radiation on a four-circle diffractometer (Rigaku AFC-5). Of the total of 2140 independent reflections, 1799 had intensities above the 2.667σ (1) level, and they were used for structure determination.

Determination of the Structure. The structure was solved by direct methods using MULTAN and refined by the block-diagonal least-square method with anisotropic temperature factors for all non-hydrogen atoms and with isotropic ones for all hydrogen atoms. The final R value was 0.053 (Tables II–V, in supplementary material section).

Registry No. 1, 40051-83-0; **2**, 19766-29-1; **3**, 39488-50-1; **6a**, 85312-20-5; **6b**, 98612-86-3; **7a**, 85312-21-6; **7b**, 98612-87-4; **8a**, 98612-88-5; **8b**, 98612-89-6; **8c**, 98612-90-9; **8d**, 98612-91-0; **9**, 98612-92-1; **10**, 98612-93-2; **11**, 98612-94-3; **12**, 98612-95-4; **13**, 98612-96-5; CH_3COCl, 75-36-5; PhCOCl, 98-88-4; $PhOCH_2COCl$, 701-99-5; 4-BrC_6H_4COCl, 586-75-4.

Supplementary Material Available: Tables II–V containing atomic coordinates, bond lengths, and bond angles for **8d** (4 pages). Ordering information is given on any current masthead page.

Variations in the Stereochemistry of the Boron Trifluoride Mediated Cyclocondensation Reaction of Aldehydes with Siloxy Dienes

Samuel Danishefsky,* Kuo-Hua Chao, and Gayle Schulte

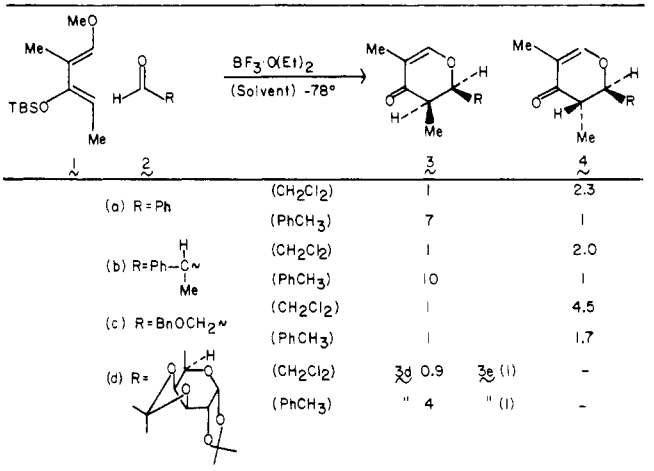
Department of Chemistry, Yale University, New Haven, Connecticut 06511

Received June 10, 1985

Variation of the Lewis Acid catalyst results in remarkable changes in the stereochemical outcome of the cyclocondensation of aldehydes with siloxy dienes.[1] Given the accessibility of the substrates which go into this reaction, the generality of the process, and the valuable functionality of the resultant products,[2] the issue of stereochemical control is of no small moment. Accordingly, we have continued to investigate the effects of modifications on the selectivity of the process. In these studies, some rather striking results were encountered. The findings are summarized herein.

This inquiry was confined to the use of boron trifluoride–etherate as the catalyst. In the first instance, we focused on the use of (*tert*-butyldimethylsilyl)oxy diene **1**. This stereochemically homogeneous diene is readily prepared from the reaction of (*E*)-1-methoxy-2-methylpent-1-en-3-one[3] with *tert*-butyldimethylsilyl triflate.[4] In all cases, reactions were carried out at −78 °C. The combined yields (see Experimental Section) of cis (**3**) and trans (**4**) products were only marginally affected by solvent changes. As recorded in Table I, a notable contrast was observed when the reaction was carried out in toluene as opposed to methylene chloride. With benzaldehyde (**2a**) and phenylpropanal (**2b**), reaction in toluene afforded a substantial increase in the proportions of cis product relative to those encountered in methylene chloride. In the case of the α-oxygenated aldehydes **2c** and **2d**, the

