1447 (s), 690 cm^{-1} (s); nmr (CCl_4) δ 1.97 (s, 3, CH_3), 6.9–7.35 (m, 10, aromatic).

Anal. Calcd for $C_{15}H_{13}N$: C, 86.92; H, 6.32; N, 6.76. Found: C, 87.02; H, 6.44; N, 6.56.

(*R*)-(+)-**2-Phenyl-2-butylisonitrile.**—Following the general procedure, 7.85 g (0.044 mol) of (*R*)-(+)-*N*-(1-methyl-1-phenylpropyl)formamide in 150 ml of DMF yielded, after distillation, 6.51 g (0.041 mol, 92%) of the optically pure isonitrile: bp 96.97° (9 mm); $[\alpha]^{24}_{5461}$ +2.87 ± 0.07° (*c* 3, dioxane); ir (neat) 2125 (s), 1498 (m), 755 (s), 692 cm^{-1} (s); nmr (CCl_4) δ 0.84 (t, 3, J = 7 Hz, CH_3), 1.67 (t, 3, J = 2 Hz, CH_3), 1.90 (m, 2, J_{AB} = 7 Hz, J_{AC} = 2 Hz, CH_2), 7.40 (m, 5, aromatic).

Anal. Calcd for $C_{11}H_{13}N$: C, 82.97; H, 8.23. Found: C, 83.08; H, 8.45.

(*E*)-**1,2-Diphenylvinylisonitrile.**—Similarly, 14.2 g (0.0637 mol) of (*E*)-*N*-(1,2-diphenylvinyl)formamide in 400 ml of DMF was treated with the DMF–$SOCl_2$ reagent, however, at −60°. The mixture was allowed to stir at −50° for 10 min prior to the addition of sodium carbonate. The mixture was taken up in 50:50 ether–pentane for the washings, and the organic layer was dried over sodium sulfate. Evaporation of the solvent gave 10.9 g (0.0532 mol, 84%) of the isonitrile, bp 109° dec (0.03 mm), which contained only a trace of the formamide. Prior to use small quantities were purified by molecular distillation at high vacuum to prevent decomposition (the isonitrile darkens on standing): ir (neat) 2105 (s), 1620 (w), 1372 (m), 689 cm^{-1}; nmr ($CDCl_3$) δ 6.94 (s, vinyl), 6.9–7.5 (m, aromatic). Mass spectral data are shown in Table II.

Anal. Calcd for $C_{15}H_{11}N$: C, 87.77; H, 5.40; N, 6.83. Found: C, 87.46; H, 5.44; N, 6.68.

(±)-**2,2-Diphenyl-1-methylcyclopropylisonitrile.**—In a like manner, 4.68 g (0.0187 mol) of racemic *N*-(2,2-diphenyl-1-methylcyclopropyl)formamide in 93 ml of DMF was treated with the thionyl chloride–DMF reagent. After the mixture had stirred for 16 hr, the contents of the flask were rinsed into a beaker with THF; 400 ml of cold water was added slowly at 0°. The precipitate was collected, washed with water, and dried to yield 4.35 g of material, mp 109–115°. Crystallization from chloroform–petroleum ether gave 3.84 g (0.017 mol, 88%) of the isonitrile: mp 118–129°; ir (CCl_4) 2120 (s), 1494 (s), 684 cm^{-1} (s); nmr ($CDCl_3$) δ 1.38 (s, 3, CH_3), 1.56 (d, 1, J_{AB} = 6 Hz, HC**H**), 1.93 (d, 1, J_{AB} = 6 Hz, **H**CH), 7.1–7.9 (m, 10, aromatic).

TABLE II

Peak	Obsd mass	Calcd mass	Anal.	Rel intensity
P + 1	206.0913	206.0924	$C^{13}C_{14}H_{11}N$	19.7
P	205.0884	205.0890	$C_{15}H_{11}N$	100.0
P − H	204.0788	204.0812	$C_{15}H_{10}N$	92.4
P − HCN	178.0745	178.0782	$C_{14}H_{10}$	32.4
P − C_7H_5N	102.0430	102.0469	C_8H_6	24.5
P − C_8H_6N	89.0378	89.0391	C_7H_5	23.6

Anal. Calcd for $C_{17}H_{15}N$: C, 87.52; H, 6.48; N, 6.00. Found: C, 87.47; H, 6.58; N, 5.94.

(*R*)-(−)-**2,2-Diphenyl-1-methylcyclopropylisonitrile.**—Similarly, 0.8354 g (0.00329 mol) of optically pure (*R*)-(−)-*N*-(2,2-diphenyl-1-methylcyclopropyl)formamide in 25 ml of DMF was treated with 0.28 ml (0.038 mol) of thionyl chloride in 1.5 ml of DMF followed by 0.81 g (0.0076 mol) of sodium carbonate. The precipitate, 0.726 g, mp 140–149°, was crystallized from benzene–petroleum ether: yield 0.537 g (0.00231 mol, 70%); mp 150.5–152°; $[\alpha]^{25}_{5461}$ −166 ±1° (*c* 1, $CHCl_3$).

Anal. Calcd for $C_{17}H_{15}N$: C, 87.52; H, 6.48; N, 6.00. Found: C, 87.47; H, 6.58; N, 5.94.

Registry No.—**3**, 32529-00-3; (*R*)-(+)-2-amino-2-phenylbutane, 10181-67-6; *N*-(1,1-diphenylethyl)formamide, 32528-92-0; (*R*)-(+)-*N*-(1-methyl-1-phenylpropyl)formamide, 32528-93-1; (±)-1-carbazido-2,2-diphenyl-1-methylcyclopropanol, 32528-94-2; (*R*)-(−) isomer, 32528-96-4; (*E*)-2,3-diphenylpropenoyl azide, 32528-95-3; (±)-*N*-(2,2-diphenyl-1-methylcyclopropyl)formamide, 32528-97-5; (*R*)-(−) isomer, 32528-98-6; (*E*)-*N*-(1,2-diphenylvinyl)formamide, 32528-99-7.

