

## Synthesis of Bisoxadiazolidinones

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In our series of studies on the reactions of three-membered heterocycles containing two heteroatoms (1-3), we have found that oxadiazolidinones are given by the reaction of oxaziridines with isocyanates in high yields. Interest in polymers connected with heterocycles, which has widely been studied recently, has led to the suggestion that polyoxadiazolidinones can be synthesized from bisoxaziridines and diisocyanates. Thus, as a fundamental investigation for the synthesis of polyoxadiazolidinones, preparation of bisoxadiazolidinones by both reactions of bisoxaziridines with phenyl isocyanate and of an oxaziridine with toluene diisocyanate have been studied along with their behaviors in hydrolysis and pyrolytic treatment.

## Results and Discussion.

## A. Bisoxadiazolidinones from Bisoxaziridines and Phenyl Isocyanate.

Only a few bisoxaziridines have been reported (4-6) and those employed in the present study including new compounds are listed in Table I. They are classified into

two types, *i.e.*, the one whose two oxaziridine rings are connected between the nitrogens and the other between the carbons.

The reaction of 3,3'-*p*-phenylenebis(2-cyclohexyloxaziridine) (**1a**) with phenyl isocyanate in *o*-xylene at 135° for 12 hours gave the bisoxadiazolidinone **2a** in 74% yield. The compound **2a** showed a strong infrared absorption band at 1740 cm<sup>-1</sup> (C=O) which is characteristic of an oxadiazolidinone ring (1). Though nmr spectrum was not obtained because of its low solubility, the mass spectrum and analytical data well support the structure.

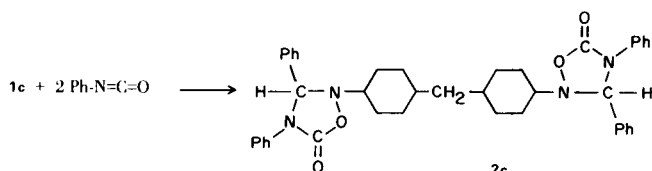
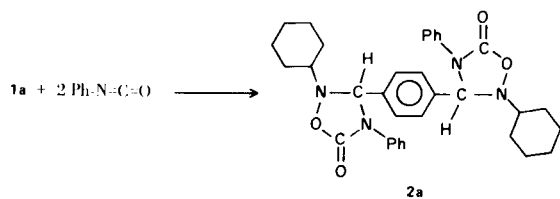
Similarly, bisoxadiazolidinone **2c** was prepared from the bisoxaziridine **1c** and the isocyanate in 89% yield.

In the reactions of bisoxaziridines **1b, d-f**, on the other hand, no cycloadduct was obtained. The results of the bisoxaziridines **1d-f** are deducible from general properties of 2-*n*-alkyloxaziridines. Not only the stability of oxaziridines but the yield of oxadiazolidinones in the reactions with phenyl isocyanate decreases with the change of the *N*-substituent in the order of *t*-, *sec*-, and *n*-alkyl group.

TABLE I  
Bisoxaziridines

Bisoxaziridine	M.p., °C	Ref.	Purity (a) (%)	Yield (b) (%)
<b>1a</b>	160 (lit. 160-161)	4	95	36
<b>1b</b>	50 (lit. 53-56)	5	95	72
<b>1c</b>	45	(c)	88	63
<b>1d</b>	-5 (d)	(c)	96	72
<b>1e</b>	84-86	(c)	83	80
<b>1f</b>	97-102	(c)	84	75

(a) Determined by iodometry. (b) Prepared by oxidation of corresponding bisimines with perbenzoic acid. (c) A new compound. (d) Freezing point.

