(7) A. G. Anderson, Jr., and G. M.-C. Cheng, *J. Org. Chem.*, **23**, 151 (1958).
(8) J. I. G. Cadogan, Special Publication 24, "Essays on Free-Radical Chemistry", The Chemical Society, London, 1970, pp 71–95.
(9) A. G. Anderson, Jr., J. A. Nelson, and J. J. Tazuma, *J. Am. Chem. Soc.*, **75**, 4980 (1953); A. G. Anderson, Jr., R. Scotoni, E. J. Cowles, and C. G. Fritz, *J. Org. Chem.*, **22**, 1193 (1957); A. G. Anderson, Jr., and R. N. McDonald, *J. Am. Chem. Soc.*, **81**, 5669 (1959).
(10) A. G. Anderson, Jr., and L. D. Grina, unpublished results.

Relative Reactivity of Substituted 2-Alkoxy- and 2-Phenoxy-3,4-dihydro-2*H*-pyrans with *tert*-Butyl Hypochlorite. Effect of Substituents on Reactivity and Products[1]

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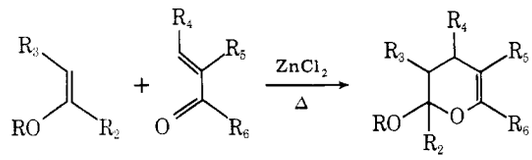
A series of substituted 3,4-dihydro-2*H*-pyrans were prepared: 2-methoxy- (**2a**), 2-methoxy-6-methyl- (**2b**), 2-methoxy-5-methyl- (**2c**), 2-methoxy-4-methyl- (**2d**), 2-methoxy-2-methyl- (**2e**), 2-methoxy-2,6-dimethyl- (**2f**), 2-ethoxy-3-methyl- (**2g**), 2-phenoxy- (**3a**), and 2-phenoxy-6-methyl-3,4-dihydro-2*H*-pyran (**3b**). The structure of each 3,4-dihydro-2*H*-pyran was discussed in terms of configuration, where applicable, and preferred conformation. Generally, addition of *tert*-butyl hypochlorite to 3,4-dihydro-2*H*-pyrans yields 1,2-addition products. However, in the 2-alkoxy-3,4-dihydro-2*H*-pyran series, an alkyl group at either position C-2 or C-6 results in some 1,4-addition product, and alkyl groups at both positions yield 1,4-addition products exclusively. The effect of substituents on the reactivity of the 3,4-dihydro-2*H*-pyran ring was determined using *tert*-butyl hypochlorite in competitive experiments with 3,4-dihydro-2*H*-pyran (**1**). The relative reactivities are **2f > 3b > 2b > 2d ≈ 2c > 1 > 2e > 2g > 2a ≈ 3a.**

Empirical observations in the course of our studies on the chemistry of 2-alkoxy-3,4-dihydro-2*H*-pyrans with various electrophilic reagents[2] has demonstrated an apparent dramatic effect of substituents on the reactivity of the 3,4-dihydro-2*H*-pyran ring, as well as on the course or outcome of the reaction.[1] The object of this study was to synthesize a series of substituted 2-alkoxy- (**2a–g**) and 2-phenoxy-3,4-dihydro-2*H*-pyrans (**3a,b**) and measure, in a relative sense with respect to 3,4-dihydro-2*H*-pyran (**1**), the effect of the substituent on both the reactivity of the 3,4-dihydro-2*H*-pyran ring system and product distribution using *tert*-butyl hypochlorite.

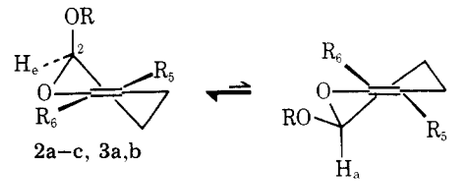
Synthesis and Structure. Substituted 2-alkoxy- and 2-phenoxy-3,4-dihydro-2*H*-pyrans generally are prepared by the thermally promoted cyclization[3] of appropriately substituted enol ethers and α,β-unsaturated aldehydes and ketones. We have found that the procedure[4] using various transition-metal salts as catalyst generally has an advantage over the thermally promoted cyclization, since both the temperature and reaction time for the cyclization can be drastically reduced. Because of this convenience, it is usually the method of choice even though the isolated yields for some of the substituted 3,4-dihydro-2*H*-pyrans are sometimes only moderate. Table I is a summary of the substituted 3,4-dihydro-2*H*-pyrans (**2a–g, 3a,b**) prepared by these procedures with the general reaction conditions and results.



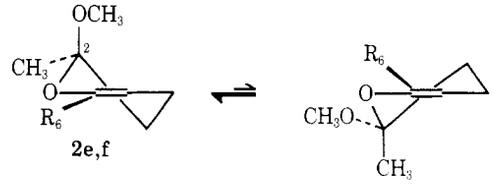
R = CH_3, CH_3CH_2, C_6H_5
R_{2-6} = H, CH_3

2a–g, 3a,b

The substituted 2-methoxy-3,4-dihydro-2*H*-pyrans **2a–c,** and the 2-phenoxy-3,4-dihydro-2*H*-pyrans **3a,b** all exist predominantly (ca. 80%, NMR analysis) in the conformation where the anomeric proton (H_e) is equatorial. The NMR signal for the anomeric C-2 proton at ca. δ 4.8 for the 2-methoxy-



(**2a–c**) and at ca. δ 5.7 for the 2-phenoxy-3,4-dihydro-2*H*-pyrans (**3a,b**) is a superficial triplet ($J_{ea} \approx J_{ee} = \sim 3$ Hz) as expected for an equatorial proton at this position. This preference in the conformational equilibrium of 2-alkoxy-3,4-dihydro-2*H*-pyrans has been previously observed[5] and is predicted by the anomeric effect (Edward–Lemieux effect).[6] Since there is also only one conformer detected (NMR and GLC analysis) for the 2-methoxy-2-methyl-3,4-dihydro-2*H*-pyran (**2e**) and its 6-methyl derivative **2f** (no anomeric



proton in either), we assume the preferential conformation of these 3,4-dihydro-2*H*-pyrans to also have the C-2 methoxy group axial (anomeric effect), requiring the C-2 methyl to be in the favorable equatorial position.

