

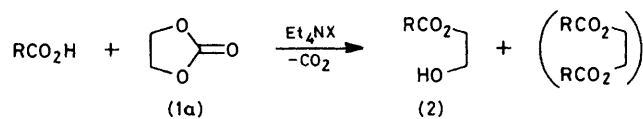
Synthetic Studies with Carbonates. Part 6.¹ Syntheses of 2-Hydroxyethyl Derivatives by Reactions of Ethylene Carbonate with Carboxylic Acids or Heterocycles in the Presence of Tetraethylammonium Halides or under Autocatalytic Conditions

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Reactions of ethylene carbonate (1a) with a variety of carboxylic acids catalysed by tetraethylammonium halides gave the corresponding 2-hydroxyethyl esters along with the diesters arising from disproportionation of the former products induced by the quaternary ammonium halides. Formation of the disproportionation products could be minimized by use of a short reaction time. The autocatalytic reactions of (1a) with strongly acidic carboxylic acids at elevated temperature gave ethylene glycol diesters selectively. Reaction mechanisms are discussed. Reactions of cyclic carbonates such as (1a) and propylene carbonate (1b) with acid anhydrides or active acyl compounds such as *p*-nitrophenyl acetate in the presence of tetraethylammonium iodide gave alkylene glycol diesters or 2-acyloxyalkyl aryl ethers in high yields. An attempt to extend this reaction to cyclohexane-1,2-diol carbonate was unsuccessful, but a reaction with 1,2-epoxycyclohexane succeeded; this enabled us to examine the stereochemistry of the reaction. Finally, *N*-2-hydroxyethylation of a series of heterocyclic compounds having acidic imino hydrogen atoms was performed, both with tetraethylammonium iodide as catalyst and without a catalyst.

ALTHOUGH ethylene oxide has been widely used for 2-hydroxyethylation, the reaction is hazardous and should be performed in a sealed tube.² Ethylene carbonate (1a) has recently been accepted as an alternative 2-hydroxyethylating agent whose m.p. (38 °C) is low enough for the reaction to be performed stoichiometrically without solvent.³ In addition, the progress of the reaction is readily monitored by observing the evolution of carbon dioxide. It has been shown that a strong nucleophilic or basic catalyst is required for 2-hydroxyethylation with the carbonate (1a).⁴ On the



SCHEME 1

other hand, we have recently reported a novel procedure for 2-hydroxyethylation of phenols involving the carbonate (1a) and neutral catalysts such as tetraethylammonium halides. As an extension of this reaction, we now report reactions of the carbonate (1a) with a series of carboxylic acids and heterocyclic compounds. Furthermore, the reactions of cyclic carbonates with acid anhydrides and with active acyl compounds have been studied. These reactions may provide us with useful intermediates for the synthesis of compounds such as willardiine⁵ and polyterephthalate, and may find application in carbohydrate chemistry; some such results⁶ have already been reported.

¹ Part 5, M. Yamada, S. Inaba, T. Yoshino, and Y. Ishido, *Carbohydrate Res.*, 1973, **31**, 151.

² A. Rosowsky, 'Heterocyclic Compounds with Three- and Four-membered Rings,' Interscience-Wiley, New York, 1964; see also F. Nerdel, J. Buddrus, G. Scherowsky, and M. Fligge, *Annalen*, 1967, **710**, 85.

³ (a) T. Yoshino, S. Inaba, H. Komura, and Y. Ishido, *Bull. Chem. Soc. Japan*, 1973, **46**, 553; (b) W. W. Carlson and L. H. Cretcher, *J. Amer. Chem. Soc.*, 1947, **69**, 1952; (c) W. W. Carlson, U.S. Pat., 2,448,767/1948 etc.

Reactions of the Carbonate (1a) with Carboxylic Acids Catalysed by Tetraethylammonium Halides.—The catalytic effects of tetraethylammonium chloride, bromide, and iodide on the reaction of the carbonate (1a) with benzoic acid were compared in order to select the best catalyst; the conditions and results are summarized in Table 1. Runs 1—3 all gave 2-hydroxyethyl benzoate as the main product, together with a small amount of ethylene glycol dibenzoate; we were able to obtain the former selectively by performing the reaction for a shorter period at a lower temperature. This

TABLE 1
Reactions of ethylene carbonate (1a) with benzoic acid

Run	X in Et ₄ NX	Conditions		Yields (%)	
		Temp. (°C)	Period (h)	2-Hydroxyethyl benzoate	Ethylene glycol dibenzoate
1	Cl ⁻	150—155	1.5	77	23
2	Br ⁻	150—155	1.0	63	27
3	I ⁻	150—155	0.3	69.5	22
4	I ⁻	140—145	0.7	86.5	

result was successfully extended to the reactions of other carboxylic acids; the conditions and results are summarized in Table 2. Predominant formation of the 2-hydroxyethyl acylates was attained in reactions under the conditions exemplified in runs 1—3. In addition, benzoic acid derivatives having electron-withdrawing substituents, such as *o*- and *p*-nitrobenzoic acids and 3,5-dinitrobenzoic acid, gave the corresponding 2-hydroxyethyl carboxylates alone in high yields at 145—150 °C.

Subsequently, we examined potential requirements

⁴ (a) S. Searles, jun., H. R. Hays, and E. F. Lutz, *J. Org. Chem.*, 1962, **27**, 2832; *J. Amer. Chem. Soc.*, 1958, **80**, 3168; (b) Dow Chem. Co., Belg. Pat., 632,941/1963 (*Chem. Abs.*, 1966, **64**, 3363); (c) M. Prystas and J. Gut, *Coll. Czech. Chem. Comm.*, 1962, **27**, 1054.

⁵ A. P. Martinez and W. W. Lee, *J. Org. Chem.*, 1965, **30**, 317.