The Base-Catalyzed Dehydrohalogenation of Two Isomeric 3,4-Dibromo-2-ethoxytetrahydropyrans[1]

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The reactions of the two isomers, 3α,4β-dibromo-2α-ethoxytetrahydropyran (**1a**) and 3α,4β-dibromo-2β-ethoxytetrahydropyran (**1b**), with refluxing ethanolic sodium ethoxide have been examined. Total yields of isolable products were 19–38%. Compound **1a** afforded *trans*-5,6-diethoxy-5,6-dihydro-2*H*-pyran (**6**), *cis*-2,5-diethoxy-5,6-dihydro-2*H*-pyran (**7c**), and *trans*-2,5-diethoxy-5,6-dihydro-2*H*-pyran (**7t**) in the relative proportion 5.6:4.8:1.6, along with a trace of 3-bromo-2-ethoxy-5,6-dihydro-2*H*-pyran (**2**). Compound **1b** furnished the same products **6**, **7c**, **7t**, and **2** in the relative proportion 1:1:16:6. The diethoxydihydropyrans were stable under the reaction conditions, but compound **2** reacted further to produce **6**, **7c**, and **7t** in the proportion 1.4:3.5:22.9.

It has been reported[4] that the reaction of hot ethanolic potassium hydroxide or sodium ethoxide with a mixture of the two isomers of 3,4-dibromo-2-ethoxytetrahydropyran **1a** and **1b** produces in poor yield a mixture containing 3-bromo-2-ethoxy-5,6-dihydro-2*H*-pyran (**2**) and a compound suggested to be 2,4-diethoxy-5,6-dihydro-2*H*-pyran (**3**) (Scheme I). Prolonged treatment of the mixture of dibromides **1a** and **1b** under these conditions led to a bromine-free product from which was isolated by distillation a diethoxydihydropyran **3**. Compound **2** was isolated in 50% yield by dropping a solution of **1a** and **1b** in toluene onto molten potassium hydroxide. Neither of the structures **2** or **3** was definitely established. Compound **2** was assigned its structure on the basis of the analogy to the behavior of α,β-dibromocarbonyl compounds in dehydrobromination reactions. A tentative assignment of the structure of **3** was based on the finding that catalytic hydrogenation of **3** gave a diethoxytetrahydropyran **5** (evidence for one double bond in **3**) and that acid hydrolysis of **3**, followed by phenylhydrazone formation from the hydrolysis product, gave a substance which contained one ethoxy group.

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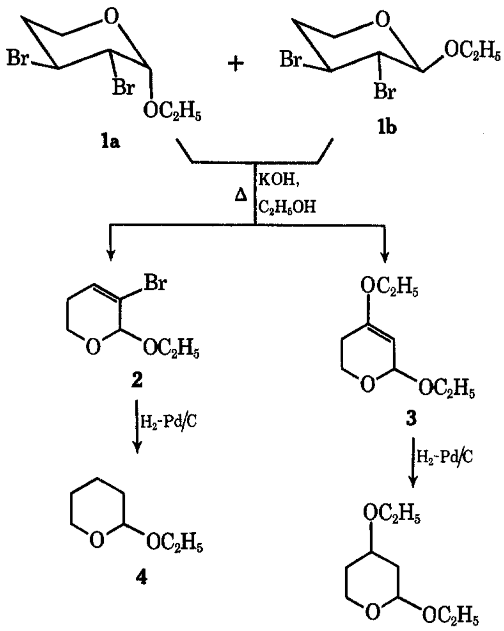
[1] Partly from the thesis of Sweet, submitted in 1968 to the Faculty of Graduate Studies, University of Alberta, as part of the requirements for the Ph.D. degree.

[2] Postdoctoral Fellow, 1968–1970.

[3] Author to whom correspondence should be directed.

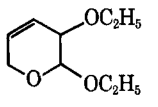
[4] G. F. Woods and S. C. Temin, *J. Amer. Chem. Soc.*, **72**, 139 (1950).

SCHEME I



In view of the ease with which enol ethers are hydrolyzed under acidic conditions,[5,6] it is expected that **3** would cleave not only at the acetal function but also at the enol ether linkage, with loss of both ethoxy groups. Hence structure **3** is not consistent with the hydrolysis data.[4]

It is also known that 1,2-dibromocyclohexane, treated with ethanolic base, is converted in reasonably good yield to 3-ethoxycyclohexene.[7] Accordingly under similar conditions, dehydrohalogenation of **1a** and **1b** might be expected to give one or more of the α,β-unsaturated ethers **6–9** as well as the monobromo compound **2**. In view of our experience and that of McElvain, *et al.*,[8] that the anomeric proton of acetals is difficult to remove by ordinary bases, the likelihood that **8** is formed seems remote but cannot be ruled out.



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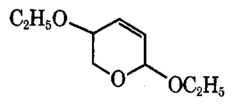

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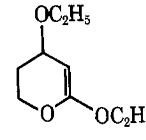

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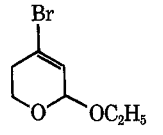

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Our interest in dihydro- and tetrahydropyrans, as well as the above anomalies, prompted a reexamination of the reactions of the dibromides **1a** and **1b** with alcoholic base. This paper reports the results obtained.

Results and Discussion

The mixture of the two isomeric 3,4-dibromo-2-ethoxytetrahydropyrans **1a** and **1b** was prepared according to published directions.[4,9] Although the minor isomer **1b**, a solid, could be separated readily in pure form by crystallization from a mixture of **1a** and **1b**, the major isomer **1a**, a liquid, was freed from contaminating **1b** only with much difficulty.