In contrast, analysis (NMR and GLC) of 2-methoxy-4-methyl-3,4-dihydro-2*H*-pyran (**2d**) indicates a diastereomeric cis/trans mixture (60:40) at the anomeric C-2 carbon. The minor diastereomer *trans*-**2d,** derived from the exo approach

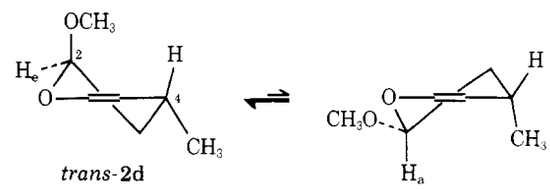


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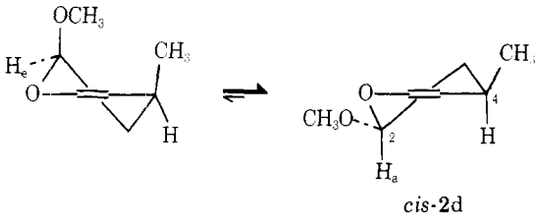
Table I. Synthesis of 2-Alkoxy- and 2-Phenoxy-3,4-dihydro-2*H*-pyrans[a]

Vinyl ether	α,β-Unsat carbonyl compd	Mole ratio, ether/carbonyl	Reaction Temp (°C)	Reaction Time (h)	Catalyst[b]	Product	Yield[c]
Methyl vinyl ether	Propenal	1.5:1	140	12		**2a**	44
Methyl vinyl ether	Methyl vinyl ketone	2:1	90	0.5	$ZnCl_2$	**2b**	35
Methyl vinyl ether	2-Methylpropenal	2.5:1	92	0.5	$ZnCl_2$	**2c**	10[d]
Methyl vinyl ether	*trans*-2-Butenal	1.2:1	200	12		**2d**	80[e]
Isopropenyl methyl ether	Propenal	2:1	60	1.5	$ZnCl_2$	**2e**	61
Isopropenyl methyl ether	Methyl vinyl ketone	1.2:1	25	5	$ZnCl_2$	**2f**	10[f]
1-Ethoxy-1-propene	Propenal	2.3:1	90	1.0	$ZnCl_2$	**2g**	68
Phenyl vinyl ether	Propenal	1.1:1	90	2.0	$ZnCl_2$	**3a**	36
Phenyl vinyl ether	Methyl vinyl ketone	1.1:1	90	0.75	$ZnCl_2$	**3b**	11[g]

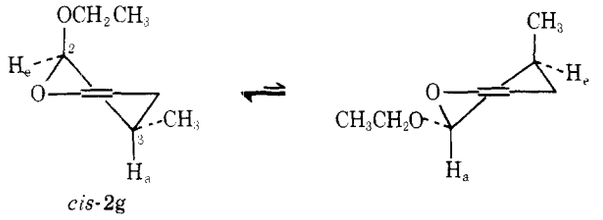
[a] Reaction conditions are described in the Experimental Section for the synthesis of 2-methoxy-2-methyl-3,4-dihydro-2*H*-pyran (**2e**), which are the general procedures described in ref 3 (no catalyst) and 4 (catalyst). [b] For reactions using 0.4 mol of α,β-unsaturated carbonyl compound, 140 mg (1 mmol) of $ZnCl_2$ was used. [c] Distilled. [d] Low yield probably due to ease of polymerization of 2-methylpropenal. [e] Using conditions described in ref 4, 2 h at 70 °C in the presence of $ZnCl_2$, the yield was 68%. [f] Crude sample contaminated with 2,4-dimethoxy-4-methyl-1-pentene that required a spinning-band distillation to purify. The isopropenyl methyl ether dimer becomes a serious side product at higher temperatures. [g] Similar yield using 150 °C for 8 h with no $ZnCl_2$ conditions.

Diels–Alder type cyclization, exists predominantly in the conformation (equatorial anomeric proton) controlled by the anomeric effect. The NMR signal for the anomeric proton (H_e) is a triplet (J = ~3 Hz) at δ 4.76. The major diastereomer *cis*-**2d**, derived from the favored endo approach, exists predominantly in the conformation where the anomeric proton is now axial. The NMR signal for H_a is a quartet (J = 7.5 and 2.5 Hz) centered at δ 4.72. In this diastereomer, the preferred equilibrium conformer is a result of the avoidance of the unfavorable 1,3-steric interaction of the axial methoxy group at C-2 and the pseudoaxial methyl group at C-4 rather than the influence of the anomeric effect.[5c,6d,7]

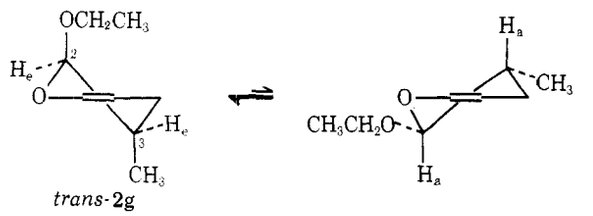


cis-2d

2-Ethoxy-3-methyl-3,4-dihydro-2*H*-pyran (**2g**) is also a diastereomeric cis/trans mixture (30:70) but at the C-3 carbon. The compounds were prepared from a cis/trans mixture of 1-ethoxy-1-propene. The product from the cis vinyl ether is *cis*-2-ethoxy-3-methyl-3,4-dihydro-2*H*-pyran (*cis*-**2g**), where the cis configuration is retained in the adduct. The trans vinyl ether leads to the *trans*-**2g** adduct. Both diastereomers exist predominantly in the conformation where the anomeric proton at C-2 is equatorial, since the signal at δ 4.71 for this proton in the trans isomer is a doublet (J_{ee} = 1.3 Hz) and the signal at δ 4.51 for the cis isomer is a doublet (J_{ea} = 4.1 Hz).

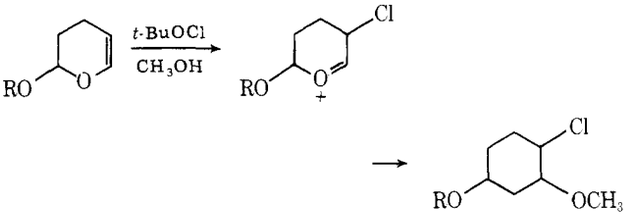


cis-2g

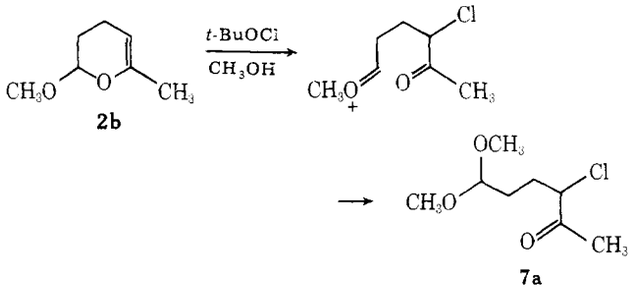


trans-2g

Reaction and Products. The choice of *tert*-butyl hypochlorite as the electrophile for this study was made because of its reactivity, convenience in preparation and handling, and our familiarity with the reaction and the resultant products.[1] Table II is a listing of the products of the reaction of *tert*-butyl hypochlorite in methanol at 0 °C with each of the 2-alkoxy- (**2a–g**) and 2-phenoxy-3,4-dihydro-2*H*-pyrans (**3a,b**), as well as with 3,4-dihydro-2*H*-pyran (**1**). Generally, addition of *tert*-butyl hypochlorite to substituted 2-alkoxy-3,4-dihydro-2*H*-pyrans in alcohol solvents yields the corresponding 1,2-addition products. The 1,2-addition products are diastereomeric mixtures (usually two major and two minor isomers) that resulted from both cis and trans addition to the olefin.