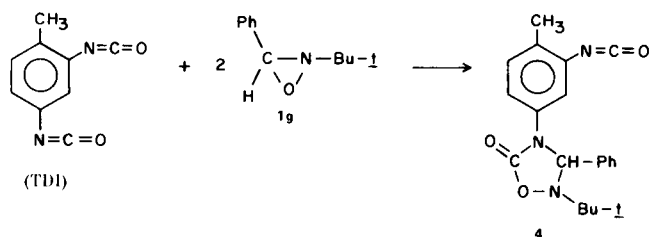


In polar solvents, 2-ethyl-3-phenyloxaziridine gave no adduct with phenyl isocyanate (1). The bisoxaziridine **1b**, though it has *t*-butyl groups on the nitrogens, seems to be relatively unstable in contrast to a stable 2-*t*-butyl-3-phenyloxaziridine (**1g**).

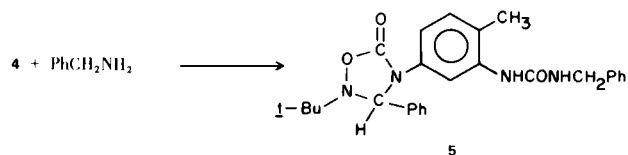
#### B. Bisoxadiazolidinone from Oxaziridine and Diisocyanate.

As another route to bisoxadiazolidinones, the reaction of 2-*t*-butyl-3-phenyloxaziridine (**1g**) with toluene-2,4-diisocyanate (TDI) was studied. The oxaziridine **1g** is one of the most stable analogs and is obtainable in high purity. Furthermore, the oxaziridine **1g** reacts with phenyl isocyanate to result in an oxadiazolidinone derivative quantitatively (1).

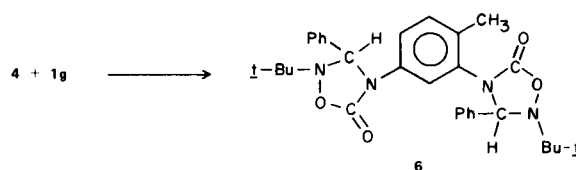
When two moles of the oxaziridine **1g** was allowed to react with one mole of TDI in refluxing benzene for 6 hours, the 1:1 cycloadduct **4** was obtained in 79% yield, showing the selective cycloaddition to the isocyanato group of 4-position.



The 1:1 adduct **4** exhibited typical absorptions of an isocyanato group and an oxadiazolidinone carbonyl group in the infrared spectrum at 2320 and 1742  $\text{cm}^{-1}$ , respectively. Molecular ion peak ( $m/e$  351) and fragmentation in its mass spectrum as well as signals in the nmr spectrum were reasonable for the structure. Further structural support was given by the treatment of the compound **4** with benzylamine. The urea derivative **5** was analyzed satisfactorily.



The 1:1 adduct **4** was allowed to react with the oxaziridine **1g** for another 14 hours in refluxing benzene and the desired bisoxadiazolidinone **6** was obtained in 67% yield, thus indicating the difference in reactivity of the isocyanato groups in TDI.



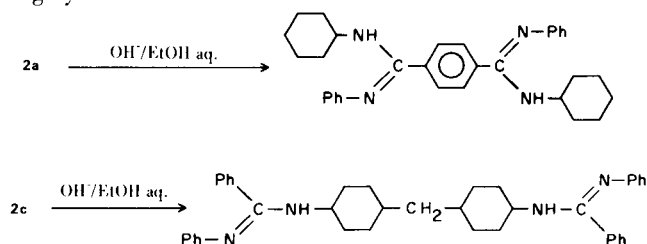
The ir spectrum of the compound **6** shows a single strong absorption band at 1750  $\text{cm}^{-1}$  ( $\text{C=O}$ ). Other spectral and analytical data are also in good agreement with the structure.

Of the diisocyanate, only TDI was studied and, in this case, the lower reactivity of the *ortho*-isocyanato group compared with the *para*-substituent is considered to be a slight hindrance for the present purpose. Hence, optimum reaction conditions including some catalysts should be sought for preparing polyoxadiazolidinones effectively.

#### C. Hydrolysis and Pyrolytic Treatment of Bisoxadiazolidinones.

Regarding properties of 1,2,4-oxadiazolidinones, we have reported that the compounds resist acidic hydrolysis but hydrolyzed under alkaline conditions or pyrolyzed to give the corresponding amidines (1).