When **1a**, contaminated with **1b** to the extent of 10%, was heated for 24 hr in a refluxing solution of sodium ethoxide in dry ethanol, a 30% yield of colorless liquid was obtained by fractional distillation. This was found by gas–liquid chromatography (glc) to consist of four substances in the molar ratio of 2.7:2.3:1:1. These were separated first by preparative glc into three fractions, the first of which was a mixture of the two major products, while the second and third were the two individual minor products. Subsequent glc with a 5-ft column separated the two major products. These four products are shown in Scheme II as compounds **6**, **7c**, **7t**, and **2**, respectively. The proportions obtained are shown in Table I.

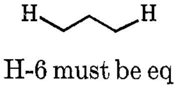
TABLE I

MOLAR PROPORTIONS OF PRODUCTS OBTAINED FROM THE BASE-CATALYZED DEHYDROBROMINATION OF 1a, 1b, AND 2

Starting material	Reaction conditions[a]	Overall yield, %	Molar proportion of 6	7c	7t	2
90% 1a 10% 1b	Δ for 24 hr	30	2.7	2.3	1	1
1a	Δ for 24 hr	19	5.6	4.8	1.6	Trace
1b	Δ for 24 hr	38	1	1	16	6
2	Δ for 24 hr	35	1.4	3.5	22.9	5.7

[a] All reactions were done in ethanol solvent containing sodium ethoxide.

The larger of the two major products was identified as *trans*-5,6-diethoxy-5,6-dihydro-2*H*-pyran (**6**) on the basis of (a) the infrared spectrum which shows no absorption in the region characteristic of vinyl ethers,[10,11] (b) the elemental analysis, (c) agreement of the 100-MHz proton magnetic resonance (pmr) spectrum and its analysis by double irradiation spin decoupling, with structure **6**, and (d) its conversion by catalytic hydrogenation to a compound identical with authentic *trans*-2,3-diethoxytetrahydropyran. The conformation of **6** is considered to be that shown in Scheme II, on the basis of (a) the long-range coupling between H-6 and H-4 requiring the geometric arrangement[12]



which suggests that H-6 must be equatorial, (b) the *anomeric effect*[13] which gives preference to the conformation in which the anomeric alkoxy group is axial or quasiaxial.[13,14]

The smaller of the two major products is considered to be *cis*-2,5-diethoxy-5,6-dihydro-2*H*-pyran (**7c**) on the basis of the following information. (a) The infrared spectrum shows no absorption in the region char-

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(5) J. Wislicenus, *Justus Liebigs Ann. Chem.*, **192**, 106 (1878).

(6) A. Ledwith and H. J. Woods, *J. Chem. Soc.*, 753 (1966).

(7) C. J. Gogek, R. Y. Moir, J. A. McRae, and C. B. Purves, *Can. J. Chem.*, **29**, 938 (1951).

(8) S. M. McElvain, R. L. Clarke, and G. D. Jones, *J. Amer. Chem. Soc.*, **64**, 1966 (1942).

(9) R. M. Srivastava, F. Sweet, T. P. Murray, and R. K. Brown, *J. Org. Chem.*, **36**, 3633 (1971).

(10) R. J. Ferrier, *J Chem. Soc.*, 5443 (1964).

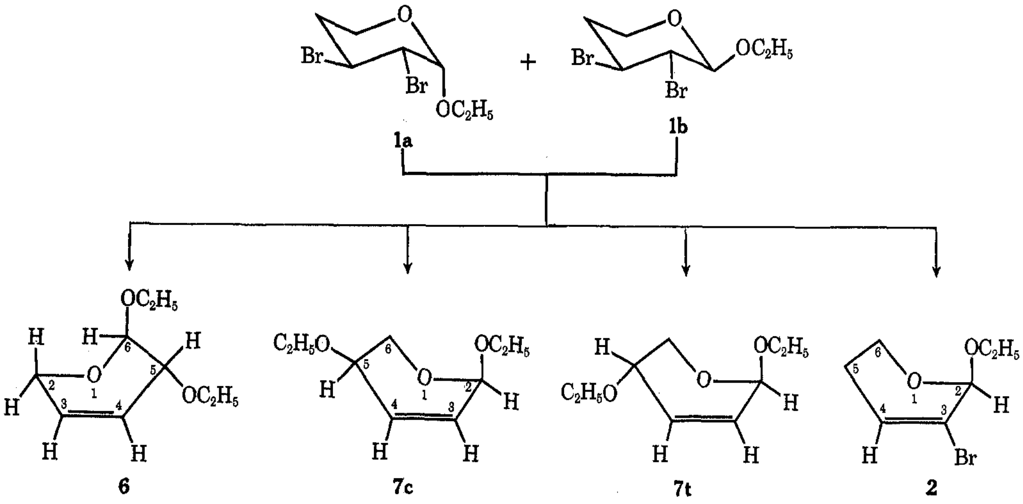
(11) M. Sharma and R. K. Brown, *Can. J. Chem.*, **44**, 2825 (1966).

(12) (a) E. W. Garbisch, Jr., *Chem. Ind. (London)*, 1715 (1964); (b) A. Rassat, C. W. Jefford, J. M. Lehn and B. Waegell, *Tetrahedron Lett.*, No. 5, 233 (1964).

(13) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Wiley, New York, N. Y., 1965, pp 375–377.

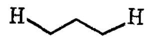
(14) R. M. Srivastava and R. K. Brown, *Can. J. Chem.*, **49**, 1339 (1971).

SCHEME II



acteristic of vinyl ethers.[10,11] (b) The elemental analysis agrees with such a structure. (c) Analysis of the 100-MHz pmr spectrum using double irradiation to locate the signal positions of the various protons agrees with such a structure and shows that the anomeric proton, H-2, is situated on a carbon atom attached to a –HC=CH– group. As well, the unusually large allylic coupling ($\sim$1.8 Hz) between H-3 and H-5 indicates that H-5 is quasiaxial because it is only in such an orientation that the σ–π overlap is maximum, generating such a large allylic coupling.[15a] (d) The preference for the conformation which has the quasiaxial orientation of the anomeric alkoxy group.[13,14] It is the *cis*- but not the *trans*-2,5-diethoxy-5,6-dihydro-2*H*-pyran which accommodates observations c and d.