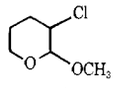
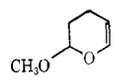
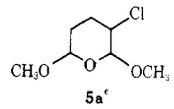
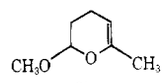
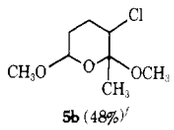
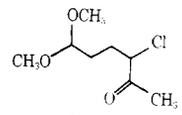
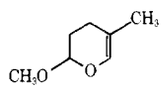
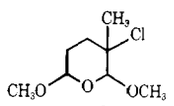
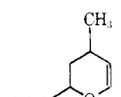
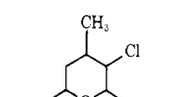
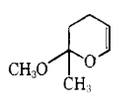
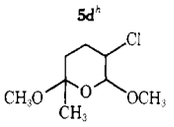
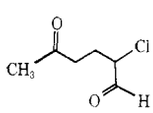
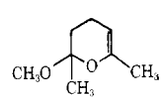
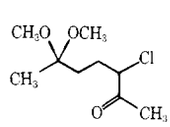
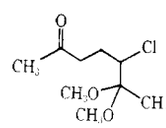
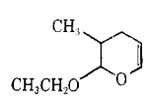
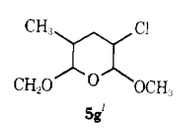
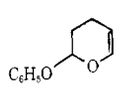
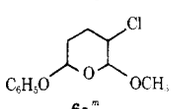
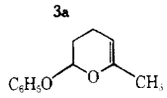
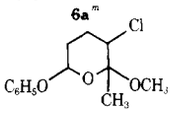
In the 2-alkoxy series, alkyl substituents at either of two positions can result in a second type of product that has formed from 1,4-addition. When a methyl group is at either C-6 as in 2-methoxy-6-methyl-3,4-dihydro-2*H*-pyran (**2b**) or C-2 as in 2-methoxy-2-methyl-3,4-dihydro-2*H*-pyran (**2e**), the second product is observed along with the 1,2-addition product. When an alkyl substituent is at both positions as is the case with 2-methoxy-2,6-dimethyl-3,4-dihydro-2*H*-pyran (**2f**), the 1,4-addition product forms *exclusively* (see Table II). It is not obvious why no 1,4-addition product was observed in the phenoxy series from 2-phenoxy-6-methyl-3,4-dihydro-2*H*-pyran (**3b**). However, at this time we can not rule out the possibility that some 1,4-addition product might be formed from a 2-alkyl or 2,6-dialkyl derivative.



2b **7a**

Products of this nature, the 1,4-addition product as well as the 1,2-addition product, may prove to be useful synthons. In

Table II. *tert*-Butyl Hypochlorite Addition to 3,4-Dihydro-2*H*-pyrans[a]

Dihydropyrans[b]	Products[b] 1,2-Addition (yield)[c]	1,4-Addition (yield)[c]
 1	 4[d]	
 2a	 5a[e]	
 2b	 5b (48%)[f]	 7a (52%)
 2c	 5c[g]	
 2d	 5d[h]	
 2e	 5e (20%)[i]	 7b (80%)[j]
 2f		 8a (75%)[k]  8b (25%)[k]
 2g	 5g[l]	
 3a	 6a[m]	
 3b	 6b[n]	

[a] Reaction conditions are those described in the Experimental Section for 2-methoxy-2-methyl-3,4-dihydro-2*H*-pyran (2e) with *tert*-butyl hypochlorite. [b] Satisfactory composition analyses (±0.4% for C, H for the 3,4-dihydro-2*H*-pyrans and for C, H, Cl for the 1,2-addition products) were submitted to the editor. The 1,4-addition products were too unstable for satisfactory composition analyses. [c] Analyzed by GLC (% of volatiles). [d] A 85:15 cis/trans mixture. [e] A 38:62 diastereomeric mixture. [f] A 6:37:45:12 diastereomeric mixture. [g] A 25:20:55 diastereomeric mixture. [h] A 19:12:12:57 diastereomeric mixture. [i] Only one diastereomer formed. This ratio of products is reversed to 80:20 5e/7b when the reaction is performed at 45 °C. [j] Very unstable. Easily converted to the dimethoxy acetal in methanol. [k] Mixture decomposes readily to *m*-cresol. [l] A 40:35:7:11:7 diastereomeric mixture. [m] A 45:37:9:8 diastereomeric mixture. [n] A 46:5:14:35 diastereomeric mixture.

addition, the effect of substituents on the course of these reactions should now enable us to predict when to expect 1,4-addition products in our ongoing studies with other electrophilic reagents.

Relative Rate Studies. Relative rate studies between each of the substituted 3,4-dihydro-2*H*-pyrans (**2a–g, 3a,b**) and 3,4-dihydro-2*H*-pyran (1) were performed to measure the effect of substituents on the reactivity of the 3,4-dihydro-2*H*-pyran ring system. Equimolar mixtures of each substituted 3,4-dihydro-2*H*-pyran (**2a–g, 3a,b**) and 3,4-dihydro-2*H*-pyran (1) were allowed to compete for an equivalent of *tert*-butyl hypochlorite. The relative ratio (GLC analyses) of product material from the substituted 3,4-dihydro-2*H*-pyran and 3,4-dihydro-2*H*-pyran was then used to determine the reactivity of the substituted pyran relative to 3,4-dihydro-2*H*-pyran. These results are summarized in Table III. There is a substantial difference in the relative rates of the variously substituted 3,4-dihydro-2*H*-pyrans that must be directly attributable to the substituent or substituents. The most significant seems to be the deactivating effect of the axial alkoxy and phenoxy groups at the anomeric C-2 position and the activating effect of an alkyl group at C-6 toward electrophilic

Table III. Relative Reactivity of Substituted 3,4-Dihydro-2*H*-pyrans[a]

Pyran	Substituent(s)	Relative rate to Pyran 1[a]	Relative rate to Pyran 2a	Relative rate to Pyran 3a
1		1.00		
2a	2-Methoxy-	0.25 ± 0.08[b]	1.00	
2b	2-Methoxy-6-methyl-	3.60 ± 1.40	14.40	
2c	2-Methoxy-5-methyl-	1.42 ± 0.14	5.68	
2d	2-Methoxy-4-methyl-	1.43 ± 0.13	5.72	
2e	2-Methoxy-2-methyl-	0.80 ± 0.21	3.20	
2f	2-Methoxy-2,6-dimethyl-	5.40 ± 1.08	21.60	
2g	2-Ethoxy-3-methyl-	0.48 ± 0.13	1.92	
3a	2-Phenoxy-	0.24 ± 0.08		1.00
3b	2-Phenoxy-6-methyl-	5.10 ± 1.03		21.25