⁶ H. Komura, T. Yoshino, and Y. Ishido, *Bull. Chem. Soc. Japan*, 1973, **46**, 550.

for the formation of diesters. The results are summarized in Table 3; 2-hydroxyethyl benzoate (2; R = Ph) was used as a model compound. The formation of ethylene glycol dibenzoate was negligible when we heated the ester (2; R = Ph) alone at 150–170 °C or together with benzoic acid at 160 °C (runs 1–3). Addition of the carbonate (1a) or the quaternary

TABLE 2

Reactions of ethylene carbonate (1a) with various carboxylic acids catalysed by tetraethylammonium iodide

Run	Acid	Reaction period ^a (min)	Yields (%) ^b	
			2-Hydroxyethyl ester	Ethylene diester
1	Acetic	60 (90)	74 (84)	(8)
2	Decanoic	35	81	
3	<i>p</i> -Methoxybenzoic	60 (90)	73 (87)	(9)
4	3,5-Dinitrobenzoic	30	87	

^a Temperature 145–150 °C in every case. ^b Of isolated products.

ammonium halide to the ester (2; R = Ph), on the other hand, resulted in dibenzoate formation (14–25%; runs 4–7) almost equivalent to that observed in the reactions listed in Tables 1 and 2. The carbonate (1a) showed a marked effect on the disproportionation of (2; R = Ph) to the dibenzoate and ethylene glycol at 200 °C, and the effect was greatly increased in the presence of tetraethylammonium iodide (run 9), in

TABLE 3

Disproportionation of 2-hydroxyethyl benzoate (HEB)

Run	Reagent	Conditions		Disproportionation ratio ^a (%)
		Temp. (°C)	Period (h)	
1	None	150–160	2	0
2	None	160 (170)	1.5(5)	2.7 (4.8)
3	BzOH ^b	160	3	0
4	(1a)	160 (200)	1.5	22 (53, c 83 ^d)
5	Et ₄ N ⁺ Cl ⁻	160	1.5	25
6	Et ₄ N ⁺ Br ⁻	160	1.5	14
7	Et ₄ N ⁺ I ⁻	160	1.5	22
8	BzOH + Et ₄ N ⁺ I ⁻ ^e	160	1.5	27
9	(1a) + Et ₄ N ⁺ I ⁻ ^f	160	1.5	54

^a Calculated from integration of the ¹H n.m.r. spectrum of the mixture. ^b BzOH:HEB 1:1. ^c (1a):HEB 1:1. ^d (1a):HEB 1:2. ^e BzOH:Et₄N⁺I⁻:HEB 1:0.2:1. ^f (1a):Et₄N⁺I⁻:HEB 1:0.2:1.

contrast to the reaction in the presence of benzoic acid (run 8). The effect of tetraethylammonium iodide was further examined with respect to other 2-hydroxyethyl carboxylates (Table 4), and it was concluded that all were susceptible to disproportionation to the corresponding dicarboxylates, and that 2-hydroxyethyl esters of carboxylic acids with larger p*K*_a values disproportionated more readily. These results are consistent with the fact that the reactions of the carbonate (1a) with benzoic

* Ethylene carbonate undergoes protonation on the carbonyl oxygen atom.⁹

⁷ A. Hilt, J. Trivedi, and K. Hamann, *Makromol. Chem.*, 1965, **89**, 177.

acids having electron-withdrawing groups gave no dibenzoates. On the other hand, a successful disproportionation of 2-hydroxyethyl *p*-nitrobenzoate was achieved by treating it with 3 mol. equiv. of the carbonate (1a) at 190–200 °C for 1.5 h, giving ethylene glycol bis-*p*-nitrobenzoate quantitatively without tetraethylammonium iodide.

The foregoing results enable us to discuss the reaction mechanism. Hilt's finding that thermal decomposition of the carbonate (1a) by a series of quaternary ammonium and metal halides involves the formation of ethylene oxide and polyethylene oxide *via* 2-halogenoethoxide⁷ has been generalized to include induction above 160 °C.^{3a,8} However, the reactions of the carbonate (1a) with carboxylic acids described here were effectively conducted around 140 °C in the presence of tetraethylammonium halides.

The reaction may be explained as shown in Scheme 2.

TABLE 4

Disproportionations of 2-hydroxyethyl esters^a

Run	Ester	p <i>K</i> _a of carboxylic acid	Disproportionation ratio (%)
1	Decanoate	4.87	55
2	Acetate	4.76	38
3	<i>p</i> -Methoxybenzoate	4.47	27
4	<i>p</i> -Toluate	4.37	21
5	Benzoate	4.20	22
6	<i>p</i> -Nitrobenzoate	3.42	12.5

^a Mixtures of tetramethylammonium iodide and the ester (0.2:1) were heated at 160 °C for 1.5 h.

Compound (1a) is decomposed by nucleophilic attack of halide ion on the methylene carbon atom, which may be assisted by hydrogen bonding between the carbonyl oxygen and the carboxylic acid,* to give the intermediate (3), which is then attacked by carboxylate ion to give the 2-hydroxyethyl carboxylate and carbon dioxide, as proposed by Gordon, through a four-centre mechanism.¹⁰ Disproportionation of the 2-hydroxyethyl carboxylates to the corresponding dicarboxylates is likely to arise or be accelerated by electrostatic interaction between the ammonium ion and the carbonyl group of the former, and an increase of polarity of the reaction system by tetraethylammonium halide or the carbonate (1a), which has a dielectric constant of 73 D at 50 °C. However, the disproportionation cannot be discussed in detail since there has been no investigation of the reactions of 2-hydroxyethyl carboxylates in the presence of neutral catalysts such as tetraethylammonium halides.

Autocatalytic Reaction.—Assuming the occurrence of a catalytic effect of acidic hydrogen on the carbonate (1a), as mentioned above, we attempted the reaction of the carbonate (1a) (in excess) with some carboxylic acids

⁸ (a) A. L. Shapiro, *Zhur. org. Khim.*, 1967, **4**, 2065; 1968, **5**, 1207; (b) K. Gulbins, G. Benzing, R. Maysenholder, and K. Hamann, *Chem. Ber.*, 1960, **93**, 1975.

⁹ G. A. Olah and A. M. White, *J. Amer. Chem. Soc.*, 1968, **90**, 1884.

