TABLE I

1- AND 1,4-SUBSTITUTED PIPERAZINES,

R	R′	B. p. °C.	B. p. Mm.	Ref. index n_D	Ref. index °C.	Method	Yield, %	Nitrogen, % Calcd.	Nitrogen, % Found	M. p., °C.	Salt Formula	Nitrogen, % Calcd.	Nitrogen, % Found
p-Br-C_6H_4-CH_2	CH_3					B	86			292–294	$C_{12}H_{17}BrN_2 \cdot 2HCl$	8.19	8.05
$(C_6H_5)_2CH$-CH_2	CH_3					C	40			278–279	$C_{19}H_{24}N_2 \cdot 2HCl$	7.93	7.80[a]
$(C_6H_5)_2C{=}CHCH_2$	CH_3	167–170	0.9	1.5807	30.5	C	71	9.58	9.85	139–140	$C_{20}H_{24}N_2 \cdot HCl$[b,c]	8.52	8.58
1-$C_{10}H_7CH_2$[d]	H	154–156	1			A	37			227–228	$C_{15}H_{18}N_2 \cdot HCl$	10.67	10.45
1-$C_{10}H_7CH_2$[d]	CH_3					B	Quant.			241[e]	$C_{16}H_{20}N_2 \cdot 2HCl$	8.94	8.73
1-$C_{10}H_7CH_2$[d]	CH_2CH_2OH					C	81			206–206.5[e]	$C_{17}H_{22}N_2O \cdot 2HCl$	8.16	8.10
1-$C_{10}H_7CH_2$[d]	1-$C_{10}H_7CH_2$[d]			[f]		A	27	7.65	7.79[g]		$C_{26}H_{26}N_2$[h]		
2-$C_{10}H_7CH_2$[d]	H	155–160	1	1.6101	25	A	33			193–195	$C_{15}H_{18}N_2 \cdot HCl$	10.67	10.31
2-$C_{10}H_7CH_2$[d]	CH_3					B	82			281[e]	$C_{16}H_{20}N_2 \cdot 2HCl$	8.94	8.83
2-$C_{10}H_7CH_2$[d]	CH_2CH_2OH					C	33			241[e]	$C_{17}H_{22}N_2O \cdot 2HCl$	8.16	8.05
2-$C_{10}H_7CH_2$[d]	2-$C_{10}H_7CH_2$[d]			[i]		A	23	7.65	7.46[j]		$C_{26}H_{26}N_2$[h]		
9-$C_{13}H_9$[k]	H					..	89			283–285[e]	$C_{17}H_{18}N_2 \cdot 2HCl$	8.67	8.47
9-$C_{13}H_9$[k]	CH_3					C	57			265–268[e]	$C_{18}H_{20}N_2 \cdot 2HBr$	6.57	6.66
9-$C_{13}H_9$[k]	CH_2CH_2OH			[l]		C	68	9.52	9.65	243–244[e]	$C_{19}H_{22}N_2O \cdot 2HCl$	7.63	7.54
9-$C_{13}H_9$[k]	9-$C_{13}H_9$[k]			[m]		A	Quant.	6.76	6.63		$C_{30}H_{26}N_2$[h]		
9-$C_{14}H_9CH_2$[n]	CH_3					C	43			254–255[e]	$C_{20}H_{22}N_2 \cdot 2HCl$	7.71	7.49
9-$C_{14}H_9CH_2$[n]	9-$C_{14}H_9CH_2$[n]			[o]		A	Quant.	6.01	6.14	283–286	$C_{34}H_{30}N_2 \cdot 2HCl$	5.20	5.25
2-C_5H_4N[p]	H	114–116	1.4	1.5888	27	A	40	25.75	25.74	275–276	$C_9H_{13}N_3 \cdot 2HCl$	17.79	17.51
2-C_5H_4N[p]	CH_3	106–107	2.7	1.5625	25	B	82			258–259	$C_{10}H_{15}N_3 \cdot 2HCl$	16.80	16.55
2-C_5H_4N[p]	2-C_5H_4N[p]	135–140	1.4	[q]		A	15	23.32	23.06	281–283	$C_{14}H_{16}N_4 \cdot 2HCl$	17.87	17.73

