Preparation of Substituted Glycolurils and Their *N*-Chlorinated Derivatives

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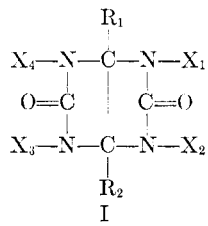
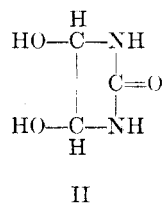
A number of new substituted glycolurils were prepared and chlorinated to the corresponding *N*-chloro derivatives for evaluation as foliage protectants.

The previously described[2] di- and tetrachloroglycoluril were found[3] to have good bactericidal activity against the test organisms *Erwinia amylovora*, *Xanthomonas phaseoli*, *Micrococcus pyrogenes* var. *aureus*, and *Escherichia coli* and some foliage protectant activity against the test organisms *Alternaria solani* and *Phytophthora infestans*. The synthesis work described in this paper was carried out to determine if a significant improvement in foliage protectant activity could be obtained by modifying the structure of the *N*-chlorinated glycoluril by introducing alkyl, aryl, carboxyl, and carboxyalkyl substituents. It was hoped that the substituents would increase the solubility of the compounds in lipids and thereby lead to increased biological activity.

Substituted glycolurils, I, where X_1–X_4 were H, and R_1 and R_2 were H, alkyl, aryl, or carboalkoxy were prepared by the reaction of the appropriate glyoxal (or diketone) with urea; examples of I where R_1 and R_2 were H, and X_1 and X_3 or X_4 were alkyl, benzyl, and carboxymethyl, were prepared by the reaction of glyoxal with an *N*-substituted urea; and, finally, examples of I where R_1 and R_2 were H and X_1 or X_1 and X_2 were alkyl, benzyl, phenyl, carboxymethyl, and (carboethoxy)-methyl were prepared by the reaction of the appropriate urea with glyoxalmonoureide (II).[4]



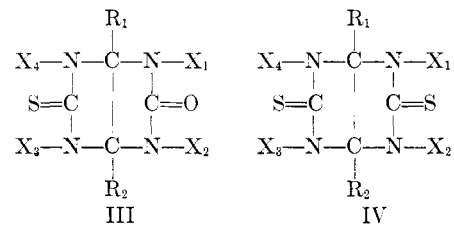
I



II

Attempts to prepare related sulfur compounds (III and IV) by analogous routes were unsuccessful except for the formation of 1-(*n*-butyl)-2-thionoglycoluril in low yield.

Previously reported methods were used to prepare 3a-methylglycoluril,[5] 1,3,4,6-tetrachloro-3a,6a-diphenylglycoluril,[6,7] 1,3,4,6-tetrachloro-3a,-6a-dimethylglycoluril,[7,8] and diethyl glycoluril-3a,-6a-dicarboxylate (V).[9]



III IV

Earlier workers[9–12] variously reported V to decompose over the range 245–272°. In the present study it was found that successive recrystallizations from water raised this decomposition temperature to 298–303°. In some experiments, 4,5-diethoxy-4,5-dicarbethoxyimidazolidin-2-one[11] (VI), decomposing at 210–211°, was obtained as the major reaction product. Support for the structure of VI comes from infrared data showing bands for carbonyl at 1740 cm.$^{-1}$, ester at 1295 cm.$^{-1}$, ether at 1100 cm.$^{-1}$, free NH at 3420 cm.$^{-1}$, and CH at 2940 cm.$^{-1}$. Some VI was also found in the mother liquors from the preparation and recrystallization of V.

Both VI[9,11] and the related 4,5-dihydroxy-4,5-dicarbethoxyimidazolidin-2-one (VII)[11] have been separately prepared and suggested as intermediates which can be further converted to V. Further confirmation that VII can serve as a common intermediate for both V and VI comes from the present work in which it was found that II, which is known to react with additional urea to form glycoluril, reacts with ethanol in the presence of hydrochloric acid to form 4,5-diethoxyimidazolidin-2-one (VIII).

The reaction of II with either hydantoic acid or ethyl hydantoate in aqueous solution gave 1-(carboxymethyl)glycoluril (IX) which could be converted to the corresponding ethyl ester (X) by reaction with ethanol. X could also be prepared by the direct reaction of II and ethyl hydantoate in ethanol.

