Ring-closure Reactions. Part 23.[1] Kinetics of Formation of Three- to Seven-membered-ring *N*-Tosylazacycloalkanes. The Role of Ring Strain in Small- and Common-sized-ring Formation

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Rates of cyclisation of a series of anions derived from *N*-tosyl-ω-bromoalkylamines to nitrogen heterocycles with three to seven members in Me_2SO–H_2O (99:1) have been studied. Rates vary markedly with ring size in the order 5 > 3 > 6 > 7 ~ 4. First-order rate constants for cyclisation have been translated into effective molarities (EM) with reference to an appropriate intermolecular model reaction. Comparison of the present results with available literature data on S_N2 ring-closure reactions leading to small- and common-sized rings reveals that the ease of formation of three-membered rings is much more structure-dependent than that of the higher homologues. This remarkable behaviour is believed to parallel the unique way in which the stability of three-membered rings is affected by structure. As a rule, the ease of cyclisation appears to bear an inverted relationship to the assumed strain energy of the ring product. The apparent opposition of this rule to earlier conclusions in the literature is discussed.

The kinetics of ring closure of short-chain bifunctional molecules *via* intramolecular nucleophilic substitution have been studied extensively since Freundlich's pioneering investigations on the cyclisation of ω-bromoalkylamines.[2] However, an extensive comparative analysis of reactivity data in this area is still prevented by the sparseness of the data, as well as by the fact that the equivalent non-cyclisation reactions required for the calculation of effective molarity (EM) have been only rarely investigated. The importance of EM as a key parameter for a meaningful discussion of reactivity in intramolecular reactions has long been recognised.[3–6]

As a part of a programme aimed at providing reliable EM data for small- (three- and four-membered) and common-sized (five- to seven-membered) ring formation we have investigated the kinetics of the base-promoted ring closure of a series of *N*-tosyl-ω-bromoalkylamines (AH) in Me_2SO–H_2O 99:1 (v/v) leading to *N*-tosylazacycloalkanes [equation (1)]. The investigation

$$\underset{\mathrm{AH}}{\mathrm{TsNH[CH_2]_{\mathit{n}-1}Br}} \overset{\mathrm{OH^-}}{\rightleftharpoons} \underset{\mathrm{A^-}}{\mathrm{TsN[CH_2]_{\mathit{n}-1}Br}} \xrightarrow{k_{intra}} \mathrm{TsN\overset{\frown}{[CH_2]_{\mathit{n}-2}CH_2}} \quad (1)$$

also includes the kinetics of alkylation of *N*-tosylbutylamine with butyl bromide under the same conditions [equation (2)]

$$\mathrm{TsN[CH_2]_3CH_3} + \mathrm{CH_3[CH_2]_3Br} \xrightarrow{k_{inter}} \mathrm{TsN([CH_2]_3CH_3)_2} \quad (2)$$

as an intermolecular model reaction.

Results

As shown by literature reports[7,8] on the kinetics of intramolecular alkylation of sulphonamide derivatives, reaction occurs unequivocally by way of the anion. In the present study anions A^- were generated *in situ* by adding an appropriate amount of Me_4NOH to dilute solutions of the parent sulphonamides AH in 99:1 Me_2SO–H_2O. Since the enhanced basicity of OH^- in the nearly aprotic solvent is such as to promote complete dissociation of acids of comparable acidity, like phenols[9] and malonic ester derivatives,[1] the reaction between AH and OH^- was assumed to be essentially quantitative, allowance being made for the amount of base used to neutralise the free acidity of the solvent (see Experimental section).

Another advantage of the use of the OH^-–Me_2SO base–solvent system is that reactions (1) proceed cleanly in the virtual absence of side reactions other than polymerisation, as shown by a recent investigation on the synthesis of many-membered *N*-tosylazacycloalkanes:[10] a 92% yield of isolated product was reported for the seven-membered ring. Further, product analysis under conditions close to those of the kinetic runs was carried out for the reaction leading to the three-membered ring. When a 8.1×10^{-4}M-solution of $TsNHCH_2CH_2Br$ in 99:1 Me_2SO–H_2O was exactly neutralised with Me_4NOH, a 100% (g.l.c.) yield of *N*-tosylaziridine was obtained, showing the absence under the given conditions of any side reactions, including nucleophile-induced ring opening and cyclodimerisation processes which are well precedented for the three-membered heterocycle.[8]