¹⁰ A. S. Gordon and W. P. Norris, *J. Phys. Chem.*, 1959, **69**, 3013.

without added catalyst. Gradual elevation of temperature above 180 °C to 200 °C induced evolution of carbon dioxide in reactions with *p*-bromo- and *p*-nitro-benzoic

TABLE 5

Autocatalytic reactions of ethylene carbonate (1a) with carboxylic acids ^a

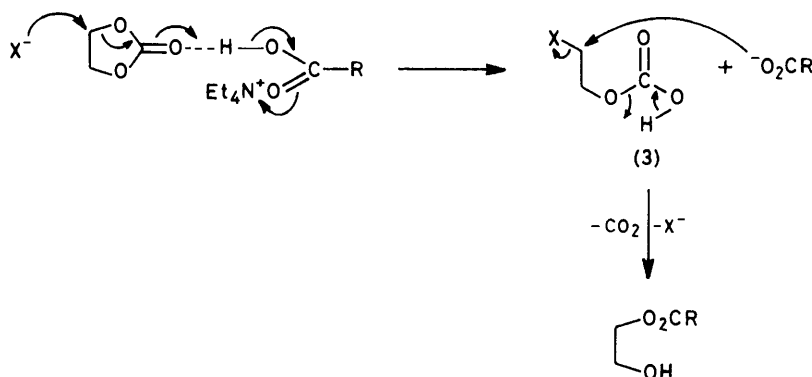
Run	Acid	p <i>K</i> _a	Conditions		Yield of ethylene diester (%)
			Temp. (°C)	Period (h)	
1	<i>p</i> -Bromobenzoic	4.00	180–220	3.5	49
2	<i>p</i> -Nitrobenzoic	3.42	180–200	1.0	98
3	3,5-Dinitrobenzoic	2.82	180–200	5.0	81

^a Temperatures raised gradually in each case.

acid and 3,5-dinitrobenzoic acid, giving the corresponding ethylene glycol dicarboxylates exclusively.

On the other hand, no reaction was induced with

mixtures of the carbonate (1a) with acetic or benzoic anhydride even at 180 °C, the substitution reaction was expected to take place in the presence of tetraethylammonium halides on the basis of the above results. The 2-halogenoethoxide formed initially should be susceptible to acylation by an acid anhydride, and subsequent nucleophilic substitution of the halide by the resulting acylate ion would give the ethylene glycol diacylate. When the carbonates (1a and b) reacted with some acid anhydrides in the presence of tetraethylammonium iodide, the desired dicarboxylates were obtained in high yields (Table 6). The reaction was also applicable to such active acyl compounds as aryl acetates and acetylimidazole. The corresponding 2-acyloxy-ethyl or -propyl aryl ethers were obtained in satisfactory yields; the rather low yield of 2-acetoxy-ethylimidazole may be attributed to its decomposition



SCHEME 2

acetic, decanoic, and benzoic acids (*cf.* Table 5). Incidentally, the autocatalytic reaction of terephthalic acid with (1a) has been said to give the bis-2-hydroxyethyl esters,¹¹ in contrast with the above result. However, a re-examination of the reaction yielded the disproportionation products, *i.e.* bis-2-hydroxyethyl ethylene diterephthalate and its telomers. The occurrence of

during distillation. The i.r. and ¹H n.m.r. spectra of the products were in good agreement with their structures. The product from the carbonate (1b) and *p*-nitrophenyl acetate was identical with the acetate of

TABLE 6

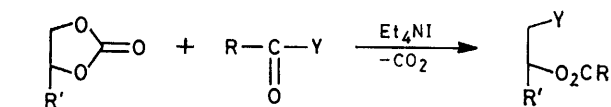
Reactions of cyclic carbonates with acid anhydrides or active acyl compounds

Run	RCOY		Conditions		Yield (%)
	R	Y	Temp. (°C)	Period (h)	
1	Me ^a	MeCO ₂	135–140	1	79.5
2	Ph ^a	PhCO ₂	150	5	97
3	Me ^b	MeCO ₂	135–140	6	77
4	Me ^a	<i>p</i> -O ₂ N·C ₆ H ₄ ·O	150	1.3	87
5	Me ^a	Imidazolyl	150	0.25	45
6	Me ^b	<i>p</i> -O ₂ N·C ₆ H ₄ ·O	165	1.5	78

^a Reaction with (1a). ^b Reaction with (1b).

2-hydroxypropyl *p*-nitrophenyl ether; the methine proton signal showed a downfield shift on acetylation.

We hoped to study the stereochemistry of the reaction by use of *cis*-cyclohexane-1,2-diyl carbonate.* However, this carbonate underwent no reaction on treatment with acetic or benzoic anhydride in the presence of a tetraethylammonium halide at 180 °C. Consequently,



(1) a; R' = H
b; R' = Me

SCHEME 3

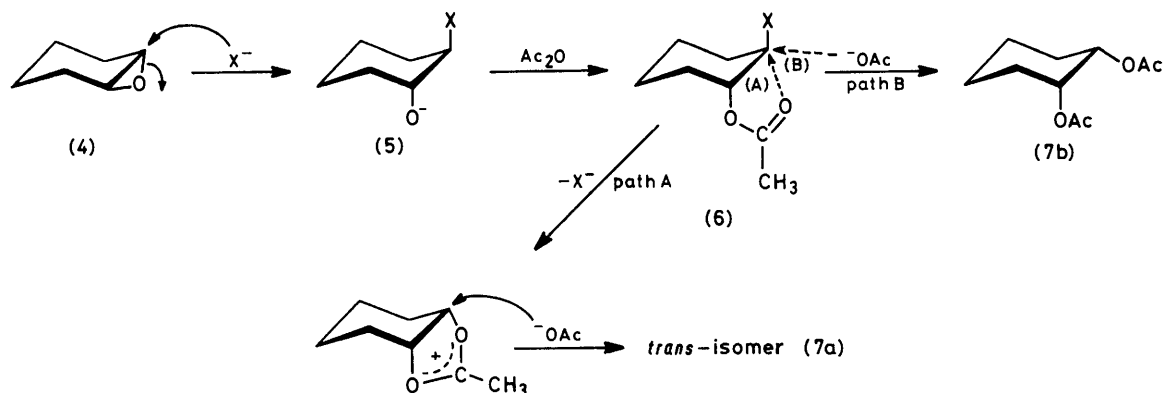
these disproportionations might be a result of the large dielectric constant of (1a) as mentioned in the previous section.

