at 278 mμ, whereas the CA-2 preparation had an even higher maximum at 340 mμ. Mixing of various amounts of CA-1 and CA-2 shifted the 340 mμ maximum of CA-2 to various corresponding lower wave lengths.

To interpret these results, one uses the working rule which states that when the absorption properties of the *cis-trans* isomers of a substance differ, "the more elongated isomer absorbs at somewhat longer wave lengths and more intensely."[12]

Haskins and Gorz[13] recently have found that such absorption data apply in their studies on *cis-* and *trans-o*-cinnamic acid. If this rule should also hold with caffeic acid, CA-1 would then appear to be the *cis* isomer and CA-2 the *trans* isomer of caffeic acid. These assignments of *cis* and *trans* to the caffeic acid isomers check with the designations in above paragraphs.

Infrared absorption spectra of the caffeic acids. To prepare samples of CA-1 and CA-2 for infrared studies, caffeic acid solution was streaked onto S & S No. 589 paper and developed in 15% acetic acid–water. The CA-1 and CA-2 zones were cut out and separately eluted with methyl alcohol. The eluate containing CA-1 was extracted with *n*-hexane, which is supposed to favor solution of the *cis* isomer.[14] The hexane was removed *in vacuo* at room temperature in the dark, and crystals of CA-1 were obtained. The methyl alcohol eluate CA-2 was concentrated *in vacuo* almost to dryness, in the dark at room temperature, and the residue was extracted several times with ethyl ether. Crystals of CA-2 were obtained after evaporation of the ether. Two milligrams of each of the crystalline CA-1 and CA-2 were mixed with 400 mg. of potassium bromide and made into pellets. These were studied with the Perkin-Elmer recording infrared spectrophotometer, Model 21.

At 814 cm.$^{-1}$, the absorption of the compound from CA-2 (*trans*) showed stronger intensity than did the absorption from compound CA-1 (*cis*). Bellamy[15] states that conjugation of the double bond with carbonyl groups has a very marked effect, and that the group —CH=CHCOOR (*cis*) absorbs near 820 cm.$^{-1}$ with sufficient regularity for this to be a useful assignment. He continues by stating that this absorption from the *cis* form is usually much weaker in intensity than that from the *trans* series. Also, at 1640 cm.$^{-1}$, CA-2 showed stronger absorption than did CA-1. Thus, the infrared data confirmed the previous indications that the CA-2 fraction was primarily the *trans* isomer, and the CA-1 fraction was mainly the *cis* isomer of caffeic acid.

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Halogenation of Glycoluril and Diureidopentane

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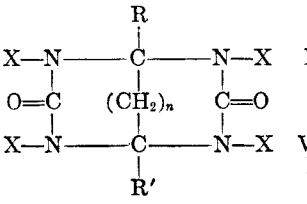
The literature reveals the preparation of 1,3,4,6-tetrachloro-3a,6a-diphenylglycoluril (I),[1,2] 1,3,4,6-tetrachloro-3a,6a-dimethylglycoluril (II),[2,3] and of 1,3,4,6-tetrachloro-3a-methyl-6a-phenylglycoluril (III)[2] but does not disclose 1,3,4,6-tetrachloroglycoluril (IV). This paper deals with the preparation of IV and some related compounds.



	R	R′	X	*n*
I	C_6H_5	C_6H_5	Cl	0
II	CH_3	CH_3	Cl	0
III	CH_3	C_6H_5	Cl	0
IV	H	H	Cl	0
V	H	H	Br	0
VI	H	H	I	0
VII	H	H	H	0
IX	CH_3	CH_3	H	1
X	CH_3	CH_3	Cl	1

We found that chlorination of aqueous suspensions of glycoluril (VII),[4–6] under a variety of conditions, gave IV. Excellent yields were obtained when the chlorination mixture was kept neutral or slightly alkaline (*p*H 7–8) by the addition of various basic materials either as solids or as solutions. Although a wide variety of alkaline materials was successfully used, a 1 to 6*N* sodium hydroxide solution was the most convenient alkali to add.

Bromination of glycoluril to 1,3,4,6-tetrabromoglycoluril (V) required somewhat more alkaline conditions (*p*H 8–11). The use of analogous techniques failed to give tetraiodoglycoluril (VI).

A clear solution resulted on treatment of an aqueous suspension of VII with half the theoretical amount of chlorine required for the preparation of IV. Further chlorination of this solution caused the precipitation of IV. Concentration of the clear solution resulted in the isolation of a dichloroglycoluril (VIII). No attempt was made to separate or characterize the possible isomers.

No material corresponding to a mono- or a trichloroglycoluril was found. Chlorination of VII to a theoretical trichloroglycoluril stage gave a solid which was readily separated into IV and VIII by extraction with water. The water solubility, at

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(2) J. W. Williams, U. S. Patent **2,649,389** (1953).

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room temperature, of IV was found to be 0.01 g./100 ml. while that of VIII was 0.27 g./100 ml.

This is the first instance that we are aware of in which a dihaloglycoluril has been isolated. Because VII was converted almost entirely into VIII before any significant amount of IV was observed, we are led to believe that other glycolurils could be similarly chlorinated. However, because of different solubility characteristics, the partial chlorination of other glycolurils might not be as easy to follow visually as was our example.

