

Configuration of *cis* and *trans* Isomers

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The attempted acid-catalyzed azeotropic removal of water from a mixture containing lactamide and chloral in refluxing toluene lead to the elimination of ammonia; both *cis*- and *trans*-5-methyl-2-(trichloromethyl)-1,3-dioxolan-4-one were isolated. A number of 1,3-dioxolan-4-ones and 1,3-oxathiolan-5-ones were obtained by cyclodehydration of aldehydes with  $\alpha$ -hydroxy- and  $\alpha$ -mercapto-carboxylic acids in the presence of boron trifluoride etherate. Geometric isomers were separated, and their configurations were determined by nuclear magnetic resonance.

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In the preceding article (1) it was shown that  $\alpha$ -hydroxy-carboxamides undergo cyclocondensation with aldehydes in the presence of *p*-toluenesulfonic acid or boron trifluoride etherate to give *cis*- and *trans*-1,3-oxazolidin-4-ones separable by chromatography. In an attempt to prepare *cis*- and *trans*-5-methyl-2-(trichloromethyl)-1,3-oxazolidin-4-one (**1a** and **1b**) from lactamide and chloral, the only products obtained were *cis*- and *trans*-5-methyl-2-(trichloromethyl)-1,3-dioxolan-4-one (**2a**) (32%) and (**2b**) (7%), separated by silica chromatography. Ammonia rather than water was eliminated.

The structures of **2a** and **2b** have been established on the basis of correct combustion analyses (CHN) and the nmr spectral characteristics, particularly the signals of the two protons in the 2- and 5-positions. For the *trans* isomer (**2b**), the combined deshielding effects of the two substituents, methyl and trichloromethyl, result in the signals from the ring-protons each appearing at lower field ( $\delta$  6.3 (2-H) and 5.0 ppm (5-H), than those from the corresponding ring-protons in the *cis* isomer (**2a**) ( $\delta$  6.1 (2-H) and 4.85 ppm (5-H)). In the infrared spectra of both **2a** and **2b**, the carbonyl bands occur at 1825-1820  $\text{cm}^{-1}$  and the C-O-(lactone) bands at 1220-1210  $\text{cm}^{-1}$ ; these data are indicative (9) of a 1,3-dioxolan-4-one structure. The electron impact-induced fragmentation of **2a** and **2b** was briefly investigated (70 eV, ion source: 170°) and found to give superimposable spectra for both isomers. The molecular ions are not observed. For both isomers, the ion  $m/e$  45 ( $\text{CO}_2$ ) gives rise to the base peak. Both

spectra exhibit ions ( $m/e$  139) corresponding to the elimination of Cl and  $\text{CO}_2$  from the molecular ions, and fragments ( $m/e$  101) corresponding to the elimination of  $\text{CCl}_3$  ( $m/e$  117). Further, both compounds give rise to the fragmentation of the abundant fragment  $\text{Cl}_3\text{C-CH}$  ( $m/e$  130).

In the literature, some uncertainty exists about the known forms of 5-methyl-2-(trichloromethyl)-1,3-dioxolan-4-one. Wallach and Heymer (2), Nencki (3), and Boesken (4), obtained a form, m.p. 45°; *cis-trans* isomerism was not observed. Baron and Hollis (5) and Cort and Stewart (6) obtained a single isomer, m.p. 88° and m.p. 82°, respectively, but not the product, m.p. 56°, reported by Shah and Alimchandani (7), who also reported another, liquid form. Correspondences in the nmr spectra of the isomers melting at 88° and 82° indicate that the geometric isomerism is the same. By applying Schoolery's rules (8), Cort and Stewart (6) conclude that these isomers have the *trans*-configuration **2b**.

Repeating the methods of Nencki (3) and Baron and Hollis (5) using ( $\pm$ )lactic acid and chloral, we obtained two isomers (a solid (m.p. 45° and 50-55°), and another, liquid form. Correspondences in the nmr spectra indicate that the geometric isomerism of the solid forms is the same as in **2b** (*trans* isomer), and the liquid forms correspond with **2a** (*cis* isomer). Attempts to crystallize the liquid form were unsuccessful. Attempts to increase the melting point of the solid forms by crystallization techniques were likewise unsuccessful. It is surmised that in preparations obtained from lactic acid and chloral in the presence of concentrated sulfuric acid, traces of acidic impurities account for the failure to obtain the two geometric isomers in form of crystalline solids melting at 34-36° and 88°, respectively.