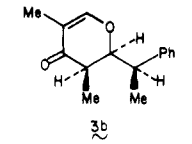
Table I



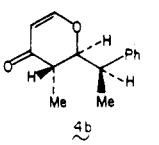
		3	4
(a) R = Ph	(CH_2Cl_2)	1	2.3
	$(PhCH_3)$	7	1
(b) R = Ph–C(H)(Me)–	(CH_2Cl_2)	1	2.0
	$(PhCH_3)$	10	1
(c) R = $BnOCH_2$–	(CH_2Cl_2)	1	4.5
	$(PhCH_3)$	1	1.7
(d) R =	(CH_2Cl_2)	3d 0.9	3e (1)
	$(PhCH_3)$	" 4	" (1)

situation is more complex. For **2c**, the methylene chloride–toluene trend is also in the same direction. However, the consequence of the effect was to erode the trans selectivity manifested in the former solvent. With the galactose-derived aldehyde **2d**, cis selectivity is manifested in both solvents; the impact of the solvent effect was only on the ratio of diastereofacial isomers (vide infra).

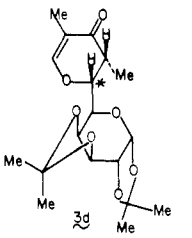
The facial sense of the reaction of **1** with aldehyde **2b** was apparently specific in both solvents. Thus, pyrones **3b** and **4b** are identical with those previously prepared.[1] The formation of these compounds corresponds to that predicted by the Cram[5] or Felkin[6] models. The structure of trans dihydropyrone **4b** had been rigorously demonstrated by its conversion to the well-known Prelog–Djerassi lactone. That the cis isomer **3b** corresponds to the same facial series had been previously inferred.[1,7]



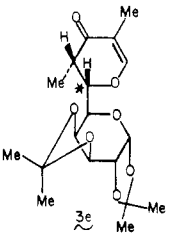
3b



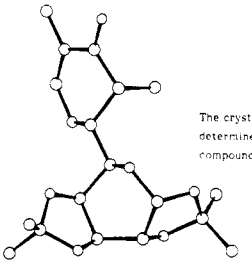
4b



3d



3e



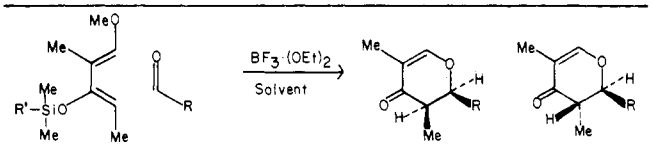
The crystallographically determined structure of compound **3d**.

The full stereochemistry of the major cis pyrone **3d**, mp 150–151 °C, was unambiguously demonstrated to be as shown by an X-ray crystallographic determination.[8] We

(1) Danishefsky, S.; Larson, E. R.; Askin, D. *J. Am. Chem. Soc.* **1982**, *104*, 6457.
(2) Larson, E. R.; Danishefsky, S. *J. Am. Chem. Soc.* **1983**, *105*, 6715.
(3) Danishefsky, S.; Yan, C. F.; Singh, R. K.; Gammill, R.; McCurry, P. Jr.; Fritsch, N.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 7001.
(4) Emde, H.; Domsch, D.; Feger, H.; FrickU.; Bötz, H.; Hergoth, H.; Hofmann, K.; Kober, W.; Krageloh, K.; Oesterle, T.; Steppan, W.; West, W.; Simchen, G. *Synthesis* **1982**, 1.
(5) Cram, D. J.; Wilson, D. R. *J. Am. Chem. Soc.* **1963**, *85*, 1245 and references therein.
(6) Chêrest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199.
(7) Danishefsky, S.; Larson, E.; Askin, D.; Kato, N. *J. Am. Chem. Soc.* **1985**, *107*, 1246.

0022-3263/85/1950-4650$01.50/0

Table II



	2		3	4
1 R'= ^{t}Bu	(a) R=Ph	CH_2Cl_2	I	2.3
5 R'=Me	(a) R=Ph	CH_2Cl_2	I	4.6
1	(b) R=Ph-CH(Me)-	CH_2Cl_2	I	2.0
5	(b) "	CH_2Cl_2	I	6.9
1	(a) R=Ph	$PhCH_3$	7	I
5	(a) R=Ph	$PhCH_3$	2.2	I
1	(b) R=Ph-CH(Me)-	$PhCH_3$	10	I
5	(b) "	$PhCH_3$	3.7	I

note in passing the anti relationship of the oxygen atoms of the two pyranoid rings. This same arrangement had been observed earlier with previously synthesized carbon-linked bis(saccharides).[9] Since NMR analysis (see Experimental Section) indicated that the isomeric structure produced was also a cis dihydropyrone, it is possibly represented by structure **3e**. The proclivity of aldehyde **2d** to afford only cis dihydropyrones with diene **1** is not understood. The solvent effect on the ratio of facial isomers is also not interpreted. These compounds are interesting in that they are carbon-linked disaccharide-like structures in which one of the saccharides is of the branched sugar type.[10]