The third product obtained in the proportion 1:7 is considered to be *trans*-2,5-diethoxy-5,6-dihydro-2*H*-pyran (**7t**) on the basis of the following evidence. (a) Elemental analysis agrees with such a structure. (b) The infrared spectrum shows no absorption in the region characteristic of vinyl ethers.[10,11] (c) The mass spectrum showed *m/e* 171, one unit less than the expected molecular weight. However, the exceptional ease with which the anomeric hydrogen (H-2) can be removed to provide a resonance-stabilized carbonium ion[15b] would account for this one unit difference. (d) The preference for the conformation possessing the quasiaxial orientation of the anomeric alkoxy group.[13,14] (e) The 100-MHz pmr spectrum and spin-decoupling experiments support structure **7t**, showing that the anomeric proton H-2 is located on a carbon atom attached to a –CH=CH– group. A small long-range coupling ($\sim$1 Hz) between H-4 and the anomeric proton H-2 indicates that these two protons are in the required



arrangement[12] and hence H-2 is equatorial. Also, the small couplings of the two C-6 protons, with H-5 ($J_{5,6\text{ ax or eq}} \sim 3$ Hz and $J_{5,6\text{ eq or ax}} \sim 2.2$ Hz) require H-5 to be gauche to both C-6 protons. In the conformation in which the anomeric alkoxy group is quasiaxial, H-5 can be gauche to both C-6 protons only if the C-5 alkoxy group is quasiaxial and hence H-5 is quasiequatorial. Only structure **7t** satisfies the above observations and since compounds **7t** and **7c** have different retention times on the glc, as well as different pmr spectra, yet their elemental analyses are identical, it is clear that they must be cis and trans isomers.

The last compound was identified as 3-bromo-2-ethoxy-5,6-dihydro-2*H*-pyran (**2**) on the basis of the following evidence. (a) The elemental analysis agreed with structure **2**. (b) The mass spectrum gave a signal at *m/e* 206 with a ^{81}Br satellite signal at *m/e* 208 of about the same intensity. (c) The infrared spectrum (neat) shows a band of medium strength of 1650 cm^{-1} for C=CBr. This agrees with the observation of absorption at 1650 cm^{-1} for the double bond in 1-bromocyclohexene.[16] (d) The 100-MHz pmr spectrum and its analysis with the aid of double irradiation spin decoupling clearly agrees with structure **2**. The quartet for the lone olefinic proton signal, with couplings of 6.0 and 2.8 Hz with the two high-field protons on C-5, shows that the bromine atom is attached to C-3 and not to C-4. If the proton were attached to C-3, its signal would be a doublet which might be split again to a small extent (<1.5 Hz) due to long-range or to allylic coupling. (e) The anomeric effect[13,14] would cause the structure to assume the conformation in which the C-2 alkoxy group is quasiaxial as shown by **2**. (f) Hydrogenation of **2** produces 2-ethoxytetrahydropyran. The evidence above confirms the structural assignment previously suggested[4] for this monobromo compound.

Following the structural determination of the products obtained from the dehydrohalogenation of **1a** containing 10% of **1b**, pure **1a** was heated for 24 hr in refluxing ethanol containing sodium ethoxide. A liquid was obtained in 19% yield, analyzing for a mixture of **6**, **7c**, **7t**, and **2** in the proportion 5.6:4.8:1.6: trace. When the period of reflux was reduced to 8 hr, the crude liquid obtained showed **2** was present in greater than trace amount.

Pure **1b** treated similarly for 24 hr gave a liquid (38% yield) which was found to be a mixture of **6**, **7c**, **7t**, and **2** in the proportion 1:1:16:6, respectively.

[15] (a) N. S. Bhacca and D. H. Williams, "Applications of Nmr Spectroscopy in Organic Chemistry," Holden-Day, San Fransisco, Calif., 1964, p 108; (b) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretations of Mass Spectra of Organic Compounds," Holden-Day, San Franscico, Calif., 1964, p 52.

[16] G. Chiurdoglu, R. Ottinger, J. Reisse, and A. Toussaint, *Spectrochim. Acta*, **18**, 215 (1962).

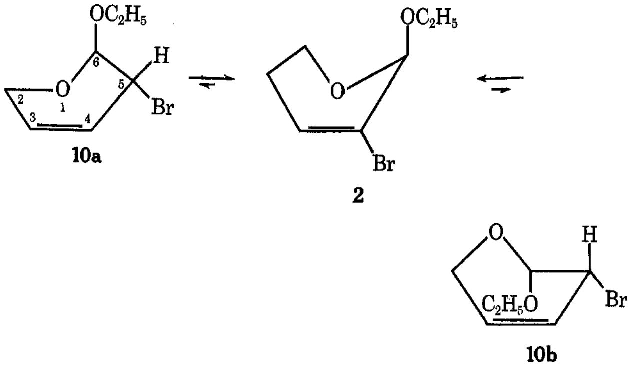
Finally, although compounds **6**, **7c**, and **7t** were found to be stable to this alkaline treatment, compound **2** was unstable. Pure **2**, heated for 20 hr under the usual alkaline conditions, provided a liquid mixture which contained **6**, **7c**, **7t**, and **2** in the proportion 1.4:3.5:22.9:5.7, along with a small amount (proportion ~1.0) of an unknown material. The above information is assembled in Table I for comparison.

How the dibromides **1a** and **1b** are converted by base to the four products shown in Scheme II is not at all clear. Since **1b** produces a high proportion of **7t** along with a fair quantity of **2** plus a minor amount of **6** and **7c**, and because **2** itself is converted under similar conditions primarily to **7t** along with a small amount of **6** and **7c**, it is reasonable to assume that **1b** first is converted into **2** which subsequently reacts further. This does not appear to be the procedure followed by **1a**, since here the bulk of the product is a nearly equal quantity of **6** and **7c**. However, the low yields (19–38%) obtained make such speculation unsatisfactory.