To study the physical characteristics of related 1,3-dioxolan-4-ones and 1,3-oxathiolan-5-ones, tribromoacetaldehyde and three substituted-phenoxyacetaldehydes were allowed to undergo cyclocondensation with glycolic, lactic, dimethylacetic, mandelic, mercaptoacetic, and 2-mercaptopropionic acids. The utilization of boron trifluoride etherate allowed the condensation to proceed

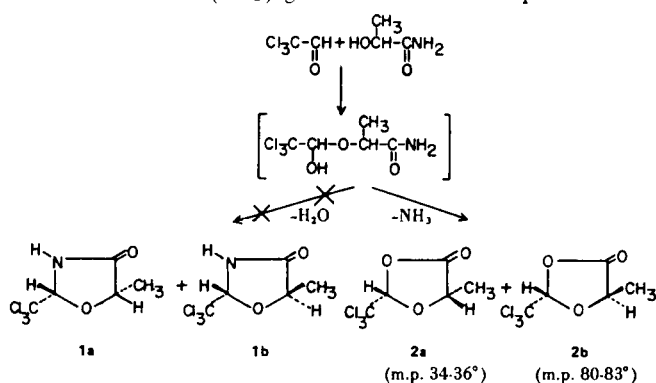
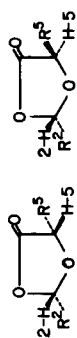