[a] Relative rate study conditions are those described in the Experimental Section for 2-methoxy-2-methyl-3,4-dihydro-2*H*-pyran (**2e**) vs. 3,4-dihydro-2*H*-pyran (**1**). [b] Standard deviation using experiments performed in triplicate.

reactions. Thus, the field effects for the axial alkoxy and phenoxy groups are electron withdrawing and for the methyl substituent directly attached to the unsaturation are electron donating as one might have predicted.[8]

When the reactivity of the alkyl-substituted 2-alkoxy- and 2-phenoxy-3,4-dihydro-2*H*-pyrans are calculated relative to 2-methoxy- (**2a**) and 2-phenoxy-3,4-dihydro-2*H*-pyran (**3a**), respectively, the effects of alkyl substituents on the 2-alkoxy- and 2-phenoxy-3,4-dihydro-2*H*-pyran ring systems are much more obvious (see Table III). For example, placing a methyl group on the 2-methoxy-3,4-dihydro-2*H*-pyran ring system at C-6 enhances the rate by a factor of ca. 14, and on the 2-phenoxy-3,4-dihydro-2*H*-pyran ring system by a factor of ca. 21.

Rate enhancements of this magnitude help explain our previous observations that peracid oxidations of 2-alkoxy-3,4-dihydro-2*H*-pyrans, which lead to 1,4-oxidation products, are sluggish compared to 2-alkoxy-6-methyl-3,4-dihydro-2*H*-pyrans,[2a] that, although 2-alkoxy-6-methyl-3,4-dihydro-2*H*-pyrans condense slowly with dimethyl acetylenedicarboxylate in refluxing toluene, 3,4-dihydro-2*H*-pyran (**1**) and its 2-alkoxy derivatives such as **2a** are seemingly inert,[2b] and, finally, that the 1,4-addition of tetracyanoethylene[9] to 2-alkoxy-6-methyl-3,4-dihydro-2*H*-pyrans occurs at ambient temperatures and become exceedingly exothermic while the 2-alkoxy-3,4-dihydro-2*H*-pyrans react slowly with no detectable exotherm and require no external cooling.[2c] In addition, these relative reactivities will help in predicting which type of substituted 2-alkoxy-3,4-dihydro-2*H*-pyrans might be expected to react with various electrophilic reagents.

Experimental Section[10]

General Comments. The 2-alkoxy- (**2a–g**) and 2-phenoxy-3,4-dihydro-2*H*-pyrans (**3a,b**) were prepared by a general method previously described.[3,4] Dihydropyrans **1** and **2a** are available from Aldrich Chemical Co. The *tert*-butyl hypochlorite was prepared,[11] dried over $CaCl_2$, and stored in the dark below 0 °C. For best results it is recommended to use freshly prepared *t*-BuOCl. All solvents were reagent grade. All reactions were performed in oven-dried glassware under a static argon atmosphere. Gas chromatography analyses (GLC) were performed on 200 × 0.3 cm (i.d.) glass columns packed with 3.8% silicon gum rubber SE-30 (methyl) supported on 60–80 mesh Chromosorb W (AW, DMCS) or 10% silicon gum rubber XE-60 (25% cyanoethyl, methyl) or on a 150 × 0.3 cm (i.d.) glass column packed with 20% Carbowax 20M supported on 80–100 mesh Chromosorb W (AW, DMCS). Distillations were accomplished with a short-path or Kugelrohr apparatus; all boiling points are uncorrected. Column chromatography was performed on 60–100 mesh Floridin magnesium silicate (Florisil) or 70–230 mesh silica gel 60 (Merck) columns by eluting with pentane–Et_2O or hexane–benzene–Et_2O. The assigned structure of each product (or mixture) was consistent with the spectral data. Composition analyses (±0.4% for C, H, Cl) for all new dihydropyrans (**2c–g** and **3a,b**) and all new 1,2-addition products (**5c–e, 5g,** and **6a,b**) were submitted to the editor. The 1,4-addition products were too unstable for satisfactory composition analyses. Significant data on all new compounds are included in the Experimental Section. Representative experiments are described to illustrate these reactions.

2-Methoxy-2-methyl-3,4-dihydro-2*H*-pyran (2e). A 200-mL glass pressure bottle[12] that contained a mixture of 22.4 g (0.4 mol) of freshly distilled propenal, 200 mg of dihydroquinone, and 140 mg of anhydrous $ZnCl_2$ was charged with ca. 70 mL (0.8 mol) of 2-methoxypropene and heated with agitation at 60 °C for 1.5 h. After allowing the pressure vessel to cool, the vessel was carefully opened and the reaction mixture was removed, washed twice with water, and dried over anhydrous $MgSO_4$. Distillation yielded 30.8 g (61%) of **2e** as a colorless oil: bp 37 °C (16 Torr); $n^{23}D$ 1.4395; IR ($CHCl_3$) 1657 cm^{-1}; NMR (100 MHz, $CDCl_3$) δ 6.19 (1 H, d with further fine splitting, J = 7 Hz), 4.85–4.66 (1 H, m), 3.25 (3 H, s), 2.40–1.40 (4 H, complex m), 1.38 (3 H, s); mass spectrum *m/e* (rel intensity) 128 (M^+, 19), 113 (3), 97 (24), 72 (100), 42 (53).

Reaction of 2-Methoxy-2-methyl-3,4-dihydro-2*H*-pyran (2e) with *tert*-Butyl Hypochlorite. To a stirred solution (0–5 °C) of 640 mg (5.0 mmol) of 2-methoxy-2-methyl-3,4-dihydro-2*H*-pyran (**2e**) in 7.5 mL of methanol was slowly added 600 mg (5.5 mmol) of *tert*-butyl hypochlorite in 1.5 mL of methanol. After 10 min the reaction mixture was partitioned between brine and petroleum ether. The organic layer was separated, washed with water, and dried ($MgSO_4$). Removal of solvent in vacuo afforded 590 mg of a pale-yellow oil. Analysis (GLC) of the oil indicated a 20:80 mixture of 1,2-addition product **5e** and 1,4-addition product **7b.** Column chromatography (silica gel) afforded 90 mg (9%) of **5e** and 398 mg (54%) of **7b** as colorless oils.

3-Chloro-2,6-dimethoxy-6-methyltetrahydropyran (5e): bp 97–99 °C (14 Torr); NMR (100 MHz, $CDCl_3$) δ 4.42 (1 H, d, $J_{2,3}$ = 8.5 Hz, pseudoaxial anomeric proton at C-2), 3.62 (1 H, d of q, J = 8.5, 2.1, 1.6 Hz, C-3 proton), 3.51 (3 H, s), 3.27 (3 H, s), 2.30–1.90 (2 H, m), 1.90–1.50 (2 H, m), 1.34 (3 H, s); mass spectrum *m/e* (rel intensity) 165 (2), 163 (7), 136 (2), 134 (4), 105 (7), 94 (2), 92 (8), 72 (100), 42 (16).

