069); ν_{max}(film)/cm^{-1} 1650 (C=C) and 1600 (aryl).

(*b*) The alcohol [**5**; R = $CH_2CH_2CH(OH)Ph$] (500 mg), diethyl ether (5 cm^3) and 97% sulfuric acid (15 drops) were stirred at room temperature for 5 days and then poured into water (20 cm^3). Extraction with diethyl ether, washing (water), drying (Na_2SO_4), and evaporation gave a pale yellow oil (307 mg) which was purified by chromatography [toluene–ethyl acetate (4:1)] to yield an oily mixture of alkenes (193 mg, 40%) (Found: C, 62.9; H, 5.7; N, 3.7; Cl, 10.6; S, 8.75. $C_{19}H_{20}ClNO_2S$ requires C, 63.1; H, 5.6; N, 3.9; Cl, 9.8; S, 8.9%); ν_{max}(film)/cm^{-1} 1660 (C=C) and 1600 (aryl).

(*c*) The alcohol [**5**; R = $CH_2CH_2CH(OH)Me$] (500 cm^3), diethyl ether (5 cm^3) and 90% sulfuric acid were stirred at −20 °C for 5 h and then at 18 °C for 48 h. Work-up as in (*b*) yielded an oil (250 mg). TLC indicated at least 3 new products, one of which gave a red spot with Brady's reagent spray. Attempted chromatography caused much loss of material and decomposition.

4-[N-(2-*Chloroprop*-2-*enyl*)-N-*tosylamino*]*butan*-2-*one* (**5**; R = CH_2CH_2COMe).—As described above, methylmagnesium iodide [from iodomethane (7.12 g)] was treated with the nitrile (**5**; R = CH_2CH_2CN) (5.0 g). The *title product* was an oil (3.3 g, 60%) (Found: C, 53.2; H, 5.6; N, 4.6; Cl, 11.1. $C_{14}H_{18}ClNO_3S$ requires C, 53.2; H, 5.7; N, 4.4; Cl, 11.2%); ν_{max}(film)/cm^{-1} 1710 (C=O); δ_H 7.3–7.8 (4 H, m, ArH), 5.4 (2 H, m, $=CH_2$), 4.0 (2 H, s, CH_2), 3.4 (2 H, t, CH_2), 2.8 (2 H, t, CH_2), 2.4 (3 H, s, Me) and 2.1 (3 H, s, Me).

4-[N-(2-*Chloroprop*-2-*enyl*)-N-*tosylamino*]*butan*-2-*ol* [**5**; R = $CH_2CH_2CH(OH)Me$].—The above ketone (4.0 g, 12.65 mmol) was treated with sodium borohydride (120 mg, 3.16 mmol) as described previously. Chromatography of the crude oil as in the previous case gave the *title product* (2.39 g, 60%) as a yellow oil (Found: C, 53.2; H, 6.3; N, 4.2; Cl, 11.3. $C_{14}H_{20}ClNO_3S$ requires C, 53.0; H, 6.3; N, 4.4; Cl, 11.15%); ν_{max}(film)/cm^{-1} 3500 (OH) and 1630 (C=C); δ_H 7.2–7.9 (4 H, m, ArH), 5.5 (2 H, m, $=CH_2$), 4.0 (2 H, s, CH_2), 3.0–3.7 (3 H, m, CH_2 + CH), 2.4 (3 H, s, Me), 2.4 (1 H, s, exch., OH), 1.5 (2 H, m, CH_2) and 1.2 (3 H, d, Me).

3-[N-(2-*Chloroprop*-2-*enyl*)-N-*tosylamino*]*propanoic Acid* (**5**; R = $CH_2CH_2CO_2H$).—The corresponding ester (**5**; R = $CH_2CH_2CO_2Me$) (5 g) was stirred at 20 °C for 24 h with methanol (75 cm^3) and aq. sodium hydroxide (300 cm^3, 2 mol dm^{-3}). The acidic fraction on work-up gave the *title acid* as a crystalline solid (4.07 g, 78%), m.p. 73–74 °C (Found: C, 49.25; H, 5.1; N, 4.5; Cl, 11.25. $C_{13}H_{16}ClNO_4S$ requires C, 49.2; H, 5.1; N, 4.4; Cl, 11.2%); ν_{max}(Nujol)/cm^{-1} 3250 (OH) and 1710 (C=O); δ_H 9.40–9.75 (1 H, br s, exch., OH), 7.2–7.8 (4 H, m, ArH), 5.55 (2 H, br s, $=CH_2$), 4.0 (2 H, s, CH_2), 3.35–3.6 (2 H, t, CH_2), 2.6–2.85 (2 H, t, CH_2) and 2.43 (3 H, s, Me).