It is well established that base-catalyzed dehydrohalogenations occur more readily if the relevant hydrogen and halogen atoms can assume a mutual trans diaxial relationship. Only in the alternate chair form can either **1a** or **1b** provide such a favorable spatial arrangement, and this would lead to an allylic bromide 5-bromo-6-ethoxy-5,6-dihydro-2*H*-pyran (**10**), which then must form the four products of Scheme II. However it is known that base-catalyzed cis elimination of halogen acid can also occur[17] and hence **1a** and **1b** could produce **2** directly by this route. The isomeric vinyl bromide, 4-bromo-2-ethoxy-5,6-dihydro-2*H*-pyran (**9**), has not been found, although it may have been produced and been less stable than the 3-bromo isomer **2**.

How **2** is induced to form the diethoxydihydropyrans **7t**, **6**, and **7c** is not clear. Since the interconversion of allylic and vinyl chlorides has been shown to occur in the presence of a strong base[18] it is possible that here also a base-catalyzed isomerization to an allyl bromide (*e.g.*, **10**) takes place (Scheme III). Such a rearrangement of a vinyl bromide to an allyl bromide has been suggested to explain the formation of an enamine from 2-bromo-3-methylbenzo[*b*]thiophene 1,1-dioxide.[19] The allyl bromide then could provide **6** by an S$_{\mathrm{N}}$2 reaction and **7c** and **7t** by an S$_{\mathrm{N}}$2′ reaction with ethoxide ion. The proportion of these products would depend upon the detailed structure of the allyl bromide. The S$_{\mathrm{N}}$2′ reactions of allylic systems and their relation to the S$_{\mathrm{N}}$2 reactions have been examined and reported.[19–22]

SCHEME III



Our attempts to isolate an intermediate allyl bromide have been unsuccessful. Reaction of **1a** (containing 10% of **1b**) with sodium ethoxide in ethanol at room temperature for 25 hr gave a product consisting of starting material containing a small amount of olefinic product. When the room temperature reaction was extended for 7 days, the product contained essentially **6** and **7c**.

Experimental Section

Boiling points are uncorrected. For liquids isolated in very small amounts by glc, the boiling points were determined by both micro boiling point technique and by heating them very slowly in a two-bulb micro distillation apparatus under vacuum, with the lower bulb immersed in a heating bath. When the liquid began to distill from the lower bulb, the bath temperature was recorded. The latter method was preferred to the usual micro boiling point method since in trial comparative runs on compounds of known boiling point it gave results more in accord with the correct values.

Analysis of products by glc was carried out with an F & M Model 700 apparatus or with an Aerograph Autoprep, Model A-700. The following columns were employed. (a) Butanediol succinate (BDS, 20%) on Gas-Chrom P (60-80 mesh) in a column $^1/_8$ in. × 12 ft. For preparative work a 0.25 in. × 6 ft (or 12 ft) column was used (BDS-P). (b) Carbowax 6000 (25%) on Gas-Chrom W (60–80 mesh) in a $^1/_8$ in. × 12 ft column (CW). For preparative work a column 0.25 in. × 6 ft (or 12 ft) was employed (CW-P). Helium was the carrier gas.

Elemental analyses were made by Mrs. Darlene Mahlow of this department. The 60-MHz pmr spectra were made by Mr. Robert Swindlehurst, and the 100-MHz pmr spectra and spin-decoupling experiments were done by Mr. Glen Bigam, both of this department. The instruments employed were the Varian A-60 MHz and Varian HR-100 MHz spectrometers. Tetramethylsilane was the reference compound. The solvent was $CDCl_3$ unless otherwise stated. All the J values reported in this paper are the approximate coupling constants determined by observation of the signal spacings on the spectrum. The infrared spectra were obtained by Mr. Robert Swindlehurst, using a Perkin-Elmer Model 421 grating spectrometer. Solvents were removed by rotary evaporator under vacuum unless otherwise stated.

***trans*-2,3-Diethoxytetrahydropyran.**—Following the general alkylation procedure previously described[23] but reversing the sequence of addition of reagents, 10 g (0.068 mol) of *trans*-2-ethoxy-3-hydroxytetrahydropyran[24] in 75 ml of dry 1,2-dimethoxyethane (DME) was added slowly (1 hr) to a stirred mixture of 11.7 g (0.075 mol) of ethyl iodide and 1.86 g (0.078 mol) of sodium hydride in 375 ml of DME kept at ~30°. The mixture was stirred overnight and then worked up as described.[23] Ordinary fractional distillation followed by a second fractional distillation with a spinning-band column gave a colorless liquid boiling at 79–80° (10 mm), yield 7.7 g (65%). Analysis by glc on the BDS column showed a slight contamination (<5%) by starting material. Use of the 12 ft preparative column (BDS-P) at 160° with a helium gas flow rate of 150 ml/min gave pure material of the same boiling point: $n^{22}\mathrm{D}$ 1.4318; 100-MHz pmr τ 5.56 (d, 1, anomeric, $J_{2,3} \sim 4$ Hz), 6.00–6.70 (m, 6, HCO),

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[17] H. C. Stevens and O. Grummitt, *J. Amer. Chem. Soc.*, **74**, 4876 (1952).

[18] M. Tanabe and R. A. Walsh, *ibid.*, **85**, 3522 (1963).

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6.82 (m, 1, HCO for H-3, $J_{3,4\ \mathrm{eq\ or\ ax}} \sim 3.0$ Hz, $J_{3,4\ \mathrm{ax\ or\ eq}} \sim 6.0$ Hz), 7.80–8.80 (m, 4, HC aliphatic), 8.78 (t, 3, HC aliphatic, $J \sim 7$ Hz), and 8.81 (t, 3, HC aliphatic, $J \sim 7$ Hz).

Anal. Calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 61.79; H, 10.64.

