with water and the aqueous phase washed with ether. The crude product was obtained by acidification of the extract with concentrated HCl followed by collection of the precipitate which was then extracted with boiling acetic acid. The insoluble product was dissolved in warm DMF (charcoal) and reprecipitated by the addition of water and cooling. It separated as colorless microprisms: 4.76 g (41%); mp 337–340 °C dec; IR (KBr) ν_{OH} 2400–3200, ν_{CO} 1675 cm^{-1}; UV (dioxane) λ_{max} 318 nm (log ϵ 4.65); ^{1}H NMR (Me_2SO-d_6) δ 8.10 (d, 1, J = 4.0 Hz, thiophene H), 7.95 (d, 1, J = 4.0 Hz, thiophene H), 7.85 (s, 1, pyrimidine H), 7.75 (d, 2, two overlapping thiophene H's), 2.68 (s, 3, SCH_3); ^{13}C NMR (Me_2SO-d_6) 171.8, 162.7, 158.7, 155.6, 147.4, 146.6, 138.0, 133.8, 133.6, 129.3, 110.5, 12.3 ppm; mass spectrum, m/e (relative intensity) 378 (100, $M^{+\cdot}$).

Anal. Calcd for $C_{15}H_{10}N_2O_4S_3$: C, 47.61; H, 2.66; N, 4.70. Found: C, 47.72; H, 2.69; N, 7.34.

2,4-Bis(5-carboxy-2-thienyl)-6-*n*-butylpyrimidine (6). The crude product was isolated from the acetic acid extract of 2,4-bis(5-carboxy-2-thienyl)-6-(methylthio)pyrimidine (5; R = COOH) obtained above by precipitation with water after treatment of the acetic acid solution with charcoal. Chromatography (silica) with THF–Et_2O, followed by recrystallization from acetic acid–water, produced colorless microprisms: 2.1 g (24% based on *n*-butyllithium used); mp 299–302 °C dec; IR (KBr) ν_{OH} 2500–3100, ν_{CO} 1675 cm^{-1}; UV (MeOH) λ_{max} 313 nm (log ϵ 4.36); ^{1}H NMR (Me_2SO-d_6) δ 8.16 (1, d, thiophene H, J = 4.0 Hz), 8.03 (1, d, thiophene H, J = 4.0 Hz), 7.91 (1, s, pyrimidine H), 7.85 (1, d, thiophene H), 7.82 (1, d, thiophene H), 2.80 (m, 2, $ArCH_2$), 1.77 (m, 2, $ArCH_2CH_2$), 1.35 (m, 2, CH_2CH_3), 0.97 (t, 3, CH_3); ^{13}C NMR (Me_2SO-d_6) 187.7, 172.4, 162.8, 162.7, 159.4, 157.6, 148.0, 147.0, 137.9, 137.6, 134.0, 133.9, 129.0, 113.0, 36.7, 30.0, 21.9, 13.8 ppm; mass spectrum, m/e (relative intensity) 388 (5, $M^{+\cdot}$).

Anal. Calcd for $C_{18}H_{16}N_2O_4S_2$: C, 55.65; H, 4.15; N, 7.21. Found: C, 55.7; H, 4.18; N, 7.18.

General Procedure for the Synthesis of Macrocycles 4, 7, and 9. A solution of the diacid (3.0 mmol) and Cs_2CO_3 (3.0 mmol) in DMF (50 mL) was evaporated to dryness on a rotary evaporator by using a steam bath. Dry DMF (250 mL) was added to the resulting dry powder followed by the α,ω-dibromo polyether, and the mixture was well stirred for 2–7 days at 60–70 °C. The DMF was removed by distillation under reduced pressure (except for **4a**) and the residue extracted with chloroform. The chloroform solution was dried (Na_2SO_4) and concentrated, and the product was purified by column chromatography (silica, EtAc) or HPLC (silica, EtAc–hexane, Prep 500).