2-Chloro-5-hexanon-1-al (7b):[13] bp 105 °C (13 Torr); IR ($CHCl_3$) 1733, 1717 cm^{-1}; NMR (60 MHz, $CDCl_3$) δ 9.43 (1 H, d, J = 1.8 Hz), 4.33 (1 H, t of d, J = 7, 1.8 Hz), 2.90–2.45 (2 H, m), singlet at 2.19 (3 H) superimposed on a multiplet at 2.45–1.50 (2 H); mass spectrum *m/e* (rel intensity) 148 (M^+, 0.5), 113 (5), 112 (5), 83 (9), 58 (26), 43 (100).

Relative Rate Study using Competitive Conditions. 2-Methoxy-2-methyl-3,4-dihydro-2*H*-pyran (2e) vs. 3,4-Dihydro-2*H*-pyran (1). To a stirred solution (0–5 °C) of 128 mg (1 mmol) of 2-methoxy-2-methyl-3,4-dihydro-2*H*-pyran (**2e**) and 84 mg (1 mmol) of 3,4-dihydro-2*H*-pyran (**1**) in 2 mL of methanol was added 108 mg (1 mmol) of *tert*-butyl hypochlorite in 0.2 mL of methanol. After 3 min the reaction mixture was worked up, as described above for the reaction with **2e,** and afforded an oil that was analyzed by GLC. The relative ratio of product material from **2e** vs. **1** was calculated by measuring the relative areas of all product peaks and then correcting these areas using predetermined response factors. These response factors[14] were determined under the analysis conditions by the use of standard solutions of known concentrations of each product or product mixture from each dihydropyran.

2-Methoxy-3,4-dihydro-2*H*-pyran (2a): bp 51 °C (80 Torr); $n^{23}D$ 1.4445; NMR (100 MHz, CCl_4) δ 6.11 (1 H, d with further fine splitting, J = 6 Hz), 4.77 (1 H, t, J = 3 Hz, equatorial anomeric proton), 4.73–4.54 (1 H, m), 3.37 (3 H, s), 2.22–1.62 (4 H, m).

2-Methoxy-6-methyl-3,4-dihydro-2*H*-pyran (2b): bp 52–54 °C (18 Torr); $n^{23}D$ 1.4447; NMR (100 MHz, CCl_4) δ 4.82 (1 H, t, J = 3 Hz, equatorial anomeric proton), 4.53–4.37 (1 H, m), 3.37 (3 H, s), 1.68 (3 H, broad singlet with fine splitting) superimposed on 2.20–1.50 (4 H, complex m).

2-Methoxy-5-methyl-3,4-dihydro-2*H*-pyran (2c):[5c] bp 56 °C (14 Torr); $n^{23}D$ 1.4483; IR (film) 1678 cm^{-1}; NMR (100 MHz, $CDCl_3$) δ 6.09–5.95 (1 H, m), 4.79 (1 H, t, J = 2.8 Hz, equatorial anomeric proton), 3.39 (3 H, s), 2.30–1.60 (4 H, m), 1.52 (3 H, br s); mass spectrum *m/e* (rel intensity) 128 (M^+, 50), 97 (37), 58 (42), 43 (80), 41 (100), 39 (75).

2-Methoxy-4-methyl-3,4-dihydro-2*H*-pyran (2d): bp 79–80 °C

(100 Torr); n^{23}_D 1.4420; NMR (100 MHz, CCl_4) δ 6.12 (0.6 H, q, J = 6.8, 2.3 Hz) overlapping 6.04 (0.4 H, q, J = 7.0, 2.3 Hz), 4.76 (0.4 H, t, J = 3 Hz, equatorial anomeric proton, trans isomer) overlapping 4.72 (0.6 H, q, J = 7.5, 2.5 Hz, axial anomeric proton, cis isomer), 4.59–4.40 (1 H, m), 3.39 (1.8 H, s, cis isomer), 3.36 (1.2 H, s, trans isomer), 2.50–2.10 (1 H, m), 2.10–1.70 (1 H, m), 1.60–1.20 (1 H, m), 1.02 (1.8 H, d, J = 6.8 Hz, cis isomer) overlapping 0.98 (1.2 H, d, J = 7.0 Hz, trans isomer); mass spectrum m/e (rel intensity) 128 (M^+, 100), 113 (51), 97 (34), 96 (28), 58 (98).

2-Methoxy-2,6-dimethyl-3,4-dihydro-2*H*-pyran (2f): bp 42 °C (1.5 Torr); n^{23}_D 1.4453; IR (film) 1685 cm^{-1}; NMR (100 MHz, $CDCl_3$) δ 4.56–4.42 (1 H, m), 3.21 (3 H, s), 1.70 (3 H, s with fine spitting), and 1.35 (3 H, s) superimposed on 2.30–1.30 (4 H, complex m); mass spectrum m/e (rel intensity) 142 (M^+, 34), 111 (40), 72 (100), 43 (60), 42 (40).

2-Ethoxy-3-methyl-3,4-dihydro-2*H*-pyran (2g): bp 52 °C (11 Torr); n^{22}_D 1.4380; IR (film) 1627 cm^{-1}; NMR (100 MHz, CCl_4) δ 6.04 (1 H, d of q, J = 6.3, 1.9 Hz), 4.71 (0.7 H, d, J_{ee} = 1.3 Hz, equatorial anomeric proton, trans isomer), and 4.51 (0.3 H, d, J_{ea} = 4.1 Hz, equatorial anomeric proton, cis isomer) superimposed on 4.75–4.45 (1 H, m), a complex system for the anisochronous ethoxy methylenes in the cis and trans isomers that includes four overlapping quartets centered at 3.86 (0.3 H, two overlapping q, J = 9.9, 7.2 Hz) and 3.76 (0.7 H, two overlapping q, J = 9.9, 7.2 Hz) and four overlapping quartets centered at 3.52 (0.7 H, two overlapping q, J = 9.0, 7.1 Hz) and 3.42 (0.3 H, two overlapping q, J = 9.0, 7.1 Hz), 2.40–1.35 (3 H, complex m), 1.18 (3 H, t, J = 7.2 Hz), 0.95 (3 H, d, J = 6.2 Hz); mass spectrum m/e (rel intensity) 142 (M^+, 15), 97 (14), 86 (70), 58 (100).

2-Phenoxy-3,4-dihydro-2*H*-pyran (3a): bp 98 °C (1 Torr); n^{20}_D 1.5931; IR (film) 1653 cm^{-1}; NMR (100 MHz, $CDCl_3$) δ 7.44–6.90 (5 H, complex m), 6.25 (1 H, d of q, J = 6.3, 2.7, 1.7 Hz), 5.69 (1 H, t, J = 3.1 Hz, equatorial anomeric proton), 4.95–4.75 (1 H, m), 2.60–1.80 (4 H, complex m); mass spectrum m/e (rel intensity) 176 (M^+, 18), 148 (3), 120 (9), 94 (56), 82 (100), 77 (20), 55 (45).

