Intramolecular Sulphonyl-amidomethylation; a New Route to Fused Heterocyclic Compounds

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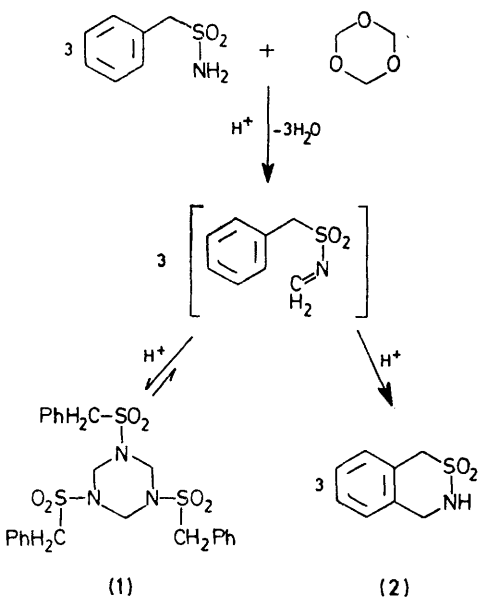
Summary Cyclization by intramolecular sulphonyl-amidomethylation at an aromatic carbon atom provides fused heterocyclic compounds in high yields.

SULPHONYL- or acylsulphonyl-amidomethylation seldom has been applied to substitution at an aromatic carbon atom.[1] The analogous intramolecular reaction has not been described hitherto. We report the latter reaction and illustrate its usefulness in the synthesis of fused heterocyclic systems.



(1) (2)

The reaction of phenylmethane sulphonamide (1 mmol) with trioxan (0·33 mmol) in methanesulphonic and acetic acids (4 : 1; 1·25 ml), stirred at 35 °C for 2 min, gave a 54% yield of the kinetic product, (**1**),[2] which was identified by comparison with an authentic sample (m.p., mixed m.p., and i.r. absorption).

When the reaction time was extended to 3 h, the thermodynamic product (**2**), resulting from intramolecular sulphonyl-amidomethylation, was isolated in 67% yield, m.p. 142—143 °C[3] (from EtOAc), M^+, *m/e* 183, δ (CF_3CO_2H) 4·48 and 4·67 (each 2H, 2 × CH_2), and 6·9—7·5 (4H, ArH). Compound (**2**) was also obtained (in 74% yield) by heating (**1**) at 35 °C in the same acidic medium.

Further studies were carried out using a stronger acid medium in increased volumes (to avoid an intermolecular process and to reduce the reaction time).† To a stirred solution of the sulphonamide (1 mmol) in methanesulphonic acid (3 ml), trioxan (0·33 mmol) in trifluoroacetic acid (1 ml) was added. After 30 min at 35 °C, the solution was cooled and added dropwise to a stirred mixture of $CHCl_3$ (10 ml) and crushed ice (20 g). The $CHCl_3$ extract was washed (ice–water and aqueous $NaHCO_3$), dried, and evaporated to give the crude product.

Phenylmethanesulphonamide furnished compound (**2**) in 66% yield. β-Phenylethanesulphonamide gave an 89% yield of 1,2,4,5-tetrahydro-3,2-benzothiazepine 3,3-dioxide (**3**), m.p. 160—162 °C (from MeOH), ν_{max} (Nujol) 3258 cm^{-1} (NH), δ ($CDCl_3$) 3·22 (4H, CH_2·CH_2), 4·33 (3H, HN·CH_2), and 7·28 (4H, ArH). This new cyclization can also be applied to *N*-monosubstituted sulphonamides as shown by the conversion (78% yield) of *N*-methylphenylmethanesulphonamide into 3-methyl-3,4-dihydro-1*H*-2,3-benzothiazine-2,2-dioxide (**4**), m.p. 74—75 °C (from Pr^i_2O), δ (CF_3CO_2H) 3·00 (3H, NMe), 4·52 and 4·62 (each 2H, NCH_2 and SCH_2), and 6·9—7·6 (4H, ArH). On the other hand, the cyclization of carboxamides, *e.g.* *N*-methylphenylacetamide, was unsuccessful.

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† The reactions were performed excluding moisture. New compounds (**3**) and (**4**) gave satisfactory analytical data.

[1] H. Hellmann, in 'Neuere Methoden der Präparativen Organischen Chemie,' ed. W. Foerst, Verlag Chemie, Weinheim, 1960, vol. II, p. 190; H. E. Zaugg, and W. B. Martin, *Org. Reactions*, 1965, **14**, 52; H. E. Zaugg, *Synthesis*, 1970, 49.

[2] O. O. Orazi and R. A. Corral, *J.C.S. Perkin I*, 1975, 772.

[3] E. Sianesi, G. Bonola, R. Pozzi, and P. Da Re, *Chem. Ber.*, 1971, **104**, 1880, prepared this compound by two other methods in 9 and 45% yields.