

reflections were scanned up to $2\theta = 66^\circ$ and led to 6223 unique structure factors ($R_{\text{sym}} = 5.6\%$) after data reduction. The corresponding normalized structure factors were calculated as usual (calcd scale factor = 0.38, mean $\langle U \rangle$ thermal factor = 0.032), and direct methods were applied. After many trials on phase sets corresponding to the highest figures of merit, we were able to develop a partial structure that gave upon F recycling procedure the whole set of atoms. The refinements of the structure were made with isotropic thermal factors for all the non-hydrogen atoms, in the first step, and then with anisotropic thermal factors with the Br and O atoms in a second step. The final R conventional factor converged to $R = 9.1\%$ for 2320 observed structural factors greater than 3σ . Due to the paucity of the data, no attempt was made to refine anisotropically the whole structure and carbon atoms were kept anisotropic.

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Supplementary Material Available: Tables of positional parameters, thermal parameters, interatomic distances, and interatomic angles for macrolactone 10 (5 pages); tables of observed and calculated structure factors (16 pages). Ordering information is given on any current masthead page.

Effect of *N*-Chloro Structure and 1-Substituent on σ -Substitution (Addition-Elimination) in Pyrroles¹

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1-Methylpyrrole was reacted with a number of different types of *N*-chloro derivatives, and σ -substitution was observed only with *N*-chloroimides. It is proposed that there is a qualitative relationship between the $\text{p}K_a$ of the *N*-chloro precursor and the reaction path. The reaction of 1-substituted pyrroles (CH_3 , C_6H_5 , $\text{C}_6\text{H}_5\text{CH}_2$, $\text{CH}_3\text{C}=\text{O}$, $(\text{CH}_3)_3\text{C}$, $\text{CH}_2=\text{CHCH}_2$, $(\text{C}_6\text{H}_5)_3\text{C}$) with *N*-chlorosuccinimide in $\text{CHCl}_3/\text{NaHCO}_3$ indicated that σ -substitution was very sensitive to electronic factors, e.g. no reaction was observed with 1-acetylpyrrole. It was not as sensitive to steric effects, and only with 1-tritylpyrrole was σ -substitution not observed. Only chlorination was observed with pyrrole itself.

Electrophilic substitution typically occurs by an $\text{S}_{\text{E}}2$ mechanism in aromatic⁴ and heteroaromatic systems.⁵ This is not the exclusive reaction path with electrophiles; addition^{6,7} and substitution by σ -substitution⁸ (addition-elimination^{6,7}) are sometimes observed. Recently we reported that the reaction of 1-methylpyrrole with *N*-chloroacetanilide gave a product (ca. 20% yield) in which the acetanilide moiety had been incorporated into the pyrrole ring by σ -substitution (addition-elimination),⁹ the

Table I. Reaction of *N*-Chloro Derivatives with 1-Methylpyrrole: Effect of *N*-Chloro Structure

<i>N</i> -chloro compound	$\text{p}K_a^a$	% yield ^c	
		base ^d	no base
<i>N</i> -chlorophthalimide (NCP)	8.30	81	66
<i>N</i> -chlorobenzotriazole	8.60	0 ^e	0 ^e
<i>N</i> -chlorosuccinimide (NCS)	9.70	74	33
<i>N</i> -chloromaleimide (NCM)	10.2 ^b	79	64
<i>N</i> -chloroacetanilide ⁹			20
<i>N</i> -chlorobenzimidazole	12.9	0 ^e	0 ^e
<i>N</i> -chlorobenzamide	14-15	NR ^f	0 ^e
<i>N</i> -chloroacetamide	15.1	NR ^f	NR ^f
<i>N</i> -chlorourea		NR ^f	NR ^f
<i>N</i> -chloro- <i>N,N'</i> -dimethylurea		NR ^f	NR ^f

^a Values taken (except where noted) from ref 29. ^b Calculated from data in ref 34. ^c Determined by ^1H NMR spectroscopy. ^d NaHCO_3 . ^e Only chloropyrroles. ^f No reaction after 48 h. ^g Pyridine as base; no reaction in the absence of base under a N_2 atmosphere.