2-Phenoxy-6-methyl-3,4-dihydro-2*H*-pyran (3b): bp 104 °C (0.8 Torr); n^{20}_D 1.5316; IR (film) 1690 cm^{-1}; NMR (100 MHz, $CDCl_3$) δ 7.40–6.86 (5 H, complex m), 5.64 (1 H, t, J = 3.1 Hz, equatorial anomeric proton), 4.72–4.56 (1 H, m), 1.69 (3 H, singlet with fine splitting) superimposed on 2.56–1.46 (4 H, complex m); mass spectrum m/e (rel intensity) 190 (M^+, 10), 120 (7), 97 (100), 96 (95), 43 (75).

3-Chloro-2,6-dimethoxy-3-methyltetrahydropyran (5c): bp 115 °C (13 Torr); NMR (100 MHz, $CDCl_3$) δ 4.86 (0.3 H, superficial t, equatorial anomeric proton at C-6), 4.72 (0.7 H, t, J = ~4 Hz, equatorial anomeric proton at C-6), 4.65 (0.7 H, s, anomeric proton at C-2), 4.44 (0.3 H, s, anomeric proton at C-2), 3.52 (0.9 H, s), 3.46 (2.1 H, s), 3.44 (2.1 H, s), 3.42 (0.9 H, s), 2.20–1.95 (2 H, m), 1.95–1.60 (2 H, m), 1.55 (0.9 H, s), 1.52 (2.1 H, s); mass spectrum m/e (rel intensity) 195 (0.6), 193 (1.9), 165 (2), 163 (6), 136 (5), 134 (15), 108 (7), 106 (21), 85 (6), 71 (13), 58 (100).

3-Chloro-2,6-dimethoxy-4-methyltetrahydropyran (5d): bp 100–110 °C (11 Torr); NMR (100 MHz, CCl_4) δ 4.75 (0.7 H, superficial d, J = ~1.5 Hz, anomeric proton at C-2), 4.57 (0.7 H, d of d, J = 9.4, 3.7 Hz, anomeric proton at C-6) superimposed on 4.62 (0.3 H, t, J = ~2 Hz, anomeric proton at C-6) and 4.58 (0.3 H, d, J = ~1.5 Hz, anomeric proton at C-2), 3.89–3.81 (0.3 H, m), 3.78–3.69 (0.7 H, m), four singlets at 3.43, 3.41, 3.38, and 3.36 (6 H), 2.00–1.07 (3 H, complex m), 1.02 (2.1 H, d, J = 6.5 Hz) overlapping 0.99 (0.9 H, d, J = 6.5 Hz); mass spectrum m/e (rel intensity) 195 (1.2), 193 (3.7), 165 (5), 163 (16), 136 (1.8), 134 (5), 121 (5), 119 (14), 94 (21), 92 (67), 85 (32), 58 (100).

3-Chloro-6-ethoxy-2-methoxy-5-methyltetrahydropyran (5g): bp 90–95 °C (11 Torr); NMR (100 MHz, CCl_4) δ 4.63 (0.5 H, d, J = 3.1 Hz, anomeric proton at C-6), 4.53 (0.5 H, d, J = 2.8 Hz, anomeric proton at C-6), 4.40 (0.5 H, d, J = 3.8 Hz, anomeric proton at C-2), 4.35 (0.5 H, d, J = 5.5 Hz, anomeric proton at C-2), 4.05–3.64 (2 H, complex m), 3.40 (1.5 H, s) and 3.38 (1.5 H, s) superimposed on 3.61–3.21 (1 H, complex m), 2.30–2.05 (1 H, m), 2.05–1.35 (2 H, m), 1.19 (1.5 H, t, J = 7.4 Hz) overlapping 1.16 (1.5 H, t, J = 7.4 Hz), 0.93 (3 H, broadened d, J = ~6 Hz); mass spectrum m/e (rel intensity) 210 (M^+, 0.4), 208 (M^+, 1.1), 179 (1.5), 177 (4.5), 165 (3), 163 (8), 99 (12), 94 (32), 92 (100), 86 (88), 72 (18), 58 (46).

3-Chloro-2-methoxy-6-phenoxytetrahydropyran (6a): Fraction no. 4 (col chrom), crystals (1st major isomer): mp 62–65 °C; NMR (60 MHz, $CDCl_3$) δ 7.50–6.80 (5 H, complex m), 5.58–5.36 (1 H, superficial t, anomeric proton at C-6), 4.60 (1 H, d, J = 4 Hz, anomeric proton at C-2), 3.82–4.14 (1 H, m), 3.27 (3 H, s), 2.84–1.45 (4 H, m). Fraction no. 8 (col chrom), oil (ca. 17% 1st major isomer and 83% 2nd major isomer): NMR (100 MHz, $CDCl_3$) δ 7.40–6.90 (5 H, complex m), 5.64 (0.8 H, t, J = 3.0 Hz, anomeric proton at C-6) overlapping 5.58 (0.2, t, J = 3.0 Hz, anomeric proton at C-6), 4.71 (0.8 H, d, J = 7.2 Hz, anomeric proton at C-2) overlapping 4.67 (0.2 H, d, J = 7.0 Hz, anomeric proton at C-2), 3.82 (1 H, q, J = ~7 Hz), 3.35 (~2.5 H, s), 3.34 (~0.5 H, s), 2.44–2.13 (2 H, m), 2.13–1.80 (2 H, m); mass spectrum m/e (rel intensity) 244 (M^+, 4), 242 (12), 213 (1.6), 211 (5), 184 (2), 182 (6), 151 (30), 149 (92), 120 (100), 107 (36), 105 (67), 94 (34), 71 (66).

3-Chloro-2-methoxy-2-methyl-6-phenoxytetrahydropyran (6b): NMR (100 MHz, $CDCl_3$) δ 7.29–6.72 (5 H, complex m), 5.42 (0.60 H, t, J = 2.5 Hz, anomeric proton at C-6), 5.34 (0.15 H, t, J = 3.2 Hz, anomeric proton at C-6) overlapping 5.28 (0.25 H, q, J = 8.5, 3.2 Hz, anomeric proton at C-6), 4.08 (0.60 H, q, J = 5, 3.5 Hz), 3.93 (0.25 H, q, J = 5, 3.5 Hz), 3.82 (0.15 H, q, J = 5, 4 Hz), 3.38 (0.45 H, s), 3.36 (0.75 H, s), 3.03 (1.8 H, s), 2.95–2.0 (2 H, m), 2.0–1.65 (2 H, m), 1.49 (0.45 H, s), 1.48 (0.75 H, s), 1.42 (1.8 H, s); mass spectrum m/e (rel intensity) 258 (M^+, 2), 256 (M^+, 6), 243 (0.7), 241 (2), 227 (5), 225 (14), 199 (3), 197 (4), 184 (1), 182 (3), 165 (34), 163 (100), 133 (36), 120 (81), 119 (65), 94 (22), 85 (35), 77 (15), 43 (19).