The trend toward formation of the cis isomer in toluene is consistent with a greater tendency for involvement of a pericyclic-like mechanism. Previus work[7] has demonstrated a connectivity between a more nearly Diels–Alder-like process and formation of cis product.

We also examined the consequences of varying the nature of the silyloxy group of the diene in reactions with **2a** and **2b**. Toward this end, the (*tert*-butyldimethylsilyl)oxy diene **1** and the (trimethylsilyl)oxy diene **5**[3] were employed (Table II). These studies were conducted with BF_3·OEt_2 as the catalyst at −78 °C in methylene chloride (wherein trans selectivity is manifested) and in toluene (−78 °C) (wherein cis selectivity is exhibited). *In each case, the diene 1 gave significantly more cis product than did diene 5.* In the experiments conducted in methylene chloride, the shift from diene **1** to diene **5** served to upgrade trans selectivity. In the toluene experiments, the consequence of shifting from diene **1** to diene **5** was that of erosion of cis specificity.

These results can also be accommodated within the framework of the mechanistic duality previously discussed.[7] With diene **1**, wherein the silicon to oxygen bond is less perturbed during the reaction than is the corresponding bond within diene **5**, a more nearly pericyclic pathway is followed, thereby favoring the cis product. In the latter diene, a greater degree of aldol or siloxonium character[7] is manifested, and the trans product is correspondingly favored.

Regardless of the precise factors that are responsible for these variations, some rather dramatic stereochemical latitude is possible. This is easily seen by comparing the BF_3·OEt_2 catalyzed reaction of diene **5** with aldehyde **2b** in methylene chloride at −78 °C (wherein the ratio of **3b–4b** is 1:6.5) with the reaction of diene **1** with the same aldehyde and the same catalyst at the same temperature in toluene (wherein the ratio of **3b–4b** is 10:1). This capability is useful in the stereoselective synthesis of polypropionates, as will soon be demonstrated.

Experimental Section[12]

Preparation of (*E*,*Z*)-3-[(*tert*-Butyldimethylsilyl)oxy]-1-methoxy-2-methyl-1,3-pentadiene (1). A solution of 1-methoxy-2-methylpent-1-en-3-one (850 mg, 6.63 mmol) and triethylamine (1.35 g, 13.34 mmol) in Et_2O (26 mL) was cooled to 0 °C and treated with *tert*-butyldimethylsilyl trifluoromethanesulfonate (1.92 g, 7.27 mmol). After being allowed to slowly warm to 15 °C over a 3-h period the reaction mixture was diluted with Et_2O (100 mL) and transferred to a separatory funnel. The lower layer (containing triethylammonium trifluoromethanesulfonate) was separated. The organics phase was washed with saturated aqueous $NaHCO_3$ solution (2 × 25 mL), dried ($MgSO_4$), and concentrated in vacuo. Kugelrohr installation (1.0 mmHg, bath temperature 70–85 °C) yielded 1.46 g (91%) of diene **1**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 6.30 (s, 1 H, 4.70 (4, *J* = 7 Hz, 1 H), 3.62 (s, 3 H, 1.67 (s, 3 H), 1.60 (d, *J* = 7 Hz, 3 H), 1.00 (s, 9 H), 0.11 (s, 6 H).

Typical Reactions of Dienes 1 and 5 under BF_3·Et_2O Catalysis in Methylene Chloride. To 5 mL of methylene chloride at −78 °C was added dropwise BF_3·Et_2O (125 μL, 1.0 mmol). This solution was then added to a solution of aldehyde (0.25 mmol) in dry CH_2Cl_2 (0.5 mL), followed by a solution of diene (0.25 mmol) in dry CH_2Cl_2 (0.5 mL) dropwise with a syringe pump. After being maintained at −78 °C for 10 min, the reaction mixture was quenched by addition of saturated $NaHCO_3$ solution (2 mL). After being allowed to warm to 25 °C, the system was diluted with brine (5 mL). The aqueous layer was further extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and evaporated. The residue was dissolved in $CDCl_3$ (0.5 mL), and the ratio of various products was determined by integration of its ^{1}H NMR spectrum.[12] Purification was accomplished by flash chromatography.