(1) Present address: Department of Chemistry, Marshall University, Huntington, West Virginia.

(2) F. B. Slezak, A. Hirsch, and I. Rosen, *J. Org. Chem.*, **25**, 660 (1960).

(3) Unpublished results by Dr. Paul H. Schuldt and co-workers at the Boyce Thompson Institute for Plant Research, Inc., Yonkers, N. Y.

(4) B. V. Reibnitz, U. S. Patent 2,731,472, January 17, 1956.

(5) L. Seekles, *Rec. trav. chim.*, **46**, 77 (1927).

(6) H. Biltz and O. Behrens, *Ber.*, **43**, 1984 (1910).

(7) J. W. Williams, U. S. Patent 2,649,389, August 18, 1953.

(8) H. B. Adkins, U. S. Patent 2,654,763, October 6, 1953.

(9) H. Biltz and G. Schiemann, *J. prakt. Chem.*, [2] **113**, 77 (1926).

(10) R. Anschutz and H. Geldermann, *Ann.*, **261**, 131 (1891).

(11) H. Geisenheimer and R. Anschutz, *ibid.*, **306**, 38 (1899).

(12) H. J. H. Fenton and W. A. R. Wilks, *J. Chem. Soc.*, **101**, 1570 (1912).

TABLE I

PREPARATION OF SUBSTITUTED GLYCOLURILS

	Product Glycoluril	Moles II	Moles Urea	Ml. H_2O	Ml. Concd. HCl	Hr. at 100°	M.P.	% Yield	—% Carbon— Calcd.	Found	—% Hydrogen— Calcd.	Found
1.	3a-Ethyl-6a-methyl-	0.86[a]	2.9[b]	900	25	48[c]	320–321	50	45.6	45.9	6.6	6.4
2.	1,3-Dimethyl-	.35	0.4[d]	180	3.5	1	254–256	27	42.4	42.5	5.9	5.8
3.	1-Isopropyl-	.5	.5[e]	200	5	0.5	248–249	51	45.6	45.7	6.6	6.6
4.	1,3-Diisopropyl	.1	.1[f]	250	3	.5	312–313	71	53.1	53.0	8.0	7.8
5.	1,4- and/or 1,6-Diisopropyl-	.2[g]	.5[e]	150	5	.5	306–307	32	53.1	52.2	8.0	7.8
6.	1-(*n*-Butyl)-	.5	.8[h]	300	10	.25	267–268[i]	32	48.5	48.8	7.1	6.9
7.	1-Benzyl-	.2	.2[j]	300	5	1	283–284	65	56.9	56.8	5.2	5.1
8.	1-Phenyl-	.25	.25[k]	500	5	0.5	300	82	55.0	55.3	4.6	4.8
9.	1,4- and/or 1,6-Dibenzyl	.05[g]	.1[j]	100	3	.3	303–305	20	67.1	67.0	5.6	5.5
10.	1-Carboxymethyl	.2	.21[l]	80	10	.25	226	43	36.0	36.2	4.0	4.1
11.	1,4- and/or 1,6-bis-(carboxymethyl)-	.1[g]	.21[l]	30	5	.2	257	14	37.2	37.1	3.9	3.8
12.	1-(Carbethoxy)methyl-	.2	.21[m]	100[n]	10	.25	217–218	41	42.2	42.2	5.3	5.4

[a] 2,3-Pentanedione. [b] Urea. [c] Room temp. [d] 1,3-Dimethylurea. [e] 1-Isopropylurea. [f] 1,3-Diisopropylurea. [g] 30% Commercial glyoxal solution. [h] *n*-Butylurea. [i] British Patent 783,051 (1957) reports m.p. 249°. [j] 1-Benzylurea. [k] Phenylurea. [l] Hydantoic acid. [m] Ethyl hydantoate. [n] Ethanol.