Reactions of Cyclic Carbonates with Active Acyl Compounds catalysed by Tetraethylammonium Halides.—Although no reaction was induced on heating equimolar

* Prepared by ester exchange of *cis*-cyclohexane-1,2-diol with (1a), with a catalytic amount of sodium hydrogen carbonate; the preparation will be reported elsewhere together with those of related compounds.

¹¹ G. E. Ham, U.S.P., 2,870,124/1959.

1,2-epoxycyclohexane (4) was used for the study since this should give the same intermediate 2-halogenocyclohexanolate ion (5) as would be expected from nucleophilic attack of halide ion on the carbonate accompanied by carbon dioxide evolution. Reactions of the epoxide (4) with acetic and benzoic anhydrides in the presence of tetraethylammonium iodide at 130–131 °C gave the corresponding *trans*-cyclohexane-1,2-diyl diesters exclusively. In order to elucidate the stereochemistry more fully, the changes in *trans*:*cis* ratio of the isomers formed by the above reaction on changing the halide ion from chloride, to bromide, to iodide was determined from the ¹H n.m.r. spectrum of each resulting mixture. The exclusive formation of the *trans*-isomer was observed



SCHEME 4

in the case of iodide, whereas both *trans*- and *cis*-isomers were formed in the cases of bromide and chloride (Table 7). Consequently, the steric course of this reaction may be considered to be as follows. The species (6) is produced in two steps [initial halide attack

TABLE 7

Effect of halide ions on the ratio of *trans*- to *cis*-cyclohexane-1,2-diyl diacetate (7) in the reaction of 1,2-epoxycyclohexane (4) with acetic anhydride ^a

X in Et ₄ NX	Diacetate		
	Crude yield (%)	% <i>trans</i> ^b	% <i>cis</i> ^b
I	98.5	100	0
Br	82	62	38
Cl	78	43	57

^a Reactions carried out in an oil-bath at 130 °C for 15 min.

^b Calculated from integration of ¹H n.m.r. spectra.

on (4) and subsequent acetylation] and then the acetoxy-group of (6) nucleophilically attacks the resultant halogenomethylene carbon atom to form a 1,3-dioxolanium ion. This is then attacked by the resulting acetate ion to give the *trans*-isomer (7a) (path A). The alternative path (B) involves direct displacement of the

halogeno-substituent of (6) by acetate ion to give the *cis*-isomer (9b). The above results indicate that the reaction might well proceed *via* path (A) with the iodide, but *via* both paths (A) and (B) with the bromide and chloride. This mechanism may also apply to the reactions of the carbonates (1a and b).

Reactions of the Carbonate (1a) with Heterocyclic Compounds catalysed by Tetraethylammonium Halides.—Polymerization products of *N*-vinyl-purine and -pyrimidine derivatives and their properties have recently become of interest, in particular with regard to their hyperchromicity in u.v. spectroscopy due to the interaction between heterocyclic base pairs, as observed in RNA and DNA,¹² and to the separation of nucleosides

by using this kind of polymer as a support for chromatography.¹³ *N*-2-Hydroxyethyl heterocycles, precursors of *N*-vinyl derivatives, have been prepared previously from the carbonate (1a) by using strong alkali as catalyst.¹⁴ In the light of Scheme 2, heterocycles having acidic imino hydrogen atoms should be able to replace carboxylic acids in the present reaction. Reactions of the carbonate (1a) with imidazole, pyrimidine, purine, and other imino derivatives catalysed by tetraethylammonium iodide gave the expected results (Table 8). Attempts to obtain monosubstituted products from uracil and hypoxanthine, which have two possible reaction sites, by using 1.2 equiv. of (1a), were successful. *N*⁶-Benzyladenine gave two isomers 2-hydroxyethylated at the 3- (23%) and the 9-positions (44%).

Autocatalytic Reactions of the Carbonate (1a) with Heterocycles.—An attempt to achieve an autocatalytic reaction of the carbonate (1a) with imidazole in view of its large nucleophilicity resulted in *N*-2-hydroxyethylimidazole even at 130 °C, accompanied by carbon dioxide evolution. Other autocatalytic reactions of (1a) with various heterocyclic compounds were then examined and found to give the corresponding *N*-2-hydroxyethylated products in high yields except in a

¹² N. Ueda, K. Nakatani, K. Kondo, K. Takemoto, and M. Imoto, *Makromol. Chem.*, 1970, **134**, 305.

¹³ (a) G. Greber and H. Schott, *Angew. Chem.*, 1870, **82**, 82; (b) R. C. Beaney, A. S. Jones, and R. T. Walker, *Nucleic Acids Research*, 1975, **2**, 699.

