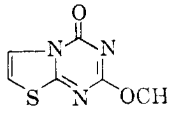
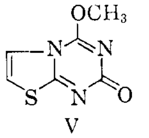
2-Aminothiazole reacted rapidly with II to form a crystalline product, $C_6H_5N_3SO_2$. The infrared spectrum showed no NH absorption. Strong bands at 1700 cm.$^{-1}$ (conjugated ring carbonyl) and 1230 cm.$^{-1}$ $\left(\mathrm{CH_3O\overset{|}{C}{=}}\right)^7$ were present, however. A strong absorption in the ultraviolet (λ_{max} 2900 Å., ϵ 11,900) suggested structure IV for this material, although the alternative structure V could not be ruled out. The former


IV


V

would be expected if initial attack occurred at the difluoromethylene group of the isocyanate. The latter would result from initial formation of the normal urea derivative followed by ring closure.

Experimental

Dimethyl azodiformate was synthesized by the oxidation of dimethyl hydrazodicarboxylate with fuming nitric acid.[8] The product melted at 10°.

Dimethyl 3,3,4,4-Tetrafluoro-1,2-diazetidine-1,2-dicarboxylate.—The procedure used was a modification of that described by Cramer[9] for the diethyl ester. To 100 g. of dimethyl azodiformate in a 400-ml. stainless steel autoclave was added under pressure 80 g. of tetrafluoroethylene. The autoclave was held at 150° for 7 hours and was then cooled. Unreacted tetrafluoroethylene was bled from the autoclave. The viscous yellow product was flash distilled at 3 mm. pressure from a flask heated with the vapor of refluxing cyclohexanol. The volatile material was dissolved in a mixture of 500 ml. of ether and 50 ml. of ethanol to which 30 ml. of a saturated aqueous solution of sodium bisulfite had been added. The solution was stirred until colorless (5 minutes). The organic layer was separated, washed with water, and dried over magnesium sulfate. The solvent was evaporated, and the product was fractionally distilled to yield 80 g. (47%) of colorless liquid, b.p. 90° (28 mm.), n^{25}D 1.3801.

Anal. Calcd. for $C_6H_6F_4N_2O_4$: C, 29.3; H, 2.5; F, 30.9; N, 11.4; mol. wt., 246. Found: C, 29.9; H, 2.8; F, 30.7; N, 10.9; mol. wt. (freezing point in benzene), 249.

Methoxydifluoromethyl Isocyanate.—The pyrolysis was carried out by dropping 80 g. of dimethyl 3,3,4,4-tetrafluoro-1,2-diazetidine-1,2-dicarboxylate at the rate of 2 ml./minute through a 25 × 300 mm. tube packed with 5-mm. sections of 7-mm. quartz tubing.[10] The internal pressure was 5 mm., and the temperature was maintained at 600°. Volatile products were condensed in a trap cooled by liquid nitrogen. The contents of the trap were distilled into a second trap at reduced pressure by allowing the first trap to warm to room temperature. The residue (32 g.) was then recycled through the pyrolysis tube. This process was repeated twice. The product in the second trap weighed 67 g. and was fractionally distilled to yield 54 g. (68%), b.p. 43–44°, and a forerun of 6 g. (7%), b.p. 41–43°.

Anal. Calcd. for $C_8H_3F_2NO_2$: C, 29.3; H, 2.5; F, 30.9; N, 11.4; mol. wt., 123. Found: C, 29.6; H, 2.4; F, 30.9; N, 11.9; mol. wt., 117.

Reaction of Methoxydifluoromethyl Isocyanate with 2-Aminothiazole.—A solution of 7.2 g. of 2-aminothiazole in 20 ml. of tetrahydrofuran was added slowly to a stirred solution of 4.40 g. of methoxydifluoromethyl isocyanate in 20 ml. of tetrahydrofuran. After an hour, a tan solid was removed by filtration and recrystallized from 200 ml. of boiling acetonitrile to yield 4.0 g. (61%) of white crystals, m.p. 240–241°.

Anal. Calcd. for $C_6H_5N_3SO_2$: C, 39.3; H, 2.8; N, 22.9; S, 17.5. Found: C, 39.3; H, 2.7; N, 22.9; S, 17.8.

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[7] L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," second edition, John Wiley and Sons, Inc., New York, N. Y., 1958, p. 117.

[8] O. Diels and P. Fritzsche, *Ber.*, **44**, 3026 (1911).

[9] R. D. Cramer, U. S. Patent 2,456,176, December 14, 1948.

[10] J. C. Kauer, U. S. Patent 2,860,154 (1958).

[CONTRIBUTION FROM THE U. S. BORAX RESEARCH CORP.]

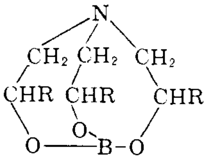
The Hydrolysis of Triisopropanolamine Borate[1]

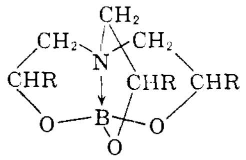
BY H. STEINBERG AND D. L. HUNTER

RECEIVED APRIL 18, 1959

Commercially available triisopropanolamine has been found by kinetic analysis to consist of a 38.1–61.9% mixture of diastereomers. The less prevalent isomer has been isolated. Triisopropanolamine borates prepared from these isomers are interpreted as diastereomers (IVa and IVb) which differ only in the configuration about one methyl-bearing carbon atom.

The borates equilibrate in water or aqueous dioxane with their products of hydrolysis, triisopropanolamine and boric acid, at widely divergent rates. The equilibrium points are approached by pseudo first-order kinetics with half-lives of 29.5 and 4080 hours in water, 11.0 and 983 hours in 60% dioxane, and 2.74 and 39.0 hours in 91% dioxane. In dilute hydrochloric acid, the hydrolyses proceed to completion at accelerated rates. This unusual hydrolytic stability is attributed to the unavailability of boron for coördination with water due to a transannular interaction of amino-nitrogen[2] and boron across the eight-membered ring (IIb). The magnitude of the transannular interaction is dependent upon the steric requirements of the isomers.