Isomerization of *trans*-2,3-Diethoxytetrahydropyran to the Cis Isomer.—A solution of 1.5 g (0.0086 mol) of *trans*-2,3-diethoxytetrahydropyran in 25 ml of absolute ethanol containing 100 mg of *p*-toluenesulfonic acid monohydrate was heated under reflux for 4 hr. To the cooled solution was added sufficient 10% ethanolic potassium hydroxide to neutralize the acid. Removal of the solvent by fractional distillation left a liquid which contained some colorless solid. An ether solution (100 ml) of this total residue was washed with water (four 5-ml portions) and dried (Na_2SO_4). The filtered solution was freed from ether by fractional distillation to provide a light yellow liquid (1.1 g, 73%). Analysis by glc on a BDS column at 125° (helium flow rate, 50 ml/min) showed two overlapping peaks in the approximate area ratio 2:1. The two peaks in order of appearance were due to *trans*- and *cis*-2,3-diethoxytetrahydropyran, respectively. This isomeric mixture boiled at 77–78° (10 mm), $n^{24}\mathrm{D}$ 1.4318.

Anal. Calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 62.12; H, 10.46.

The 60-MHz pmr spectrum showed two anomeric proton signals, one at τ 5.21 (d, $J \sim 3.5$ Hz) for the cis isomer, the other at τ 5.55 (d, $J \sim 4.0$ Hz) for the trans isomer. The signal area ratio was 2:1.

3-Bromo-2-ethoxy-5,6-dihydro-2*H*-pyran (2).—This was prepared essentially by the method of Woods and Temin.[4] From 16.5 g (0.057 mol) of a 3:1 isomeric mixture of **1a** and **1b** there was obtained 7.7 g of a yellowish liquid. Glc on a BDS column showed two peaks in the area ratio 3:1. Fractional distillation by a Vigreux column gave two fractions.

The first fraction (4.48 g, 38%) was an oil: bp 84–85° (8 mm): $n^{26}\mathrm{D}$ 1.4880 [lit.[4] bp 88° (10 mm), $n^{21}\mathrm{D}$ 1.4900; lit.[25] bp 100–101° (20 mm), $\eta^{21.5}\mathrm{D}$ 1.4903].

Anal. Calcd for $C_7H_{11}O_2Br$: C, 40.60; H, 5.36; Br, 38.60. Found: C, 40.65; H, 5.37; Br, 38.47.

The infrared spectrum (neat) showed a band at 1650 cm^{-1} (C═C—Br); 100-MHz pmr τ 3.77 (q, 1, HC═C< for H-4, $J_{2,4} < -0.5$ Hz, $J_{4,5\ \mathrm{eq}} \sim 6.0$ Hz, $J_{4,5\ \mathrm{ax}} \sim 2.8$ Hz), 5.18 (apparent singlet, 1, anomeric for H-2, $J_{2,5\mathrm{ax}} \sim 1.5$ Hz, $J_{2,6\ \mathrm{eq}} \sim 1$ Hz), 5.90–6.30 (m, 1, HCO for H-6 ax, $J_{6\ \mathrm{ax},\ 6\ \mathrm{eq}} \sim -12$ Hz), 6.10–6.40 (m, 1, HCO for H-6 eq), 6.30–6.64 (m, 2, HCO), 7.40–7.80 (m, 1, HC aliphatic for H-5 ax, $J_{5\ \mathrm{ax},\ 5\ \mathrm{eq}} \sim -18$ Hz, $J_{5\ \mathrm{ax},\ 6\ \mathrm{ax}} \sim 11$ Hz, $J_{5\ \mathrm{ax},\ 6\ \mathrm{eq}} \sim 6$ Hz), 7.90–8.20 (m, 1, HC aliphatic for H-5 eq, $J_{5\ \mathrm{eq},\ 6\ \mathrm{ax}} \sim 4$ Hz, $J_{5\ \mathrm{eq},\ 6\ \mathrm{eq}} \sim 1.5$ Hz), 8.77 (t, 3, HC aliphatic, $J \sim 7$ Hz). The computer simulation, using the observed chemical shifts and coupling constants, gave a spectrum closely similar to that obtained experimentally.

The second fraction (2.05 g, 12.4%) was a light yellow liquid, bp 108–110° (6.5 mm). The 60-MHz pmr spectrum indicated it to be essentially **1a** containing a small amount of impurity (unknown).

Dehydrobromination of 3,4-Dibromo-2-ethoxytetrahydropyran (1a and 1b).—Sodium metal (8 g, 0.35 g-atom) was dissolved in 150 ml of dry ethanol. To this, cooled to room temperature, was added a solution of 25 g (0.09 mol) of **1a** containing 10% of the isomer **1b**,[9] in 25 ml of dry ethanol. The mixture was heated under reflux for 24 hr, during which time it developed a deep amber color, and sodium bromide precipitated. Part of the solvent (100 ml) was removed by fractional distillation at atmospheric pressure, and the residue when diluted with 200 ml of ether deposited more of the salt. The solid was separated and the filtrate diluted with 200 ml more of ether, was washed with water (eight 25-ml portions) and dried ($MgSO_4$). This was then separated from the solid and freed from solvent. Fractional distillation of the residue gave fraction a, 2.8 g, bp 94° (12 mm), and fraction b, 1.8 g, bp 90° (9 mm), combined yield ~30% assuming both fractions to be a diethoxydihydropyran. Analysis by glc (CW column at 150°, helium flow rate, 55-60 ml/min) showed both fractions to be the same, giving three main peaks (A, B, C) in the area ratio 5:1:1 in order of appearance, plus two very minor peaks of shorter retention time (1.5 and 8.5 min) comprising <3% of the combined areas. Preparative glc (CW-P column, 12 ft), under the same conditions as for the glc analysis above, separated the three major peaks having retention times of 13, 16.5, and 18.5 min, respectively. Only 10-μl injections could be made at a time for effective separation.

The **major component A** on reinjection gave the same characteristic broad peak observed when the above mixture was analyzed by glc, bp 83–85° (10 mm) by the two-bulb method.

Anal. Calcd for $C_9H_{16}O_3$: C, 62.76; H, 9.37. Found: C, 63.04; H, 9.44.