¹⁴ (a) M. Imoto and K. Takemoto, *Synthesis*, 1970, 173; (b) N. Ueda, K. Kondo, K. Takemoto, and M. Imoto, *Makromol. Chem.*, 1968, **120**, 13, 21; 1969, **128**, 42; (c) J. Pitha and P. O. Tso, *J. Org. Chem.*, 1968, **33**, 1341.

few cases. The results are summarized in Table 9. The 2-hydroxyethylation sites on each heterocycle were established by comparison of u.v. absorption spectra with those of the corresponding known *N*-glycosyl

TABLE 8

Reactions of ethylene carbonate (1a) with heterocyclic compounds catalysed by tetraethylammonium iodide

Run	Heterocycle (H)	Conditions			Product	
		(1a)/(H)	Temp. (°C)	Period (h)	HO-[CH ₂] ₂ posn.	Yield (%)
1	Imidazole	1.1	130	0.3	1	50
2	2-Hydroxy-pyridine	1.1	150	1.5	1	75.5
3	Adenine	1.2	150	2.5	9	87
4	<i>N</i> ⁶ -Benzyladenine	1.1	150	1.0	3	23
					9	44
5	4-Methoxy-2(1 <i>H</i>)-pyrimidone	1.1	150	1.5	1	63.5
6	Phthalimide	1.1	145	1.5	1	95
7	Phthalimide ^a	1.1	145	2.0	1	80

^a Carried out with propylene carbonate (1b) in place of (1a); the product was the corresponding 2-hydroxypropyl derivative.

derivatives (*cf.* Table 10). Judged from these satisfactory yields and the simplicity of the reaction procedure, this autocatalytic reaction is advantageous from the synthetic standpoint in comparison with the catalysed reactions described above. The usefulness of such

TABLE 9

Reactions of ethylene carbonate (1a) with heterocyclic compounds in the absence of catalyst

Run	Heterocycle (H)	Conditions			Product	
		(1a)/(H)	Temp. (°C)	Period (h)	HO-[CH ₂] ₂ posn.	Yield (%)
1	2-Hydroxy-pyridine	1.0	170	1.5	1	52
2	Imidazole	1.1	130	1.7	1	56
3	4-Methoxy-2(1 <i>H</i>)-pyrimidone	1.1	150	1.0	1	75
4	Adenine	2.0	150	1.3	9	92
5	<i>N</i> ⁶ -Benzyladenine	5.0	150	1.0	3	3
					9	88
6	Hypoxanthine	2.2	150	3.5	1 and 9	81.5
7	Hypoxanthine	1.2	150	7	9	72.5
8	Uracil	2.2	160	2	1 and 3	98.5

a reaction has also been shown in the synthesis of nucleosides and their analogues.¹⁵

EXPERIMENTAL

¹H N.m.r. spectra were taken with a Varian T-60 apparatus for solutions in deuteriochloroform or hexadeuteriodimethyl sulphoxide (tetramethylsilane or sodium 2,2-dimethyl-2-silapentane-1-sulphonate as internal standard). Methylene protons of 2-hydroxyethyl carboxylates (RCO₂-CH₂^β-CH₂^α-OH) and heterocycles (=N-CH₂^β-CH₂^α-

OH) are designated as H^α and H^β as indicated. I.r. spectra were recorded with a Hitachi EPI-S2 spectrometer.

Data for 2-hydroxyethyl esters and ethylene diesters not given here, and the results of other reactions not listed in the Tables, are available as Supplementary Publication No. SUP 22018 (9 pp.).*

Reactions of Ethylene Carbonate (1a) with Carboxylic Acids catalysed by Tetraethylammonium Halides. General Procedure.—A mixture of the carbonate (1a) (2.0 g, 22 mmol) and a carboxylic acid (20 mmol) was heated at 150–155 °C together with the quaternary salt (3.6 mmol) until the evolution of CO₂ ceased. After heating for 30 min more, the mixture was dissolved in ethyl acetate (100 ml), and the solution was washed with water, from which the quaternary salt was recovered quantitatively. The organic layer was dried (MgSO₄) and concentrated *in vacuo*. From the residue the two products, the corresponding 2-hydroxyethyl carboxylate and ethylene glycol diester, were isolated

TABLE 10

U.v. data (λ/nm; aqueous soln.) for *N*-2-hydroxyethyl heterocyclic compounds

Deriv. of	pH 1		pH 7		pH 12	
	λ _{max.} (log ε)	λ _{min.} (log ε)	λ _{max.} (log ε)	λ _{min.} (log ε)	λ _{max.} (log ε)	λ _{min.} (log ε)
4-Methoxy-2(1 <i>H</i>)-pyrimidone	270 (3.96)	235 (3.04)	277.5 (3.81) ^c	237 (2.78)	272.5 (3.88)	244 (3.23)
<i>N</i> ⁶ -Benzyladenine (9-isomer)	268 (4.30) ^a	236 (3.62)	271 (4.28) ^{a,d}	233 (3.22)	271 (4.32) ^a	242 (3.85)
<i>N</i> ⁶ -Benzyladenine (3-isomer)	287 (3.28)	242 (3.28)	296 (4.37) ^e	253 (3.88)	290 (4.23) ^a	250 (3.53)
Hypoxanthine ^b	252 (4.20)	225 (3.76)	254 (4.12) ^f	230 (3.75)	260 (4.18)	239 (3.06)
2-Hydroxy-pyridine	282 (3.78)	242 (2.70)	299 (3.73) ^g	244 (2.37)	298 (3.65)	251 (2.74)

^a Determined in EtOH. ^b 1,9-Disubstituted derivative.

^c 1-(2,3,5-Tri-*O*-benzoyl-β-D-arabinofuranosyl)-4-methoxy-2(1*H*)-pyrimidone had λ_{max.} 276 nm (log ε 3.80) (T. Y. Shen, H. M. Lewis, and W. V. Ruyle, *J. Org. Chem.*, 1965, **30**, 835), ^d *N*⁶-Benzyladenosine had λ_{max.} 265 nm (log ε 4.30) (N. Nakazaki, M. Sekiya, T. Yoshino, and Y. Ishido, *Bull. Chem. Soc. Japan*, 1973, **46**, 3858). ^e 3,*N*⁶-Dibenzyladenine had λ_{max.} 293 and 218 nm (log ε 4.24 and 4.35) (N. J. Leonard, K. C. Carraway, and J. P. Helgson, *J. Heterocyclic Chem.*, 1965, **2**, 291). ^f 1-Methylinosine had λ_{max.} 251 nm (log ε 4.02). ^g *N*-Methyl-2-pyridone had λ_{max.} 295 nm (log ε 3.64) (L. C. Anderson, *J. Amer. Chem. Soc.*, 1949, **71**, 343).