Recrystallization from dry acetonitrile generally gave the products (Tables I and II) as colorless prisms. Compound **4a** was obtained by concentration of the reaction mixture followed by precipitation of the crude product by adding 3 volumes of water. This macrocycle was purified by crystallization from dry Me_2SO followed by a second recrystallization from pyridine.

Potassium Thiocyanate Complex (1:1) of Cyclic *O,O'*-Ethylenebis(oxyethylene) 2,2'-Bifuryl-5,5'-dicarboxylate (9d). An acetone (5 mL) solution containing cyclic *O,O'*-ethylenebis(oxyethylene) 2,2'-bifuryl-5,5'-dicarboxylate (**9d**; 160 mg, 0.476 mmol) and potassium thiocyanate (46.3 mg, 0.476 mmol) was heated under reflux for 4 h an then cooled to room temperature. The product precipitated as colorless microneedles: 180 mg (87%); mp 251–253 °C dec; IR (KBr) ν_{SCN} 2030, ν_{CO} 1710 cm^{-1}; UV (MeOH) λ_{max} 222 nm (log ϵ 4.24), 323 (4.50), 336 sh (4.40); ^{1}H NMR (Me_2SO-d_6) δ 7.49 (d, 2, J = 3.6 Hz, furan H_4), 7.17 (d, 2, furan H_3), 4.32 (m, 4, CO_2CH_2), 3.70 (m, 4, $CO_2CH_2CH_2$), 3.66 (s, 4, CH_2CH_2).

Anal. Calcd for $C_{17}H_{16}NO_8SK$: C, 47.10; H, 3.72; N, 3.23. Found: C, 47.18; H, 3.75; N, 3.22.

Potassium Thiocyanate Complex (1:1) of Cyclic *O,O'*-Oxybis(ethyleneoxyethylene) 2,2'-Bifuryl-5,5'-dicarboxylate (9e). An acetone (2 mL) solution containing cyclic *O,O'*-oxybis(ethyleneoxyethylene) 2,2'-bifuryl-5,5'-dicarboxylate (**9e**; 100 mg, 0.263 mmol) and potassium thiocyanate (26.0 mg, 0.267 mmol) was stirred for 30 min, with the formation of a precipitate. After the mixture was cooled in an ice bath, the product was collected as colorless prisms: 95 mg (75%); mp 210–211 °C dec; IR (KBr) ν_{SCN} 2027, ν_{CO} 1715 cm^{-1}; UV (MeOH) λ_{max} 224 nm (log ϵ 4.20), 324 (4.52), 338 sh (4.37); ^{1}H NMR ($CDCl_3$) δ 7.36 (2, d, furan H_4, J = 3.7 Hz), 6.73 (2, d, furan H_3), 4.62 (4, m, CO_2CH_2), 3.90 (4, m, $CO_2CH_2CH_2$), 3.84 (s, 8, OCH_2CH_2O).

Anal. Calcd for $C_{19}H_{20}NO_9SK$: C, 47.79; H, 4.22; N, 2.93. Found: C, 47.70; H, 4.27; N, 2.92.

Registry No. **1** (R = Li), 82093-90-1; **1** (R = Br), 82093-91-2; **1** (R = Cl), 82093-92-3; **1** (R = CO_2H), 82093-93-4; **1** (R = H), 78570-43-1; **1** (R = CHO), 82093-94-5; **1** (R = COCl), 82093-95-6; **1** (R = CH_2OH), 82093-96-7; **2**, 82093-97-8; **3**, 82093-98-9; **4a**, 82093-99-0; **4b**, 82094-00-6; **4c**, 82094-01-7; **4d**, 82094-02-8; **5** (R = CO_2H), 82094-03-9; **5** (R = H), 82094-04-0; **5** (R = Li), 82094-05-1; **6**, 82094-06-2; **7a**, 82094-07-3; **7b**, 82094-08-4; **7c**, 82094-09-5; **8** (X = O), 50738-83-5; **8** (X = O) dicesium salt, 82094-10-8; **8** (X = S), 3515-34-2; **8** (X = S) dicesium salt, 82094-11-9; **9a**, 82094-12-0; **9b**, 82094-13-1; **9c**, 82094-14-2; **9d**, 82094-15-3; **9d**·KSCN, 82094-61-9; **9e**, 82094-16-4; **9e**·KSCN, 82094-63-1; **9f**, 82094-17-5; 1,2-bis(2-bromoethoxy)ethane, 31255-10-4; bis[2-(2-bromoethoxy)ethyl] ether, 31255-26-2; 1,2-bis[(2-bromoethoxy)ethoxy]ethane, 57602-02-5.