Ia, R = H
b, R = CH_3


IIa, R = H
b, R = CH_3

Brown and Fletcher[3] have stated that triethanolamine borate could exist either as structure Ia in which the BO_3 group is planar or the tetrahedral counterpart IIa resulting from a nitrogen–boron transannular interaction. More recently Lucchessi and DeFord[4] have demonstrated an equilibrium between the planar and tetrahedral forms of triethanolamine borate in which water or butanol

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[1] Presented in part before the Division of Organic Chemistry, 128th Meeting of the American Chemical Society, Minneapolis, Minn., Sept., 1955.

[2] Transannular interactions of amino-nitrogen and carbonyl groups have been reported for eight and nine-membered rings [N. J. Leonard, *et al.*, THIS JOURNAL, **76**, 630, 5708 (1954)].

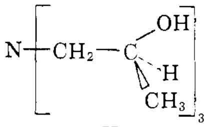
[3] H. C. Brown and E. A. Fletcher, *ibid.*, **73**, 2808 (1951).

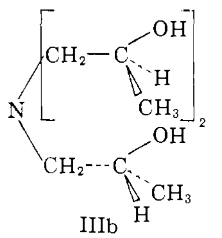
[4] C. A. Lucchessi, Doctoral Dissertation Series Publication No. 13, 109; Northwestern Univ. (D. D. Deford), 1955.

favored structure Ia and aprotic solvents favored structure IIa.

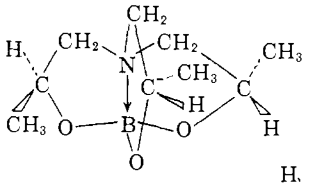
From the inertness of the nitrogen atom toward methyl iodide and the slow reaction with methanesulfonic acid in nitrobenzene, Brown and Fletcher concluded that a transannular bond must be present. Similar intramolecular nitrogen–boron interactions also have been suggested to rationalize the otherwise unexplainable hydrolytic stability of β-aminoethyl diphenylborinate,[5] β-aminoethyl di-α-naphthylborinate,[5a,6] β-aminoethyl phenyl-α-naphthylborinate,[5a,6] 5-β-aminoethoxy-10,11-dihydrodibenzo[b,f]borepin,[7] diethanolamine hexaneboronate[8] and both monomeric[9] and polymeric[5b] diethanolamine benzeneboronate. The present work based upon the unusually slow rate of hydrolysis of triisopropanolamine borate (IIb) provides independent support for the existence of a transannular bond in molecules of this kind.

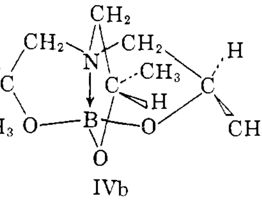
Triisopropanolamine contains three equivalent asymmetric centers and thus can exist as four optical isomers: diastereomer IIIa and its enantiomorph in which the configuration about the asymmetric carbon atoms are identical or diastereomer IIIb and its enantiomorph in which the configuration of one carbon atom is reversed.


IIIa


IIIb

Thus, it is possible that the boric acid ester prepared from commercially available triisopropanolamine would consist of a mixture of diastereomers, the symmetrical racemate IVa, derived from IIIa, and the unsymmetrical racemate IVb, derived from IIIb, differing only in the spatial relationship of one hydrogen atom and one methyl group which are thrust out from the three fused five-membered rings.


IVa


IVb

Results

Synthetic.—Repeated recrystallization of triisopropanolamine (Union Carbide Chemicals Co.) from anhydrous ether led to the isolation of about 4% of a crystalline material with a considerably higher melting point (96–99°) than that reported in the literature (15–30°,[10] 48–52°,[11] 58°[12,13]). The elemental analysis, neutralization equivalent, molecular weight and infrared spectrum substantiated the structure of a tripropanolamine.

The high melting amine, presumably IIIa or IIIb, as well as the diastereomeric mixture of amines (IIIa plus IIIb) were converted to the borates by the azeotropic removal of water from a toluene mixture of the amines and boric acid. Repeated recrystallization of the diastereomeric mixture of borates (IVa plus IVb) from a variety of solvents indicated a partial concentration of one of the isomers; however, a clean separation could not be made.

Hydrolyses in Water.—The hydrolyses were conveniently followed by the periodic removal of aliquots from water solutions of the esters and titration of the triisopropanolamine produced. The ester derived from the high melting amine[14] equilibrated with its products of hydrolysis at 9.93% reaction (Fig. 1). The pseudo first-order rate constant (0.0235 hr.$^{-1}$) was determined from the straight line of a plot of log $(ax_\mathrm{e} + x(a - x_\mathrm{e}))/(x_\mathrm{e} - x))$ *versus* t utilizing the equilibrium expression[15] for a first-order reaction (hydrolysis) opposed by one of the second order (esterification).

Equilibration of the "fast" isomer precluded a facile isolation of the "slow" isomer by selective hydrolysis, and thus in the absence of a pure sample of "slow" ester the rate constant for the "slow" isomer was obtained from data for the hydrolysis of the mixture of the isomeric amine borates (IVa and IVb). Utilizing the usual integrated expression[16] for a first-order process, a plot of log $(a - x)$ *versus* t (Fig. 1) reveals an initially steep straight line which sharply decreases in slope between 5.8 and 32 hours. The original interpretation[17] of this phenomenon concluded that a hydrolytically reactive impurity[18] gave rise to the initial

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[5] (a) R. L. Letsinger, I. Skoog and N. Remes, THIS JOURNAL, **76**, 4047 (1954); (b) R. L. Letsinger and I. Skoog, *ibid.*, **77**, 2491 (1955); (c) C. S. Rondestvedt, R. M. Scribner and C. E. Wulfman, *J. Org. Chem.*, **20**, 9 (1955).

