

# Dichloroacetaldehyde in the Mannich Reaction

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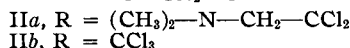
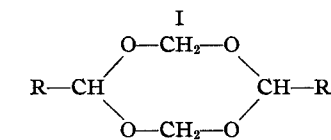
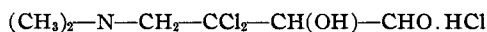
2,6-Bis-substituted-1,3,5,7-tetroxocanes are prepared from dichloroacetaldehyde.

DICHLOROACETALDEHYDE is reported by Logan and Schaeffer to undergo simultaneously an aldol-type reaction and the Mannich reaction to give the  $\alpha$ -hydroxyaldehyde (I) (1). This work was repeated, and the same compound (m.p. 177.5–178.5° dec.) was obtained; but the assigned structure did not agree with infrared and NMR data. No carbonyl or hydroxyl absorption bands were observed in the infrared spectrum, and no aldehyde proton was detected in the NMR spectrum. Furthermore, the four isolated sets of protons in the NMR spectrum are incompatible with I.

A strong infrared band system consisting of five absorptions centered at 9.12  $\mu$  (Table I) indicates the presence of an alkyl ether. Cyclic ring deformation vibrations related to the ether stretching mode generate the four additional satellite bands centered at 9.12  $\mu$ . Thus, the infrared data suggest the compound has the structure of IIa. The NMR chemical shifts and assignments in support of structure IIa are as follows:  $\delta = 4.12$  (1) tertiary protons on C<sub>2</sub> and C<sub>6</sub>,  $\delta = 4.6$  (2) methylene protons on C<sub>4</sub> and C<sub>8</sub>,  $\delta = 5.4$  (2) methylene groups on C<sub>2</sub> and C<sub>6</sub>,  $\delta = 6.5$  (6) N-methyl groups.

In addition, the compound readily gave formaldehyde 2,4-dinitrophenylhydrazone at room temperature. IIa but not I would be expected to give this derivative. Further support for the structural assignment is provided by Pinner, who reported (2) that chloral and formaldehyde react in concentrated sulfuric acid to give the tetroxocane (IIb).

**Biological Test Results.**—The compound IIa showed no antimicrobial activity against a number of organisms when tested at 100 mcg./ml. This testing procedure has been described by Blanton and Nobles (3).



## EXPERIMENTAL

**2,6-Bis-(1,1-dichloro-2-dimethylaminoethyl)-1,3,5,7-tetroxocane Dihydrochloride.**—Following the directions of Logan and Schaeffer, dichloroacetaldehyde, dimethylamine hydrochloride, and formaldehyde gave after recrystallization a pure compound, m.p. 177.5–178.5° dec.

*Anal.*—Calcd. for C<sub>12</sub>H<sub>24</sub>Cl<sub>6</sub>N<sub>2</sub>O<sub>4</sub>: C, 30.47; H, 5.11; Cl, 14.99; N, 5.92; total chloride, 44.97; mol. wt. 473.082. Found: C, 30.59; H, 5.09; Cl, 15.09; N, 5.64; total chloride, 44.61; neut. equiv., 235.

To a solution of the above compound (2.36 Gm., 0.005 mole) in aqueous alcohol was added at room temperature a solution of 2,4-dinitrophenylhydrazine (3.96 Gm., 0.02 mole). There was obtained after one recrystallization from alcohol 1.34 Gm. (64%) of formaldehyde 2,4-dinitrophenylhydrazone, m.p. 164–164.5°. A mixed melting point was not depressed.

*Anal.*—Calcd. for C<sub>7</sub>H<sub>8</sub>N<sub>4</sub>O<sub>4</sub>: C, 40.01; H, 2.88; N, 26.66. Found: C, 40.06; H, 3.11; N, 26.30.

**2,6-Bis-(trichloromethyl)-1,3,5,7-tetroxocane.**—Following the procedure of Pinner, chloral hydrate, formaldehyde, and sulfuric acid gave after recrystallization from acetic acid a pure compound, m.p. 188–189°.

*Anal.*—Calcd. for C<sub>6</sub>H<sub>6</sub>Cl<sub>6</sub>O<sub>4</sub>: C, 20.31; H, 1.70; Cl, 59.95; mol. wt. 354.856. Found: C,

TABLE I.—INFRARED SPECTRA OF 2,6-BIS-SUBSTITUTED-1,3,5,7-TETROXOCANES<sup>a</sup>

Vibration	IIa R = (CH <sub>3</sub> ) <sub>2</sub> N-CH <sub>2</sub> -CCl <sub>2</sub>	IIb R = CCl <sub>3</sub>
>NH <sup>+</sup> Cl <sup>-</sup>	4.3 $\mu$ broad, m	
C—H bending	7.4, 7.5 $\mu$ w w	7.4, 7.5 $\mu$ m w
C—O—C stretching	8.36, 8.80, 9.12, 9.50, 10.02 s m vs m m	8.50, 8.67, 9.10, 9.50, 9.84 s m vs s s
>CCl <sub>2</sub> stretching	11.45, 11.9 vs vs	
—CCl <sub>3</sub> stretching		12.4 broad, vs
Unassigned	7.65, 7.9, 8.02, 10.44, 13.2, 13.9 w m m m w broad m	7.74, 7.82, 10.16, 10.48, 10.96, 14.1 w w m m m w

<sup>a</sup> Run as mineral oil mull on a Perkin-Elmer model 21 spectrometer. Intensities of peaks are: vs (very strong), s (strong), m (medium), w (weak).

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<sup>1</sup> The numbers in parentheses are relative intensities of the NMR absorption peaks. The spectrum was run in D<sub>2</sub>O on a Varian model A-60 spectrometer.

20.55; H, 1.74; Cl, 59.89; mol. wt. (osmometer), 344.

## REFERENCES

- (1) Logan, A. V., and Schaeffer, W. D., *J. Am. Chem. Soc.*, **74**, 5538(1952).
- (2) Pinner, A., *Ber.*, **31**, 1931(1898).
- (3) Blanton, C. D., and Nobles, W. L., *J. Pharm. Sci.*, **53**, 1130(1964).