Table I

## 1,3-Dioxolan-4-ones

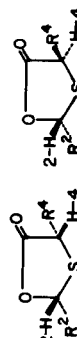


Compound	R <sup>2</sup>	R <sup>5</sup>	Isomer	Yield, %	M.p., °C	Formula	Carbon		Hydrogen		Chlorine		Nmr Positions in Deuteriochloroform (δ)		
							Calcd.	Found	Calcd.	Found	Calcd.	Found	2-H	5-H	5-H
<b>2a</b>	Cl <sub>3</sub> C	CH <sub>3</sub>	cis	7	34-36	C <sub>5</sub> H <sub>5</sub> Cl <sub>3</sub> O <sub>3</sub> (a)	27.3	27.0	2.3	2.3	—	—	6.1	4.85	1.45 (CH <sub>3</sub> )
<b>2b</b>	Cl <sub>3</sub> C	CH <sub>3</sub>	trans	32	80-83	C <sub>5</sub> H <sub>5</sub> Cl <sub>3</sub> O <sub>3</sub> (a)	27.3	27.3	2.3	2.2	—	—	6.3	5.0	1.45 (CH <sub>3</sub> )
<b>3a</b>	Br <sub>3</sub> C	C <sub>6</sub> H <sub>5</sub>	cis	6	101-104	C <sub>10</sub> H <sub>7</sub> Br <sub>3</sub> O <sub>3</sub>	28.9	28.8	1.7	1.7	—	—	6.17	5.93	ca. 7.5 (C <sub>6</sub> H <sub>5</sub> )
<b>3b</b>	Br <sub>3</sub> C	C <sub>6</sub> H <sub>5</sub>	trans	7	92-94	C <sub>10</sub> H <sub>7</sub> Br <sub>3</sub> O <sub>3</sub>	28.9	28.5	1.7	1.6	—	—	6.6	6.05	ca. 7.5 (C <sub>6</sub> H <sub>5</sub> )
<b>4a</b>	4-Cl-C <sub>6</sub> H <sub>4</sub> -OCH <sub>2</sub>	CH <sub>3</sub>	cis	28	53-55	C <sub>11</sub> H <sub>11</sub> ClO <sub>4</sub>	54.4	54.5	4.5	4.5	14.6	15.0	5.9	4.43	1.5 (CH <sub>3</sub> )
<b>4b</b>	4-Cl-C <sub>6</sub> H <sub>4</sub> -OCH <sub>2</sub>	CH <sub>3</sub>	trans	23	37-40	C <sub>11</sub> H <sub>11</sub> ClO <sub>4</sub>	54.4	54.5	4.5	4.6	14.6	14.7	5.9	4.58	1.5 (CH <sub>3</sub> )
<b>5</b>	4-Cl-C <sub>6</sub> H <sub>4</sub> -OCH <sub>2</sub>	H	—	41	50-53	C <sub>10</sub> H <sub>9</sub> ClO <sub>4</sub>	52.5	52.6	3.9	3.8	15.5	15.6	5.9	4.27	4.52 (H)
<b>6a</b>	2,4-Cl <sub>2</sub> -C <sub>6</sub> H <sub>3</sub> -OCH <sub>2</sub>	CH <sub>3</sub>	cis	40	57-60	C <sub>11</sub> H <sub>10</sub> Cl <sub>2</sub> O <sub>4</sub>	47.6	47.8	3.6	3.6	25.6	25.5	5.93	4.48	1.5 (CH <sub>3</sub> )
<b>6b</b>	2,4-Cl <sub>2</sub> -C <sub>6</sub> H <sub>3</sub> -OCH <sub>2</sub>	CH <sub>3</sub>	trans	19	45-47	C <sub>11</sub> H <sub>10</sub> Cl <sub>2</sub> O <sub>4</sub>	47.6	47.6	3.6	3.5	25.6	25.8	6.0	4.80	1.5 (CH <sub>3</sub> )
<b>7</b>	2,4-Cl <sub>2</sub> -C <sub>6</sub> H <sub>3</sub> -OCH <sub>2</sub>	H	—	46	53-54	C <sub>10</sub> H <sub>8</sub> Cl <sub>2</sub> O <sub>4</sub>	45.6	45.6	3.0	3.0	—	—	6.0	4.27	4.65 (H)
<b>8a</b>	2,4-Cl <sub>2</sub> -C <sub>6</sub> H <sub>3</sub> -OCH <sub>2</sub>	C <sub>6</sub> H <sub>5</sub>	cis	52	105-107	C <sub>16</sub> H <sub>12</sub> Cl <sub>2</sub> O <sub>4</sub>	56.6	56.7	3.5	3.6	20.9	21.2	5.93	5.27	ca. 7.5 (C <sub>6</sub> H <sub>5</sub> )
<b>8b</b>	2,4-Cl <sub>2</sub> -C <sub>6</sub> H <sub>3</sub> -OCH <sub>2</sub>	C <sub>6</sub> H <sub>5</sub>	trans	32	68-71	C <sub>16</sub> H <sub>12</sub> Cl <sub>2</sub> O <sub>4</sub>	56.6	56.6	3.5	3.6	20.9	21.3	6.10	5.65	ca. 7.5 (C <sub>6</sub> H <sub>5</sub> )
<b>9a</b>	2-Cl-4-CH <sub>3</sub> -C <sub>6</sub> H <sub>3</sub> -OCH <sub>2</sub>	C <sub>6</sub> H <sub>5</sub>	cis	31	71-73	C <sub>17</sub> H <sub>15</sub> ClO <sub>4</sub>	64.0	64.3	4.7	4.4	11.1	11.5	5.95	5.3	ca. 7.5 (C <sub>6</sub> H <sub>5</sub> )
<b>9b</b>	2-Cl-4-CH <sub>3</sub> -C <sub>6</sub> H <sub>3</sub> -OCH <sub>2</sub>	C <sub>6</sub> H <sub>5</sub>	trans	9	77-78	C <sub>17</sub> H <sub>15</sub> ClO <sub>4</sub>	64.0	64.0	4.7	4.7	—	—	6.05	5.45	ca. 7.5 (C <sub>6</sub> H <sub>5</sub> )
<b>10</b>	2-Cl-4-CH <sub>3</sub> -C <sub>6</sub> H <sub>3</sub> -OCH <sub>2</sub>	H	—	61	42-44	C <sub>11</sub> H <sub>11</sub> ClO <sub>4</sub>	54.4	54.4	4.5	4.5	14.6	15.0	5.95	4.25	4.53 (H)
<b>11</b>		CH <sub>3</sub>	—	80	oil	C <sub>13</sub> H <sub>15</sub> ClO <sub>4</sub>	57.7	57.7	5.5	5.5	—	—	5.8	1.5	1.5 (CH <sub>3</sub> )

(a) *Anal.* Calcd.: N, 0.0. Found: <0.1.