Similar decarboxylation from bisoxadiazolidinones was observed in their alkaline hydrolyses giving bisamidines in high yields.



Thermogravimetric analyses of bisoxadiazolidinones **2a** and **2c**, however, indicated that the thermal decomposition caused not the loss of carbon dioxide but the release of two moles of phenyl isocyanate (see Experimental).

It is predictable from the above facts that polyoxadiazolidinones may be hydrolyzed into polyamidines losing carbon dioxide but depolymerized when heated strongly.

## EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Ir, nmr, and mass spectra were obtained on a JASCO IR-E spectrophotometer, a JEOL JNM-3H-60 spectrometer, and a Hitachi RMU-6E spectrometer, respectively. Thermogravimetric analysis (TGA) was carried out in a nitrogen stream at a heating rate of 1.25°/min. with a Rigaku Denki Thermoflex DG-Cl-H.

## Materials.

Phenyl isocyanate and toluene-2,4-diisocyanate were purchased from a commercial source and were distilled just before their use. The bisimines employed as starting materials for bisoxaziridines were all prepared by condensation of the appropriate dialdehyde and amine or aldehyde and diamine.

Bisoxaziridines **1a-f** were prepared by oxidation of the corresponding bisimines with perbenzoic acid according to the Pews' method (8). Melting points, purities determined by iodometry and yields are given in Table I.

2-*t*-Butyl-3-phenyloxaziridine (**1g**) was prepared from *N-t*-butylbenzylideneamine as reported in the preceding paper (1).

## Preparation of Bisoxadiazolidinones.

3,3'-*p*-Phenylenebis(2-cyclohexyl-4-phenyl-1,2,4-oxadiazolidin-5-one) (**2a**).

The bisoxaziridine **1a** (17 mmoles) was treated with phenyl isocyanate (68 mmoles) in *o*-xylene (20 ml.) at 135° for 12 hours under a nitrogen stream. After the removal of the solvent and the excess of the isocyanate, a small amount of hexane was added to the residue, which was allowed to stand to precipitate colored solid. The solid was filtered and washed with refluxing acetone and methanol to give the bisoxadiazolidinone **2a** (74%), colorless powder (from pyridine), m.p. slowly decomposes above 230°; ir (Nujol): 1740 cm<sup>-1</sup> (C=O); mass spectrum (70 eV): *m/e* 566 (M<sup>+</sup>, calcd. 566), 478 (M<sup>+</sup> - 2 CO<sub>2</sub>), 447 (M<sup>+</sup> - PhNCO), 403 (447 - CO<sub>2</sub>), 328 (M<sup>+</sup> - 2 PhNCO).

*Anal.* Calcd. for C<sub>34</sub>H<sub>38</sub>N<sub>4</sub>O<sub>4</sub> (566): C, 72.06; H, 6.76; N, 9.89. Found: C, 71.89; H, 6.73; N, 9.77.

2,2'-(4,4'-Methylenedicyclohexylene)bis(3,4-diphenyl-1,2,4-oxadiazolidin-5-one) (**2c**).

The reaction mixture of the bisoxaziridine **1c** (17 mmoles) and phenyl isocyanate (68 mmoles) treated in *o*-xylene (25 ml.) at 125° for 10 hours was concentrated *in vacuo* and the resultant precipitate was recrystallized from acetone to give colorless needles (56%), m.p. 188°; ir (Nujol): 1740 cm<sup>-1</sup> (C=O); nmr (deuteriochloroform):  $\tau$  7.7-9.1 (m, 20, CH<sub>2</sub> and 2 C<sub>6</sub>H<sub>9</sub>), 6.6-7.2 (m, 2, 2 NCH of cyclohexyl), 4.12 (s, 2, 2 CH), 2.5-3.0 (20, 4 Ph); mass spectrum (70 eV): *m/e* 418 (M<sup>+</sup> - 2 PhNCO), 386 (418 - O<sub>2</sub>).