Chlorination of the related diureidopentane (IX), prepared by the method of de Haan,[7] gave tetrachlorodiureidopentane (X) but, because of the great insolubility of the materials involved, the chlorination proceeded with greater difficulty.

The products described are relatively stable. Pure, dry samples of IV and VIII have been kept in stoppered clear-glass vials at room temperature for as long as two years with only a 5–10% loss of available chlorine. However, mixtures with wet, strongly alkaline materials (sodium metasilicate and sodium metasilicate pentahydrate) resulted in rapid decomposition of IV and VIII, which, on occasion, became violent.

EXPERIMENTAL[8]

Glycoluril (VII). A stirred solution of 30% aqueous glyoxal (2250 g., 11.6 mole) and urea (1900 g., 31.7 mole) in 4 l. of water was heated to 85–95° and maintained at this temperature for 20–30 min. while concentrated hydrochloric acid (25–45 ml.) was added as needed to maintain the solution at *p*H 1.5–2.0. Cooling, filtering, and recrystallizing from water with the aid of decolorizing carbon gave 850–900 g. (52–55%) of white crystalline VII, decomposing at 300°.

Tetrachloroglycoluril (IV). A stirred suspension of VII (71 g., 0.5 mole) in 3200 ml. of water was treated with chlorine (150 g., 2.1 mole) at the rate of 20–40 g./hr. while 6*N* sodium hydroxide solution was added at such a rate as to maintain the mixture at *p*H 7–8, as measured with a *p*H meter. The resulting white solid was filtered, washed twice with 1-l. portions of water, and dried to give 136 g. (97%) of IV, decomposing slowly above 280°.

Anal. Calcd. for $C_4H_2Cl_4N_4O_2$: C, 17.2; H, 0.7; Cl, 50.7; N, 20.0. Found: C, 17.5; H, 0.8; Cl, 50.5; N, 20.2. Infrared examination did not show the NH band (3170 cm.$^{-1}$) present in VII.

Dichloroglycoluril (VIII). This was carried out as in the preparation of IV except that 78 g. (1.1 mole) of chlorine was used. The solution was filtered to remove traces of IV and concentrated under vacuum at 50° to a volume of about 200 ml. The resulting solid was filtered, washed with two 100-ml. portions of water, and dried to give 90 g. (85%) of VIII, melting with rapid decomposition at 180°.

Anal. Calcd. for $C_4H_4Cl_2N_4O_2$: C, 22.8; H, 1.9; Cl, 33.6; N, 26.5. Found: C, 22.5; H, 1.6; Cl, 33.0; N, 26.0.

Tetrabromoglycoluril (V). A stirred suspension of VII (7.1 g., 0.05 mole) in 2200 ml. of water was treated with bromine (80.0 g., 0.5 mole) over a 3-hr. period while the mixture was maintained at *p*H 9–10. The resulting solid after filtering, washing with two 500-ml. portions of water, and drying gave 17.2 g. (75%) of V melting at 292–295° with decomposition.

Anal. Calcd. for $C_4H_2Br_4N_4O_2$: C, 9.8; H, 0.4; Br, 69.6. Found: C, 10.5; H, 0.8; Br, 65.5.

Tetrachlorodiureidopentane (X). A stirred suspension of IX (56 g., 0.3 mole) in 3 l. of water was treated with chlorine (110 g., 1.55 mole) over a 4-hr. period while the mixture was maintained at *p*H 5–8. The white solid was filtered, washed with several portions of water and dried to give 87 g. (90%) of X melting at 210° with decomposition.

Anal. Calcd. for $C_7H_8Cl_4N_4O_2$: Cl, 44. Found: Cl, 41.5.

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(7) T. de Haan, *Rec. trav. chim.*, **27**, 162 (1908).

(8) All melting points are uncorrected. Elemental and infrared analysis by the Diamond Alkali Company Research Analytical Laboratory.

C-73: A Metabolic Product of *Streptomyces albulus*

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C-73 is a crystalline compound which accompanies cycloheximide and E-73 in the broths of *Streptomyces albulus*. The three compounds have identical carbon skeletons. C-73 has an aromatic ring in place of the cyclohexanone ring which is common to cycloheximide and E-73. The structure of C-73 is shown (I.)

The isolation of the five fractions designated as A-73 (fungicidin), B-73, C-73, D-73 (cycloheximide), and E-73 from the culture filtrates of *Streptomyces albulus* has been described earlier.[1] Among these, E-73 showed pronounced antitumor activity in experimental animals and its structure has been elucidated.[2] The present paper deals with the chemical nature of C-73.

C-73 (I) is a pale yellow crystalline solid sparingly soluble in common organic solvents. Elementary analysis corresponds to the empirical formula $C_{15}H_{17}O_4N$. Its occurrence with cycloheximide in the culture broths and the close similarity between their empirical formulae $C_{15}H_{17}O_4N$ and $C_{15}H_{23}O_4N$ suggested a possible structural relationship between the two.

The ultraviolet spectrum of C-73 has maxima at 262 and 345 mμ (ϵ = 10,870 and 4,550 respectively). The infrared spectrum shows bands at 5.80, 5.90, 6.10, and 6.26 μ among others. The substance shows bright yellow fluorescence under ultraviolet light. It gives a dark green color with alcoholic ferric chloride, indicating the presence of a phenolic group. C-73 is soluble in aqueous alkali to give bright yellow solutions.

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(2) K. V. Rao, *J. Am. Chem. Soc.*, in press.