3-Chloro-6,6-dimethoxy-2-heptanone (8a) and 5-Chloro-6,6-dimethoxy-2-heptanone (8b) Mixture.[15] Column chromatography (Florisil) yielded a 75:25 mixture of 3a/3b: IR (film) 1720 cm^{-1}; NMR (60 MHz, $CDCl_3$) δ 4.31 (0.75 H, q, J = 9, 6 Hz), 3.41 (0.25 H, q, J = 9, 2 Hz), 3.20 (6 H, s), 2.84–2.45 (0.25 H, m), 2.38 (2.25 H, s), 2.18 (0.75 H, s) superimposed on 2.4–1.4 (3.5 H, br m), 1.31 (3 H, br s); mass spectrum m/e (rel intensity) 127 (6), 121 (0.5), 119 (1.5), 100 (12), 89 (4), 78 (6), 58 (23), 43 (100).

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Registry No.—**1,** 110-87-2; **2a,** 4454-05-1; **2b,** 28194-35-6; **2c,** 38328-65-3; *cis*-**2d,** 38113-08-5; *trans*-**2d,** 38320-49-9; **2e,** 64331-96-0; **2f,** 64331-95-9; *cis*-**2g,** 60582-02-7; *trans*-**2g,** 60582-03-8; **3a,** 2720-53-8; **3b,** 64332-01-0; *cis*-**4,** 6559-29-1; *trans*-**4,** 6559-30-4; **5a,** 64331-94-8; **5b** isomer 1, 64331-93-7; **5b** isomer 2, 61092-60-2; **5b** isomer 3, 61092-61-3; **5b** isomer 4, 64331-92-6; **5c,** 64331-91-5; **5d,** 64331-90-4; **5e,** 64332-02-1; **5g,** 64332-00-9; **6a** isomer 1, 64331-99-3; **6a** isomer 2, 64331-98-2; **6a** isomer 3, 64331-97-1; **6a** isomer 4, 64331-83-5; **6b** isomer 1, 64331-82-4; **6b** isomer 2, 64331-81-3; **6b** isomer 3, 64331-80-2; **6b** isomer 4, 64331-79-9; **7a,** 61092-68-0; **7b,** 64331-78-8; **8a,** 64331-77-7; **8b,** 64331-76-6; *tert*-butyl hypochlorite, 507-40-4; methyl vinyl ether, 107-25-5; isopropenyl methyl ether, 116-11-0; *cis*-1-ethoxy-1-propene, 4696-25-7; *trans*-1 ethoxy-1-propene, 4696-26-8; phenyl vinyl ether, 766-94-9; propenal, 107-02-8; methyl vinyl ketone, 4170-30-3; 2-methylpropenal, 78-85-3; *trans*-2-butenal, 123-73-9; 5-chloro-6,6-dimethoxy-2-hexanone, 64331-75-5; 3-chloro-2,6-heptadione, 19995-88-1.

References and Notes

(1) Part 6 in the series "The Chemistry of 2-Alkoxy-3,4-dihydro-2*H*-pyrans". For part 5, see: A. J. Duggan and S. S. Hall, *J. Org. Chem.*, **42,** 1057 (1977).
(2) (a) S. S. Hall and H. C. Chernoff, *Chem. Ind. (London)*, 896 (1970); (b) S. S. Hall and A. J. Duggan, *J. Org. Chem.*, **39,** 3432 (1974); (c) Unpublished observations in this laboratory (S. S. Hall, A. J. Duggan, and J. S. R. Zilenovski) on the reactivity of tetracyanoethylene with 2-alkoxy- and 2-alkoxy-6-methyl-3,4-dihydro-2*H*-pyrans.
(3) (a) R. I. Longley, Jr., and W. S. Emerson, *J. Am. Chem. Soc.*, **72,** 3079 (1950); (b) W. E. Parham and H. E. Holmquist, *ibid.*, **73,** 913 (1951); (c) C. W. Smith, D. G. Norton, and S. A. Ballard, *ibid.*, **73,** 5267 (1951); (d) W. S. Emerson, G. H. Birum, and R. I. Longley, Jr., *ibid.*, **75,** 1312 (1953).
(4) Y. Morita, R. Kikumoto, H. Ohba, A. Nakamura, K. Fukuda, and T. Nomura, U.S. Patent 3 816 464 (1974); German Patent 2 163 515 (1973); Japanese Patent 7 368 573 (1973).
(5) (a) Vu Moc Thuy and P. Maitte, *Bull. Soc. Chim. Fr.*, 4423 (1970); (b) N. M. Shetchmann, E. A. Victorama, E. A. Karakhanov, N. Kvorostakina, and N. S. Zefirov, *Dokl. Akad. Nauk. SSSR, Ser. Khim.*, **196,** 367 (1971); (c) G. Descotes, J.-C. Martin, and N. Mathicolonis, *Bull. Soc. Chim. Fr.*, 1077 (1972); (d) G. Desimoni, L. Astolfi, M. Cambieri, A. Gamba, and G. Tacconi, *Tetrahedron*, **29,** 2627 (1973); (e) A. J. Duggan and S. S. Hall, *J. Org. Chem.*, **40,** 2234 (1975).
(6) (a) J. T. Edward, *Chem. Ind. (London)*, 1102 (1955); (b) R. U. Lemieux and N. J. Chü, Abstracts, 133rd National Meeting of the American Chemical Society, San Francisco, Calif., April 1958, p 31N; (c) E. L. Eliel, N. L. Allinger, S. J. Argyl, and G. A. Morrison, "Conformational Analysis", Wiley-Interscience, New York, N.Y., 1965, p 375; (d) S. Wolfe, A. Rauk, L. M. Tel, and I. G. Csizmadia, *J. Chem. Soc. B*, 136 (1971).
(7) J. Castells, F. Camps, and F. Sanchez Ferrando, *An. R. Soc. Esp. Fis. Quim., Ser. B*, **66,** 175 (1970).
(8) J. March, "Advanced Organic Chemistry", McGraw-Hill, New York, N.Y., 1977, pp 20–22, and references cited therein.
(9) J. K. Williams, D. W. Wiley, and B. C. McKusick, *J. Am. Chem. Soc.*, **84,**