[a] Calcd.: C, 64.58; H, 7.42. Found: C, 64.58; H, 7.70. [b] This compound readily forms a monohydrate, m. p. 86–87° (isopropyl alcohol). [c] Calcd. for $C_{20}H_{24}N_2HCl \cdot H_2O$: C, 69.24; H, 7.85. Found: C, 69.30; H, 7.89. [d] Naphthylmethyl. [e] Melted with decomposition. [f] Solid, m. p. 163–164.5°. [g] Calcd.: C, 85.20; H, 7.16. Found: C, 85.20; H, 7.10. [h] Formula of base. [i] Solid, m. p. 159–60.5°. [j] Calcd.: C, 85.20; H, 7.16. Found: C, 85.20; H, 7.18. [k] Fluorenyl. [l] Solid, m. p. 143–144°. [m] Solid, m. p. 291–292° dec. [n] Phenanthryl. [o] Solid, m. p. 253–254°. [p] Pyridyl. [q] Solid, m. p. 124–126°.

1-(9-Fluorenyl)-piperazine.—A solution of 10 g. (0.03 mole) of 1-(9-fluorenyl)-4-carbethoxypiperazine in 100 cc. of concentrated hydrochloric acid was refluxed for sixty hours. The acid solution was concentrated *in vacuo* to yield 7 g. (89%) of crystalline 1-(9-fluorenyl)-piperazine which after recrystallization from anhydrous ethanol melted at 283–285° dec.

Acknowledgment.—The authors wish to thank Mr. E. F. Shelberg and the members of the Microanalytical Department for the microanalyses and Mr. Morris Freifelder for conducting the autoclave experiment.

Summary

The synthesis of a number of 1-substituted, 1,4-symmetrical disubstituted and 1,4-unsymmetrical disubstituted piperazines as histamine antagonists is described. These compounds were prepared by one of three methods from piperazine or 1-carbethoxypiperazine.

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[CONTRIBUTION FROM ROHM & HAAS COMPANY]

Transetherification Reactions. Alcohols with Certain β-Alkoxy Esters

BY W. J. CROXALL, J. O. VAN HOOK AND R. LUCKENBAUGH[1]

The condensation of acetylene with ethyl carbonate[2] provides a convenient synthesis for ethyl β,β-diethoxypropionate (I)[3] and ethyl α,α-diethoxysuccinate. This paper is the first of a series concerned with the chemistry of these esters.

During work on the isolation of the pure propionate (I) from the reaction of acetylene with ethyl carbonate,[2] it was observed that a mixture of ethyl β-ethoxyacrylate (IV) and the propionate (I) was completely converted to the latter compound by treatment with ethanol and a catalytic amount of sodium ethoxide. It was also shown that acrylate–propionate mixtures upon distillation from a catalytic amount of sodium bisulfate were readily converted to ethanol and the acrylate (IV).[2] Further verification of the reversible nature of this system was obtained in the present work when it was demonstrated that mixtures of ethanol and the acrylate (IV) in the presence of sodium bisulfate, boron trifluoride or sulfuric acid were converted to ethyl β,β-diethoxypropionate. Similar results were realized with 1-butanol and the acrylate in which case ethyl β-ethoxy-β-butoxypropionate was isolated as the main product.

The mobility of the above acrylate–propionate system suggested that the beta ethoxy groups of these esters should be capable of replacement by other alkoxy groups. Actually, this supposition has been realized, the results of which are herein reported.

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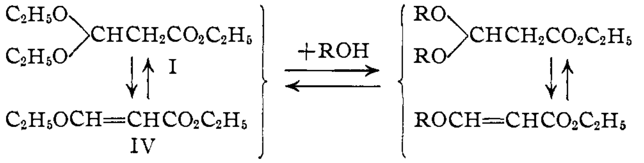
[2] Croxall and Schneider, THIS JOURNAL, **71**, 1256 (1949).