Reaction of Chloral Hydrate with Cyanoguanidine

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Reaction of chloral hydrate with cyanoguanidine (molar ratio 2:1) proceeded smoothly in refluxing carbon tetrachloride to give a 3:1 reaction product, $C_8H_7Cl_9N_4O_3$ (**6**). With 15% hydrochloric acid, **6** formed the hydrochloride. Monodehydration of **6** with thionyl chloride in refluxing carbon tetrachloride gave (2*S*,4*S*,6*R*)-2,6,7,9-tetrahydro-2,4,6-tris(trichloromethyl)-8*H*-[1,3,5]triazino[1,2-*c*][1,3,5]oxadiazin-8-one (**7**). A brief analysis of the spectral and single-crystal X-ray crystallographic data is presented.

On mechanistic grounds, reaction of chloral hydrate with cyanoguanidine (dicyandiamide) may give rise to a variety of acyclic and cyclic 3:1 addition–condensation products, depending on whether (a) more than two of the nitrogens participate in the initial addition reaction, (b) hydration of the cyano (C≡N) group takes place, (c) ring closure of the initial acyclic 1:1, 2:1, or 3:1 reaction product results in the formation of six-membered rings, and (d) further addition of one or more chloral units to these ring structures in one or more of their tautomeric forms occurs.

A recent paper[1] describes the synthesis from chloral hydrate and cyanoguanidine (molar ratio 2.17:1) of 3,6-dihydro-4-[(1-hydroxy-2,2,2-trichloroethyl)amino]-6-imino-2-(trichloromethyl)-2*H*-1,3,5-oxadiazine (**2**). The cy-

(1) Dovlatyan, V. V.; Papoyan, T. Z.; Tarkhanyan, G. K. *Chem. Heterocycl. Comp. (Engl. Transl.)* **1975**, *11*, 415; *Chem. Abstr.* **1975**, *83*, 97226 (1975).