A disadvantage, however, of the use of 99:1 Me_2SO–H_2O for kinetic measurements arises from the fact that u.v. spectral changes accompanying closure of A^- are obscured by Me_2SO absorption. On the other hand, ring closures were found to be too fast for measurement by conventional techniques: the usual method based on argentimetric titration of the bromide ion released could not be applied. The problem was solved by matching a visual acid–base indicator (InH) to the reactions under study and monitoring the disappearance of the basic form In^- by stopped-flow spectrophotometry. The rationale of the method has been illustrated previously.[11] Briefly, under a given set of experimental conditions the concentration of In^- is proportional to that of A^-, so that the rate of disappearance of the former may be equated to that of the latter. The proportionality between $[In^-]$ and $[A^-]$ was ensured (i) by running the cyclisation reaction of a given A^- in the presence of a substantial amount of its conjugate acid AH, and (ii) by using an indicator sufficiently less acidic than AH that only a very small, but analytically detectable, amount was converted into its basic form In^-. It was found that 2-chloro-4-nitroaniline (anionic form $\lambda_{max.}$ 468 nm, $\varepsilon_{max.}$ 3.4×10^4 l mol^{-1} cm^{-1}) was a suitable indicator for the cyclisation reactions leading to the five-, six-, and seven-membered rings, and for the reaction between

Table 1. Rate and EM data for the formation of *N*-tosylazacycloalkanes in Me_2SO–H_2O (99:1 v/v) at 25 °C

n[a]	k_{intra}/s^{-1}[b]	EM/mol l^{-1}[c]
3	87.6 ± 3.0	1.92×10^3
4	(2.69 ± 0.09) × 10^{-2}	0.59
5	630 ± 30	1.38×10^4
6	12.9 ± 0.4	2.82×10^2
7	(6.21 ± 0.01) × 10^{-2}	1.36
Inter[d]	(4.57 ± 0.05) × 10^{-2}	

[a] Ring size. [b] Runs in triplicate. [c] Calculated as k_{intra}/k_{inter}. [d] Relative to the alkylation of *N*-tosylbutylamine with butyl bromide; rate constant in 1 mol^{-1} s^{-1}.

$TsNH[CH_2]_3CH_3$ and $CH_3[CH_2]_3Br$. A more acidic indicator, 2,6-di-t-butyl-4-methylphenol (anionic form $\lambda_{max.}$ 332 nm, $\varepsilon_{max.}$ 5.9×10^3 l mol^{-1} cm^{-1}) was required by the reactions leading to the three- and four-membered rings, on account of the higher acidity of the parent *N*-tosyl-ω-bromoalkylamines relative to that of the higher homologues.

The results of kinetic experiments are listed in Table 1. Occasional replacement of KOH or NaOH for Me_4NOH showed negligible effects on rates, thus revealing the unimportance of ion-pairing under the reaction conditions.

Discussion

Reliable rate and EM data have been obtained for ring-closure reactions involving intramolecular displacement of bromide ion by an anionic nitrogen nucleophile leading to rings in the three- to seven-membered range. Measurements refer to conditions where the complicating interference of incomplete conversion of AH into A^-, as well as of side reactions such as polymerisation, is virtually absent.

The ease of formation of the saturated nitrogen heterocycles varies in the order 5 > 3 > 6 > 7 ~ 4. This order is, at least in part, consistent with previous kinetic studies,[7,8] and might have been expected in view of the increasing difficulties met in the preparation of the open-chain precursors AH, where concurrent cyclisation is the main side reaction (see Experimental section).

The EM data from the present work are conveniently compared in the Figure with all the corresponding EM data for intramolecular nucleophilic substitution reactions leading to saturated carbocycles and heterocycles (Scheme). Because of the scarcity of data, we have also included the lactonisation of ω-bromoalkanoate ions,[11,12] where a trigonal carbon is present in the chain backbone. It should be borne in mind that the data for the cyclisation of ω-bromoalkylamines and for the base-promoted cyclisation of chlorohydrins are quoted in Kirby's review[4] as belonging to class γ, which means that they are believed to be reliable to within one order of magnitude. Note also that closure of $(EtO_2C)_2\bar{C}CH_2CH_2Br$ to the three-membered carbocycle is too fast to be measured. The EM value of 2×10^5M quoted in the Figure represents a lower reactivity limit based on the minimum value of 100:1 assigned[13] to the relative rates of closure of three- and five-membered rings.