[6] R. L. Letsinger and N. Remes, THIS JOURNAL, **77**, 2489 (1955).

[7] R. L. Letsinger and I. H. Skoog, *ibid.*, **77**, 5176 (1955).

[8] W. L. Ruigh, C. E. Erickson, F. Gunderloy and M. Sedlak, WADC Technical Report 55-26, Part II, May, 1955.

[9] O. C. Musgrave and T. O. Park, *Chemistry & Industry*, 1552 (1955).

[10] Eastman Kodak Co.

[11] K. Krasuskii, *J. Gen. Chem.* (*U.S.S.R.*), **6**, 460 (1936).

[12] F. Barbe, *Chim. & ind.* (*Paris*), **63**, 492 (1950).

[13] Union Carbide Chemicals Co.

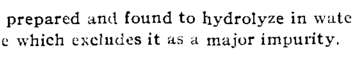
[14] For convenience, the more rapidly hydrolyzing diastereomer of triisopropanolamine borate and the high melting amine from which it is derived shall be referred to as the "fast" isomers and the slowly hydrolyzing racemate and its amine as the "slow" isomers.

[15] S. Glasstone, "Textbook of Physical Chemistry," 2nd Ed., D. Van Nostrand Co., Inc., New York, N. Y., 1948, p. 1071.

[16] An expression for an irreversible process may be used here since the data are concerned with a portion of the reaction sufficiently removed from the equilibrium point so that the back reaction has not yet become significant.

[17] H. Steinberg and D. L. Hunter, *Ind. Eng. Chem.*, **49**, 174 (1957).

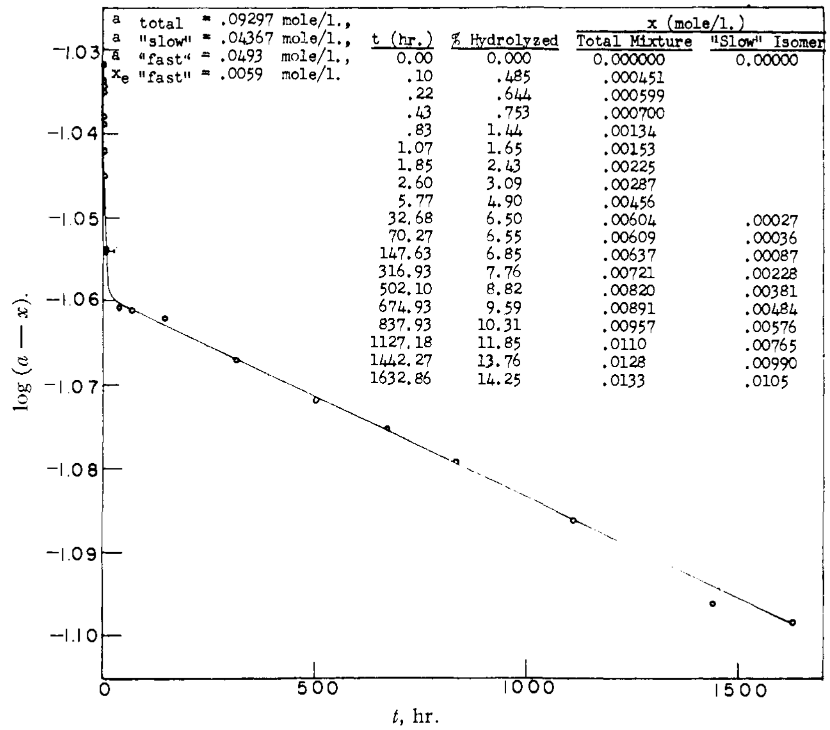
[18] In ref. 3 it was believed that triethanolamine purified by distillation contained some secondary amine. In ref. 8, a diethanolamine product was isolated from a reaction employing triethanolamine. However, tri-(diisopropanolamine) biborate,



$$\left[\mathrm{NH(CH_2\overset{\overset{CH_3}{|}}{C}HO)_2BO\overset{\overset{CH_3}{|}}{C}HCH_2}\right]_2\mathrm{NH}$$

has since been prepared and found to hydrolyze in water at a rate too fast to measure which excludes it as a major impurity.

rapid hydrolysis. The rate constant obtained for the "slow" isomer was consequently in error. A more accurate hydrolysis rate constant for the "slow" isomer may be obtained as follows.



a total = .09297 mole/l.,
a "slow" = .04367 mole/l.,
a "fast" = .0493 mole/l.,
x_e "fast" = .0059 mole/l.

t (hr.)	% Hydrolyzed	x (mole/l.) Total Mixture	x (mole/l.) "Slow" Isomer
0.00	0.000	0.000000	0.00000
.10	.485	.000451	
.22	.644	.000599	
.43	.753	.000700	
.83	1.44	.00134	
1.07	1.65	.00153	
1.85	2.43	.00225	
2.60	3.09	.00287	
5.77	4.90	.00456	
32.68	6.50	.00604	.00027
70.27	6.55	.00609	.00036
147.63	6.85	.00637	.00087
316.93	7.76	.00721	.00228
502.10	8.82	.00820	.00381
674.93	9.59	.00891	.00484
837.93	10.31	.00957	.00576
1127.18	11.85	.0110	.00765
1442.27	13.76	.0128	.00990
1632.86	14.25	.0133	.0105

Fig. 1.—Rate of hydrolysis of triisopropanolamine borate (mixture of racemates) in water at 25°.