Typical Reactions of Dienes 1 and 5 under BF_3·OEt_2 Catalysis in Toluene. The reactions were conducted as above except that toluene was used instead of methylene chloride. As above, ratios were determined by NMR analysis of the total reaction mixture after workup.

Typical combined yields of the two major products from each reaction: 3a, 4a (60%); **3b, 4b** (70%); **3c, 4c** (73%); **3d, 3e** (85%).

Spectral Properties of Individual Compounds. 3a: previously described.[7] **4a**: previously described.[7] **3b**: previously described.[7] **4b**: previously described.[7] **3c**: ^{1}H NMR (250 MHz, $CDCl_3$ δ 7.35 (s, 5 H), 7.23 (s, 1 H), 4.76 (d, *J* = 12.1 Hz, 1 H), 4.64 (d, *J* = 12.1 Hz, 1 H), 3.79 (dd, *J* = 11.2, 2.5 Hz, 1 H), 3.70 (dd, *J* = 11.2, 4.5 Hz, 1 H), 3.59 (ddd, *J* = 4.5, 3.4, 2.5 Hz), 2.0 (qd, *J* = 7.4 (d), 3.4 (d) Hz, 1 H), 1.67 (d, *J* = 1 Hz, 3 H), 1.05 (d, *J* = 7.4 Hz, 3 H); IR ($CDCl_3$) 1709, 1668, 1623 cm^{-1}; MS, *m*/*e* 246 (M^+). **4c**: ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C) δ 7.36 (m, 5 H), 7.25 (s, 1 H), 4.68 (d, *J* = 12.1 Hz, 1 H), 4.56 (d, *J* = 12.1 Hz,

(8) The methodology used to solve the structure is given in the Experimental Section. Fractional coordinates, isotropic temperature coordinates ×10^4 (Table 1), bond distances (Table 2), bond angles (Table 3), torsional angles (Table 4), and anisotiopic temperature factors (Table 5) are provided in the supplementary material.

(9) Danishefsky, S.; Maring, C.; Barbachyn, M.; Segmuller, B. *J. Org. Chem.* **1985**, *49*, 823.

(10) In principle, detachment of the galactosidal segment from the branched segment should be possible and would provide a route to optically pure branched sugar derivatives in either the D or the L configuration.

(11) For a recent account of the reaction of simple (enyloxy)silanes with aldehydes, see: Heathcock, C. H.; Hug, K. T.; Flippin, L. A. *Tetrahedron Lett.* **1985**, 5973.

(12) Commercial chemicals were used as obtained without further purification, except for solvents, which were purified and dried, where appropriate, before use by standard methods. Preparative column chromatography was carried out on silica gel 60 GF 254 (E. Merck). Routine Fourier transform ^{1}H NMR spectra were determined on a Bruker WM 250-MHz instrument. All shifts are reported relative to solvent. IR spectra were measured in solution ($CDCl_3$) on a Perkin-Elmer 1420 spectrophotometer using NaCl cells. Mass spectra were determined on an Hewlett-Packard 5895 GC/MS system.