In spite of the foregoing limitations, a fairly clear picture emerges from the data, showing that closures of four-membered and larger rings are much less structure-dependent than closures of three-membered rings. Interpretation of the data requires a distinction of general factors from factors that are confined either to specific reactions or to specific ring sizes. First of all, consideration of the entropy contribution to ring closure is required on the basis of the number of internal rotors frozen upon cyclisation.[1,3,5] This number is $n - 1$ for $TsN\bar{-}[CH_2]_{n-1}Br$, $(EtO_2C)_2\bar{C}[CH_2]_{n-1}Br$, and $H_2N[CH_2]_{n-1}Br$,

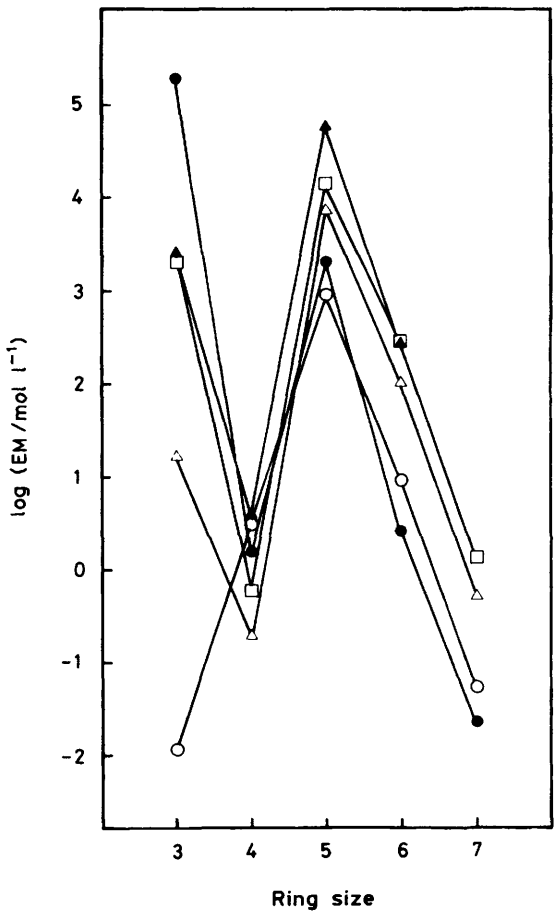
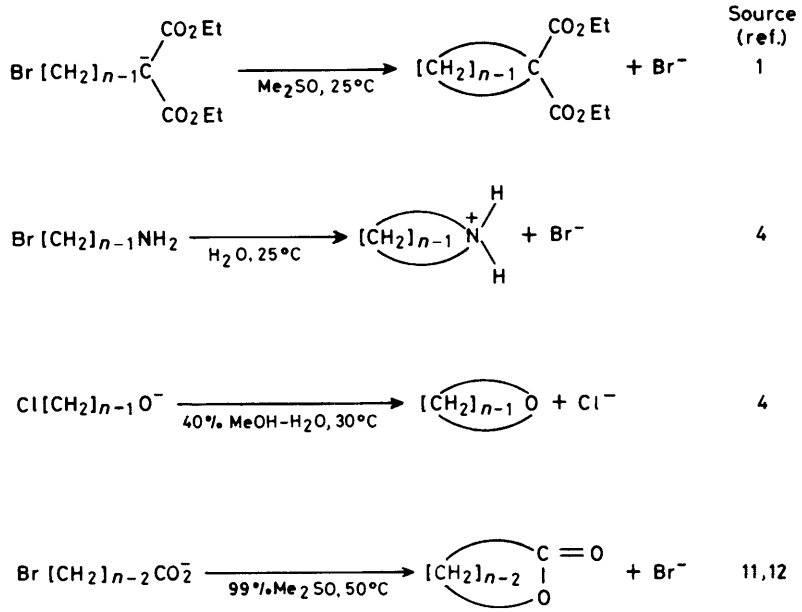