2210 (1962).
(10) The IR spectra were determined with a Perkin-Elmer Model 237B and a Beckmann Model IR-9 infrared recording spectrophotometers. The NMR spectra were determined at 60 MHz with a Varian Associates Model T-60 and at 100 MHz with a Varian Associates Model HA-100 NMR spectrometers. The chemical shifts are expressed in δ values (parts per million) relative to a Me_4Si internal standard. The mass spectra were obtained with a Consolidated Electronics Corp. Model 110-21B and a Varian Associates Model CH5 mass spectrometer. Gas chromatographic analyses (GLC) were performed on a Hewlett-Packard Model 402 high-efficiency chromatograph with a flame-ionization detector attached to a Hewlett-Packard Model 3380A integrator.
(11) M. J. Mintz and C. Walling, *Org. Synth.*, **49**, 9 (1969).
(12) Washed in dilute NaOH solution, rinsed three times with distilled water, and oven dried immediately prior to use.
(13) Refluxing **7b** in methanol for 3 h yielded 5-chloro-6,6-dimethoxy-2-hexanone (89%): IR (film) 1717 cm^{-1}; NMR (60 MHz, $CDCl_3$) δ 4.36 (1 H, d, J = 6 Hz), 4.13–3.77 (1 H, complex m), 3.49 (6 H, s), 2.97–2.44 (2 H, complex m), 2.20 (3 H, s) superimposed on 2.44–1.46 (2 H, complex m); mass spectrum *m/e* (rel intensity) 165 (4), 164 (2), 163 (14), 162 (5), 127 (15), 107 (19), 105 (53), 75 (100), 47 (46), 43 (62).
(14) D. Jentzsch, "Gas Chromatographie", Franckh'sche Verlagshandlung, Stuttgart, 1968, pp 61–62 and 98.
(15) This mixture is rather unstable. A refrigerated methanolic solution of **8a** and **8b** slowly decomposed to *m*-cresol in a few weeks. A stirred mixture of **8a** and **8b** in methanol at 25 °C for 4 days yielded 3-chloro-2,6-heptadione (83%): IR (film) 1725 cm^{-1}; NMR (60 MHz, $CDCl_3$) δ 4.33 (1 H, d of d, J = 8, 5.5 Hz), 2.9–2.4 (2 H, m), 2.35 (3 H, s) and 2.18 (3 H, s) superimposed on 2.4–1.7 (2 H, m), which after 24 h storage neat in a refrigerator had also decomposed to *m*-cresol.

Isoquinolines. 7.[1] Reaction of Ethylene Oxide with Isoquinolines. Novel Isoquinolone and Oxazolidine Formation

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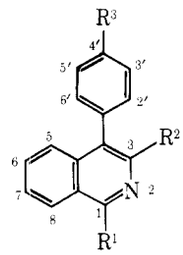
Aprotic deamination of 3-amino-1-bromo-4-nitrophenylisoquinoline (**6**) followed by partial reduction yielded 4-aminophenyl-1-bromoisoquinoline (**8**), and complete reduction yielded 4-aminophenylisoquinoline (**9**). Isoquinolines **8** and **9** when treated with excess ethylene oxide in acetic acid afforded 4-[*p*-bis(2-hydroxyethyl)amino]phenyl-2-(2-hydroxyethyl)-1-isoquinolone (**15a**) and 2-(2-acetoxyethyl)-4-[*p*-bis(2-hydroxyethyl)amino]phenyl-1-isoquinolone (**15b**). Evidence for a mechanism involving an oxazolidine intermediate is presented. When isoquinoline (**17**) was similarly treated with ethylene oxide, 2,3-dihydro-10b*H*-oxazolo[2,3-*a*]isoquinoline (**19**) was obtained.

In the course of preparing potential CNS antitumor agents, we recently reported that amine **1** afforded diol **2**, whereas amine **3** yielded a mixture of diol **4** and triol **5** when treated with excess ethylene oxide.[1] In continuation of this



Compd	R^1	R^2	R^3
1	Br	$NHCOCH_3$	NH_2
2	Br	$NHCOCH_3$	$N(CH_2CH_2OH)_2$
3	H	$NHCOCH_3$	NH_2
4	H	$NHCOCH_3$	$N(CH_2CH_2OH)_2$
5	H	$NH(CH_2)_2OH$	$N(CH_2CH_2OH)_2$
6	Br	NH_2	NO_2
7	Br	H	NO_2
8	Br	H	NH_2
9	H	H	NH_2
10a	Br	H	$N(CH_2CH_2OH)_2$
10b	Br	H	$NHCH_2CH_2OH$
10c	H	H	$N(CH_2CH_2OH)_2$

program we required isoquinolines lacking the 3-amino group. The deamination of **6**[2a] with isoamyl nitrite in dry THF yielded **7** (27–43%).[2b] Stannous chloride reduction of **7** yielded **8** (81%), and catalytic hydrogenation of **8** gave **9** (90%). Treatment of either **8** or **9** with excess ethylene oxide in acetic acid overnight at room temperature did not yield the expected isoquinoline diols **10a** or **10c** but gave isoquinolones **15a** and **15b** as shown in Scheme I. In particular, **8** afforded a mixture of **15a** and **15b** in 51 and 25% yield, respectively. The yield of **15a** from **9** was somewhat lower (34%). The reaction between isoquinolines and related compounds with epoxides has been previously observed,[3a–d] but only in one instance was isoquinolone formation noted.[4]

With the addition of excess sodium acetate to the reaction, monoacetate **15b** constituted as much as 50% of the product mixture. Compound **15b** could not be chromatographed on silica gel without extensive (50%) hydrolysis to **15a** and appeared thermally labile toward intermolecular acylation. Evidence for the intermolecular acylation was provided by the mass spectrum of **15b** which at 60 °C showed the expected molecular ion (*m/e* 410) and $M^+ - CH_2OH$ (*m/e* 379) as prominent peaks, but at 110 °C peaks assignable to a diacetate (*m/e* 452 M^+, *m/e* 421 $M^+ - CH_2OH$) and triacetate (*m/e* 494 M^+) of **15a** were also observed. In view of the instability of **15b**, mixtures of **15a** and **15b** were gently saponified to **15a** and treated with $SOCl_2$ in CH_3CN to give mustard **16** (49%) as shown in Scheme I.

A suggested mechanism for the transformation of **8** (X = Br) and **9** (X = H) to isoquinolones **15a** and **15b** is incorporated in Scheme I. Pertinent to the mechanism are the following observations: Diol **10a** can be isolated as the initial product in the reaction of **8** and ethylene oxide after short (2 h) reaction times. Prior to this study, solvent incorporation into isoquinolone products had not been reported, but the isolation and characterization of isoquinolone **15b** implicates intermediates **12–14** in the mechanism and precludes consideration of **11** as an intermediate in isoquinolone formation. Although a hydride transfer (X = H) has been suggested as the penultimate step in the reaction of **9** and ethylene oxide, the observation that no isoquinolone products are formed under conditions that rigorously exclude oxygen would argue for an oxidation step (X = OH or OOH) prior to oxazolinium

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