first such example in pyrrole chemistry.^{10,11} Addition-elimination reactions have been previously observed in benzene derivatives,⁶⁻⁸ polyaromatic hydrocarbons,^{6,7,8d} furans,¹²⁻¹⁴ benzofurans,^{15,16} and indoles.¹⁷⁻¹⁹

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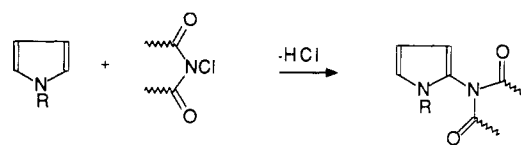
Subsequently we showed that in the presence of NaHCO₃, the reaction of 1-methylpyrrole with *N*-chlorosuccinimide (NCS) or *N*-chlorophthalimide (NCP) occurred predominately by σ -substitution.²⁰ An element effect pertained since only halogenation was observed with the *N*-iodo and *N*-bromo derivatives.²⁰ In this work the influence of pyrrole structure (1-substituent) and the nature of the *N*-chloro derivative on a σ -substitution is examined.

Influence of *N*-Chloro Structure. 1-Methylpyrrole (2) was reacted with the *N*-chloro derivatives of phthalimide,²¹ succinimide, maleimide,²¹ benzotriazole,²² benzimidazole,²³ benzamide,²⁴ acetamide,²⁵ and *N,N'*-dimethylurea²⁶ in CDCl₃ containing NaHCO₃. The product distribution was determined by ¹H NMR (Table I). σ -Substitution products precipitated upon addition of petroleum ether to the crude reaction residue. Included in Table I are the p*K*_a's (where available) of the *N*-chloro precursors (see below). The reaction with *N*-chloroacetanilide has been reported and is included in Table I for comparison. Previously we proposed that an ion pair is initially formed composed of a σ -complex and a nitrogen anion.⁹ Collapse of the ion pair gave a 2,5-addition compound which eliminated HCl to give the addition-elimination product.⁹

Table I indicates that σ -substitution was principally observed when the *N*-chloro derivative of a nitrogen compound with relatively acidic hydrogens was used. In contrast when the *N*-chloro precursor was a very weak acid, no reaction took place in the presence of base. The p*K*_a of the *N*-chloro precursor should be a measure of the leaving group character of the nitrogen anion formed. Table I indicates a relationship between p*K*_a and the occurrence of σ -substitution. But in view of the paucity of data and the uncertainty²⁶ in some of the values, this trend can only be considered to be qualitative at present.

On the basis of these results we propose that the initial process is nucleophilic attack by the pyrrole ring on the chlorine atom of the *N*-chloro derivative to give an ion pair. This is an X-philic reaction,²⁷ which would be favored by *N*-chloro derivatives which contain good leaving groups and by pyrroles bearing substituents which increase the

Scheme I



1, R = H	a = NCS	2 a - c
2, R = CH ₃	b = NCP	3 a - c
3, R = C ₆ H ₅	c = NCM	4 a - c
4, R = C ₆ H ₅ CH ₂		5 a - c
5, R = <i>t</i> -C ₄ H ₉		6 a - c
6, R = CH ₂ =CH-CH ₂		
7, R = CH ₃ C=O		
8, R = (C ₆ H ₅) ₃ C		

Table II. Reaction of Pyrroles with *N*-Chloroimides: Effect of 1-Substituent on Yield of σ -Substitution Product