Table II

## 1,3-Oxathiolan-5-ones



Compound	R <sup>2</sup>	R <sup>4</sup>	Isomer	Yield, %	M.p., °C	Formula	Carbon		Hydrogen		Chlorine		Nmr Positions in Deuteriochloroform (δ)		
							Calcd.	Found	Calcd.	Found	Calcd.	Found	2-H	4-H	4-H
<b>12a</b>	Cl <sub>3</sub> C	CH <sub>3</sub>	cis	36	35-36	C <sub>5</sub> H <sub>5</sub> Cl <sub>3</sub> SO <sub>2</sub>	25.5	25.5	2.1	2.1	45.2	45.1	5.83	4.15	1.75 (CH <sub>3</sub> )
<b>12b</b>	Cl <sub>3</sub> C	CH <sub>3</sub>	trans	50	63-65	C <sub>5</sub> H <sub>5</sub> Cl <sub>3</sub> SO <sub>2</sub>	25.5	25.6	2.1	2.1	45.2	45.0	5.73	4.20	1.65 (CH <sub>3</sub> )
<b>13</b>	Cl <sub>3</sub> C	H	—	54	32-33	C <sub>4</sub> H <sub>3</sub> Cl <sub>3</sub> SO <sub>2</sub> (a)	—	—	—	—	48.1	47.8	5.8	4.0	3.7 (H)
<b>14</b>	4-Cl-C <sub>6</sub> H <sub>4</sub> -OCH <sub>2</sub>	H	—	11	45-48	C <sub>10</sub> H <sub>9</sub> ClSO <sub>3</sub> (b)	—	—	—	—	14.5	14.9	5.8	3.92	3.6 (H)
<b>15</b>	2,4-Cl <sub>2</sub> -C <sub>6</sub> H <sub>3</sub> -OCH <sub>2</sub>	H	—	40	59-61	C <sub>10</sub> H <sub>8</sub> Cl <sub>2</sub> SO <sub>3</sub> (c)	43.6	43.6	2.8	2.9	25.4	25.3	5.8	4.18	3.62 (H)

(a) *Anal.* Calcd.: S, 14.4. Found: 14.9; (b) *Anal.* Calcd.: S, 13.1. Found: 13.0; (c) *Anal.* Calcd.: S, 11.4. Found: 11.6.

smoothly at ambient temperature. This method as described by Farines and Soullier (9), has been applied to the preparation of 1,3-dioxolan-4-ones (Table I) and 1,3-oxathiolan-5-ones (Table II). Mixtures containing *cis* and *trans* isomers were readily separated by silica chromatography. In every case, the *trans* isomers had higher R<sub>f</sub> values than the corresponding *cis* isomers; in this respect their behavior parallels that of *cis*- and *trans*-1,3-oxazolidin-4-ones (1). Spraying of treated thin-layer plates with freshly prepared potassium permanganate in aqueous acetone, followed by warming of the plates with a heat gun proved to be a reliable and quick technique to develop the plates and to determine accurately the purity and movement characteristics of the *cis* and *trans* isomers.

In the infrared spectra of all 4-dioxolanones, the carbonyl stretching vibration is observed in the range of 1830-1805 cm<sup>-1</sup>. For the 5-oxathiolanones, the carbonyl absorption is shifted to somewhat longer wave lengths and is found near 1800-1785 cm<sup>-1</sup>. The C-O stretching mode of both the dioxolanones and oxathiolanones gives rise to strong absorption bands in the region 1220-1190 cm<sup>-1</sup>.

As has been noted for **2a** and **2b** (above), the principal feature in all the *cis* and *trans* isomers is the shift to high field of protons on the ring-carbon atoms that are *cis*, and to lower field of protons that are *trans* to each other. The compounds in which both R<sup>5</sup> and R<sup>4</sup> are hydrogen show vicinal coupling of 7-8 Hz and long range coupling to proton 2-H of about 2 Hz. In general, the signals due to the protons on C-5 of the dioxolanones are shifted to a considerably lower field, by about 0.6 ppm, than those of the protons on C-4 of the oxathiolanones.

#### EXPERIMENTAL

Representative methods of synthesis are described for **2a,b**, **4a,b** and **15**.

*cis*-5-Methyl-2-(trichloromethyl)-1,3-dioxolan-4-one (**2a**) and *trans*-5-Methyl-2-(trichloromethyl)-1,3-dioxolan-4-one (**2b**).