The infrared spectrum showed no absorption between 1610 and 1690 cm^{-1} (no vinyl ether) and no absorption above 3100 cm^{-1} (no OH).

The 60-MHz pmr spectrum showed two anomeric proton signals, one at τ 5.08 (m, $W_{1/2} \sim 5$ Hz), the other at τ 5.22 (d, $J \sim 2.7$ Hz) in the area ratio 0.85:1.0, respectively, indicative of two substances.

Glc with a 0.25 in. × 50 ft column containing 10% neopentyl glycol sebacate on Gas-Chrom W (acid washed) at 150° and with helium gas flow rate of 60 ml/min separated the two components but only if no greater than 20 μl amounts were used for each injection. Four peaks of retention times 51, 55, 61, and 64 min were observed. The first two were the major peaks and were separated and isolated in small amount, while the latter two very minor peaks could not be isolated. Quantities of the major components obtained were insufficient for a boiling point determination.

The first of the two major components of A.—The infrared spectrum (neat) showed very weak bands at 1732, 1700, and 1592 cm^{-1}. The Raman spectrum (neat) showed a medium intensity band at 1664 cm^{-1} (>C═C< stretching); 100-HMz pmr τ 3.95–4.30 (m, 2, HC═C for H-3 and H-4), 5.24 (d, 1, anomeric for H-6, $J_{5,6} \sim 2.5$ Hz), 5.87 (m, 2, HCO, $W_{1/2} \sim 7$ Hz), 5.98–6.60 (m, 6, HCO), 8.75 (t, 3, HC aliphatic, $J \sim 7$ Hz), and 8.78 (t, 3, HC aliphatic, $J \sim 7$ Hz).

Anal. Calcd for $C_9H_{16}O_3$: C, 62.76; H, 9.37. Found: C, 62.94; H, 9.68.

The second of the two major components of A.—No elemental analysis due to the minute amount isolated. The infrared spectrum (neat) showed the same three weak bands at 1730, 1700, and 1592 cm^{-1} as did the first major component of A; 100-MHz pmr τ 3.98 (d, 1, HC═C for H-4, $J_{3,4} \sim 10$ Hz, $J_{2,4} \sim 1$ Hz), 4.28 (d of t, 1, HC═C for H-3, $J_{2,3} \sim 2$ Hz, $J_{3,5} \sim 1.8$ Hz), 5.11 (m, 1, anomeric for H-2, $W_{1/2} \sim 6$ Hz), 5.80–6.70 (m, 7, HCO), 8.88 (t, 3, HC aliphatic, $J \sim 7$ Hz), and 8.91 (t, 3, HC aliphatic $J \sim 7$ Hz).

Component B.—Colorless liquid; reinjection gave one symmetrical peak in the glc. The amount of B was insufficient for a boiling point determination.

Anal. Calcd for $C_9H_{16}O_3$: C, 62.76; H, 9.37. Found: C, 62.40, 62.29; H, 9.77, 9.47.

The infrared spectrum (neat) showed very weak absorption at 1740 cm^{-1}; the mass spectrum *m/e* 171 for M − 1; 100-MHz pmr τ 3.89 (q, 1, HC═C for H-4, $J_{3,4} \sim 10$ Hz, $J_{4,6} \sim 1$ Hz, $J_{2,4} \sim 1$ Hz), 4.07 (q, 1, HC═C for H-3, $J_{2,3} \sim 2.5$ Hz), 5.02 (d, 1, HC, anomeric for H-2), 5.92 (q, 1, HCO for H-6 ax, $J_{6\ \mathrm{ax},\ 6\ \mathrm{eq}} \sim 12$ Hz, $J_{5,6\ \mathrm{ax}} \sim 3$ Hz), 6.13 (q, 1, HCO for H-6 eq, $J_{5,6\ \mathrm{eq}} \sim 2.2$ Hz), 6.15–6.62 (m, 5, HCO), 8.88 (t, 3, HC, aliphatic, $J \sim 7$ Hz), and 8.90 (t, 3, HC aliphatic, $J \sim 7$ Hz).

Component C.—Colorless liquid, bp 85–86° (8 mm).

Anal. Calcd for $C_7H_{11}O_2Br$: C, 40.60; H, 5.36; Br, 38.60. Found: C, 40.44; H, 5.44; Br, 38.87.

The mass spectrum had *m/e* 206, *m/e* 208 (^{81}Br satelite). Infrared and 100-MHz pmr spectra were identical with those obtained for compound **2** prepared above.

Hydrogenation of Component A.—A quantity of A (1.53 g, 0.0089 mol), isolated by glc, was dissolved in 50 ml of 95% ethanol. To this was added 500 mg of 5% palladium on charcoal. The mixture was shaken with hydrogen at 40 psi for 2 hr at room temperature. The catalyst was removed and the solvent separated by frational distillation. The weight of the residual oil indicated nearly quantitative yield of hydrogenated product. Glc analysis (BDS column at 120°, helium flow rate, 60 ml/min) showed only two peaks in the area ratio 1.0:0.85 with retention times of 7.5 and 9 min, respectively. Separation was achieved with a BDS-P column (0.25 in × 12 ft) at 140° with a helium gas flow rate of 72–75 ml/min, and 25-μl quantities for each injection. The material appearing first was *trans*-2,3-diethoxytetrahydropyran, a colorless liquid, bp 76° (10 mm), $n^{21}\mathrm{D}$ 1.4317.

Anal. Calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 62.15; H, 10.52.

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The material of longer retention time, *cis*-2,5-diethoxytetrahydropyran, by glc analysis was found to contain ~5% of *trans*-2,3-diethoxytetrahydropyran, bp 75° (10 mm), n^{22}_{D} 1.4313.

Anal. Calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 61.91; H, 10.55.