1-substituent	<i>N</i> -chloroimide	% yield ^a	
		base ^b	no base
H	NCS	0 ^c	0 ^c
H	NCP	0 ^c	0 ^c
CH ₃	NCS	65 (74)	(33)
CH ₃	NCP	48 (81)	(66)
CH ₃	NCM ^d	71 (79)	(64)
C ₆ H ₅	NCS	27 (35)	(6)
C ₆ H ₅	NCP	13	6
C ₆ H ₅	NCM ^d	28	8
C ₆ H ₅ CH ₂	NCS	45 (52)	(20)
C ₆ H ₅ CH ₂	NCP	56	20
C ₆ H ₅ CH ₂	NCM ^d	53	19
CH ₃ C=O	NCS	NR ^e	0 ^c
CH ₂ =CHCH ₂	NCS	49 (68)	(17)
CH ₂ =CHCH ₂	NCP	63	19
CH ₂ =CHCH ₂	NCM ^d	50	16
<i>t</i> -C ₄ H ₉	NCS	47 (65)	(28)
<i>t</i> -C ₄ H ₉	NCP	15	5
<i>t</i> -C ₄ H ₉	NCM ^d	43	19
(C ₆ H ₅) ₃ C	NCS	0 ^c	0 ^c

^aReactions run in CDCl₃ and yields are for isolated products. Values in parentheses determined by ¹H NMR spectroscopy. ^bNaHCO₃. ^cOnly chloropyrroles. ^d*N*-Chloromaleimide. ^eNo reaction after 48 h.

electron density of the ring (see below).

The *N*-chloro derivatives of benzotriazole and benzimidazole were exceptions to this trend as evidenced by reaction with 2 to give complex mixtures of products. *N*-Chlorobenzotriazole has been reported to react with indoles by an electron-transfer pathway.²⁸ It is possible that these two *N*-chloro heterocycles reacted faster by this route than by the reaction under study, and for this reason no σ -substitution is observed.

Table I reveals that the yield of σ -substitution product decreased in the absence of added base, indicating, as previously noted, that a competing acid-catalyzed process was also taking place.^{9,20}

Influence of Pyrrole Structure. The steric and electronic effects of nitrogen substituents on σ -substitution were probed by reacting a series of 1-substituted pyrroles (Scheme I) with *N*-chlorosuccinimide (NCS) in CDCl₃ (Table II). It has previously been proposed that σ -substitution occurs because ion-pair collapse is competitive with deprotonation of the σ -complex. Since pyrrole (1) reacted to give chloropyrroles under all conditions, de-

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protonation was the faster process. Proton transfer from nitrogen acids is faster than from carbon acids,²⁹ which is likely the reason why σ -substitution is not observed when pyrrole reacts with NCS or NCP.

No reaction was detected by ¹H NMR spectroscopy between 1-acetylpyrrole (7) and NCS after 48 h in the presence of NaHCO₃. As stated above the initial step is nucleophilic attack by the pyrrole ring on the chlorine atom of the *N*-chloro compound. The electron-withdrawing acetyl group lowers the electron density and the reactivity of the pyrrole ring. The results in this study indicate that the formation of ion pairs is very sensitive to the nucleophilic character of the pyrrole ring. In contrast, in the absence of base, 1-acetylpyrrole (7) reacted readily with NCS in an acid-catalyzed reaction to give chloropyrroles. The pyrrole ring of 7 can displace succinimide from protonated NCS but is not nucleophilic enough to displace the succinimidyl anion from NCS.

Of the pyrroles which underwent σ -substitution, 1-phenylpyrrole (3) gave the smallest yield, and the reaction was complete in 24 h compared to 4 h with 2.²⁰ This result is most probably attributable to the inductive effect of the phenyl group, which would be expected to make the pyrrole ring less nucleophilic and also destabilize the initially formed ion pair.

Steric effects were examined in the reactions of 1-*tert*-butylpyrrole (5) and 1-tritylpyrrole (8) with NCS. A 65% yield (¹H NMR) of σ -substitution product was obtained when 1-*tert*-butylpyrrole was reacted with NCS, compared to a 74% yield with 2.

In contrast the reaction with 1-tritylpyrrole (8) gave only chloropyrroles, indicating that only when extremely large groups are present does ion-pair collapse not take place. Whereas 2-chloro- and 3-chloro-1-tritylpyrrole were isolated in a ratio of 2:1, bromination of 8 with pyridinium bromide perbromide gave almost exclusively the 3-bromo-1-tritylpyrrole,³⁰ most likely as a result of the differing size of the halogens.

