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Catalyzed ring transformation of cyclic *N*-aryl-azadiperoxides with participation of α,ω -dithiols†

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$\text{Co}(\text{OAc})_2$ -catalyzed ring transformation reaction of 10-aryl-7,8,12,13-tetraoxa-10-azaspiro[5.7]tridecanes with α,ω -dithiols (ethane-1,2-, propane-1,3-, butane-1,4-, pentane-1,5-, and hexane-1,6-dithiols, 3,6-dioxaoctane-1,8-dithiol) giving 3-aryl-1,5,3-dithiazacyclanes was studied.

Cyclic peroxides attract attention for their antimalarial,¹ anti-bacterial,² and antitumor³ activities. Among numerous cyclic peroxides, heteroatomic cyclic peroxides occupy a special place owing to their high biological activities.⁴ The methods of synthesis of heteroatom-containing cyclic peroxides are limited. Recently,^{5–10} nitrogen- and sulfur-containing cyclic di- and triperoxides with antitumor activity have been synthesized.^{5–9} The development of efficient methods for the preparation of new cyclic hetero-di(tri)peroxides^{5–10} promotes active investigation of their transformations. It was shown that the reduction of silatriperoxycycloalkanes with PPh_3 affords siladiperoxycycloalkanes;¹¹ the reaction of spiro{adamantane-[2,3']-(pentaioxacane)} with *o*-phenylenediamine results in the synthesis of benzodioxazocine.⁵ The implemented conversion of pentaioxacane with *o*-phenylenediamine to benzodioxazocine⁵ suggests that cyclic *N*-containing peroxides can be involved in reactions with binucleophilic reagents, in particular α,ω -dithiols, to give new heterocycles. In contrast to the previously described methods of synthesis^{5–10} and transformation of the peroxide ring,^{5,11} this work for the first time discusses the method of catalytic conversion of tetraoxazaspirotridecane to dithiazacycloalkanes.

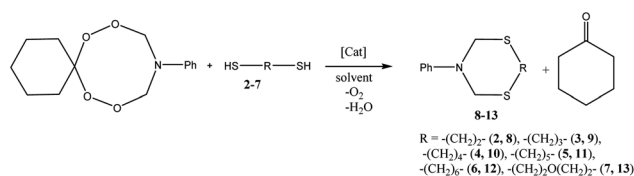
It was shown by preliminary experiments that the reaction of 10-phenyl-7,8,12,13-tetraoxa-10-azaspiro[5.7]tridecane **1** with ethane-1,2-dithiol **2** does not proceed without a catalyst. The reaction of azadiperoxide **1** with ethane-1,2-dithiol **2** catalyzed by $\text{Sm}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$, H_2SO_4 or $\text{BF}_3 \cdot \text{Et}_2\text{O}$ in THF as a solvent affords 3-phenyl-1,5,3-dithiazepane **8** in 10–15% yield (Scheme 1, Table 1). It was found that the yield of 3-phenyl-1,5,3-dithiazepane¹² is affected by the nature of the catalyst. When the reaction is carried out in a polar solvent (MeOH) in the presence of catalytic amounts of $\text{Sm}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$, H_2SO_4 or $\text{BF}_3 \cdot \text{Et}_2\text{O}$, the yield of the target product **8** increases to 30%. In the presence of the $\text{Co}(\text{OAc})_2$ catalyst, the

yield of heterocycle **8** is 85%. When AlCl_3 or CuCl catalysts are used, the yields of heterocycle **8** are 55% and 75%, respectively (Table 1). Under these conditions, cyclohexanone is formed and O_2 is released (Scheme 1). All reactions were carried out at room temperature for 20 h.

A probable pathway to the synthesis of 3-phenyl-1,5,3-dithiazepane **8** from 10-phenyl-7,8,12,13-tetraoxa-10-azaspiro[5.7]tridecane **1** includes¹³ coordination of the peroxide oxygen atom to the central atom of the catalyst, nucleophilic addition of ethane-1,2-dithiol to the resulting carbocation,^{14,15} and the subsequent ring closure giving heterocycle **8** (Scheme 2).

