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REGIOSPECIFIC OXIDATIVE CYCLIZATION OF N-METHANESULFONYL-ALKYLAMINES: A NEW METHOD OF PYRROLIDINE RING CONSTRUCTION

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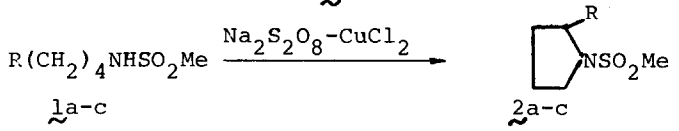
Summary. N-Methanesulfonylalkylamines cyclize regiospecifically into N-methanesulfonylpyrrolidines in one-pot oxidation reaction in $Na_2S_2O_8$-$CuCl_2$.

In context of our investigations of the remote oxidative functionalization of ketones[1], alkanoic acids and their derivatives[2] at non-activated C-atom providing the new approach to γ- and δ-diketones[1] and lactones[2], we have studied oxidation of N-methanesulfonylalkylamines in $Na_2S_2O_8$-$CuCl_2$.

We have found that N-methanesulfonylalkylamines 1 under the action of $Na_2S_2O_8$-$CuCl_2$ (molar ratio 1:$Na_2S_2O_8$:$CuCl_2$=1:1:1) cyclize regiospecifically into N-methanesulfonylpyrrolidines 2.



1a-c 2a-c

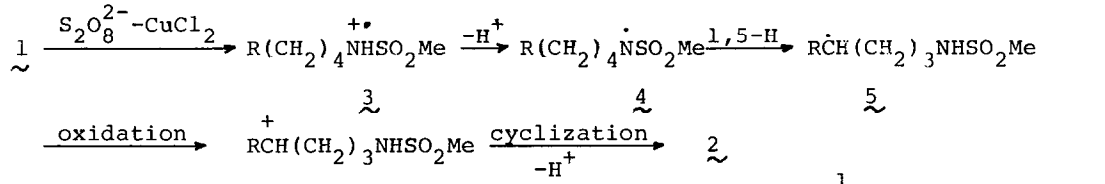
R= H(a), Me(b), Et(c).

Of the substrates studied 1b undergoes oxidative cyclization most easily. Yields of sulfonylpyrrolidines from 1a,c are 1.5-fold lower (Table).

Table. Oxidation of sulfonylalkylamines 1a-c in $Na_2S_2O_8$-$CuCl_2$.

Substrate	Conversion, (%)	Cyclization products, yields (%) based on 1 converted (on the starting 1)[3]
1a	27	2a, 82 (22)
1b	39	2b, 94 (37)
1c	37	2c, 71 (26)

The suggested mechanism of the reaction involves generation of N-centred cation radicals 3, that are converted in sulfonamidyl radicals 4[4]. These radicals undergo 1,5-H shift to C-centred radicals 5. Sulfonylpyrrolidines 2 are formed as a result of oxidation of 5 to corresponding carbocations and subsequent cyclization.



Careful investigation of reaction products by means of ^{1}H NMR (250 MHz) and g.l.c. demonstrated the absence of corresponding 2-R-N-methanesulfonylpiperidines 6a,b that are isomers of 2b,c. This indicates the competitive 1,6-H shift in 4 is hardly probable.

Unlike oxidation of 1 we observed no pyrrolidines in reactions of $Na_2S_2O_8$-$CuCl_2$ system with alkylamines $R(CH_2)_4NH_2$ themselves[5] or N-acetylalkylamines[6].

The reaction studied represents a quite unique example of the completely regiospecific rearrangement of heterocentred radicals.

Smooth hydrolysis of 2 to corresponding 2-R-pyrrolidines on boiling with HBr-PhOH and simplicity of experimental procedure enable us to consider this reaction as a new effective method of pyrrolidine ring construction.

Typical procedure. A solution of 11.9 g (0.05 mole) of $Na_2S_2O_8$ in 50 ml of water was added dropwise to a stirred mixture of 8.25 g (0.05 mole) of 1b and 8.55 g (0.05 mole) of $CuCl_2 \cdot 2H_2O$ in 100 ml of water at 90°. The mixture was kept at the same temperature for 5 h, cooled to 20° and extracted with ether (2 x 100 ml) and $CHCl_3$ (100 ml), combined extracts were dried ($MgSO_4$). The residue (8.1 g) after solvent removal was analysed with ^{1}H NMR and g.l.c.; yield 2b 94% on 1b converted, conversion 39%. The solution of this residue in 100 ml of toluene was treated with 0.75 g (0.031 mole) of NaH to remove unreacted 1b as a N-Na-salt. The mixture was filtered off, evaporation of solvent afforded 2.98 g (0.018 mole) of pure 2b; ms: 163 (M^+); ^{1}H NMR ($CDCl_3$, TMS, 250 MHz): 1.15 (d, 3H), 1.60-2.00 (m, 4H), 2.70 (s, 3H), 3.20 (m, 2H), 3.66 (m, 1H) p.p.m. 1b was recovered upon acidification of its Na-salt.

References and Notes.

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