TABLE II

CHLORINATION OF SUBSTITUTED GLYCOLURILS

	Product Glycoluril	Moles Starting Glycoluril	Ml. H_2O	Moles Cl_2	Temp.	M.P.	% Yield	—% Carbon— Calcd.	Found	% Hydrogen Calcd.	Found	—% Chlorine— Calcd.	Found
1.	1,3,4,6-Tetrachloro-3a-methyl-	0.1	2000	0.45	Room	147–148[a]	77	20.4	20.5	1.4	1.6	48.3	48.3
2.	1,3,4,6-Tetrachloro-3a-ethyl-6a-methyl-	.1	2000	.45	35	205–208[a]	93	26.1	26.6	2.5	2.5	44.1	43.4
3.	4,6-Dichloro-1,3-dimethyl-	.02	150	.056	Room	114–116	77	..	..	..	..	29.7	29.6
4.	3,4,6-Trichloro-1-isopropyl-	.05	900	.1	0–10	125–126[b]	87	29.2	29.5	3.2	3.4	36.9	36.7
5.	4,6-Dichloro-1,3-diisopropyl-	.05	900	.127	Room	148–149[a]	95	40.7	41.4	5.4	5.7	24.1	23.1[c]
6.	1-(*n*-Butyl)-3,4,6-trichloro-	.01	200	.043	0–10	67–68[b]	93	31.9	32.3	3.7	3.9	35.3	35.1
7.	1-Benzyl-3,4,6-trichloro-	.05	1000	.21	Room	160–161[a]	99	39.4	39.8	2.7	3.0	31.8	31.5
8.	3,4,6-Trichloro-1-phenyl-	.01	200	.056	50	140–141[d]	80	37.4	37.3	2.2	2.3	..	..
9.	1,3,4,6-Tetrachloro-3a,6a-dicarbethoxy-	.01	200	.056	Room	162–163[a]	88	28.3	29.2	2.4	2.5	33.4	32.2[c]

[a] Recrystallized from benzene. [b] Recrystallized from chloroform–carbon tetrachloride. [c] Further recrystallization did not improve these analyses indicating that these compounds are slightly underchlorinated. [d] Recrystallized from chloroform–hexane.

Chlorination of aqueous suspensions of I under conditions of controlled pH gave the desired *N*-chlorinated analogs.

1,3,4,6 - Tetrachloro - 3a,6a - dimethylglycoluril proved to be the most effective foliage protectant of the group described while tetrachloroglycoluril remained the best bactericide of the group.

Experimental[13]

General Procedure for the Preparation of Substituted Glycolurils.—Glyoxalmonoureide or the appropriate dicarbonyl compound, and the appropriate urea derivative were refluxed in an acidified solution, cooled, the solid filtered and washed with, or recrystallized from, ethanol. Experimental details used with this general procedure, melting points, yields, and analytical data obtained are summarized in Table I.

1-(*n*-Butyl)-2-thionoglycoluril.—Glyoxalmonoureide (1.2 g., 0.01 mole), *n*-butylthiourea (2 g., 0.015 mole), and water (20 ml.) were heated 10 min. at 80–90° while keeping the solution at pH 1–3 by the dropwise addition of concd. hydrochloric acid. The solution was evaporated *in vacuo* and the residue was recrystallized from ethanol to give a white solid decomposing at 184–185° which was believed to be the hydrochloride of the desired product. A solution of 1 g. of the hydrochloride in 3 ml. of water was brought to a pH of about 8 by the dropwise addition of 6 *N* sodium hydroxide. A 0.5-g. portion of the resulting solid was recrystallized from 3 ml. of ethanol to give the desired product decomposing at 171°.

Anal. Calcd. for $C_8H_{14}N_4OS$: C, 44.8; H, 6.6. Found: C, 44.7; H, 6.8.

4,5-Diethoxyimidazolidin-2-one (VIII).—Glyoxalmonoureide (23.6 g., 0.2 mole), absolute ethanol (200 ml.), and 6 *N* hydrochloric acid (1 ml.) were refluxed 10 min. The solution was cooled, concentrated to 50 ml. *in vacuo*, chilled, and the product filtered and recrystallized from 20 ml. of absolute ethanol to give 6.6 g. (19%) of VIII melting at 159–160°.

(13) All melting points are uncorrected. Analyses by the Research Analytical Laboratory of Diamond Alkali Co.

Anal. Calcd. for $C_7H_{14}N_2O_3$: C, 48.3; H, 8.1; N, 16.1. Found: C, 48.6; H, 7.7; N, 16.1.