Figure. EM Profiles for the formation of diethyl cycloalkane-1,1-dicarboxylates (●), cyclic ethers (▲), *N*-tosylazacycloalkanes (□), cyclic ammonium ions (△), and lactones (○). The EM value for the three-membered ring in the series (●) represents a lower reactivity limit (see text)

but is $n - 2$ for $^-O_2C[CH_2]_{n-2}Br$ and $^-O[CH_2]_{n-1}Cl$, because no rotational entropy is associated to the symmetrical C–O^- bond. The entropy contribution of an internal rotor amounts to 4.5 cal mol^{-1} K^{-1},[3,5] which corresponds to a rate factor of nearly 10, and cyclisation of short chains involves an almost complete freezing of internal rotors.[5] Hence the formation of lactones and of cyclic ethers is entropically favoured by one order of magnitude on average, in comparison with the formation of carbocycles and of nitrogen heterocycles having equal ring size, but possessing an additional rotor.

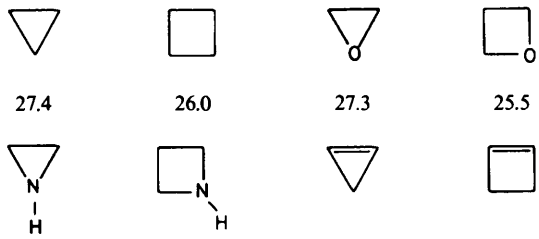
On the other hand, there is a rate-depressing influence on lactonisation exerted by the cisoid conformation of the ester function being formed.[14] In the absence of such influence, the points for the lactones would presumably be shifted upwards by some two orders of magnitude. Analogous considerations apply to the formation of the six- and seven-membered 1,1-bis(ethoxycarbonyl)cycloalkanes. Here it has been suggested that 1,3-diaxial-type interactions of the quasi-axial ethoxycarbonyl group raise the free energy of the six-membered transition state (but not that of the five-membered homologue),[1] and are likely to act in a similar way in the seven-membered-ring case.

It appears therefore that if a rough correction were made for entropic and specific structural factors, the EM data reported in the Figure for four-membered and larger rings would lie in a much narrower range than actually observed for each ring size. Accordingly, EM values in the neighbourhood of 1M for ring size 4, $10^{3.5}$M for ring size 5, 10^2M for ring size 6, and 1M for ring



Scheme.

Table 2. Ring strain energies of small rings (kcal mol^{-1})[a]



27.4	26.0	27.3	25.5
26.9	25.2[b]	54	30

[a] Data from J. D. Cox and G. Pilcher, 'Thermochemistry of Organic and Organometallic Compounds,' Academic Press, London, 1970, and A. S. Pell and G. Pilcher, *Trans. Faraday Soc.*, 1965, **61**, 71. [b] Estimated from S. W. Benson, F. R. Cruickshank, D. M. Golden, G. R. Haugen, H. E. O'Neal, A. S. Rodgers, R. Shaw, and R. Walsh, *Chem. Rev.*, 1969, **69**, 279.

size 7 would be taken as representative of 'normal' intramolecular nucleophilic substitutions, at least for first-row elements as nucleophiles. Such behaviour is exhibited to close approximation by the anions $A^-(n = 4—7)$, a series where specific structural factors are apparently unimportant.

That the inherent efficiencies of neighbouring C^-, O^-, N^-, and N nucleophiles are quite similar is not really surprising as long as five- to seven-membered transition states are involved, as the latter can presumably accommodate without severe distortions the linear nucleophile/carbon/leaving-group arrangement imposed by rear-side attack in S_N2 reactions. But in the four-membered ring case, which should deviate markedly from a linear arrangement, the foregoing results would hardly be expected on the basis of the present state of knowledge of directionality of S_N2 reactions.[15]

The situation in the closures of three-membered rings is more complex. Here the EM range is much wider than found for the larger ring sizes, and a very pronounced sensitivity of the ease of formation of three-membered rings to structure effects is observed. Comparison with the relative insensitivity to structural changes of the ease of formation of the four-membered rings is striking, in view of the fact that cyclopropane and cyclobutane, and their oxa and aza congeners, have similar strain energies (Table 2). This is in keeping with the general properties of three-membered rings, which often exhibit unusual chemical behaviour in comparison with four-membered and higher homologues.[16]