The 5% impurity could be removed by injection of 10-μl quantities into a BDS-P column (0.25 in. × 6 ft) at 120°; helium gas flow rate, 50 ml/min: bp (pure *cis*-2,5-diethoxytetrahydropyran) 75–76° (10 mm); n^{22}_{D} 1.4314; 100-MHz pmr τ 5.37 (t, 1, anomeric for H-2, $J_{2,3\ \mathrm{ax\ or\ eq}} \sim 2.7$ Hz, $J_{2,3\ \mathrm{eq\ or\ ax}} \sim 2.3$ Hz), 6.10–6.90 (m, 7, HCO), 8.0–8.7 (m, 4, HC aliphatic), 8.86 (t, 3, HC aliphatic, $J \sim 7$ Hz), and 8.90 (t, 3, HC aliphatic, $J \sim 7$ Hz).

Dehydrobromination of Pure 1b.—Pure **1b** (25 g, 0.09 mol) was dehydrobrominated as described for the 9:1 mixture of **1a** and **1b** above, except that 80 ml of ethanol was used to dissolve **1b**. The reaction afforded 8 g of brown liquid. Fractional distillation gave 6 g of colorless liquid, bp 88–89° (10 mm). Glc analysis showed this to be a mixture of A, B, and C in the ratio 1:18:3, yield ~38%.

Hydrogenation of a Mixture of Components B and C Obtained from the Dehydrobromination of Pure 1b.—A mixture of B and C (1.35 g), separated from A by glc, was hydrogenated for a period of 4 hr at 40 psi in ethanol containing 0.75 g of potassium hydroxide (to prevent acid-catalyzed isomerization) and 500 mg of 5% palladium on charcoal. The reaction mixture was worked up as in the hydrogenation of A above, affording 0.7 g of crude liquid. Analysis by glc (BDS column at 145°, helium gas flow, 100 ml/min) showed only two peaks in the area ratio of 1.0:7.5. The first peak (minor component) showed a retention time identical with that of 2-ethoxytetrahydropyran.[26] The major component, *trans*-2,5-diethoxytetrahydropyran, was isolated by glc with a BDS-P column (0.25 in. × 12 ft): bp 85–86° (10 mm); n^{25}_{D} 1.4318; mass spectrum *m/e* 174; 100-MHz pmr τ 5.38 (q, 1, anomeric for H-2, $J_{2,3\ \mathrm{eq}} \sim 2.5$ Hz, $J_{2,3\ \mathrm{ax}} \sim 3.5$ Hz), 6.00–6.80 (m, 7, HCO), 7.85–8.25 (m, 2, HC aliphatic for H-3 eq and H-4 eq[27,28]), 8.25–8.65 (m, 2, HC aliphatic for H-3 ax and H-4 ax[27,28]), and 8.80 (t, 6, HC aliphatic, $J \sim 7$ Hz).

Anal. Calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 61.96; H, 10.62.

Dehydrobromination of Pure 1a.—Pure **1a** (45 g, 0.16 mol) was dehydrobrominated as described for the 9:1 mixture of **1a** and **1b** above. The brown liquid (12 g) was distilled to give three fractions: (a) 4.2 g, bp 86–87° (9.5 mm); (b) 0.75 g, bp 85° (7.5 mm); and (c) 0.15 g, bp 68–70° (2.5 mm). The combined yield was 19%. Glc of each fration with a CW column at 150° showed each to be composed of components A and B plus a trace of C. Overall proportion of A:B ~ 0:0.8.

Isomerization of *trans*-2,5-Diethoxytetrahydropyran.—A solution of 400 mg of *trans*-2,5-diethoxytetrahydropyran (obtained from the hydrogenation of components B and C above) in 7 ml of absolute ethanol containing 50 mg of *p*-toluenesulfonic acid monohydrate was heated under reflux for 4 hr. The cooled solution was basified with 10% alcoholic potassium hydroxide. The ether (100 ml) extract was washed with water (five 3-ml portions) and dried (Na_2SO_4). Removal of the drying agent, and then the solvent by fractional distillation at atmospheric pressure, gave a light yellow oil. Analysis by glc, using a BDS column, showed two overlapping peaks in the area ratio ~1.0:0.75. This mixture was isolated by glc with the BDS-P column.

Anal. Calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 62.00; H, 10.40.

Glc with a BDS-P column (0.25 in. × 6 ft) at 105°, gas flow rate 55 ml/min and with 5–6-μl injection quantities, gave a small amount of the larger component. The 100-MHz pmr was identical with that of *cis*-2,5-diethoxytetrahydropyran obtained from the hydrogenation of component A above.

Reaction of 3-Bromo-2-ethoxy-5,6-dihydro-2*H*-pyran (2) with Sodium Ethoxide in Ethanol.—To a cooled solution of sodium (0.81 g, 0.035 g-atom) in 15 ml of dry ethanol was added an absolute ethanol (5 ml) solution of 2 g (0.01 mol) of **2**. This was heated under reflux for 20 hr, and then most of the solvent was removed by fractional distillation. The cooled residue, when diluted with ether (25 ml), deposited sodium bromide. The ether filtrate was washed with water (six 5-ml portions) until free of base and then dried (Na_2SO_4). Removal of the solvent by fractional distillation gave a colorless liquid. This was distilled under vacuum in a two-bulb micro boiling point apparatus, affording 0.6 g of colorless liquid, bp 80–85° (8 mm). The glc analysis showed four peaks in the area ratio 1.0:4.9:22.9:5.7 with retention times 6.8, 13, 15.5, and 17.5 min, respectively. The last three were coincident with those of components A, B, and C above. These were separated by glc and the liquids were identified as A, B, and C by their pmr spectra. The first peak of retention time 6.8 min was not isolated or identified.

Registry No.—**1a**, 31599-27-6; **1b**, 31599-28-7; **2**, 32513-73-8; **6**, 32513-74-9; **7c**, 32513-75-0; **7t**, 32513-76-1; *trans*-2,3-diethoxytetrahydropyran, 32513-77-2, 32513-78-3 (cis isomer); *cis*-2,5-diethoxytetrahydropyran, 32513-79-4, 32513-29-4 (trans isomer).

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