If the presence of the unhydrolyzed "slow" isomer does not alter the equilibrium position of the "fast" isomer, the equilibrium concentrations for the "fast" ester and amine in the hydrolyses of the pure "fast" ester and the mixture of esters may be equated in a mass law expression (1). Substitution of

$$K_{\text{eq}} = \frac{[\text{amine}_{\text{in mixt}}]_e^2}{[\text{ester}_{\text{in mixt}}]_e} = \frac{[\text{amine}_{\text{pure}}]_e^2}{[\text{ester}_{\text{pure}}]_e} \quad (1)$$

the equilibrium concentrations for the pure "fast" amine and ester (amine = 0.00727 mole/l., ester = 0.0659 mole/l.) and the equilibrium concentration of the "fast" amine in the hydrolysis of the mixture (0.0059 mole/l., obtained from the intersection of the extrapolation of the two straight lines of Fig. 1) leads to a value of 0.0434 mole/l. for the equilibrium concentration of the "fast" ester in the mixture. The initial concentration of the "fast" ester is thus 0.0493 mole/l. or 53.0% of the total mixture. It is now possible to re-evaluate the total data of Fig. 1 for the slow isomer. In the equilibrium expression 2 for the "fast" ester $[E_f]_t$ and "fast" amine $[A_f]_t$ at time

$$K_{\text{eq}} = [A_f]_t[\text{BA}]_t/[E_f]_t \quad (2)$$

t, the concentration of the boric acid $[\text{BA}]_t$ may be substituted with its equivalent, the sum of the concentrations of the "fast" and "slow" amines which in turn is equivalent to x_{total} of Fig. 1. In addition, as the "slow" ester hydrolyzes, the boric acid produced represses the hydrolysis of the "fast" ester from its equilibrium position and the concentration of the "fast" ester is increased by an amount equivalent to the decrease in concentration of the "fast" amine.

$$[E_f]_t = [E_f]_e + ([A_f]_e - [A_f]_t)$$

and since $[E_f]_e + [A_f]_e = a_f$, substitution in (2) gives

$$[A_f]_t = \frac{K_{\text{eq}}a_f}{x_{\text{total}} + K_{\text{eq}}}$$

A final substitution of $x_{\text{total}} - [A_s]_t$ for $[A_f]_t$ gives equation 3

$$[A_s]_t = x_{\text{total}} - \frac{K_{\text{eq}}a_f}{x_{\text{total}} + K_{\text{eq}}} \quad (3)$$

which allows the calculation of the data for the "slow" isomer (Fig. 1). A plot of log $(a-x)$ *versus* t for the "slow" isomer gives an excellent straight line for the complete 1600-hour time period.

Further treatment of the data of Fig. 1 for the "fast" isomer leads to a rate constant of 0.0240 hr.$^{-1}$ which is in good agreement with the 0.0235 hr.$^{-1}$ value already obtained for the pure "fast" ester.

Hydrolyses in Aqueous Dioxane.—Hydrolyses were performed in 60 and 91% (by volume) aqueous dioxane in order to make direct comparisons of hydrolytic stability with a series of water-insoluble esters whose rates in aqueous dioxane have been reported.[17] The ester mixture utilized in these hydrolyses was recrystallized twice from benzene as compared to five recrystallizations for the sample used in the aqueous hydrolysis. The isomeric composition thus differed and by the method used in the aqueous hydrolyses was found to be 42.2% "fast." This value in addition to the equilibrium concentration (0.00764 mole/l.) of "fast" amine in 60% dioxane obtained from Fig. 2 allow the calculation of the rate data for the pure isomers utilizing the equilibrium expression of reference 15 and the usual integrated expression for a first-order process (modified by equation 3), respectively.

The data for the hydrolysis in 91% dioxane (Fig. 3) were similarly treated to give pseudo first-order hydrolysis rate constants for the "fast" and "slow" isomers, respectively, obtained graphically from slopes of the appropriate plots. However, the equilibration of the "slow" ester with its products of hydrolysis is evident by the zeroing of the slope after 215 hours (57.5% hydrolysis) and thus the use of the expression for an irreversible process should lead to a smaller rate constant than is actually operative. Indeed the use of the equilibrium expression gives a rate constant of 0.0178 hr.$^{-1}$ as compared to 0.0146 hr.$^{-1}$ obtained originally.

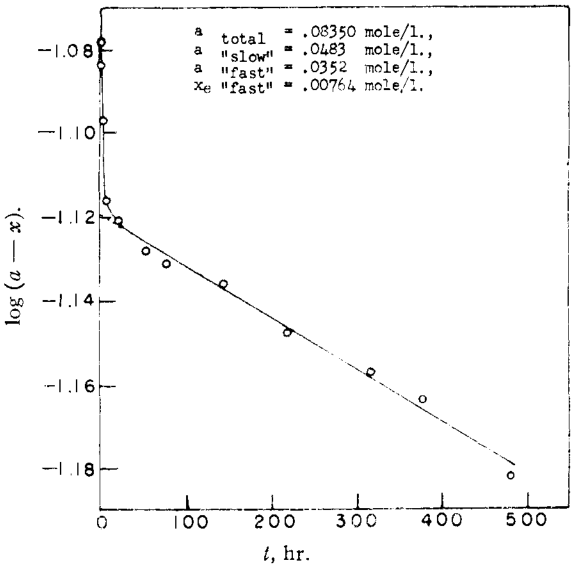


Fig. 2.—Rate of hydrolysis of triisopropanolamine borate (mixture of racemates) in 60% aqueous dioxane at 25°.