Infrared support for this structure is given by bands for NH at 3475 cm.$^{-1}$, carbonyl at 1735 cm.$^{-1}$, ether at 1095 cm.$^{-1}$, and CH_3 and CH_2 at 2995 cm.$^{-1}$ and 2875 cm.$^{-1}$.

General Procedure for the Chlorination of Glycolurils.—A stirred suspension of the glycoluril in water was treated with chlorine for 0.5 to 1.5 hr. while 1 or 3 *N* sodium hydroxide was added at such a rate as to maintain the mixture in the range pH 8–9. The resulting solid was filtered, washed with water, dried, and recrystallized. The experimental details used with this general procedure, melting points, yields, and analytical data observed are summarized in Table II.

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Addition of Silicon Hydrides to Olefinic Double Bonds. VII. Addition to Chloro- and Dichlorobutenes

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In the presence of platinum catalysts, silicon hydrides react with allylic chlorides in a highly complex way. The products obtained from 1-chlorobutene-2, 3-chlorobutene-1, 1,4-dichlorobutene-2, and 3,4-dichlorobutene-2 were found to include numerous compounds. The formation of the various compounds is explained as due to a series of allyl rearrangements, eliminations of chloride from allylic chlorides and double bond migrations during the reaction.

During the preparation of 3-chloropropylsilicon compounds by means of the addition of silicon hydrides (usually as chlorosilanes) to allyl chloride, propylene is formed in the presence of a platinum catalyst[2,3] or in the presence of palladium,[2-4] rhodium,[4] ruthenium,[4] or nickel.[4] The yield of propylene is dependent to some extent upon the structure of the silicon hydride[2] and to a far greater extent upon the catalyst.[2,4]

In an effort to increase our understanding of the reaction, this study was carried out with chloroplatinic acid with linear chloro- and dichlorobutenes as well as with allyl chloride.

The formation of propylene as outlined by equation I has been proposed.[2,4] β-Chloroisopropyltrichlorosilane was prepared by chlorination of isopropyltrichlorosilane and used as a solvent during the addition of trichlorosilane to allyl chloride. The reaction proceeded normally in every respect, and the solvent was recovered quantitatively and unchanged. The scheme of equation 1 may therefore be eliminated from further consideration because the last step did not occur under the conditions which form propylene.

$$\equiv SiH + CH_2{=}CHCH_2Cl \longrightarrow \equiv SiC(CH_3)(CH_2Cl)-H \longrightarrow \equiv SiCl + CH_2{=}CHCH_3 \quad (1)$$

Methallyl chloride may be used instead of allyl chloride. It adds the hydride smoothly, but forms little or no isobutylene.[2] Methyldichlorosilane was added to allyl chloride dissolved in benzyl chloride and toluene was not found as a by-product. Because neither methallyl chloride nor benzyl chloride entered into metathetical reactions described by equation 2, it seems most unlikely that propylene from allyl chloride formed in this way.

$$\equiv SiH + ClCH_2CH{=}CH_2 \longrightarrow \equiv SiCl + CH_3CH{=}CH_2 \quad (2)$$

The hypothesis already advanced,[2] which assumes that the addition reaction may start by nucleophilic attack by a hydride ion upon the double bond of the olefin, therefore persists.

The hydride ion originates as a silane hydrogen. If completely ionized by the catalyst, it would give rise with allyl chloride to a carbanion which is thought to tautomerize according to the scheme:

$$\equiv SiH, Pt, CH_2{=}CHCH_2Cl \rightleftharpoons \begin{cases} :\bar{C}H_2CH_2CH_2Cl \xrightarrow{\equiv SiH} \text{Adducts} \\ \updownarrow \\ CH_3\bar{C}HCH_2Cl \longrightarrow CH_3CH{=}CH_2 + Cl^- \end{cases} \quad (3)$$

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(2) J. W. Ryan, G. K. Menzie, and J. L. Speier, *J. Am. Chem. Soc.*, **82**, 3601 (1960).

(3) A. D. Petrov, V. A. Ponomarenko, B. A. Sokolov, and G. V. Odabashyan, *Izvest. Akad. Nauk., S.S.S.R.*, **10**, 1206 (1957).

(4) A. D. Petrov, Kh. M. Minachev, V. A. Ponomarenko, B. A. Sokolov, and G. V. Odabashyan, *Doklady Akad. Nauk., S.S.S.R.*, **112** (2), 273 (1957).