[3] McElvain and Clarke (*ibid.*, **69**, 2657 (1947)) have shown the difficulties encountered in preparing this compound in good yield.

When the propionate (I) and an alcohol of higher boiling point than ethanol are fractionated from a catalytic amount of sodium bisulfate a transetherification reaction occurs and there is obtained ethanol and an ethyl β-alkoxyacrylate whose alkoxy group corresponds to the alcohol employed. However, if the fractionation is interrupted after removal of the theoretical amount of ethanol and the sodium bisulfate catalyst is destroyed before proceeding with the final distillation, there is isolated an ethyl β,β-dialkoxypropionate as the predominant product. Although the ethyl esters are the main products isolated, small amounts of the transesterification-transetherification products (alkyl β-alkoxyacrylate and alkyl β,β-dialkoxypropionate) are also formed. Similar results are obtained when the acrylate (IV) or mixtures of this acrylate and the above propionate (I) are used. That transetherification and not transesterification has occurred was demonstrated for the reaction product obtained from 1-butanol and the propionate (I), namely, ethyl β-butoxyacrylate. Hydrogenation of this compound gave ethyl β-butoxypropionate which upon saponification yielded ethanol and β-butoxypropionic acid. Likewise, characterization of the ethyl β,β-dialkoxypropionate type, showing that transetherification had taken place, was accomplished with ethyl β,β-dibutoxypropionate. Saponification of this propionate gave ethanol and an oily acid which upon heating evolved carbon dioxide and yielded dibutyl acetal. The over-all exchange reaction may be represented as



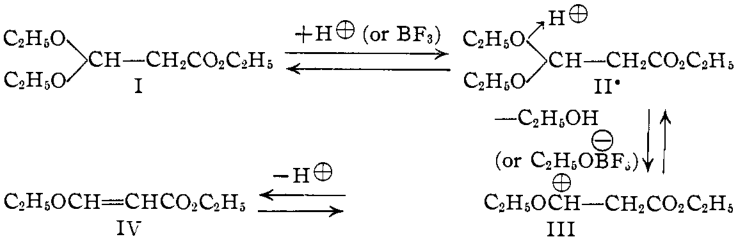
Attempts to apply the transetherification reaction to ethyl ethoxymaleate[2] or ethyl α,α-diethoxysuccinate[2] by use of sodium bisulfate were only partially successful. Alcohols with boiling points below 150° did not undergo this reaction. With higher boiling alcohols these esters underwent simultaneous transetherification and transesterification to give alkyl alkoxymaleates.

A boron trifluoride ether complex was found to be an excellent catalyst for the transetherification of the acrylate (IV), the propionate (I), ethyl ethoxymaleate and ethyl α,α-diethoxysuccinate. With this catalyst only the ethyl esters of the β,β-dialkoxypropionates and α,α-dialkoxysuccinates were obtained. No corresponding acrylates were isolated and all attempts to cleave the dialkoxypropionates to alkoxyacrylates in the presence of this catalyst resulted in high boiling oils. In view of these results no attempts were made to employ this catalyst in the preparation of the alkoxymaleates. Confirmation of a transetherification reaction occurring in the succinate series was established for ethyl α,α-dialloxysuccinate. Saponification of this succinate gave ethanol; the resulting acid in this case was not isolated.

With strong acid catalysts, such as sulfuric acid, the products were those which would be formed by both transetherification and transesterification. This type of change was observed with the acrylate (IV), the propionate (I), ethyl ethoxymaleate and ethyl α,α-diethoxysuccinate. With the acrylate (IV) and propionate (I), poor yields of alkyl β-alkoxyacrylates were obtained; higher boiling products were evident in these cases. With the maleate and succinate, however, good yields of alkyl alkoxymaleates were realized. Basic catalysts, as demonstrated with sodium and magnesium alkoxides, were found to accomplish both transetherification and transesterification. With these catalysts alkyl β-alkoxyacrylates or alkyl alkoxymaleates were the products if the catalysts were allowed to remain during the final fractionation. On the other hand, alkyl β,β-dialkoxypropionates and alkyl α,α-dialkoxysuccinates were the isolated products when the reaction was conducted in the presence of excess alcohol and the catalyst destroyed before fractionation.