Steric effects and the generality of this new reaction were studied further by examining the reaction of 1-phenyl-, 1-benzyl-, 1-*tert*-butyl-, and 1-allylpyrrole with *N*-chlorosuccinimides (Table II). Yields are generally lower than with 2 (Table II) and in the absence of base, chlorination is favored to a greater extent than with 2. Overall the results indicate that this is a general reaction pathway for pyrroles having the appropriate substituents. Table II indicates that this reaction is more sensitive to electronic effects than to steric effects.

Experimental Section

Infrared spectra were taken on a Perkin-Elmer 1320 instrument. A Varian T-60 and an XL-100 FT were used to record ¹H NMR spectra. Melting points were taken on a Fisher-John hot stage apparatus and are uncorrected. Pyrrole (1), 1-methylpyrrole (2), NCS, and 1-phenylpyrrole (3) were commercially available. NCS and 3 were used without further purification, and 1 and 2 were distilled from zinc dust prior to use. 1-Acetyl-,³¹ 1-benzyl-,³² 1-*tert*-butyl-,³³ 1-allyl-,³³ and 1-tritylpyrrole³⁰ were prepared by literature procedures. Phthalimide,²¹ maleimide,²¹ benzotriazole,²²

benzimidazole,²³ benzamide,²⁴ acetamide,²⁴ urea,²⁵ and *N,N'*-dimethylurea²⁵ were converted to their respective *N*-chloro derivatives.

General Reaction Method. To the pyrrole (0.2 mmol) in 1.0 mL of CDCl₃ (with or without NaHCO₃) was added the *N*-chloro derivative (0.2 mmol). The mixture was stirred in the dark until it tested negatively with a KI/ethanol/acetic acid solution. Reactions generally took 4–8 h except for 1-phenylpyrrole (3) (24 h). Yields were then obtained by ¹H NMR analysis. Preparative-scale reactions were run using 5 mmol each of pyrrole and *N*-chloro derivative in 25 mL of chloroform (washed with water and dried over CaCl₂) containing NaHCO₃ (0.8 g). The reaction mixture was washed three times with water, and the chloroform was removed under reduced pressure. Addition of petroleum ether (50–70 °C) precipitated the σ -substitution product (recrystallized from ethanol). The reaction of 1-methylpyrrole (2) with *N*-chloromaleimide gave an oil, which was purified by column chromatography on silica gel (chloroform–ethyl acetate (7:3 v/v) solvent). The following products were isolated and identified by their spectral properties (see Scheme I).

***N*-(1-Methyl-1*H*-pyrrol-2-yl)succinimide (2a):** 65% yield; mp 163–164 °C; ¹H NMR (CDCl₃) δ 6.72 (m, 1 H, J_{3-5} = 2.1 Hz, J_{4-5} = 3.2 Hz, C5H), 6.20 (m, 2 H, J_{3-4} = 4.0 Hz, J_{3-5} = 2.1 Hz, J_{4-5} = 3.2 Hz, C3H and C4H), 3.43 (s, 3 H, NCH₃), 2.83 (s, 4 H) ppm; IR (KBr) 1715, 1585, 1525, 1465, 1410, 1400, 1320, 1265 cm⁻¹.

***N*-(1-Methyl-1*H*-pyrrol-2-yl)phthalimide (2b):** 48% yield; mp 205–206 °C; ¹H NMR (CDCl₃) δ 7.89 (m, 4 H), 6.73 (m, 1 H, C5H), 6.22 (m, 2 H, C3H and C4H), 3.52 (s, 3 H, NCH₃) ppm; IR (KBr) 1720, 1640, 1580, 1520, 1500, 1465, 1310, 1265 cm⁻¹.

***N*-(1-Methyl-1*H*-pyrrol-2-yl)maleimide (2c):** yield 71%; orange oil; ¹H NMR (CDCl₃) δ 6.74 (m, 3 H), 6.14 (m, 2 H, C3H and C4H), IR (neat) 1710, 1560, 1500, 1440, 1400, 1310 cm⁻¹.