1 H), 4.14 (ddd, J = 12.8, 4.4, 2.4 Hz, 1 H), 3.70 (dd, J = 11.2, 4.4 Hz, 1 H), 2.74 (dq, J = 12.8, 6.9 Hz, 1 H), 1.67 (d, J = 1.0 Hz, 3 H), 1.10 (d, J = 6.9 Hz, 3 H). **3d**: ^{1}H NMR (250 MHz, CDCl3, 25 °C) δ 7.20 (s, 1 H), 5.52 (d, J = 5.1 Hz, 1 H), 4.67 (dd, J = 7.9, 2.4 Hz, 1 H), 4.60 (dd, J = 9.6, 3.2 Hz, 1 H), 4.43 (dd, J = 6.3, 4.4 Hz, 1 H), 4.39 (dd, 8.4, 1.8 Hz, 1 H), 4.35 (dd, J = 5.1, 2.6 Hz, 1 H), 3.96 (dd, J = 9.8, 1.7 Hz, 1 H), 2,63 (dq, J = 7.4, 3.1 Hz, 1 H), 1.67 (s, 3 H), 1.55 (s, 3 H), 1.44 (s, 3 H), 1.38 (s, 3 H), 1.35 (s, 3 H), 1.15 (d, J = 7.4 Hz, 3 H); IR ($CDCl_3$) 1663, 1620 cm^{-1}; MS, m/e 354 (M^+). **3e**: ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C) δ 7.12 (s, 1 H) 5.50 (d, J = 4.9 Hz, 1 H), 4.64 (dd, J = 7 = 7.9, 2.3 Hz, 1 H), 4.42 (dd, J = 9.7, 3.1 Hz, 1 H), 4.36 (dd, J = 7.9, 1.5 Hz, 1 H), 4.31 (dd, J = 4.8, 2.5 Hz, 1 H), 4.04 (dd, J = 9.6, 1.3 Hz, 1 H), 2.78 (dq, J = 7.4, 3.2 Hz, 1 H), 1.65–1.26 (m, 18 H); IR ($CDCl_3$) 1665, 1625 cm^{-1}; MS, m/e 364 (M^+).

Crystallographic Determination of Compound 3d. A needle-shaped crystal of dimension 0.6 × 0.6 × 0.4 mm was mounted on a glass rod. Diffraction measurements were made on an Enraf-Nonius CAD-4 fully automated diffractometer using graphite monochromatized Mo Kα radiation (λ = 0.71073 Å). The unit cell was found by using 25 randomly selected reflections and has a = 6.004 (1) Å, b = 16.051 (6) Å, and c = 9.755 (2) Å, with β = 100.17 (2)°. The volume is 925 (1) Å^3 and the calculated density is 1.272 g/cm^3 for Z = 2. Systematic extinctions, as estimated density and the presence of chirality were the criteria used to establish the space group as $P2_1$, with one molecule of composition $C_{18}H_{26}O_7$ comprising the asymmetric unit.

There were 2493 reflections collected with $2\theta \leq 52°$, with 1712 (69%) observed ($I \geq 3\sigma I$). The structure was solved by direct methods, using MULTAN80.[13] All 25 non-hydrogen atoms were observed on the electron-density map based on the phasing of 158 reflections ($E_{min} \geq 1.59$).

Carbon and oxygen atoms were refined anisotropically. Hydrogen atoms were calculated by using SDP[14] program HYDRO and added to the structure factor calculations. Full-matrix refinement of the non-hydrogen atoms and addition of the hydrogen atoms to the structure factor calculations, without refinement of their positions, has resulted in convergence to a standard crystallographic residual of 0.062 and a weighted residual of 0.075. The indications from residual electrons density point to disorder in the molecule. All intramolecular bond distances and angles are within normal ranges.

A perspective drawing of compound **3d**[15] is given in the text. Tables 1–5[16] containing the final X-ray parameters, bond distances, bond angles, torsional angles, and anisotropic temperature factors are provided as supplementary material.

Acknowledgment. This work was supported by PHS Grant CA 28824. NMR spectra were obtained through the auspices of the Northeast Regional NSF/NMR Facility at Yale University, which was supported by NSF Chemistry Division Grant CHE 7916210.

Registry No. 1, 98703-75-4; **2a**, 100-52-7; **2b**, 93-53-8; **2c**, 60656-87-3; **2d**, 4933-77-1; **3a**, 83378-98-7; **3b**, 80160-78-7; **3c**, 83379-01-5; **3d**, 98687-79-7; **3e**, 98757-20-1; **4a**, 83379-03-7; **4b**, 80160-77-6; **4c**, 83379-05-9; **5**, 72486-93-2; BF_3, 7637-07-2; (*E*)-1-methoxy-2-methylpent-1-en-3-one, 56279-35-7; *tert*-butyldimethylsilyl trifluoromethanesulfonate, 69739-34-0.

Supplementary Material Available: A prospective drawing of compound **3d** with numbered atoms and tables containing fractional coordinates, temperature factors, bond distances, torsional angles, and anisotropic temperature factors for **1** (7 pages). Ordering information is given on any current masthead page.

