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DICHOTOMY ON INTRAMOLECULAR AROMATIC SUBSTITUTION CAUSED BY THE SMILES REARRANGEMENT

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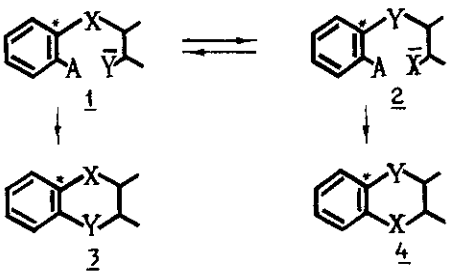
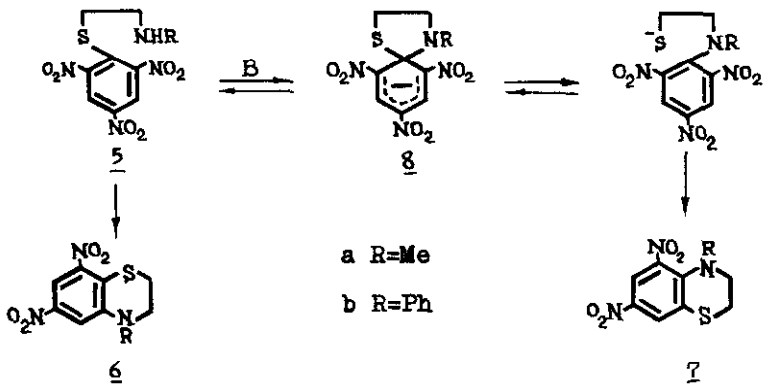
Intramolecular aromatic nucleophilic substitution represents the final step in the synthesis of six-membered bi- and polycyclic systems with two heteroatoms in one cycle and follows the following scheme:



Until the 30's it seemed accepted that the structure of intermediate condensation product 1 or 2 is sufficiently reliable for the determination of the structure of a cyclic product. Yet as has become obvious after Smiles' studies, the rearrangement 1 ⇌ 2 (the Smiles rearrangement[1]) may take place prior to final cyclization which to a considerable extent devalues the latter criterion. Hence in principle in case of a label in molecules 1 or 2 one may expect the formation of two isomeric cyclic compounds 3 and/or 4. In practice, however, more often is the case when only one isomer is formed regardless of whether 1 or 2 undergoes cyclization. Due the reversible Smiles rearrangement the formation of two cyclic isomers was registered on cyclisation of non-symmetrically substituted catechol- and

dithiocatechol-derivatives, when the difference in nucleophility of both anionic centers was insignificant (X=Y=O [2] or S [3]). So far there have been only some indications that on cyclization of the isomeric 2-amino-4-methylphenyl picryl ether and 2-hydroxy-4-methylphenyl picramide two isomeric phenoxazines may be formed (X=O, Y=NH_2) [4].

We found what seems to be the first convenient model with differnt heteroatoms X and Y (X=S, Y=NHR) for the study of intramolecular nucleophilic cyclization both with and without the preliminary Smiles rearrangement, namely, 1-(β-N-R-aminoethylthio)-2,4,6-trinitrobenzene (5). Thus, cyclization of (5a) [5] may be carried out with formation of 6,8- [6] or/and 5,7-dinitro-4-methyl-2,3-dihydrobenzo-1,4-thiazines [7] (6a and 7a respectively); the ratio of isomers is to a great extent dependent of the strength of the base and solvent (Table).



The formation of Meisenheimer spiro-complex 8a under the action of strong base on the hydrochloride of 5a is registered in DMSO-d_6 (pmr): shift of $H^{3(5)}$ singlet from 9.16 to 8.38 ppm is the most specific: UV λ_{max}^{MeOH} 443 and 520 nm (shoulder). On employment of a weak base (pyridine) the spiro-complex is obviously not formed and cyclization is not accompanied by the Smiles rearrangement.