***N*-(1-Phenyl-1*H*-pyrrol-2-yl)succinimide (3a):** 27% yield; mp 145–147 °C; ¹H NMR (CDCl₃) δ 7.30 (m, 5 H), 6.83 (m, 1 H, J_{3-5} = 1.8 Hz, J_{4-5} = 3.2 Hz, C5H), 6.16 (m, 2 H, J_{3-4} = 3.8 Hz, J_{3-5} = 1.8 Hz, J_{4-5} = 3.2 Hz, C4H and C3H), 2.68 (s, 4 H) ppm; IR (KBr) 1710, 1590, 1440, 1390, 1340 cm⁻¹.

***N*-(1-Phenyl-1*H*-pyrrol-2-yl)phthalimide (3b):** 13% yield; mp 157–158 °C; ¹H NMR (CDCl₃) δ 7.71 (m, 4 H), 7.25 (m, 5 H), 6.90 (m, 1 H, C5H), 6.37 (m, 2 H, C4H and C3H) ppm; IR (KBr) 1710, 1590, 1490, 1390, 1315 cm⁻¹.

***N*-(1-Phenyl-1*H*-pyrrol-2-yl)maleimide (3c):** yield 28%; mp 180 °C; ¹H NMR (CDCl₃) δ 7.27 (m, 5 H), 6.87 (m, 1 H, C5H), 6.63 (s, 2 H), 6.30 (m, 2 H, C4H and C3H) ppm; IR (KBr) 1710, 1560, 1430, 1390, 1310 cm⁻¹.

***N*-(1-Benzyl-1*H*-pyrrol-2-yl)succinimide (4a):** 41% yield; mp 144–145 °C; ¹H NMR (CDCl₃) δ 7.18 (m, 5 H, arom), 6.75 (m, 1 H, J_{3-5} = 1.9 Hz, J_{5-4} = 2.8 Hz, C5H), 6.19 (m, 2 H, J_{3-5} = 1.9 Hz, J_{5-4} = 2.8 Hz, J_{4-3} = 3.6 Hz, C4H and C3H), 4.90 (s, 2 H), 2.55 (s, 4 H) ppm; IR (KBr) 1700, 1560, 1440, 1390, 1310 cm⁻¹.

***N*-(1-Benzyl-1*H*-pyrrol-2-yl)phthalimide (4b):** 56% yield; mp 137–139 °C; ¹H NMR (CDCl₃) δ 7.76 (m, 4 H), 6.82 (m, 5 H), 6.72 (m, 1 H, C5H), 6.25 (m, 2 H, C4H and C3H), 4.92 (s, 2 H) ppm; IR (KBr) 1710, 1600, 1430, 1380, 1300 cm⁻¹.

***N*-(1-Benzyl-1*H*-pyrrol-2-yl)maleimide (4c):** yield 53%; mp 120–122 °C; ¹H NMR (CDCl₃) δ 7.14 (m, 5 H), 6.60 (s, 2 H), 6.67 (m, 1 H, C5H), 6.15 (m, 2 H, C4H and C3H), 4.80 (s, 2 H) ppm; IR (KBr) 1710, 1440, 1390, 1280 cm⁻¹.

***N*-(1-*tert*-Butyl-1*H*-pyrrol-2-yl)succinimide (5a):** 47% yield; mp 145–147 °C; ¹H NMR (CDCl₃) δ 6.87 (m, 1 H, J_{3-5} = 2.1 Hz, J_{5-4} = 3.3 Hz, C5H), 6.05 (m, 2 H, J_{3-5} = 2.1 Hz, J_{5-4} = 3.3 Hz, J_{4-3} = 3.5 Hz, C4H and C3H), 2.77 (s, 4 H), 1.46 (s, 9 H) ppm; IR (KBr) 1710, 1430, 1390, 1310 cm⁻¹.