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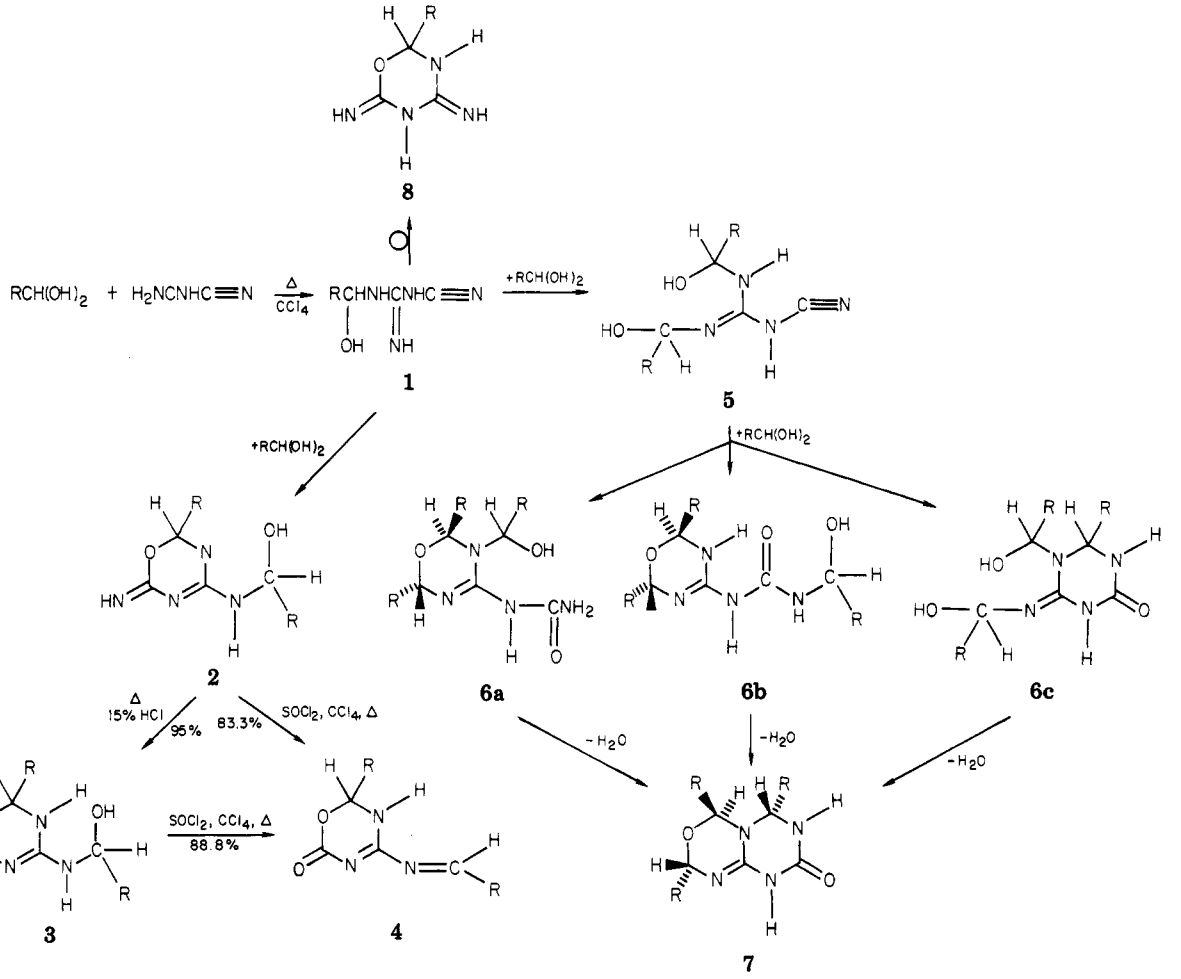
Scheme I[a]



[a] R = CCl_3.

cloaddition was viewed to proceed through the acyclic 1:1 addition product **1**. The assignment of structure **2** was based on elemental (Cl, N) and infrared spectral data and further chemical transformations leading to 2,3-dihydro-4-[(1-hydroxy-2,2,2-trichloroethyl)amino]-2-(trichloromethyl)-6*H*-1,3,5-oxadiazin-6-one (**3**) and 2,3-dihydro-4-[(trichloroethylidene)amino]-2-(trichloromethyl)-6*H*-1,3,5-oxadiazin-6-one (**4**, Scheme I).

The present reinvestigation provides evidence that the structural assignments of **2**–**4** are incorrect, and alternatives are proposed.

Results and Discussion

Reactions of chloral hydrate with cyanoguanidine in refluxing carbon tetrachloride always gave uniform products that melted with decomposition at 172–174 °C. The product reported[1] had a melting point of 173 °C dec, and analytical data (C, H, Cl, N) indicated the molecular formula $C_8H_7Cl_9N_4O_3$ (3:1 reaction product **6**) rather than molecular formula $C_6H_6Cl_6N_4O_2$ (**2**, 2:1 reaction product). Although no intermediates have been detected in the course of the reaction by earlier workers[1] or in the present work, the formation of **6** by a multistep mechanism involving addition–hydration–dehydration sequences appears plausible.

No molecular ion (M^+) or pseudomolecular ion, $(M + H)^+$, is observed in the mass spectrum of **6** obtained by electron impact (EI) and chemical ionization (CI), respectively. However, the field-desorption (FD) mass spectrum shows the molecular ion at m/z 522 (M^+; nine-chlorine isotope pattern). In the EI and FD mass spectra of **6**, the ion at m/z 405 with a six-chlorine isotope pattern is due to the loss of the trichloromethyl (CCl_3) group from the molecular ion. The significant ion at m/z 259 is due to the loss from the molecular ion of chloral (CCl_3CHO) and trichloromethyl (CCl_3).

