# Bifunctionalization of α,ω-Sulphonamides *via* Kinetically Controlled Reaction of α,ω-Bis(*N*-nitrososulphonamides)

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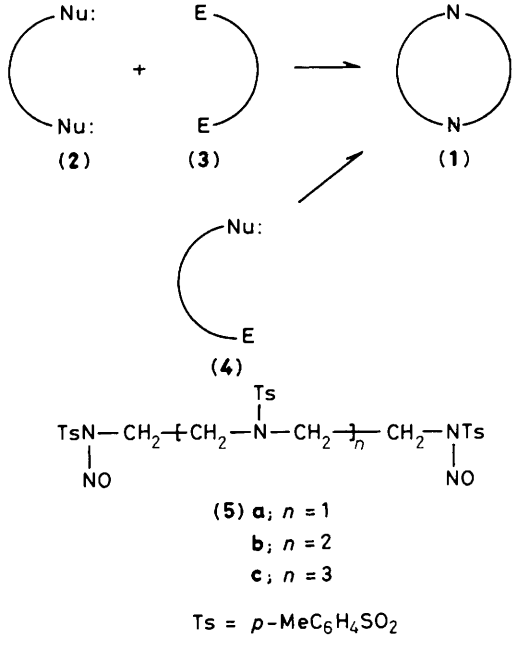
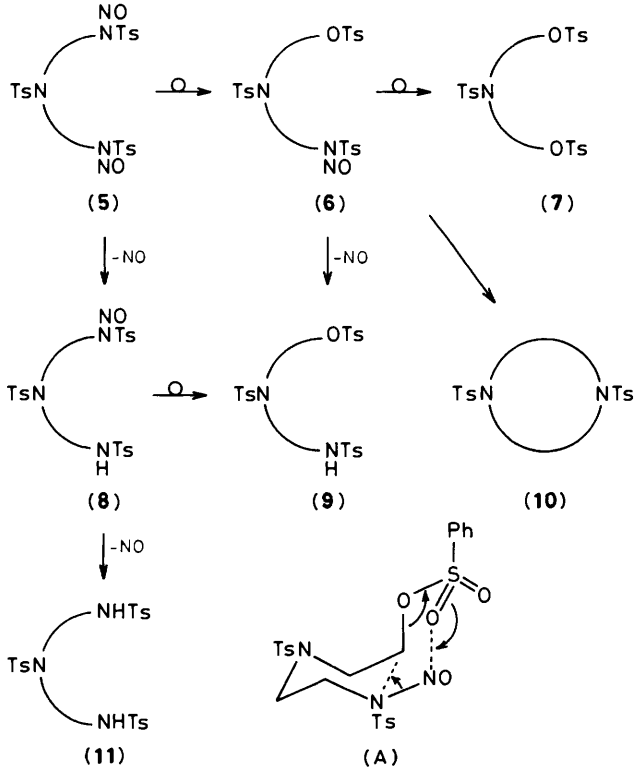
α,ω-Bis(*N*-nitrososulphonamides) in hot benzene were converted into α,ω-disulphonates and bifunctional α-sulphonate-ω-sulphonamides, in good yields, by intramolecular *N*-nitrososulphonamide–sulphonate rearrangement.

Macrocyclic polyamines, *e.g.* (**1**), are crown ether analogues, and have been the subject of recent publications.[1] Syntheses of (**1**) so far have relied on the conventional[2] intermolecular reaction of a nitrogen nucleophile (**2**) with an electrophile (**3**), in view of the lack of methods for preparing bifunctional molecules (**4**) with arbitrary chain length. The availability of a bifunctionalization starting from (**2**) would have great synthetic utility.

In our efforts to refine the intramolecular rearrangement of *N*-nitrososulphonamides to sulphonates,[3] the yields for which decrease markedly[3c,d] for the higher alkyl congeners, we found that *p*-$MeC_6H_4SO_2N(NO)CH_2CH_2Br$, which was derived by *N*-nitrosation of the corresponding sulphonamide, rearranges to *p*-$MeC_6H_4SO_3CH_2CH_2Br$ in hot (75 °C) benzene solution in high yield (80%). This result stimulated us to extend the reaction to the α,ω-bis-(*N*-nitrososulphonamides) (**5**), prepared from the corresponding sulphonamides, since there is the possibility of both release of,† and rearrangement involving, the *N*-nitroso group at either end. Monitoring by



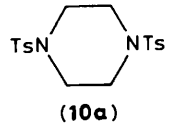



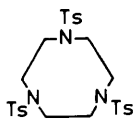

**Scheme 1.** The circles on the arrows denote rearrangement.

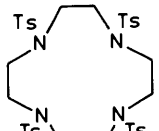
**Table 1.** The reactions of (**5a—c**) in several solvents.[a]

| Entry | Compd. | Solv. | *t*/h | % Yield[b] (7) | (9) | (10) | (11) |
|---|---|---|---|---|---|---|---|
| 1 | (**5a**) | $C_6H_6$ | 24 | 0 | 46 | 47 | 7 |
| 2 | (**5a**) | $C_6H_6$[c] | 14 | 0 | 26 | 9 | 46 |
| 3 | (**5a**) | MeCN | 5 | 0 | 0 | Trace[d] | >90[d] |
| 4 | (**5a**) | $CCl_4$ | 23 | 0 | 40[d] | 40[d] | 20[d] |
| 5 | (**5b**) | $C_6H_6$ | 32 | 56 | 36 | 0 | 8 |
| 6 | (**5c**) | $C_6H_6$ | 29 | 43 | 41 | 0 | 15 |

[a] Heated at *ca.* 70 °C. [b] Isolated yield unless otherwise noted. [c] In the presence of traces of water. [d] Judged from t.l.c.




† In general, the *N*-nitroso group is thermally sensitive, with release of NO gas.

t.l.c. and product analysis (Scheme 1, Table 1) showed that: (i) the rearrangement occurs in high yield in benzene (entries 1,5,6); (ii) the kinetically controlled reaction provides the disulphonates (**7**) and monosulphonates (**9**) in almost equal amounts (entries 5,6); (iii) dipolar solvents (entries 3,4) and benzene containing a trace of a proton source favour release of the *N*-nitroso group (entry 2); (iv) the mononitroso-monosulphonate (**6a**), formed by rearrangement at one end, can intramolecularly cyclize to afford directly the piperazine derivative (**10a**), possibly *via* the intramolecular pericyclic reaction shown in structure (A). That the direct formation of (**10a**) from (**6a**) is governed by conformational preference *via* the energetically favourable ten-membered transition state (A) is supported by the fact that the higher congeners (**9b,c**) did not give the cyclic compound (**10**) in hot benzene without base. In the presence of base ($K_2CO_3$–dimethylformamide), however, the sulphonamide–sulphonates (**9b,c**) gave the corresponding cyclic compounds (**10b,c**) in 90 and 95% yields, respectively. The diamine (**10a**) was alternatively prepared by the reaction of $p$-$MeC_6H_4SO_3CH_2CH_2Br$ with *N,N'*-ditosyl-ethane-1,2-diamine in 98% yield ($K_2CO_3$–dimethylformamide). Compounds (**7**) may be used as building blocks for macrocyclization by the conventional method,[2b] and so the present kinetically controlled bifunctionalization method provides versatile general synthons for macrocyclic polyamines.

*Received, 22nd February 1985; Com. 240*

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