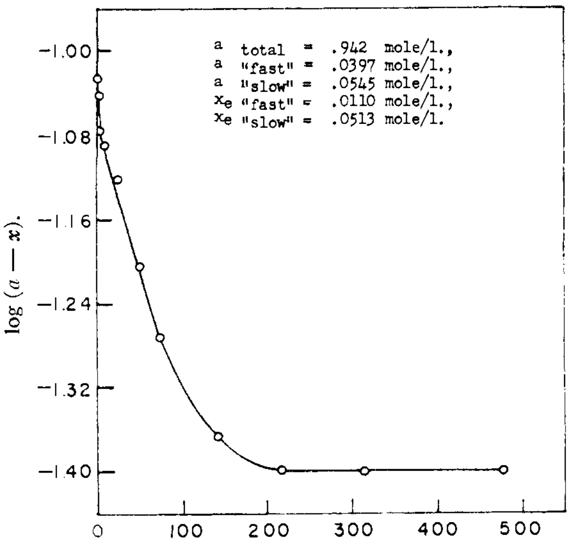


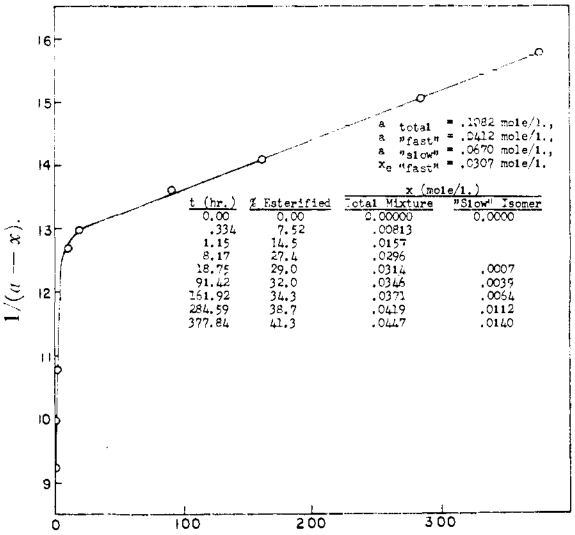
Fig. 3.—Rate of hydrolysis of triisopropanolamine borate (mixture of racemates) in 91% dioxane at 25°.

Acid-catalyzed Hydrolysis.—The hydrolysis of the isomeric mixture of triisopropanolamine borates (42.2% "fast") in the presence of one equivalent of hydrochloric acid was followed by titration of the unconsumed acid as a function of time. Since equilibration is precluded by neutralization of the triisopropanolamine, the usual expression for an irreversible first-order process may be used to treat the data for the individual isomers. Rate constants for the "fast" and "slow" isomers, respectively, were obtained from slopes of the appropriate plots.

The hydrolytic data of the acid-catalyzed hydrolysis also can be used as a check on the 42.2% "fast"–57.8% "slow" isomeric composition of the twice recrystallized borate obtained from the hydrolyses in aqueous dioxane. The concentration obtained from extrapolation to zero time of a plot of log total $(a-x)$ *versus* t should correspond to 57.8% of the total initial concentration. The value thus obtained corresponded to 53.3% "slow."

Esterification in Water.—The reverse reaction, the esterification of boric acid with triisopropanolamine, was followed by the periodic removal of aliquots from an equimolar solution of boric acid and "fast" amine in water and titration of the free amine as a function of time. The rate constant can be obtained by employing the equilibrium expression[15] for a second-order reaction opposed by one of the first order and plotting log $(a^2-xx_e)/(x_e-x)$ *versus* t. A straight line is thus defined and allows calculation of the second-order rate constant for the esterification of the "fast" amine.

The esterification data for the racemic mixture of amines is presented in Fig. 4 utilizing the usual expression for a second-order process.[16]



t (hr.)	% Esterified	x (mole/l.) Total Mixture	x (mole/l.) "Slow" Isomer
0.00	0.00	0.00000	0.0000
.334	7.52	.00813	
1.15	14.5	.0157	
8.17	27.4	.0296	
18.75	29.0	.0314	.0007
91.42	32.0	.0346	.0039
161.92	34.3	.0371	.0064
284.59	38.7	.0419	.0112
377.84	41.3	.0447	.0140

Fig. 4.—Rate of esterification of triisopropanolamine (mixture of racemates) in water at 25°.

Once again assuming the presence of the slowly esterifying amine does not influence the equilibrium point of the "fast" isomer, the equilibrium concentrations of "fast" amine and ester may be equated as in expression 1 to give an equilibrium concentration of "fast" amine of 0.0105 mole/l. The initial concentration of "fast" amine is thus 0.0412 mole/l. or 38.1% of the total mixture of amines.

It is now possible to further evaluate the data of Fig. 4 utilizing the initial concentration (0.0670 mole/l.) of the "slow" amine. The slope of the straight line defined by a plot of $1/a-x$ *versus* t is the second-order constant for the "slow" amine.

Discussion

The inordinate stability of both the "fast" and "slow" isopropanolamine borates is evident by comparison of their hydrolysis rate constants to the open-chain analog, triisopropyl borate. Isopropyl borate[17] hydrolyzes $>1.06 \times 10^5$ times as fast as the "fast" isomer and $>1.47 \times 10^7$ times as fast as the "slow" isomer even though the steric requirements for the attack of water on the boron atom are greater in the open-chain ester which has

TABLE I

SUMMARY OF HYDROLYTIC DATA

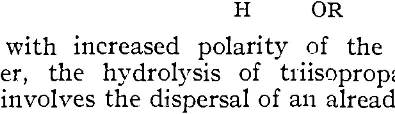
	Hydrolysis						Esterification					
	"Fast" isomer			"Slow" isomer			"Fast" isomer			"Slow" isomer		
Medium	k, hr.$^{-1}$	$t_{1/2}$, hr.	Relative rate[a]	k, hr.$^{-1}$	$t_{1/2}$, hr.	Relative rate[a]	k_2, l. mole^{-1} hr.$^{-1}$	$t_{1/2}$, hr.	Relative rate[b]	k_2, l. mole^{-1} hr.$^{-1}$	$t_{1/2}$, hr.	Relative rate[b]
Water	0.0235	29.5[c]	138	1.70×10^{-4}	4080	1.0	10.3	2.32	980	0.0105	1420	1
60% dioxane	.0628	11.0[c]	371	7.05×10^{-4}	983	4.15						
91% dioxane	.253	2.74[c]	1490	0.0178	39.0	105						
Water, 1.0 equiv. HCl	.384	1.81	2260	2.88×10^{-3}	241	16.9						

[a] Based on the rate of hydrolysis of the "slow" isomer in water, 1.70×10^{-4} hr.$^{-1}$ ≈ 1. [b] Based on the rate of esterification of the "slow" isomer, 0.0105 l. mole^{-1} hr.$^{-1}$ ≈ 1. [c] Due to equilibration, the actual half-life would be obtainable only in dilute solution. The half-life given is the time for 50% reaction if the reverse reaction were not operative.