(13) MULTAN80 system of computer programs for the automatic solution of crystal structures from X-ray diffraction data: Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J. P.; Woolfson, M. M.

(14) Programs used were the Enraf-Nonius SDP program library (version 18).

(15) UPLOT structure plotting package: Kearsley, S. K. Yale University, 1985.

(16) SKKPUB structural parameters and errors: Kearsley, S. K. Yale University, 1985.

Synthesis of 3,4-Dihydro-3,3,4-trichloroquinolin-2(1*H*)-ones and Their Conversion to Indeno[1,2,3-*de*]quinolin-2(3*H*)-ones

Johannes L. C. Marais and Benjamin Staskun*

Department of Chemistry, University of the Witwatersrand, Johannesburg, South Africa

Received February 28, 1985

Recently we treated difluorooxyborane **1a** with sulfuryl chloride to form 3,4-dihydro-3,3,4-trichloroquinolin-2-(1*H*)-one **2a**.[1] Erratic results were encountered in the earlier experiments and have led to the adoption of a procedure using added concentrated H_2SO_4 to effect a more rapid and reproducible reaction. Application of the modified method to difluorooxyboranes **1b–e** led to the corresponding formerly inaccessible **2b–e** in 20–70% yields; the structures of the products were assigned from their spectroscopic data.[2]

The function of the acid catalyst may be rationalized in terms of the mechanism[1] suggested for the conversion of **1** to **2**. Ion A (Scheme I), once it is generated from **1** and SO_2Cl_2, reacts via two distinct and competitive pathways: with hydrogen chloride it transforms to B (route a), the precursor of amide **3**, otherwise it cyclizes to ion C (route b), furnishing (ultimately) the 3,4-dihydroquinolinone **2**. The postulation that B forms at a significantly faster rate than does C in this dichotomy would account for chlorinated 3-keto amide **3** being the chief product. We speculate further that H_2SO_4 (unlike HCl) facilitates ionization of intermediate B to re-form A (Scheme I, route c). The deliberate introduction of an adequate quantity of concentrated H_2SO_4 into the reaction (in contrast to the fortuitous production of the acid from SO_2Cl_2 in the original[1] procedure) thus results in an increased yield of **2** at the expense of **3**. In support of this analysis, **1b** and SO_2Cl_2 were reacted with retention of hydrogen chloride and exclusion of moisture, i.e., under conditions favoring formation of amide(s) **3**, and H_2SO_4 was then added to the mixture; the major product was now 3,4-dihydroquinolinone **2b** contaminated with only minor **3a** and **3b**.

In a relatively large scale preparation, **1b** (10.6 mmol) was reacted with an excess of SO_2Cl_2 in the presence of concentrated H_2SO_4 to provide, after chromatography, **2b** (7.6 mmol). Also eluted from the column were two byproducts, viz., quinolin-2-one **4** and the hitherto inaccessible 3,4-dihydro-4-hydroxyquinolin-2(1*H*)-one (**5**). Product **4** is thought to arise in the reaction by loss of Cl^+ from an intermediate species (D, Scheme II),[3] whereas **5** probably resulted from fortuitous hydrolysis of **2b** during workup. Indeed, **5**[4] was subsequently prepared in excellent (~90%) yield by refluxing **2b** in aqueous acetone containing silver nitrate.

Two of the 3,4-dihydroquinolinones, viz., **2b** and **2e**, were tested as precursors for the indeno[1,2,3-*de*]quinolin-2-one **7** system. Compound **2b** in concentrated H_2SO_4 reacted in the manner of **2a**[1] likewise affording a ring-cleavage

(1) Staskun, B. *J. Org. Chem.* **1980**, *45*, 2482.

(2) The formulation of **2a** has been confirmed by an X-ray structure determination (Denner, L.; Marais, J. L. C.; Staskun, B., unpublished results).

(3) Staskun, B.; Meltzer, P. C. *Tetrahedron* **1977**, *33*, 2429.

(4) The related 3,4-dihydro-4-hydroxy-1-methyl-4-phenyl-3,3,6-trichloroquinolin-2-one is a possible intermediate in the cyclization of 2-(*N*-methyl)dichloroacetamido-5-chlorobenzophenone (Podesva, C.; Solomon, C.; Vagi, K. *Can. J. Chem.* **1968**, *46*, 435.

0022-3263/85/1950-4652$01.50/0