*Anal.* Calcd. for C<sub>41</sub>H<sub>44</sub>N<sub>4</sub>O<sub>4</sub> (656): C, 74.97; H, 6.75; N, 8.53. Found: C, 74.74; H, 6.67; N, 8.23.

2-*t*-Butyl-3-phenyl-4-(4-methyl-3-isocyanatophenyl)-1,2,4-oxadiazolidin-5-one (**4**).

To a solution of the oxaziridine **1g** (68 mmoles) in 13 ml. of benzene, a solution of toluene-2,4-diisocyanate (30 mmoles) in benzene (7 ml.) was added dropwise over 20 minutes under a nitrogen stream. The mixture was refluxed for 6 hours and then cooled to precipitate crystalline oxadiazolidinone **4**, which was filtered and washed with hexane (79%). The filtrate was determined to contain 32 mmoles of the unreacted **1g** by iodometry. Recrystallization of the filtered solid from benzene-hexane gave colorless needles, m.p. 163-165°; ir (Nujol): 2320 (-NCO) and

1742 cm<sup>-1</sup> (C=O); nmr (deuteriochloroform):  $\tau$  8.75 (s, 9, *t*-Bu), 7.78 (s, 3, CH<sub>3</sub>), 4.12 (s, 1, CH), 2.6-2.9 (m, 8, aromatic protons); mass spectrum (70 eV): *m/e* 351 (M<sup>+</sup>, calcd. 351), 295 (M<sup>+</sup> - C<sub>4</sub>H<sub>8</sub>), 250 (M<sup>+</sup> - CO<sub>2</sub> - Bu), 177 (M<sup>+</sup> - TDI).

Elemental analysis of the compound **4** was not satisfactory at it has an isocyanato group sensitive to humidity. Isocyanate content determined with butylamine by a titrimetric method was 10.6% (calcd. 11.9%).

Reaction of the Oxadiazolidinone **4** with Benzylamine.

The mixture of the compound **4** (4.3 mmoles), benzylamine (14 mmoles), and benzene (25 ml.) was refluxed for one hour under nitrogen atmosphere. The solid precipitated upon cooling was filtered and recrystallized from ethanol-water to afford 2-*t*-butyl-3-phenyl-4-(4-methyl-3-*N'*-benzylureidophenyl)-1,2,4-oxadiazolidin-5-one (**5**) (87%), colorless needles, m.p. 156-157°; ir (Nujol): 3320 (NH), 1765 (C=O), and 1640 cm<sup>-1</sup> (C=O); nmr (DMSO-d<sub>6</sub>):  $\tau$  8.80 (s, 9, *t*-Bu), 7.91 (s, 3, CH<sub>3</sub>), 5.71 (d, 2, *J* = 5.7 Hz, N-CH<sub>2</sub>), 3.64 (s, 1, CH), 2.5-3.1 (m, 13, aromatic protons), 2.2 (s, 1, NH), 1.8 (s, 1, NH); mass spectrum (70 eV): *m/e* 414 (M<sup>+</sup> - CO<sub>2</sub>), 281 (M<sup>+</sup> - 177), 177 (**1g**<sup>+</sup>), 174 (TDI<sup>+</sup>).

*Anal.* Calcd. for C<sub>27</sub>H<sub>30</sub>N<sub>4</sub>O<sub>3</sub> (458): C, 70.72; H, 6.59; N, 12.22. Found: C, 70.61; H, 6.37; N, 12.21.

Preparation of 4,4'-(2,4-Toluene)bis(2-*t*-butyl-3-phenyl-1,2,4-oxadiazolidin-5-one) (**6**).