Kirby[4] used a directionality argument to explain why EM for the formation of oxirane is much larger than that of the aziridinium ion. The greater efficiency of neighbouring O^- was attributed to its greater directional flexibility, due to the presence of three electron pairs, any one of which can be utilised for bonding to the electrophile, whereas neutral N has only one electron pair. In accord with the foregoing argument, one would expect the directional flexibility of N^- to be intermediate between those of O^- and N. The experimental data reported in the Figure contradict this prediction. The EM value for closure of *N*-tosylaziridine is not lower than that for closure of oxirane. In fact it would be higher if the entropic advantage of $^-OCH_2CH_2Cl$ were taken into account. If one considers further the well established[17] view that nitranions use an electron pair in a *p* orbital rather than a non-bonded pair for bonding to electrophiles, the inconsistency of predictions based on a presumptive relation between directional flexibility and the formal number of electron pairs of the nucleophile is apparent.

We may wonder instead whether and to what an extent the widely spread EM values related to closures of three-membered rings reflect different stabilities of the rings themselves. Unfortunately, available strain energies of small ring compounds from thermochemical data are scanty. Nevertheless, some observations and conjectures will provide useful insights into the question.

2-*Ethanolide*.—No strain energy data are available for the lactones. It is well known, however, that α-lactones are reactive intermediates which can be detected spectroscopically only under special circumstances,[18] whereas the four-membered β-lactones can be synthesised and isolated under unexceptional conditions. Moreover, although substitution of a 'naked' oxygen atom for a methylene in cyclopropane or cyclobutane does not affect appreciably the strain energies (see oxirane and

oxetane in Table 2), comparison of the strain energies of cyclopropene and cyclobutene clearly shows that a four-membered ring structure tolerates far better than a three-membered one the introduction of trigonal carbon atoms in the backbone.* It appears therefore safe to assume that 2-ethanolide will be much more strained than either oxirane or 3-propanolide. The latter, in turn, should be only slightly more strained than oxetane.

Diethyl Cyclopropane-1,1-dicarboxylate.—A well established property of cyclopropane, which has raised much experimental and theoretical interest, is its ability to enter into π-type conjugation with adjacent π-electron systems such as carbonyl, phenyl, *etc.*[19] Conjugation requires the plane of the cyclopropyl ring to be parallel to the π-orbital of the conjugating group. Such a conjugation would be expected to stabilise the cyclopropane derivative to a significant extent. On the other hand, it has been shown that the conjugative ability of cyclobutane, if any, is much smaller than that of cyclopropane.[19] The cyclopropane diester is therefore suggested to be the least strained three-membered ring system among those considered in the present discussion; little or no effect of this sort is expected to operate in the four-membered ring case.

Oxirane, N-Tosylaziridine, and Aziridinium Ion.—As the *N*-tosyl group is not expected to exert a profound influence on the strain energy of the aziridine ring, one would predict the strain energies of oxirane and *N*-tosylaziridine to be similar. On the other hand, aziridine has been reported[20] to be about 3 pK_a units less basic than its four-, five-, and six-membered homologues, which have virtually identical basicities. This shows that protonation at nitrogen decreases the inherent stability of the aziridine ring by *ca.* 4 kcal mol^{-1}, but has no effect on azetidine.

On the basis of these considerations we conclude that the stability order among three-membered rings is diethyl cyclopropane-1,1-dicarboxylate > *N*-tosylaziridine ~ oxirane > aziridinium ion > 2-ethanolide. Since this order strictly corresponds to the sequence of EM values obtained, it is apparent that the ease of ring closure closely parallels the stability of the ring being formed.

In view of the limited number of cases considered, it could be objected that the foregoing conclusion suffers from meagre experimental support. However, as far as the rate-enhancing effect of the ethoxycarbonyl groups on the formation of the cyclopropane derivative is concerned, the effect appears to be quite general, occurring whenever a carbon nucleophile bears an electron-accepting conjugating group. Several additional examples do exist where the rates of closure of three-membered rings are unusually high, being in all cases higher than those of the corresponding five-membered rings. They have been discussed by Stirling,[13,21] who was the first to discover this effect and to provide a convincing interpretation. Such an effect is possibly present with sulphur[22] but not with nitrogen[7] nucleophiles.