In addition to the broad signals of four exchangeable (DCl) protons at δ 9.3 (s, 1 H, NH), 8.5 (s, 2 H, NH_2), and 7.7 (s, 1 H, OH), the ^1H NMR spectrum (60 M Hz, Me_2SO-d_6) of **6** shows the signals of three saturated CH protons at δ 5.6 (d, 1 H, CH, $J_{CH,OH}$ = 6 Hz), 5.7 (s, 1 H, CH), and 5.7 (d, 1 H, CH, $J_{6,5}$ = 6 Hz).

The characteristic absorption band of a nitrile near 2200 cm^{-1} is absent from the infrared spectrum (KBr pellet) of **6**, indicating that the C≡N group (a) participated in the reaction with an amino group to form an acyclic or cyclic guanidine structure or (b) underwent hydration to give a urea.

Although these observations limit the number of possible structures for the 3:1 reaction product (**6**) of chloral with cyanoguanidine, they do not allow for unambiguous structure assignment.

Treatment of **6** with 15% hydrochloric acid (95 °C, 15 min) gave the corresponding hydrochloride in 93.5% yield as evidenced by the presence in the molecule of ten chlorine atoms, one of which can be determined titrimetrically as chloride ion (Cl^-). In general, the spectroscopic behavior of the hydrochloride closely resembles that of its precursor **6**.

Furthermore, by using again the reported[1] conditions, we obtained a product, **7**, from both **6** and its hydrochloride

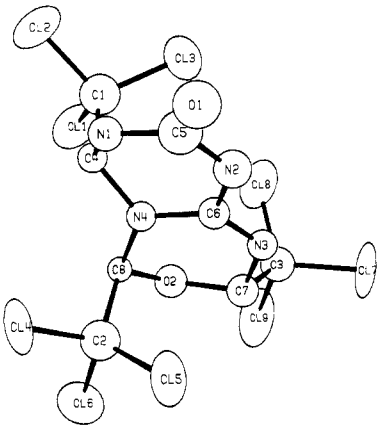


Figure 1. ORTEP plot of X-ray crystallographic structure for **7** (H atoms are excluded).

and thionyl chloride in refluxing carbon tetrachloride. The uniform product of molecular formula $C_8H_5Cl_9N_4O_2$ (**7**) had the same melting characteristics (mp 244–245 °C dec) as that assigned to structure **4** by previous investigators (lit.[1], mp 245 °C dec, Scheme I).

The EI mass spectrum of **7** shows no molecular ion. An ion of m/z 387 with a six-chlorine isotope pattern is due to loss of CCl_3. Other significant ions in the spectrum are at m/z 359 (loss of CCl_3CO), 241 (loss of CCl_3CHO and CCl_3), 214 (loss of CCl_3CHO, CCl_3, and HCN), 146 (CCl_3CHO^+), and 117 (CCl_3^+). The CI mass spectrum shows a pseudomolecular ion at m/z 505 $(M + H)^+$. Ions at m/z 469 (eight-chlorine isotope pattern) and 435 (seven-chlorine isotope pattern) are due to loss of HCl and Cl_2, respectively, from the protonated molecular ion. In the FD mass spectrum, the ion at m/z 504 with a nine-chlorine isotope pattern is due to the molecular ion (relative abundance 9%). The significant ion at m/z 387 (relative abundance 100%) is due to the loss of CCl_3 from the molecular ion.

Its ^{1}H NMR spectrum (60 MHz, Me_2SO-d_6) shows the signals of three saturated CH protons at δ 5.4 (d, 1 H, CH, $J_{4,3}$ = 6 Hz), 5.72 (s, 1 H, CH), and 6.12 (s, 1 H, CH) and two exchangeable (DCl) protons corresponding to the lines at δ 10.6 (s, 1 H, NH) and 9.3 (s, 1 H, NH), completing the spectrum of **7**.