by fractional distillation or recrystallization (yields shown in Table 2). When the reaction was performed at 140–145 °C and stopped just after the theoretical volume of CO₂ had been evolved, the 2-hydroxyethyl carboxylate alone was isolated. The products were as follows: 2-hydroxyethyl benzoate, b.p. 101–104 °C at 0.4 mmHg (lit.,¹⁶ 176–180 °C at 20 mmHg), δ 3.90 (H^α) and 4.40 (H^β); ethylene dibenzoate, b.p. 151–153 °C at 0.4 mmHg, m.p. 71.5–73 °C (lit.,¹⁶ 73 °C), δ 4.68 (4 H, s); 2-hydroxyethyl acetate, b.p. 83.5 °C at 12 mmHg (lit.,¹⁷ 187–189 °C), δ 3.80 (H^α) and 4.21 (H^β); ethylene diacetate, b.p. 77–80 °C at 13 mmHg (lit.,¹⁷ 77.1 °C at 10 mmHg), δ 4.28 (4 H, s); 2-hydroxyethyl decanoate, b.p. 115–117 °C at 0.4 mmHg (Found: C, 66.95; H, 11.3. C₁₂H₂₄O₃ requires C, 66.95; H, 11.2%), δ 3.77 (H^α) and 4.21 (H^β); 2-hydroxyethyl *p*-methoxybenzoate, b.p. 148–149 °C at 0.7 mmHg

¹⁶ J. E. Millington and F. L. M. Pattison, *Canad. J. Chem.*, 1965, **34**, 1532.

¹⁷ Beilstein, B II, 1943, 141.

* For details of Supplementary Publications see Notice to Authors No. 7, *J.C.S. Perkin I*, 1976, Index issue.

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(lit.,¹⁸ 149—150 °C at 0.4 mmHg); *ethylene bis-p-methoxybenzoate*, m.p. 115—116 °C (from ethyl acetate) (Found: C, 65.45; H, 5.6. C₁₈H₁₈O₆ requires C, 65.45; H, 5.5%), δ 4.61 (4 H, s); *2-hydroxyethyl 3,5-dinitrobenzoate*, m.p. 132.5—133.5 °C (from ethanol) (Found: C, 42.0; H, 2.95; N, 10.95. C₉H₈N₂O₇ requires C, 42.2; H, 3.15; N, 10.95%), δ 3.95 (H^a) and 4.61 (H^b).

Disproportionation of 2-Hydroxyethyl Carboxylates.—The reactions are exemplified as follows. 2-Hydroxyethyl benzoate (170 mg, 1 mmol) was heated together with tetraethylammonium iodide (50 mg, 0.2 mmol) at 160 °C for 1.5 h. The mixture was then dissolved in chloroform, washed with water, and dried (MgSO₄), and evaporated *in vacuo* to a syrup; the ratio of 2-hydroxyethyl benzoate to ethylene dibenzoate was calculated from n.m.r. integration. The results are summarized in Tables 3 and 4.

Autocatalytic Reactions of the Carbonate (1a) with Carboxylic Acids. General Procedure.—A reaction of the carbonate (1a) (30—50 mmol) and a carboxylic acid (10 mmol) was brought about by raising the bath temperature from 150 to 220 °C; CO₂ evolution began at ca. 180 °C. Heating was continued until gas evolution ceased. Crystallization of the resulting mixture from ethyl acetate, unless otherwise noted, gave the corresponding ethylene dicarboxylate in the yields shown in Table 5. Ethylene glycol formed concomitantly was detected by g.l.c. [Hitachi K-53 apparatus; 10% of SE-30 on Chromosorb W (60—80 mesh); carrier gas N₂ at 1.5 atm; oven temperature 150 °C; injection temperature 200 °C]. *Ethylene bis-p-bromobenzoate* had m.p. 155—156.5 °C (Found: C, 45.0; H, 2.85. C₁₆H₁₂Br₂O₄ requires C, 44.9; H, 2.8%), $\nu_{\text{C=O}}$ 1 711 cm⁻¹ (ester) (no hydroxy-absorption); δ 4.63 (4 H, s). *Ethylene bis-p-nitrobenzoate* had m.p. 142—143.5 °C (Found: C, 53.1; H, 3.1; N, 7.9. C₁₆H₁₂N₂O₈ requires C, 53.35; H, 3.35; N, 7.8%), $\nu_{\text{C=O}}$ 1 724 cm⁻¹ (ester) (no hydroxy-absorption); δ 4.76 (4 H, s). *Ethylene bis-3,5-dinitrobenzoate* had m.p. 170.5—171.5 °C (Found: C, 42.85; H, 2.4; N, 12.55. C₁₆H₁₀N₄O₁₀ requires C, 42.65; H, 2.25; N, 12.45%), $\nu_{\text{C=O}}$ 1 730 cm⁻¹ (ester) (no hydroxy-absorption); δ [(CD₃)₂SO] 4.06 (4 H, s). In the cases of acetic acid, decanoic acid, and benzoic acid, no CO₂ evolution was observed on heating with (1a) even at 200—215 °C. Exceptionally, the bath temperature could not be kept above 140 °C in the first case, as a result of the low b.p. of the acid.

Re-examination of the Autocatalytic Reaction of the Carbonate (1a) with Terephthalic Acid.—A mixture of the carbonate (1a) (3.50 g, 40 mmol) and terephthalic acid (1.67 g, 10 mmol) was heated at 190—195 °C for 2 h (oil-bath), then triturated with ethyl acetate (50 ml) to precipitate a white powder (telomers) (yield 100 mg, m.p. 215—220 °C), δ [(CD₃)₂SO] 4.69br (s, ethylene protons of ester) and ca. 3.7br and 4.3br (2-hydroxyethyl group); the area ratio of the former singlet to the latter pair of signals was 22:28. The filtrate was washed with aqueous m-sodium hydroxide then water saturated with sodium chloride, and dried (MgSO₄) and evaporated to give a crystalline mass; recrystallization afforded *bis-2-hydroxyethyl ethylene diterephthalate* (1.28 g, 57%); m.p. 118—120 °C (from ethanol) (Found: C, 59.45; H, 5.15. C₂₂H₂₂O₁₀ requires C, 59.2; H, 4.95%), δ [(CD₃)₂SO] 4.70 (4 H, [CH₂]₂ of ester).