The conclusion that the stability of the ring being formed is closely paralleled by the ease of ring closure needs clarification, since it is apparently in marked contrast to earlier conclusions[1,23,24] that product rings are not suitable models of the transition states in S_N2 ring-closure reactions leading to small rings. However, it applies strictly to comparisons of the ease of formation of rings of equal size belonging to diverse reaction series. With reference to the Figure, one could say that it is restricted to 'vertical trends.' But if the rates of formation of rings of different sizes belonging to the same series are considered (horizontal trends), the rule fails dramatically when applied to cyclisations of the shorter chains, which appear to reach the transition state rather easily, in spite of the high strain energies of the ring products. Thus, intramolecular S_N2 reactions exhibit interesting and somewhat intriguing properties with respect to the effect of ring strain on the ease of ring closure, which deserve careful attention in any detailed description of transition states in S_N2 reactions.

* A satisfactory interpretation of this phenomenon is given by M. J. S. Dewar (*J. Am. Chem. Soc.*, 1984, **106**, 669). In a discussion of the concept of σ conjugation and of its chemical implications, he describes the structure of cyclopropane as σ aromatic, but that of cyclobutane as σ antiaromatic.

Experimental

^{1}H N.m.r. spectra were taken with a Bruker WP-80 SY instrument. High-resolution mass spectrometric measurements were obtained with a Kratos MS-80 spectrometer. G.l.c. analyses were carried out with a Varian Vista 6000 flame ionisation instrument. U.v. spectrophotometric measurements were carried out with a Cary 219 or a Varian DMS-90 instrument, with thermostatted cell compartments. Fast reactions were followed with a Durrum D-110 stopped-flow spectrophotometer, matched with a Biomation 805 waveform recorder and a Hewlett-Packard 1207B storage oscilloscope.

Elemental analyses were performed by the Servizio Microanalisi of the Area della Ricerca del C.N.R., Montelibretti, Roma.

Materials.—Reagent grade Me_2SO (Erba RP) was thoroughly purged with argon and then degassed under vacuum for 1 h. The mixed solvent (Me_2SO–H_2O 99:1 v/v) and the Me_4NOH stock solution, (2.2×10^{-2}M in aqueous 98% Me_2SO) were prepared and handled as before.[9] The 'free acidity' of the mixed solvent, determined by a spectrophotometric titration method,[9] was in the range (4—6) × 10^{-4}M, depending on the batch.

Butyl bromide (Erba RP), phenol (Erba RP), 1,3-dibromopropane (Eastman), 1,4-dibromobutane (Merck), toluene-*p*-sulphonamide (Erba RP), toluene-*p*-sulphonyl chloride (Erba RP), and 2-bromoethylamine hydrobromide (Aldrich) were reagent grade commercial samples.

N-Tosyl-6-bromohexylamine (AH; $n = 7$) was available from a previous investigation.[10] *N*-Tosyl-2-bromoethylamine (AH; $n = 3$) was obtained in 61% yield from toluene-*p*-sulphonyl chloride and 2-bromoethylamine hydrobromide following a literature procedure;[7] m.p. 92—93 °C (from CCl_4) (lit.,[7] 93—94 °C). 1-Bromo-4-phenoxybutane was prepared in 68% yield from sodium phenoxide and 1,4-dibromobutane;[25] b.p. 90—91 °C at 0.4 mmHg, m.p. 39—41.5 °C (lit.,[25] 41 °C).

N-Tosyl-3-bromopropylamine (AH; $n = 4$) was prepared by treating the potassium salt of toluene-*p*-sulphonamide with 1,3-dibromopropane in Me_2SO at 50 °C according to a procedure[10] which proved successful for the higher members of the series ($n \geq 7$). Elution of the crude product on silica gel with $CHCl_3$ gave *N-tosyl-3-bromopropylamine* (25%), m.p. 65—66.5 °C (from CCl_4), δ($CDCl_3$) 7.8 and 7.4 (4 H, ArH), 5.2 (br t, 1 H, NH), 3.4 (t, 2 H, CH_2Br), 3.1 (q, 2 H, CH_2N), 2.4 (s, 3 H, $ArCH_3$), and 2.0 (m, 2 H, central CH_2) (Found: C, 41.3; H, 4.9; N, 4.7. $C_{10}H_{14}BrNO_2S$ requires C, 41.1; H, 4.8; N, 4.8%). A forerun of *N*-tosylazetidine was also obtained (9%); m.p. 119—121 °C (lit.,[7] 119—120 °C).