In summary, the formation of **7** appears to be the result of the formal loss from **6** of 1 molar equiv of water. On the basis of the available spectroscopic evidence, it is possible to construct 11 structures (tautomers excluded) for **7**. For example, addition of 2 molar equiv of chloral to the intermediate 1:1 addition–cyclization product **8**, in any one of its tautomeric forms, followed by monodehydration may lead to eight structures for the monodehydrated 3:1 reaction product **7**. Alternatively, dehydration of several acyclic 3:1 reaction products resulting from **5** and chloral may lead to three additional monodehydrated 3:1 reaction products **7**. Although undetected in the course of the reaction, the formation from chloral hydrate and cyanoguanidine of intermediates including **1**, **5**, **6**, and **8** is quite reasonable.

In order to determine the structure of **7** unequivocally, we performed an X-ray crystallographic analysis[2] on a colorless prismatic crystal obtained from *p*-dioxane. (See the paragraph at the end of paper about supplementary material.) An ORTEP view of the molecular structure of **7** is shown in Figure 1 (hydrogen atoms are not included). The structure of **7** has several interesting aspects. The

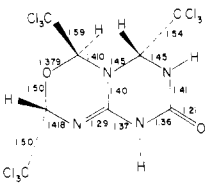


Figure 2. Bond distances in angstroms for **7**.

compound is composed of two six-membered rings with one nitrogen and one carbon atom common to both rings. The ORTEP view illustrates that the fused-ring system is not planar. A least-squares fit of various atoms to planes shows that there are two major planar regions: namely, the atoms of the *s*-triazine moiety with the exception of carbon 4 and the atoms of the 1,3,5-oxadiazine portion with the exception of carbon 6. The dihedral angle between the planes of the two rings is 10.4°. The trichloromethyl groups exist in an all-axial alternating trans arrangement.

The bond distance (Figure 2) between the bridgehead carbon atom (C-6) and the nitrogen atom (N-3) of the oxadiazine ring portion is considerably shorter (1.29 Å) than that between C-6 and the nitrogen atom (N-2) of the *s*-triazine ring moiety (1.37 Å), indicating a higher degree of double bond character between C-6 and N-3 than between C-6 and N-2.

Since **7** is the result of the formal loss from **6** of water, the number of possible structures for precursor **6** is limited to three (tautomers excluded), namely, the 1,3,5-oxadiazines **6a** and **6b**[3] and the hexahydro-*s*-triazinone **6c**. However, the available spectral information (IR, ^{1}H NMR, ^{13}C NMR, and EI, CI, and FD mass spectra) is insufficient to rigorously establish the structure of the initial 3:1 condensation product, **6**, of chloral with cyanoguanidine.

Experimental Section

Melting points were determined on a Thomas-Hoover apparatus and are uncorrected.

Infrared absorption was measured on a Digilab FTS-15B spectrometer.

NMR Spectra were recorded on a Varian EM-360 spectrometer in dimethyl-d_6 sulfoxide solvent by using a 5-min sweep time and a 0.5-s filter time. Chemical shifts are expressed in parts per million (δ) downfield from internal tetramethylsilane.

Electron-impact (EI) and chemical-ionization (CI) mass spectra were obtained on a Finnigan 4000 mass spectrometer by direct introduction via a solid probe. Methane was the reagent gas for the CI spectra.

Field-desorption mass spectra were obtained on a Varian 731 mass spectrometer. The emitter current was 15 mA.

Reaction of Chloral Hydrate with Cyanoguanidine. Preparation of 6. A mixture of 10.1 g (0.120 mol) of cyanoguanidine (dicyandiamide, Aldrich) and 43.0 g (0.260 mol) of chloral hydrate in 240 mL of carbon tetrachloride was stirred and refluxed for 4 h. The reaction mixture was chilled (10 °C) and filtered. The filter cake was washed with hot water and dried to give 21.0 g (46%, based on chloral hydrate) of colorless solid: mp 172–174 °C dec; IR (KBr) no absorption between 2500–1800 cm^{-1}, major absorption bands at 3340 (br), 1670 (with shoulder at 1700), 1530 (with shoulder at 1560), and 820 (with shoulder at 810) cm^{-1}. Anal. Calcd for $C_8H_7Cl_9N_4O_3$ (mol wt 526.25): C, 18.26; H, 1.34; Cl, 60.63; N, 10.65. Found: C, 18.5; H, 1.4; Cl, 59.7; N, 11.2.