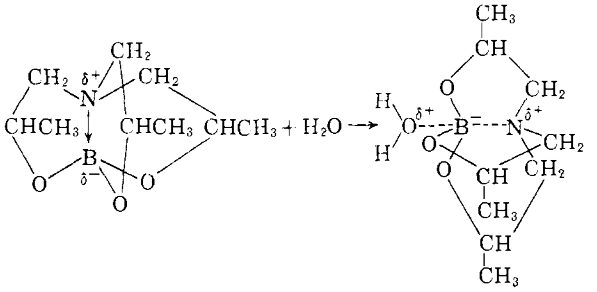
freely rotating isopropyl groups as compared to the bicyclic structure Ib in which the isopropyl groups are tied back in a ring. This unusual hydrolytic stability is attributed to the unavailability of boron for coördination with water due to a transannular interaction of nitrogen and boron across the eight-membered ring (structures IIb, IVa and IVb).

Examination of Fisher–Hirschfelder–Taylor atomic models indicates a decided interference of methyl and methylene groups in the unsymmetrical racemate IVb. The alleviation of the strain produced by this interference might alter the extent of the nitrogen–boron interaction which would be expected to reflect in a difference in rate of hydrolysis of the two diastereomeric borates IVa and IVb. In Table I, which contains a summary of the rate data, it is seen that the "fast" ester hydrolyzes at 138 times the rate of the "slow" ester in water, 89.4 times the rate of the "slow" ester in 60% dioxane and 14.2 times the rate in 91% dioxane. It is further seen that for the neutral hydrolyses the rates for both isomers increase with decreasing polarity of the solvent. It is possible that the dioxane may catalyze the reaction by forming a complex (dioxanate) with the ester which is more susceptible to hydrolysis than the original intramolecular complex.

A more probable explanation can be found by a consideration of charge distribution and solvent effects. It has previously been found that boric acid esters in general hydrolyze more rapidly in 60% than in 91% aqueous dioxane.[17] Since the hydrolysis of an ester involves the formation of a transition state with a charge separation from two previously neutral molecules, the rate should increase with increased polarity of the solvent.[19] However, the hydrolysis of triisopropanolamine borate involves the dispersal of an already existing charge separation and consequently an increase in polarity of the solvent should result in a decrease in the rate of hydrolysis.[19] Furthermore it would be expected that the isomer with the greatest nitrogen–boron interaction and consequently the greatest charge separation to start would be most effected by the change in solvent polarity. Thus the "slow" isomer whose rate of hydrolysis is increased by factors of 4 and 105 in proceeding to 60 and 91% dioxane as compared to factors of 2.7 and 11 for the "fast" isomer might be expected to have the greater transannular interaction.[20]



$$H_2O + (RO)_3B \longrightarrow \overset{H\ \ \delta_+}{\underset{H}{\ }}O-\overset{OR}{\underset{OR}{B}}\overset{\delta_-}{-}OR$$



An unequivocal assignment of diastereomers IVa and IVb to the "fast" and "slow" esters cannot be made at this time. In addition, it is not obvious from examination of atomic models whether the methyl–methylene interference tends to increase or decrease the transannular interaction. However, if in the production of triisopropanolamine from propylene oxide and ammonia, the purely statistical possibilities of isomer distribution are not too greatly altered by the asymmetry present in the intermediate mono- and diisopropanolamines, a mixture containing 25% of the symmetrical (IIIa) and 75% of the unsymmetrical (IIIb) amines would be expected. Thus the "fast" amine which comprises 38.1% of the mixture of amines might be assigned the symmetrical configuration IIIa and the "slow" amine the unsymmetrical configuration IIIb. The consequences of such an assignment are that the methyl–methylene interference present in structure IVb leads to a greater interaction of the nitrogen and boron orbitals and consequently decreases the rate of hydrolysis as compared to the symmetrical ester IVa.

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(19) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, N. Y., 1953, p. 346.

(20) Acid catalysis would also be expected to be more pronounced in the isomer with the greatest nitrogen–boron interaction since protonization of the amino nitrogen would destroy the transannular interaction and leave the boron atom in an electron deficient state, a condition already at least partially present in the other isomer. The acceleration of "slow" isomer rate in acid medium by a factor of 16.9 *versus* the factor of 16.3 for the "fast" isomer does not bear out this contention.

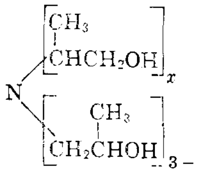
The acceleration of the rate of hydrolysis of triethanolamine borate by acid is of the same order of magnitude. Reference 17 reported a half-life of 2.17 minutes for the acidic hydrolysis. F. Hein and R. Burkhardt [*Z. anorg. Chem.*, **268**, 159 (1952)] found the freezing point depression of a 0.107 molar solution of the ester to increase with time and level after 271 minutes. Assuming 99% hydrolysis at that time and compensating for the temperature differential the half-life would be 28.8 minutes which leads to a factor of 13.

