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# Catalyzed ring transformation of cyclic *N*-aryl-azadiperioxides with participation of $\alpha,\omega$ -dithiols†

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Co(OAc)<sub>2</sub>-catalyzed ring transformation reaction of 10-aryl-7,8,12,13-tetraoxa-10-azaspiro[5.7]tridecane with  $\alpha,\omega$ -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,<sup>1</sup> antibacterial,<sup>2</sup> and antitumor<sup>3</sup> activities. Among numerous cyclic peroxides, heteroatomic cyclic peroxides occupy a special place owing to their high biological activities.<sup>4</sup> The methods of synthesis of heteroatom-containing cyclic peroxides are limited. Recently,<sup>5–10</sup> nitrogen- and sulfur-containing cyclic di- and triperoxides with antitumor activity have been synthesized.<sup>5–9</sup> The development of efficient methods for the preparation of new cyclic hetero-di(tri)peroxides<sup>5–10</sup> promotes active investigation of their transformations. It was shown that the reduction of silatriperoxycycloalkanes with PPh<sub>3</sub> affords siladiperoxycycloalkanes;<sup>11</sup> the reaction of spiro{adamantane-[2,3']-(pentaoxacane)} with *o*-phenylenediamine results in the synthesis of benzodioxazocine.<sup>5</sup> The implemented conversion of pentaoxacane with *o*-phenylenediamine to benzodioxazocine<sup>5</sup> suggests that cyclic *N*-containing peroxides can be involved in reactions with binucleophilic reagents, in particular  $\alpha,\omega$ -dithiols, to give new heterocycles. In contrast to the previously described methods of synthesis<sup>5–10</sup> and transformation of the peroxide ring,<sup>5,11</sup> this work for the first time discusses the method of catalytic conversion of tetraoxazaspirotridecane to dithiazacycloalkanes.

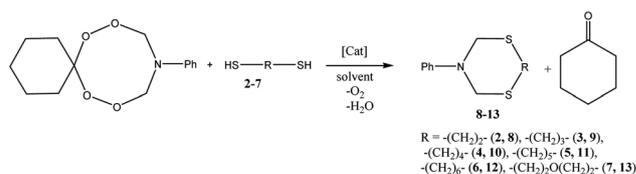
It was shown by preliminary experiments that the reaction of 10-phenyl-7,8,12,13-tetraoxa-10-azaspiro[5.7]tridecane **1** with ethane-1,2-dithiol **2** does not proceed without a catalyst. The reaction of azadiperoxide **1** with ethane-1,2-dithiol **2** catalyzed by Sm(NO<sub>3</sub>)<sub>3</sub>·6H<sub>2</sub>O, H<sub>2</sub>SO<sub>4</sub> or BF<sub>3</sub>·Et<sub>2</sub>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-dithiazepane<sup>12</sup> 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 Sm(NO<sub>3</sub>)<sub>3</sub>·6H<sub>2</sub>O, H<sub>2</sub>SO<sub>4</sub> or BF<sub>3</sub>·Et<sub>2</sub>O, the yield of the target product **8** increases to 30%. In the presence of the Co(OAc)<sub>2</sub> catalyst, the

yield of heterocycle **8** is 85%. When AlCl<sub>3</sub> 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<sub>2</sub> 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** includes<sup>13</sup> coordination of the peroxide oxygen atom to the central atom of the catalyst, nucleophilic addition of ethane-1,2-dithiol to the resulting carbocation,<sup>14,15</sup> and the subsequent ring closure giving heterocycle **8** (Scheme 2).

Under conditions including 5 mol% of Co(OAc)<sub>2</sub>, 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-dithiazacycloalkanes<sup>16</sup> **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-azacyclotridecane<sup>16</sup> **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]tridecane **14–24**, which produced 3-aryl-1,5,3-dithiazepanes<sup>12</sup> **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  $\alpha,\omega$ -dithiols.

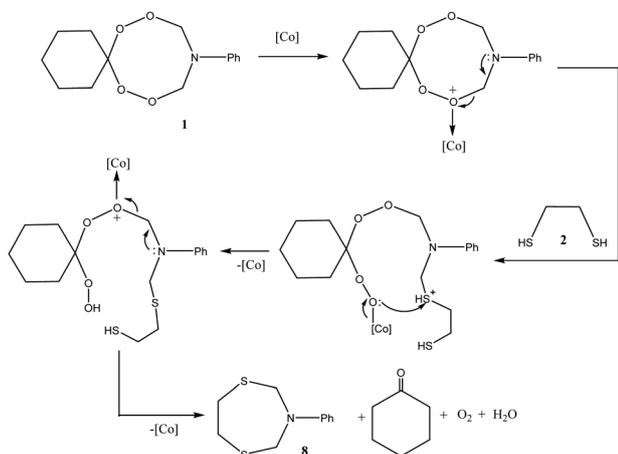
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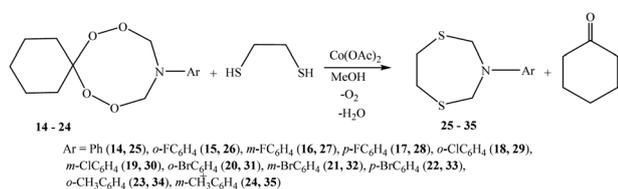


**Table 1** Effect of the catalyst and solvent nature on the yield of 3-phenyl-1,5,3-dithiazacyclanes (~20 °C, 20 h)

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

In conclusion, we demonstrated that on treatment with  $\alpha,\omega$ -alkanedithiols and the Co(OAc)<sub>2</sub> 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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