N-Tosyl-5-bromopentylamine (AH; $n = 6$). Similar alkylation of the potassium salt of toluene-*p*-sulphonamide with 1,5-dibromobutane afforded *N-tosyl-5-bromopentylamine* (2.4%), m.p. 72.5—73.5 °C (from CCl_4). Its ^{1}H n.m.r. spectrum in $CDCl_3$ was similar to that of AH ($n = 4$) except that the signal due to the central methylene protons at δ 2.0 was replaced by a broad 6 H multiplet at δ 1.8—1.2 (Found: C, 45.15; H, 5.5; N,

4.3. $C_{12}H_{18}BrNO_2S$ requires C, 45.0; H, 5.7; N, 4.4%). The major product isolated was *N*-tosylpiperidine (42%), m.p. 98—99 °C after sublimation under vacuum (lit.,[7] 99 °C).

N-*Tosyl*-4-*bromobutylamine* (AH; $n = 5$). All attempts at alkylating the potassium salt of toluene-*p*-sulphonamide with 1,4-dibromobutane afforded *N*-tosylpyrrolidine as the sole product, m.p. 121—122 °C after sublimation under vacuum (lit.,[26] 123 °C). Similar results were obtained when 1,4-dibromobutane was replaced by either 1-bromo-4-chlorobutane or 1-chloro-4-iodobutane. The title compound could be prepared in low yield by the following procedure. Alkylation of the potassium salt of toluene-*p*-sulphonamide with 1-bromo-4-phenoxybutane afforded *N*-tosyl-4-phenoxybutylamine (56%), m.p. 71—73 °C, ^{1}H n.m.r. as expected. Treatment of the latter with BBr_3 in CH_2Cl_2 at −20 °C, followed by elution from silica gel with $CHCl_3$, gave the bromo-derivative (1.4%), m.p. 49—51 °C. Comparison of the ^{1}H n.m.r. spectrum with those of the next homologues confirmed the structure (M^+, 305.0090. Calc. for $C_{11}H_{16}BrNO_2S$: *M*, 305.0081). A large amount of *N*-tosylpyrrolidine was also obtained in this case.

N-*Tosylbutylamine* was obtained in 78% yield by the reaction of butyl bromide with the potassium salt of toluene-*p*-sulphonamide in Me_2SO at 50 °C; m.p. 43—44 °C after sublimation under vacuum (lit.,[27] 43 °C).

N-*Tosylaziridine*. A solution of $TsNH[CH_2]_2Br$ (1.39 g, 5 mmol) in Me_2SO (20 ml) was added dropwise at room temperature with vigorous stirring to Me_2SO (80 ml) to which a solution of KOH (0.33 g, 5 mmol) in water (1 ml) had been added. The mixture was then diluted with brine and ice, extracted several times with $CHCl_3$, washed with water, and dried (Na_2SO_4). Removal of the solvent left *N*-tosylaziridine (0.80 g, 82%), m.p. 51—52 °C [from benzene–petroleum (1:4)] (lit.,[28] 52 °C).

Kinetics.—Typically, one syringe of the stopped-flow apparatus was charged with a solution of a given AH (*ca.* 2.4×10^{-3}M) containing the proper indicator (*ca.* 6×10^{-5}M), and the other with a solution of Me_4NOH (*ca.* 1.3×10^{-3}M), so that after mixing the concentration of AH in the stopped flow cell was approximately equal to that of A^- (*ca.* 6×10^{-4}M). Good first-order behaviour was obtained in all cases up to at least 80% conversion. The kinetics of the intermolecular model reaction were followed in a similar way with a conventional spectrophotometric apparatus, using a 30-fold excess of butyl bromide.

Product Analysis.—A 8.1×10^{-4}M-solution of $TsNH[CH_2]_2Br$ in 99% Me_2SO containing a known amount of tridecane (internal standard) was neutralised with Me_4NOH at 25 °C. After 2 min the solution was diluted with brine, carefully extracted with $CHCl_3$, washed with water, dried (Na_2SO_4), and filtered. The filtrate was carefully concentrated to a small volume for g.l.c. analysis. This was carried out on a column (1 m × 3.2 cm 5% OV-101 on Chromosorb W 100—120) operated in the interval 130—190 °C. The chromatogram consisted of only two peaks, that of the internal standard and that of the expected product. After corrections for the molar response factor, the chromatogram indicated a 100 ± 1% yield of *N*-tosylaziridine.

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