***N*-(1-*tert*-Butyl-1*H*-pyrrol-2-yl)phthalimide (5b):** 15% yield; mp 140–142 °C; ¹H NMR (CDCl₃) δ 7.90 (m, 4 H), 6.90 (m, 1 H, C5H), 6.12 (m, 2 H, C4H and C3H), 1.52 (s, 9 H) ppm; IR (KBr) 1715, 1430, 1390, 1300 cm⁻¹.

***N*-(1-*tert*-Butyl-1*H*-pyrrol-2-yl)maleimide (5c):** yield 43%; mp 143–144 °C; ¹H NMR (CDCl₃) δ 6.89 (m, 1 H, C5H), 6.80 (s, 2 H), 6.10 (m, 2 H, C4H and C3H), 1.50 (s, 9 H) ppm; IR (KBr) 1710, 1440, 1390, 1280 cm⁻¹.

***N*-(1-Allyl-1*H*-pyrrol-2-yl)succinimide (6a):** 49% yield; mp 106–107 °C; ¹H NMR (CDCl₃) δ 6.67 (m, J_{3-5} = 1.8 Hz, J_{4-5} = 3.1 Hz, C5H), 6.18 (m, 1 H, J_{4-3} = 3.7 Hz, J_{4-5} = 3.1 Hz, C4H), 6.04 (m, 1 H, J_{3-5} = 1.8 Hz, J_{3-4} = 3.7 Hz, C3H); allyl group 5.79 (m, 1 H, J_{1-3} = 16.4 Hz, J_{1-2} = 10.8 Hz, J_{1-4} = 5.3, =CH), 5.05

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(m, 2 H, $J_{1-3} = 16.4$ Hz, $J_{3-4} = 1.8$ Hz, $J_{2-4} = 1.8$ Hz, $J_{1-2} = 10.8$ Hz, $=CH_2$), 4.25 (m, 2 H, $J_{1-4} = 5.3$ Hz, $J_{2-4} = J_{3-4} = 1.8$ Hz, CH_2) ppm; IR (KBr) 1710, 1430, 1390, 1310 cm^{-1} .

N-(1-Allyl-1*H*-pyrrol-2-yl)phthalimide (6b): 63% yield; mp 120–121 °C; 1H NMR ($CDCl_3$) δ 7.87 (m, 4 H), 6.75 (m, 1 H, $J_{3-5} = 2.0$ Hz, $J_{4-5} = 2.9$ Hz, C5H), 6.24 (m, 2 H, $J_{3-5} = 2.0$ Hz, $J_{4-5} = 2.9$ Hz, $J_{3-4} = 3.8$ Hz, C4H and C3H); allyl group 5.83 (m, 1 H, $=CH$), 5.01 (m, 2 H, $=CH_2$), 4.35 (m, 2 H, CH_2) ppm; coupling constants same as in 6a; IR (KBr) 1720, 1580, 1440, 1390, 1310 cm^{-1} .

N-(1-Allyl-1*H*-pyrrol-2-yl)maleimide (6c): yield 50%; mp 75–76 °C; 1H NMR ($CDCl_3$) δ 6.70 (s, 2 H), 6.65 (m, 1 H, $J_{4-5} = 3.3$ Hz, $J_{3-5} = 2.1$ Hz, C5H), 6.23 (m, 2 H, $J_{4-5} = 3.3$ Hz, $J_{3-5} =$

2.1 Hz, $J_{3-4} = 4.2$ Hz, C4H and C3H); allyl group 5.75 (m, 1 H, $=CH$), 5.00 (m, 2 H, $=CH_2$), 4.30 (m, 2 H, CH_2) ppm; coupling constants same as in 6a; IR (KBr) 1710, 1440, 1390, 1320 cm^{-1} .