A mixture containing 4.9 g. (0.055 mole) of lactamide, 7.4 g. (0.05 mole) of chloral and 0.1 g. of *p*-toluenesulfonic acid in 400 ml. of toluene was refluxed for 15 hours. The reaction mixture was concentrated to dryness and subjected to silica chromatography (Silica gel: Grace, grade 62; eluent (by volume); hexane (80), ethyl acetate (16), tetrahydrofuran (4)) to give 3.5 g. (32%) of **2b** as a colorless crystalline solid, m.p. 80-83°; ir (potassium bromide): no NH, 1820 (C=O) and 1220 cm<sup>-1</sup> (C-O-); nmr (DMSO-d<sub>6</sub>): 1.45 (3, CH<sub>3</sub>), 5.0 (1, CHCH<sub>3</sub>) and 6.3 ppm (1, CH-CCl<sub>3</sub>). The second fraction consisted of 0.8 g (7%) of **2a**, m.p. 34-36° (from hexane); ir (potassium bromide): 1825 (C=O) and 1210 cm<sup>-1</sup> (C-O-), no NH; nmr (DMSO-d<sub>6</sub>): 1.45 (3, CH<sub>3</sub>), 4.85 (1, CH-CH<sub>3</sub>) and 6.1 ppm (1, CH-CCl<sub>3</sub>); mass spectrum (70 eV): M/e 139, 141, 143 (M+·-ClCO<sub>2</sub>); 117, 119, 121 (CCl<sub>3</sub>); 130, 132, 134 (CCl<sub>3</sub>-CH); 111, 112; 101 (M+·3Cl's); 83, 85; 73; 63; 45 (CO<sub>2</sub>, base peak).

*cis*-2-(4-Chlorophenoxy)methyl-5-methyl-1,3-dioxolan-4-one (**4a**) and *trans*-2-(4-Chlorophenoxy)methyl-5-methyl-1,3-dioxolan-4-one (**4b**).

To a solution of 17.05 g. (0.07 mole) of 4-chlorophenoxyacetaldehyde (1, 10) in 100 ml. of ether was added 9.0 g. (0.1 mole) of lactic acid dissolved in 50 ml. of tetrahydrofuran. To the clear solution was added 15 g. (0.105 mole) of boron trifluoride etherate. After 24 hours at ambient temperature, the reaction mixture was washed with aqueous sodium bicarbonate, dried, concentrated, and subjected to silica chromatography.

The first fraction that emerged from the column, 4.0 g. (23%), was **4b**, m.p. 37-40° (from hexane); ir (potassium bromide): 1810 (C=O), 1600 (C=C) and 1210 cm<sup>-1</sup> (C-O-); nmr (deuteriochloroform): 1.5 (3, CH<sub>3</sub>), 4.1 (2, CH<sub>2</sub>O), 4.58 (1, CH-CH<sub>3</sub>), 5.9 (1, CH-CH<sub>2</sub>) and 7.0 ppm (4, CH=).

The second fraction, 4.8 g. (28%), **4a**, melted at 53-55° (from hexane); ir the same as **4b**; nmr (deuteriochloroform): 1.5 (3, CH<sub>3</sub>), 4.1 (2, CH<sub>2</sub>O), 4.43 (1, CH-CH<sub>3</sub>), 5.9 (1, CH-CH<sub>2</sub>) and 7.0 ppm (4, CH=).

2-(2,4-Dichlorophenoxy)methyl-1,3-oxathiolan-5-one (15).

A solution containing 10.25 g. (0.05 mole) of 2,4-dichlorophenoxyacetaldehyde, 5.1 g. (0.055 mole) of mercaptoacetic acid and 15 g. (0.15 mole) of boron trifluoride etherate in 250 ml. of ether was stirred at ambient temperature for two hours, washed with aqueous sodium bicarbonate dried, and concentrated. Trituration with hexane gave 5.6 g. (40%) of **15**, as an off-white crystalline solid, m.p. 59-61° (from ether-hexane); ir (potassium bromide): 1785 (C=O) and 1590 cm<sup>-1</sup> (C=C); nmr (deuteriochloroform): 3.62 and 4.18 (2, CH<sub>2</sub>S), 5.8 (1, CH), 4.2 (2, CH<sub>2</sub>O) and ca. 7.0 ppm (3, CH=); mass spectrum (70 eV): m/e 278, 280 (M+); 204, 206; 175, 177; 162, 164; 145, 147; 133, 135.

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