An alternative synthesis of 6a has been realised according to the following scheme:

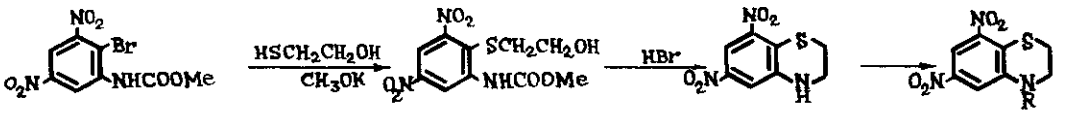


Table. The ratio of isomers 6a:7a and the total yield (%) on nucleophilic cyclization of 5a·HCl (UV spectra).

base \ solvent	HMPTA	DMF	t-BuOH	MeOH	C_6H_6	THF
t-BuOK	-	100:0 86	86:14 16	-	25:75 40	0:100 32
NEt_3	68:32 13	67:33 80	30:70 [8] 19	24:76 [8] 20	-	-
Py	-	0:100 53	0:100 44	4:96 82	0:100 2	0:100 17

The decrease of nucleophility of amino-group in initial amino thioether 5 reduces the possibility of the preliminary rearrangement. Nucleophilic cyclization of 1-(β-N-phenylaminoethylthio)-2,4,6-trinitrobenzene(5b) almost entirely goes with preliminary Smiles rearrangement and formation of 5,7-dinitro-4-phenyl-2,3-dihydrobenzo-1,4-thiazine [9] (7b): mixture of 7b and its 6,8-dinitro isomers (6b) in ratio 95:5 is formed only on heating in pyridine. The structure of 6b [10] was confirmed by the alternative synthesis following the same scheme as 6a.

Spiro-complex 8b was obtained on treatment of 5b by equimolar amount of potassium tert.-butoxide as the stable potassium salt; in the pmr spectrum (DMSO-d_6) $H^{3(5)}$ signal shifts from 8.72 of initial 5b to 8.48 ppm of 8b; UV λ_{max}^{MeOH} 441 and 530 nm (shoulder).[11]

References and Notes

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5. Prepared as hydrochloride from β-N-methylaminoethanthiole and picryl chloride in the presence of equimolar amounts of MeONa at -70°; yield 85%, mp 167 -167.5°. All new compounds gave satisfactory elemental analysis.
6. Mp. 117° (CCl_4); pmr (DMSO-d_6) δ : 8.07 (1H, d, J=2.5 Hz; 7-H), 7.55 (1H, d, J=2.5 Hz; 5-H), 3.80 (2H, m; NCH_2), 3.14 (2H, m; SCH_2), 3.16 (3H, s; NMe); UV λ_{max}^{MeOH} 265 nm (ε 14,500), 315 nm (ε 8,400) and 445 nm (ε 4,100).
7. Mp. 169-169.5° ($CHCl_3$-CCl_4, 1:4); pmr (DMSO-d_6) δ : 8.41 (1H, d, J=2.5 Hz; 6-H), 8.07 (1H, d, J=2.5 Hz; 8-H), 3.92 (2H, m; NCH_2), 3.20 (2H, m; SCH_2), 2.90 (3H, s; NMe); UV λ_{max}^{MeOH} 282 nm (ε 9,800), 312 nm shoulder (ε 5,000) and 398 nm (ε 10,200).
8. 96 hours at 20°, for other cases - 4 hours in boiling solvent in the presence of three base equivalents; in HMPTA - at 150°.
9. Mp. 169-169.5° ($CHCl_3$-CCl_4, 1:1); pmr ($CDCl_3$) δ : 8.24 (2H, s; 6- and 8-H), 4.13 (2H, m; NCH_2), 3.17 (2H, m; SCH_2), 6.9-7.4 (5H, m; Ph).
10. Mp. 160° ($CHCl_3$-CCl_4, 1:1); pmr ($CDCl_3$) δ : 8.37 (1H, d; J=2.5 Hz; 7-H), 7.53 (1H, d, J=2.5 Hz; 5-H), 4.06 (2H, m; NCH_2), 3.16 (2H, m; SCH_2), 7.1-7.5 (5H, m; Ph).
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