TABLE II

EQUILIBRIUM CONSTANTS FOR THE HYDROLYSES AND ESTERIFICATIONS AT 25°

	"Fast"			"Slow"		
	From equilibrium concentrations		From rates of hydrolysis and esterification	From equilibrium concentrations		From rates of hydrolysis and esterification
Medium	Hydrolysis	Esterification		Hydrolysis	Esterification	
Water	0.802×10^{-3}	3.60×10^{-3}	2.28×10^{-3}	$>3.32 \times 10^{-3}$	<0.201	0.0162
60% dioxane	2.12×10^{-3}			$>5.62 \times 10^{-3}$		
91% dioxane	4.22×10^{-3}			0.822		

The possibility that the high melting "fast" amine is one of the primary alcohols (V) resulting from reverse opening of the propylene oxide ring in its synthesis from propylene oxide and ammonia



V, x = 1, 2 or 3

is excluded on the basis of the large amount of the high melting product (38.1%) found to be present in the commercial product. Such a reverse opening has not been obtained[11] and would be expected to occur to the extent of a few per cent. if at all.[21] The hydrolysis of an ester derived from a tribasic acid and trifunctional alcohol which in addition possesses a basic nitrogen capable of salt formation with the acid may well be a complex of equilibria involving partially esterified fragments and their salts. The internal consistency of the data is a partial testimonial to the simplicity of the actual system; that is, the importance of the over-all equilibrium between boric acid, amine and triisopropanolamine borate which indicates the rupture of the first B–O linkage to be the rate-determining step. However, the error in this simplifying assumption is implied by the discrepancy in equilibrium constants for the "fast" isomer when calculated from the rate constants of the forward and reverse reactions and the actual equilibrium concentrations observed in the hydrolysis and esterification (Table II). The actual isolation of partially esterified species would allow direct determination of the importance of these intermediates on the kinetics of hydrolysis and work along these lines is in progress.

Experimental

Wherever possible, manipulations were performed in a dry-box or under protection of calcium chloride or Ascarite tubes.

Isolation of "Fast" Triisopropanolamine.—The isomeric mixture of amines as obtained from the Union Carbide Chemicals Co. was repeatedly recrystallized from anhydrous ether to give a 3.6% recovery of hard colorless granules melting at 96–99°.

Anal. Calcd. for $C_9H_{21}O_3N$: C, 56.51; H, 11.07; N, 7.32; neut. equiv., 191; mol. wt., 191. Found: C, 56.96; H, 11.32; N, 7.58; neut. equiv., 194; mol. wt., 195 (micro Rast in camphor).[22]

The infrared spectrum (Perkin–Elmer model 21, film between NaCl windows) showed major bands at 2.98, 3.37, 3.42, 3.56, 7.10, 7.29, 7.48, 7.86, 8.50, 8.78 and 9.45 μ. This spectrum was almost superimposable upon the spectrum of the isomeric mixture of amines.

Preparation of Triisopropanolamine Borate from Isomeric Mixture of Amines.—The theoretical amount of water (26 ml.) was azeotropically removed with the aid of a Dean–Stark water trap from a mixture of 92 g. (0.481 mole) of freshly distilled (b.p. 197–200° (30 mm.), literature[12] 190° (23 mm.)) triisopropanolamine, 29.7 g. (0.481 mole) of boric acid and 100 ml. of toluene. Most of the toluene (72 ml.) was then removed by distillation and the residue crystallized from 110 ml. of benzene to give 73.5 g. of white crystalline material. Two recrystallizations from benzene followed by washing with petroleum ether (b.p. 20–40°) and drying at reduced pressure resulted in 47.1 g. (49% yield) of white needles melting at 154–157°. A portion of the product was recrystallized three more times from benzene, m.p. 155.6–157.6°.

The ester was analyzed for boron by titration of boric acid in the presence of mannitol after fusion in sodium carbonate[17] and also by titration of boric acid derived from the methyl borate distillate from treatment of the ester with methanol and sulfuric acid.[23] The product sublimes at 135° at 0.2 mm., is very soluble in acetone and chloroform, less soluble in benzene and ether, slightly soluble in carbon tetrachloride, and insoluble in petroleum ether (b.p. 20–40°). The infrared spectrum (Beckman IR-4, KBr wafer) had major bands at 3.36, 3.41, 6.83, 7.23, 7.52, 7.98, 8.70 and 9.08 μ.

Anal. Calcd. for $C_9H_{18}O_3NB$: C, 54.30; H, 9.11; N, 7.04; B, 5.44; mol. wt., 199. Found: C, 53.60; H, 9.29; N, 7.01; B, 5.37 (fusion), 5.44 (distillation); mol. wt., 206.[22]

Preparation of Triisopropanolamine Borate from "Fast" Triisopropanolamine.—A 2-g. (10.5 mmoles) sample of the isolated triisopropanolamine melting at 96–99° was refluxed with 0.65 g. (10.5 mmoles) of boric acid in 25 ml. of toluene. The theoretical amount of water (0.56 ml.) was separated in the water trap in 45 minutes. After stripping the toluene, the residue was recrystallized from benzene and dried at reduced pressure to give 1.4 g. (67% yield) of white needles melting at 144–147° (closed tube); infrared spectrum (Beckman IR-4, KBr wafer): 3.40, 3.51, 6.13, 6.87, 7.26, 7.61, 7.97, 8.75 and 9.25 μ.

Anal. Calcd. for $C_9H_{18}O_3NB$: B, 5.44; mol. wt., 199. Found: B, 5.21 (fusion); mol. wt., 215.[22]

Preparation of Tri-(diisopropanolamine) Biborate.—Union Carbide Chemicals Co. diisopropanolamine was repeatedly recrystallized from anhydrous ether to give large hard crystals melting at 41–44°; neut. equiv., calcd. 133, found 134.

A sample of the recrystallized amine (25 g., 0.188 mole) was treated as above with 7.75 g. (0.125 mole) of boric acid and 100 ml. of toluene. After removal of the theoretical amount of water (6.8 ml.) and stripping of the solvent, the residue solidified to a clear hard glass.

Anal. Calcd. for $C_{18}H_{39}O_6N_3B_2$: N, 13.06; B, 5.04. Found: N, 13.50; B, 5.02.[23]

Tri-(diisopropanolamine) biborate cannot be made by solution of the amine and boric acid in water. In addition, the ester prepared by azeotropic water removal is immediately hydrolyzed in water.