Reactions of the Carbonates (1a and b) with Carboxylic

Anhydrides. General Procedure.—An acid anhydride (10 mmol) was treated with (1a or b) (11 mmol) at 135—140 °C in the presence of tetraethylammonium iodide (3.6 mmol), until CO₂ evolution ceased. The mixture was dissolved in acetone or benzene (50 ml), and the precipitate of quaternary iodide was recovered almost quantitatively. The filtrate was concentrated *in vacuo*, and the residue was subjected to distillation or recrystallization to give the corresponding ethylene or propylene diester in the yields shown in Table 6: ethylene diacetate, b.p. 77—78 °C at 13 mmHg (lit.,¹⁷ b.p. 190.5 °C); ethylene dibenzoate, m.p. 71.5—73 °C (from ethanol) (lit.,¹⁸ 70.5—71.5 °C); propylene diacetate, b.p. 71.5—75 °C at 10 mmHg (lit.,¹⁹ b.p. 186 °C at 758 mmHg), δ 1.28 (H-3, J_{2,3} 6.0 Hz), 2.14 (OAc), 4.13 (H-1, J_{1,1'} 12.0, J_{1,2} 6.0 Hz), 4.33 (H-1', J_{1',2} 4.0 Hz), and 5.17 (H-2).

Reactions of the Carbonates (1a and b) with Active Acyl Compounds. General Procedure.—Reactions of an active acyl compound (10 mmol) with (1a or b) (11 mmol) in the presence of tetraethylammonium iodide (3.6 mmol) were performed at 150 °C (1a) or 170 °C (1b) in the same way as described above. *N-2-Acetoxyethylimidazole* had b.p. 106.5—112 °C at 0.55—0.6 mmHg (Found: C, 54.65; H, 6.85; N, 18.0. C₉H₁₀N₂O₂ requires C, 54.55; H, 6.55; N, 18.15%).

2-(p-Nitrophenoxy)ethyl acetate had m.p. 83.5—84.5 °C (from ethanol) (Found: C, 53.8; H, 4.65; N, 6.25. C₁₀H₁₁NO₅ requires C, 53.55; H, 4.9; N, 6.2%), δ 4.23 (2 H) and 4.63 (2 H). *2-Acetoxypropyl p-nitrophenyl ether* had m.p. 68—70.5 °C (from ethanol) (Found: C, 55.1; H, 5.25; N, 5.95. C₁₁H₁₃NO₅ requires C, 55.25; H, 5.5; N, 5.85%), δ 1.39 (H-3, J_{2,3} 6.8 Hz), 4.10 (H-1, J_{1,2} 4.5 Hz), 4.12 (H-1', J_{1',2} 5.5 Hz), 5.17 (H-2), and 2.09 (OAc); this was identical with a specimen prepared by acetylation of 2-hydroxypropyl *p*-nitrophenyl ether (see later).

2-Hydroxypropyl p-Nitrophenyl Ether and its Acetate from the Carbonate (1b) and p-Nitrophenol.—A mixture of the carbonate (1b) (1.10 g, 10 mmol) and *p*-nitrophenol (1.40 g, 1.8 mmol) was heated at 155—160 °C for 1.5 h. The mixture was dissolved in chloroform (50 ml) and the solution was washed with water, dried (MgSO₄), and evaporated. The residue was recrystallized to give the *product* (1.10 g, 56%), m.p. 78—79 °C (from ethanol) (Found: C, 54.8; H, 5.4; N, 7.25. C₉H₁₁NO₄ requires C, 54.8; H, 5.6; N, 7.1%), δ 1.32 (3 H, d, Me) and 3.9—4.3 (3 H, AB₂X₃, -CH₂-CH=). This product (2.0 g, 10 mmol) was treated with acetic anhydride (2 ml)-boron trifluoride-diethyl ether (3 drops) in chloroform (20 ml) with cooling in an ice-bath for 24 h. The mixture was poured into ice-water and stirred for 1 h. The organic layer was then washed with aqueous m-sodium hydroxide and water saturated with sodium chloride, dried (MgSO₄), and evaporated. Recrystallization afforded the acetate (74%), m.p. 69—70 °C (from ethanol).

Reactions of 1,2-Epoxy-cyclohexane (4) with Acetic or Benzoic Anhydride.—On heating a mixture of the epoxide (4) (1.0 g, 10 mmol), an acid anhydride (11 mmol), and tetraethylammonium iodide (1.8 mmol) at 130—135 °C, vigorous boiling for a few minutes was observed, and the mixture was further heated for 10—15 min. The resulting mixture was extracted with chloroform (50 ml), and the extract was washed with water, dried (MgSO₄) and evaporated. The residue was distilled under reduced pressure or

¹⁸ W. A. Jacobs and M. Heidelberger, *J. Biol. Chem.*, 1915, **21**, 465.

¹⁹ B. M. Tronow and N. C. Ssigatullin, *Chem. Ber.*, 1929, **62**, 2853.

recrystallized, affording the corresponding *trans*-cyclohexane-1,2-diyl diester. *trans*-Cyclohexane-1,2-diyl diacetate (7a) (1.60 g, 80%) had b.p. 75–77.5 °C at 0.53 mmHg (lit.,²⁰ 120 °C at 12 mmHg); $\nu_{\text{C=O}}$ (NaCl) 1740, $\nu_{\text{C-O-C}}$ 1240 and 1040 cm^{-1} ; δ 4.65 (methine protons) and 2.02 (s, OAc); the *trans*-dibenzoate (1.90 g, 60%) had m.p. 87–88 °C (from ethanol) (lit.,²¹ 71.5 °C); $\nu_{\text{C=O}}$ (KBr) 1713, $\nu_{\text{C-O-C}}$ 1272 and 1110 cm^{-1} ; δ 5.30 (methine protons).