6,6-*Dichloro*-N-*tosylazepan*-4-*one* 7.—3-[*N*-(2-Chloroprop-2-enyl)-*N*-tosylamino]propanoic acid (**5**; R = $CH_2CH_2CO_2H$) (1.0 g, 3.15 mmol) was stirred under nitrogen at 35–40 °C for 18 h with thionyl chloride (25 cm^3). After removal of excess of thionyl chloride under reduced pressure, the residue was dissolved in dry, alcohol-free dichloromethane (25 cm^3) and the solution was stirred at room temperature while anhydrous aluminium chloride (1.0 g, 7.5 mmol) was added during 5 min. After being stirred for 2.5 h, the reaction mixture was worked up as usual and the *title product* (0.59 g, 56%) was recrystallised from propan-2-ol to give crystalline material, m.p. 109–110 °C (Found: C, 46.5; H, 4.4; N, 4.25; Cl, 21.15%; M^+, 335.014 76. $C_{13}H_{15}Cl_2NO_3S$ requires C, 46.4; H, 4.5; N, 4.15; Cl, 21.1%; *M*, 335.014 93); ν_{max}(Nujol)/cm^{-1} 1695 (C=O) and 1590 (C=C aryl); δ_H 7.35–7.9 (4 H, m, ArH), 4.2 (2 H, s, CH_2), 3.7 (2 H, s, CH_2), 3.5–3.7 (2 H, t, CH_2), 2.5–2.75 (2 H, t, CH_2) and 2.45 (3 H, s, Me).

6-*Chloro*-1,2,3,7-*tetrahydro*-N-*tosylazepin*-4-*one* (**8**; R = Cl).—The previous azepanone 7 (0.15 g), sodium carbonate (50 mg), water (10 cm^3) and THF (10 cm^3) were stirred at ambient temperature for 2 h. Extraction with dichloromethane and work-up yielded the *title product* as pale yellow crystals (95%), m.p. 98 °C (Found: C, 52.75; H, 4.6; N, 4.35; Cl, 12.3. $C_{13}H_{14}ClNO_3S$ requires C, 52.1; H, 4.65; N, 4.65; Cl, 11.9%); ν_{max}(Nujol)/cm^{-1} 1715 (C=O), 1660 (C=C) and 1600 (C=C aryl); δ_H 7.25–7.8 (4 H, m, ArH), 6.3 (1 H, s, =CH), 4.3 (2 H, s, CH_2), 3.4–3.6 (2 H, t, CH_2), 2.7–2.95 (2 H, t, CH_2) and 2.45 (3 H, s, Me).

1,2,3,7-*Tetrahydro*-6-*methoxy*-N-*tosylazepin*-4-*one* (**8**; R = OMe).—The dichloroazepine 7 (1.0 g, 2.98 mmol), sodium

carbonate (320 mg, 3.02 mmol) and methanol (15 cm^3) were stirred at room temperature for 15 h. After addition of water (excess) and extraction with dichloromethane, the usual work-up gave the title product (0.725 g, 82%), which crystallised from propan-2-ol as a yellow solid, m.p. 122–123 °C (Found: C, 56.8; H, 5.5; N, 4.5%; M^+, 295.087 83. $C_{14}H_{17}NO_4S$ requires C, 56.9; H, 5.8; N, 4.7%; M, 295.088 12); ν_{max}(Nujol)/cm^{-1} 1715 (C=O), 1660 (C=C) and 1600 (C=C aryl); δ_H 7.2–7.8 (4 H, m, ArH), 5.35 (1 H, s, =CH), 4.2 (2 H, s, CH_2), 3.6 (3 H, s, OMe), 3.5 (2 H, t, CH_2), 2.8 (2 H, t, CH_2) and 2.5 (3 H, s, Me).

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