Hydrochloride of 6. A slurry of 80.0 g (0.152 mol) of **6** in 800 mL of 15% hydrochloric acid was stirred at ambient temperature for 4 h without apparent reaction. The mixture was subsequently heated, resulting, at 80 °C, in a syrupy suspension. After 15 min at 95 °C, heating was discontinued, and the mixture was stirred at ambient temperature for 12 h and filtered. The filter cake was washed with cold water and dried to give 80.0 g (93.5%) of white

(2) Molecular Structure Corp., College Station, TX.

(3) Suggested by Reviewer I.

amorphous solid: mp 149–151 °C dec; IR (KBr) major bands at 3390, 3220, 2920 (br), 1720, 1645, 1535, and 800 (with shoulder at 830) cm^{-1}; EI and CI mass spectra are identical with that of **6**. Anal. Calcd for $C_8H_8Cl_{10}N_4O_3$ (mol wt 562.71): C, 17.08; H, 1.43; Cl^-, 6.03; N, 9.96. Found: C, 17.3; H, 1.7; Cl^-, 5.7; N, 9.7.

(2*S*,4*S*,6*R*)-2,6,7,9-Tetrahydro-2,4,6-tris(trichloromethyl)-8*H*-[1,3,5]triazino[1,2-*c*][1,3,5]oxadiazin-8-one (7). To a stirred mixture of 148.0 g (0.281 mol) of **6** in 2436 mL of dry carbon tetrachloride was added 93.0 g (0.782 mol) of thionyl chloride. The mixture was heated to reflux. After approximately 15 min, a clear solution was obtained. Heating with stirring was continued for 6 h, after which time the precipitate that had formed was removed by filtration. The filter cake was washed with water and dried to give 86.2 g (60.4%) of off-white solid: mp 245 °C dec; IR (KBr) major absorption bands at 3420, 3240, 3090, 2960, 2880 (br), 1690 (with shoulder at 1710), 1490, 850, and 830 cm^{-1}. Anal. Calcd for $C_8H_5Cl_9N_4O_2$ (mol wt 508.23): C, 18.91; H, 0.99; Cl, 62.78; N, 11.02. Found: C, 19.1; H, 1.0; Cl, 62.4; N, 11.2.

X-ray Structure Determination of 7. Compound **7** was recrystallized from *p*-dioxane, resulting in colorless prismatic crystals of $C_8H_5Cl_9N_4O_2$ (plus dioxane solvate). The crystals are orthorhombic: space group *Pccn*, a = 18.94 (3) Å, b = 30.798 (4) Å, c = 11.550 (2) Å, z = 8. A total of 5150 reflections were collected, of which 4413 were considered as statistically significant. Data collection was performed with Cu Kα radiation (λ = 1.541 84 Å) on an Enraf-Nonius CAD4 computer-controlled κ-axis diffractometer equipped with a graphite crystal incident beam monochromator. Data were collected to a maximum 2θ of 112.0°. The structure was solved by direct methods and has been refined anisotropically to give an R factor of 0.12. Hydrogen atoms were not included in the calculations. Two solvent molecules (dioxane) were located and refined. A difference Fourier map suggested the presence of an addition solvent molecule; however, attempts to locate and refine a third solvent molecule were unsuccessful.

Acknowledgment. We thank Dr. Carter Cook, University of Illinois, Urbana, IL, for providing field-desorption mass spectrometry service. The cooperation of the Molecular Structure Corp. in performing the X-ray crystallographic analysis is appreciated.

Registry No. 7, 81956-39-0; cyanoguanidine, 461-58-5; chloral hydrate, 302-17-0.