Effect of Tetraethylammonium Halides on the Reaction of the Epoxide (4) with Acetic Anhydride.—A mixture of the epoxide (4) (196 mg, 2 mmol), acetic anhydride (204 mg, 2 mmol), and tetraethylammonium iodide, bromide, or chloride (0.4 mmol) in a small test tube was heated at 130 °C for 15 min in an oil-bath, then treated as described above. The yields of crude diacetate (7) were 98.5, 82, and 78%, respectively, corresponding well with those indicated by integration of the methine proton n.m.r. signals near δ 4.65 (in CCl_4). The ratios of the *trans*-isomer (7a) to the *cis*-isomer (7b) of the product were also calculated, from integration of the n.m.r. signals due to the equatorial (δ 2.20) and the axial acetyl groups (δ 2.08); the ratios were 100 : 0, 62 : 38, and 43 : 57, respectively.

N-2-Hydroxyethylation of Heterocycles catalysed by Tetraethylammonium Iodide. General Procedure.—The heterocyclic compound (10 mmol), the carbonate (1a) (0.97 g, 11 mmol), and tetraethylammonium iodide (1.0 g, 3.6 mmol) were heated together in dimethylformamide (40 ml) under reflux until CO_2 evolution ceased. In the cases of succinimide, phthalimide, and 2-hydroxypyridine, the solvent was then evaporated off *in vacuo* and acetone (50 ml) was added to the residue to separate the quaternary iodide. In the cases of adenine and hypoxanthine, on the other hand, aqueous 90% ethanol (50 ml) was added to the residue, and the resulting crystals were filtered off and recrystallized from ethanol. Conditions and products are shown in Table 8.

N-2-Hydroxyethylimidazole had b.p. 125–127 °C at 0.65 mmHg (lit.,²² 181–184 °C at 4 mmHg); δ 3.85 (H^α) and 4.03 (H^β). *N-2-Hydroxyethyl-2-pyridone* had b.p. 137–138 °C at 0.65 mmHg (Found: C, 60.55; H, 6.2; N, 10.5. $\text{C}_7\text{H}_9\text{NO}_2$ requires C, 60.4; H, 6.5; N, 10.05%); δ 3.80 (H^α) and 4.11 (H^β). *N-2-Hydroxyethyladenine* had m.p. 245 °C (from ethanol) (lit.,¹⁴ 238–239 °C), δ 3.78 (H^α) and 4.27 (H^β). *N-2-Hydroxyethylphthalimide* had m.p. 126 °C (from carbon tetrachloride) (lit.,²³ 126–127 °C), δ 3.90 (H^α and H^β).

In the case of 4-methoxy-2(1H)-pyrimidone, the resulting 1-(2-hydroxyethyl)-4-methoxy-2(1H)-pyrimidone was purified

by column chromatography on silica gel (80 times the weight of the sample) in chloroform–ethanol (5 : 1) to give a semicrystalline syrup (Found: C, 49.5; H, 5.9; N, 16.5. $\text{C}_7\text{H}_{10}\text{N}_2\text{O}_3$ requires C, 49.4; H, 5.9; N, 16.45%), $\nu_{\text{C=O}}$ 1660, $\nu_{\text{C-N}}$ 1700, ν_{OH} 3400 cm^{-1} ; δ (CDCl_3) 3.82br (8 H, s, 4-OMe, CH_2CH_2 , and OH), 5.80 (H-5, d, J 9.0 Hz), and 7.58 (H-6, d).

In the case of the reaction with *N*⁶-benzyladenine, the resulting mixture was treated as in the case of adenine. The residue obtained by the evaporation of the acetonitrile solution was dissolved in ethanol (40 ml)–acetone (20 ml). *N*⁶-Benzyl-3-(2-hydroxyethyl)adenine (0.32 g, 23%) was obtained as the first crop by keeping the solution in a refrigerator for 2 days; m.p. 231–234 °C (Found: C, 62.55; H, 5.6; N, 25.5. $\text{C}_{14}\text{H}_{15}\text{N}_5\text{O}$ requires C, 62.45; H, 5.6; N, 26.0%), δ 3.90 (H^α) and 4.60 (H^β). After concentration of the filtrate to half volume, the precipitated crystals were recrystallized to give *N*⁶-benzyl-9-(2-hydroxyethyl)adenine (0.60 g, 44%); m.p. 134–135 °C (from ethanol) (Found: C, 62.15; H, 5.4; N, 26.1%), δ 3.84 (H^α) and 4.23 (H^β).

The reaction of the carbonate (1b) with phthalimide performed as above gave *N-2-hydroxypropylphthalimide* (80%); m.p. 83–84 °C (from ethanol–acetone) (Found: C, 64.1; H, 5.3; N, 7.1. $\text{C}_{11}\text{H}_{11}\text{NO}_3$ requires C, 64.4; H, 5.4; N, 6.85%).

Autocatalytic N-2-Hydroxyethylation of Heterocyclic Compounds. General Procedure.—To a solution of a heterocyclic compound (10 mmol) in dimethylformamide (10–50 ml) was added the carbonate (1a) (11–30 mmol) (Table 9), and the mixture was heated in an oil-bath until CO_2 evolution ceased. After heating for a further *ca.* 15 min, dimethylformamide was evaporated off *in vacuo*, and the residue was purified as above. The reactions of imidazole and 2-hydroxypyridine were performed without solvent. The results are summarized in Table 9. U.v. spectral data of the products are in Table 10.

1,9-Bis-2-hydroxyethylhypoxanthine had m.p. 184–186 °C (Found: C, 47.75; H, 5.0; N, 25.0. $\text{C}_9\text{H}_{12}\text{N}_4\text{O}_3$ requires C, 48.2; H, 5.4; N, 24.5%), δ 4.04 (H^α) and 3.62 (H^β). *1,3-Bis-2-hydroxyethyluracil* had m.p. 149.5–150.5 °C (from ethanol–*n*-hexane) (lit.,¹⁴ 154 °C), δ 3.98 (H^α) and 3.57 (H^β).

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