Registry No. 1, 109-97-7; 2, 96-54-8; 2a, 116625-45-7; 2b, 116625-46-8; 2c, 122845-00-5; 3, 635-90-5; 3a, 122845-01-6; 3b, 122845-02-7; 3c, 122845-03-8; 4, 2051-97-0; 4a, 122845-04-9; 4b, 122845-05-0; 4c, 122845-06-1; 5, 24764-40-7; 5a, 122845-07-2; 5b, 122845-08-3; 5c, 122845-09-4; 6, 7435-07-6; 6a, 122845-10-7; 6b, 122845-11-8; 6c, 122845-12-9; 7, 609-41-6; 8, 85684-89-5; NCP, 3481-09-2; NCS, 45514-70-3; NCM, 45514-70-3; 2-chloro-1-tritylpyrrole, 122845-13-0; 3-chloro-1-tritylpyrrole, 122845-14-1; chloropyrrole, 122845-15-2; 1-acetylchloropyrrole, 122845-16-3.

Serial Radical Cyclization of Branched Carbohydrates. 1. Simple Pyranoside Diquinanes¹

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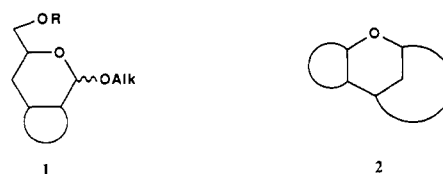
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The 2-deoxy-3-ketopyranoside **5** is converted efficiently into two multiply branched derivatives containing functionalized alkyl substituents at C2 and geminally at C3. For substrates bearing a 2-iodoethyl group at C2 and, at C3, axial vinyl and equatorial cyanomethyl groups, reaction with tri-*n*-butyltin hydride causes deiodination, and the resulting carbon-centered radical adds serially to the vinyl group and thence to the nitrile. A diquinane fused to the pyranoside ring thereby results. If aldehyde and amido groups are used instead of nitrile, the reaction takes a different course.

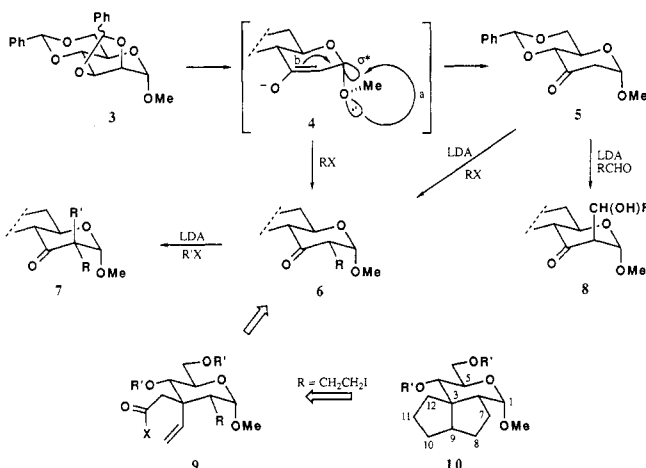
Introduction

The use of carbohydrate derivatives in the synthesis of carbocycles has been a theme of interest in this laboratory for several years.^{3,4} That the target products are furnished in optically active forms is an obvious outcome of this strategy. Therefore our attention has been focused on developing synthetic strategies that exploit the stereocontrolling properties of carbohydrates and also utilize the wide panoply of functional groups, actual or latent, that they possess. For example, in the case of annulated pyranosides, such as **1** (Scheme I), we suggested that, because of the anomeric effect, the conformational preference of the system should be dominated by the pyranoside moiety.⁵ This expectation formed the basis for our synthetic work on actinobolin, where functionalization of the carbocyclic annulus relied on that stereocontrolling principle,⁶ and for our earlier enantiodivergent synthesis of chrysanthemic acid enantiomers.⁷ Structure **2** symbolizes a bis-annulated pyranoside, used in construction of the trichothecane ring system,⁸ which demonstrated the range of functional groups that can be elaborated and utilized. In this and the accompanying⁹ paper, we report the preparation of some bis-annulated pyranosides,¹⁰ different

Scheme I



Scheme II



from **2**, that have been prepared as potential precursors for a wide variety of naturally occurring polyquinanes.¹¹

Serial Radical Cyclizations

For some time, we have been intrigued by the keto sugar methyl 4,6-*O*-benzylidene-2-deoxy- α -D-erythro-hexo-

(1) This work is supported by a grant from NIH (GM 37380).
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