Supplementary Material Available: Complete X-ray data on compound **7** are available, including tables of fractional atomic coordinates for nonhydrogen atoms, thermal parameters, bond lengths, bond angles, intermolecular contacts, mean planes, and torsion angles (10 pages). Ordering information is given on any current masthead page.

Reaction of Isoquinoline Enamides with Electrophiles

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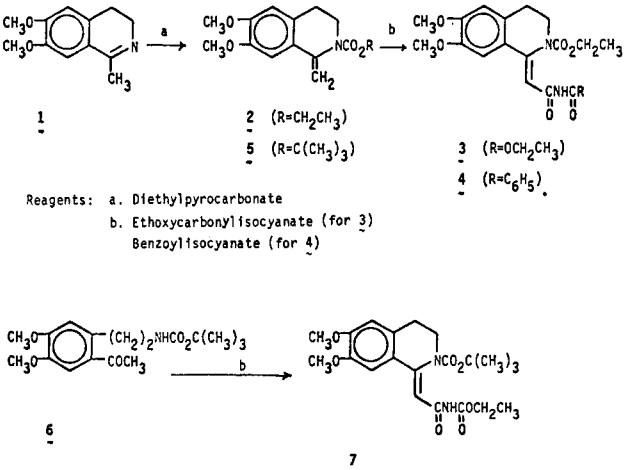
The reaction of isoquinoline enamides with acyl isocyanates yields vinylogous amides through carbon–carbon bond formation between the β carbon of the enamide and the isocyanate carbonyl. Enamide formation occurs between 1-benzyl-3,4-dihydroisoquinolines and phenylacetic anhydride. However, a *N*,*C*-bis(phenylacetyl) derivative is formed with phenylacetyl chloride. The reaction occurs through preferential reaction of phenylketene with the enamine tautomer of the 1-benzyl-3,4-dihydroisoquinoline at the carbon terminus, followed by *N*-acylation. The equilibrium is demonstrated by deuterium NMR.

While the photochemistry of enamides has been well studied and has led to a variety of preparatively useful reactions,[1] the thermal reactions of simple enamides have been relatively neglected. Brossi has described the facile hydration of isoquinoline enamides to form [(acetylphenyl)ethyl]acetamides,[2] and Ninomiya has successfully brominated the β carbon of an enamide using *N*-bromosuccinimide.[3] Barton has shown that the β carbon of enamides is successfully acetoxylated using lead tetraacetate,[4] while other enamides undergo rearrangements with thallium(III).[5] In this report we describe the reactions of enamides with strongly electrophilic acyl isocyanates and their putative reaction with phenylketene.

Scheme I



The reaction between 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline (**1**) and diethyl pyrocarbonate gave an excellent yield of the enamide **2** as the only product. Enamide **2** was treated with ethoxycarbonyl isocyanate in an inert solvent, and a product rapidly crystallized in 56%

(1) (a) Lenz, G. R. *Synthesis* **1978**, 489. (b) Ninomiya, I. *Heterocycles* **1974**, *1*, 105. Ninomiya, I.; Naito, T. *Kagaku Ryoiki Zokan* **1979**, *123*, 69.

(2) (a) Brossi, A.; Würsch, J.; Schnider, O. *Chimia* **1958**, *12*, 114. (b) Brossi, A.; Dolan, L. A.; Teitel, S. *Org. Synth.* **1977**, *56*, 3.

(3) Ninomiya, I.; Naito, T.; Kiguchi, T.; Mori, T. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1696.

(4) (a) Boar, R. B.; McGhie, J. F.; Robinson, M.; Barton, D. H. R.; Horwell, D. C.; Stick, R. V. *J. Chem. Soc., Perkin Trans 1* **1975**, 1237. (b) Boar, R. B.; McGhie, J. F.; Robinson, M.; Barton, D. H. R. *Ibid.* **1975**, 1242.

(5) Back, T. G.; Edwards, D. E.; MacAlpine, G. A. *Tetrahedron Lett.* **1977**, 2651.

0022-3263/82/1947-3049$01.25/0