General Hydrolysis Procedure.—Ester samples were weighed directly into volumetric flasks and dissolved in and diluted to the mark with freshly boiled distilled water, 60% by volume, or 91% by volume aqueous dioxane[24] which were previously maintained at 25°. The 0.07 to 0.09 molar solutions were maintained at 25° in a constant temperature bath and aliquots were periodically removed and titrated with either 0.1 or 0.025 N hydrochloric acid to methyl red end-point.

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(21) Reference 19, p. 342.

(22) E. P. Clark, "Semimicro Quantitative Organic Analysis," Academic Press, Inc., New York, N. Y., 1943, p. 82.

(23) L. H. Thomas, *J. Chem. Soc.*, 820 (1946).

(24) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., New York, N. Y., 1941, p. 368.

For the hydrolysis in acid medium, the sample was diluted with water, the calculated amount of 0.25 *N* hydrochloric acid added and then further diluted to the mark with water. Aliquots were titrated with either 0.1 or 0.025 *N* sodium hydroxide to methyl red end-point.

General Esterification Procedure.—Equal molar amounts of the appropriate amine and boric acid were weighed directly into a volumetric flask and diluted to the mark with freshly boiled distilled water previously maintained at 25°. Aliquots periodically removed from the 25° solutions were titrated with 0.025 *N* hydrochloric acid to the methyl red end-point.

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ANAHEIM, CALIF.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS, THE STATE UNIVERSITY]

An Oxygen-18 Tracer Study of the Isomerization of Cyclopropylcarbinyl Benzenesulfonate

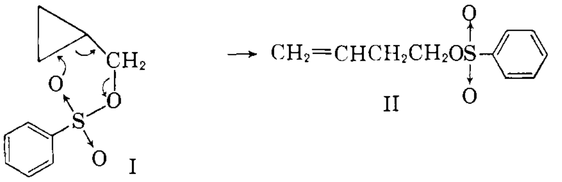
BY DONALD B. DENNEY AND EUGENE J. KUPCHIK[1]

RECEIVED JULY 31, 1959

Cyclopropylcarbinyl benzenesulfonate (I), labeled with excess oxygen-18 in the ether position of the ester group, was isomerized at *ca.* 90° to 3-butenyl benzenesulfonate (II). Hydrogenation of II followed by reductive cleavage with sodium in liquid ammonia gave *n*-butyl alcohol which contained one-third of the excess oxygen-18 originally present in I. Compound I was also found to isomerize to cyclobutyl benzenesulfonate (III) at room temperature. Reductive cleavage of III with sodium in liquid ammonia gave cyclobutanol which contained one-third of the excess oxygen-18 originally present in I. These results show that complete equilibration of the excess oxygen-18 occurred during the isomerization of I to II and I to III. The mechanistic implications of these results are discussed.

The chemistry of small ring compounds has been the subject of considerable research during the past decade. One of the most interesting aspects of this subject has been the facile interconversion of cyclopropylcarbinyl, cyclobutyl and allycarbinyl derivatives. The more recent developments and their theoretical implications have been discussed in considerable detail.[2]

Bergstrom and Siegel[3] have observed that cyclopropylcarbinyl benzenesulfonate (I), in contact with anhydrous potassium carbonate at 20°, isomerizes to the extent of 90% in 24 hours to a mixture which consists predominately of 3-butenyl benzenesulfonate (II). These workers suggested that II may have been formed by an intramolecular rearrangement.



I

II

Infrared and other analytical data indicated that a second substance, isomeric with II, was present in the crude isomerization product. This second substance was presumed to be cyclobutyl benzenesulfonate.

It was the purpose of this research to examine more closely the products of this isomerization in the hope of confirming the formation of cyclobutyl benzenesulfonate. It was also hoped that information concerning the mechanism of this reaction could be obtained by studying the isomerization of cyclopropylcarbinyl benzenesulfonate, labeled with excess oxygen-18 in the ether position of the ester group.

In an initial attempt to isomerize I to II, a methylene chloride solution of labeled I was allowed to remain in contact with anhydrous potassium carbonate at room temperature for 65 hours. The infrared spectrum of the product differed markedly from that of an authentic sample of 3-butenyl benzenesulfonate. For example, whereas the latter compound had an absorption band at 6.1 μ, due most probably to the isolated carbon–carbon double bond, the product did not have a band in this region. Furthermore, on attempted hydrogenation of the product in methanol with 10% palladium-on-charcoal as the catalyst, only 11.1% of the theoretical quantity of hydrogen was absorbed. A known sample of 3-butenyl benzenesulfonate easily absorbed the theoretical quantity of hydrogen. The absorption band at 6.1 μ was completely absent after hydrogenation. The infrared spectrum of the hydrogenated material was essentially identical to that of an authentic sample of *n*-butyl benzenesulfonate.

In another attempt to isomerize I to II, a sample of I (no solvent) was allowed to remain in contact with anhydrous potassium carbonate for 68 hours at room temperature. No absorption band at 6.1 μ appeared in the infrared; however, changes in the spectrum did occur. This was shown to be due to the formation of cyclobutyl benzensulfonate.

The isomerization of labeled I to II was finally accomplished by heating a mixture of labeled I (no solvent) and anhydrous potassium carbonate on a steam-bath for 7 hours. The isomerization was followed by observing the appearance of the absorption band at 6.1 μ. The infrared spectrum of the product was essentially identical to that of an authentic sample of 3-butenyl benzenesulfonate. The yield was 77.7%. Since gas appeared to be evolved during the reaction, it appears likely that some elimination occurred with the formation of

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(1) Alfred P. Sloan Fellow in Chemistry, 1956–1957; E. I. du Pont Teaching Fellow, 1957–1958.

(2) J. D. Roberts, Abstracts, Sixteenth National Organic Chemistry Symposium, Seattle, Wash., pp. 1–10.

(3) C. G. Bergstrom and S. Siegel, THIS JOURNAL, **74**, 145 (1952).