Under conditions including 5 mol% of $\text{Co}(\text{OAc})_2$, 20 °C, MeOH, and 20 h, 10-phenyl-7,8,12,13-tetraoxa-10-azaspiro[5.7]tridecane **1** was allowed to react with propane-1,3- **3**, butane-1,4- **4**, pentane-1,5- **5**, and hexane-1,6-dithiols **6**, which furnished the corresponding 3-phenyl-1,5,3-dithiazacycloalkanes¹⁶ **9–12** in 83–89% yields (Table 1). The ring transformation reaction of azadiperoxide **1** with 3,6-dioxo-1,8-octanedithiol **7** (monooxa derivative is shown in the scheme) under the conditions described above resulted in the synthesis of 6-phenyl-1,11-dioxo-4,8-dithia-6-azacyclotridecane¹⁶ **12** in 91% yield (Scheme 1).

The discovered ring transformation reaction of azadiperoxide **1** with ethane-1,2-dithiol **2** was also carried out for 10-aryl-7,8,12,13-tetraoxa-10-azaspiro[5.7]tridecanes **14–24**, which produced 3-aryl-1,5,3-dithiazepanes¹² **25–35** in 76–90% yields (Scheme 3).



Scheme 1 Ring transformation reaction of 10-phenyl-7,8,12,13-tetraoxa-10-azaspiro[5.7]tridecane with α,ω -dithiols.

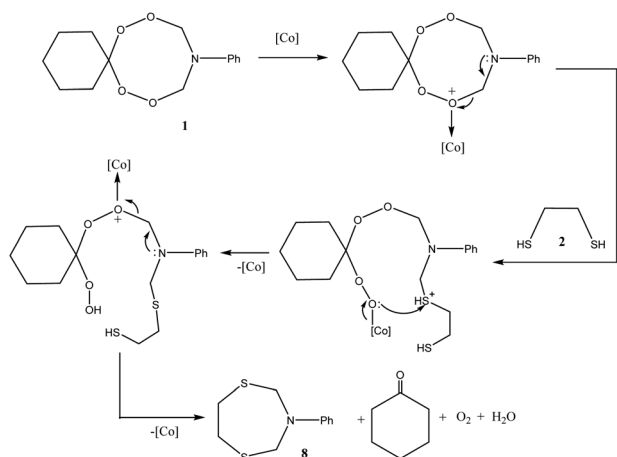
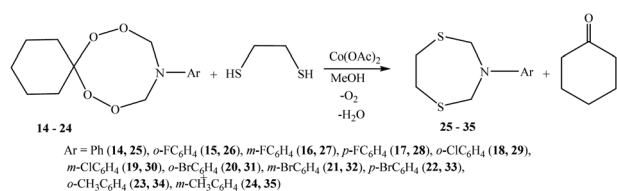
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Table 1 Effect of the catalyst and solvent nature on the yield of 3-phenyl-1,5,3-dithiazacyclanes (~20 °C, 20 h)

No.	Compound	[Cat]	Solvent	Yield, %
1	8	AlCl ₃	THF	45
2	8	AlCl ₃	MeOH	55
3	8	Co(OAc) ₂	THF	79
4	8	Co(OAc) ₂	MeOH	85
5	8	BF ₃ ·OEt ₂	THF	15
6	8	BF ₃ ·OEt ₂	MeOH	30
7	8	CuCl	THF	68
8	8	CuCl	MeOH	75
9	8	H ₂ SO ₄	THF	13
10	8	H ₂ SO ₄	MeOH	25
11	8	Sm(NO ₃) ₃ ·6H ₂ O	THF	10
12	8	Sm(NO ₃) ₃ ·6H ₂ O	MeOH	20
13	8	—	THF	—
14	8	—	MeOH	—
15	9	Co(OAc) ₂	MeOH	87
16	10	Co(OAc) ₂	MeOH	79
17	11	Co(OAc) ₂	MeOH	83
18	12	Co(OAc) ₂	MeOH	89
19	13	Co(OAc) ₂	MeOH	91

**Scheme 2** Probable synthesis mechanism for 3-phenyl-1,5,3-dithiazepane **8**.**Scheme 3** Ring transformation reaction of 10-aryl-7,8,12,13-tetraoxa-10-azaspiro[5.7]tridecanes with ethane-1,2-dithiol.

In conclusion, we demonstrated that on treatment with α,ω -alkanedithiols and the Co(OAc)₂ catalyst, azadiperoxides are converted to *N*-aryl-substituted 1,5,3-dithiazamacroheterocycles in high yields.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgements

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