A mixture of the oxadiazolidinone **4** (4.3 mmoles), the oxaziridine **1g** (12 mmoles) and benzene (20 ml.) was refluxed for 14 hours under a nitrogen stream. The mixture was concentrated and the crystalline bisoxadiazolidinone **6** precipitated upon addition of ether to the mixture. Recrystallization of the compound from benzene gave colorless granules (67%), m.p. 200-201°; ir (Nujol): 1750 cm<sup>-1</sup> (C=O); nmr (deuteriochloroform):  $\tau$  8.84 (s, 9, *t*-Bu), 8.77 (s, 9, *t*-Bu), 8.04 (s, 3, CH<sub>3</sub>), 4.50 (s, 1, CH), 4.34 (s, 1, CH), 2.5-3.0 (m, 13, aromatic protons); mass spectrum (70 eV): *m/e* 528 (M<sup>+</sup>, calcd. 528), 351 (M<sup>+</sup> - **1g**), 307 (351 - CO<sub>2</sub>), 295 (351 - C<sub>4</sub>H<sub>8</sub>).

*Anal.* Calcd. for C<sub>31</sub>H<sub>36</sub>N<sub>4</sub>O<sub>4</sub> (528): C, 70.43; H, 6.86; N, 10.60. Found: C, 70.55; H, 6.86; N, 10.60.

Alkaline Hydrolysis of Bisoxadiazolidinones **2a** and **2c**.

To a solution of the bisoxadiazolidinone **2a** (3.5 mmoles) in ethanol (50 ml.), 2*N* potassium hydroxide (10 ml.) was added and the mixture was refluxed for 24 hours followed by extraction (chloroform) and concentration *in vacuo* to give crystalline solid (89%). Recrystallization from benzene-hexane gave *p*-bis(*N*-cyclohexyl-*N'*-phenylamidino)benzene (**3a**), colorless needles, m.p. 191-193°; ir (Nujol): 3420 (NH) and 1618 cm<sup>-1</sup> (C=N); nmr (deuteriochloroform):  $\tau$  7.5-9.3 (m, 20, 2 C<sub>6</sub>H<sub>10</sub>), 5.7-6.4 (broad, 2, 2 NCH), 5.4-6.0 (broad, 2, 2 NH), 2.4-3.6 (m, 14, aromatic protons). The third signal disappeared upon addition of deuterium oxide; mass spectrum (70 eV): *m/e* 478 (M<sup>+</sup>, calcd. 478), 395 (M<sup>+</sup> - C<sub>6</sub>H<sub>11</sub>), 319 (395 - Ph), 313 (395 - C<sub>6</sub>H<sub>10</sub>).

*Anal.* Calcd. for C<sub>32</sub>H<sub>38</sub>N<sub>4</sub> (478): C, 80.29; H, 8.00; N, 11.71. Found: C, 80.16; H, 7.93; N, 11.55.

Similarly, the alkaline hydrolysis of the bisoxadiazolidinone **2c** (4.1 mmoles) resulted in 4,4'-bis( $\alpha$ -phenyliminobenzylamino)-dicyclohexylmethane (**3c**) (90%), whose recrystallization could not be done satisfactorily because of its low solubility, colorless powder, m.p. 50-57°; ir (Nujol): 1615 cm<sup>-1</sup> (C=N); mass spectrum (70 eV): *m/e* 568 (M<sup>+</sup>, calcd. 568), 476 (M<sup>+</sup> - PhNH), 388 (M<sup>+</sup> - PhC=NPh), 373 (M<sup>+</sup> - PhC(NH)=NPh), 291 (PhC(=NPh)-NH-C<sub>6</sub>H<sub>10</sub>CH<sub>2</sub><sup>+</sup>).

Thermogravimetric Analysis of Bisoxadiazolidinones **2a** and **2c**.

The thermogravimetric analysis of the bisoxadiazolidinone **2a** (76 mg.) was performed in nitrogen atmosphere at a heating rate of 1.25°/minutes. Weight loss of the compound began at 178° and continued till 278° and amounted to 47.4% (calcd. for the loss of two moles of phenyl isocyanate, 42.0%). The DTA curve showed an endothermic transition point at about 230°. The same treatment of the bisoxadiazolidinone **2c** (84 mg.) showed the weight loss of 38.1% (calcd. for the loss of two moles of phenyl isocyanate, 36.2%) during 164° to 267°. The DTA curve had an endothermic transition point at about 207°.

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