The results obtained with the various catalysts and a variety of alcohols are summarized in Table I. Of all the alcohols employed in this work only tertiary alcohols failed to undergo either a transetherification or transesterification reaction. Mercaptans were found to react in the same manner as the alcohols.

The course of the transetherification reaction with acid type catalysts such as sodium bisulfate and boron trifluoride is thought to proceed as follows: the first step of which is the establishment of the following equilibrium



The propionate (I) forms an oxonium ion (II) by addition of a proton. Loss of ethanol from II gives a carbonium ion (III) which by elimination of a proton produces the acrylate (IV). The formation of the dialkoxypropionate and the alkoxyacrylate when a higher boiling alcohol is employed in this reversible system is obvious.

With sodium alkoxide the course of the transetherification phase is initially an attack by an

TABLE I

PRODUCTS FROM EXCHANGE REACTIONS

Alkyl β-Alkoxyacrylates, $ROCH{=}CHCO_2R'$

R	R'	Catalyst	B. p. (uncor.) °C.	Mm.	% Yield	$n^{20}D$
n-C_4H_9–	C_2H_5–	$NaHSO_4$	136	30	72	1.4489
s-C_4H_9–	C_2H_5–	$NaHSO_4$	99	9	73	1.4420
C_8H_{17}–[a]	C_2H_5–	$NaHSO_4$	93	1	53	1.4513
C_6H_{11}–[b]	C_2H_5–	$NaHSO_4$	93–98	0.1	80	1.4810
$C_2H_5OC_2H_4$–	C_2H_5–	$NaHSO_4$	71–74	1	72	1.4542
ClC_2H_4–	C_2H_5–	$NaHSO_4$	81–84	1	76	1.4740
$ClCH_2CHClCH_2$–	C_2H_5–	$NaHSO_4$	61–64	5	24	1.4621
n-C_4H_9–	n-C_4H_9–	NaOR	113–115	4	39	1.4505
s-C_4H_9–	s-C_4H_9–	NaOR	67–69	1	39	1.4476
C_8H_{17}–[a]	C_8H_{17}–[a]	NaOR	140–143	1	53	1.4569
n-$C_{10}H_{21}$–	n-$C_{10}H_{21}$–	NaOR	200	1	79	(M. p. 28–29°)
$(CH_3)_2NC_2H_4$–	$(CH_3)_2NC_2H_4$–	NaOR	138–139	1	62	1.4717
$C_6H_5CH_2$–	$C_6H_5CH_2$–	NaOR	168–178	0.1	67	1.5679
n-$C_4H_9OC_2H_4$–	n-$C_4H_9OC_2H_4$–	$Mg(OR)_2$	147–153	1	55	1.4560
Alkyl β,β-Dialkoxypropionates $(RO)_2CH{-}CH_2CO_2R'$						
n-C_4H_9–	C_2H_5–	$Et_2O{\cdot}BF_3$	92–94	0.3	73	1.4230
n-C_5H_{11}–	C_2H_5–	$Et_2O{\cdot}BF_3$	107–109	0.2	68	1.4337
n-C_4H_9–	n-C_4H_9–	$Mg(OR)_2$	121–125	0.6	66	1.4282
C_6H_{11}–[b]	C_6H_{11}–[b]	NaOR	158–173	0.7	69	1.4810
C_8H_{17}–[a]	C_8H_{17}–[a]	NaOR	160–174	0.03	86	1.4460
$CH_2{=}CHCH_2$–	C_2H_5–	$NaHSO_4$	60–66	1	63	1.4410
Alkyl β-Alkylthioacrylates $RSCH{=}CH{-}CO_2R'$						
n-C_4H_9–	C_2H_5–	$NaHSO_4$	100–107	2	51	1.4990
n-C_8H_{17}–	C_2H_5–	$NaHSO_4$	130–132	0.2	75	1.4941
$C_{12}H_{25}$–[g]	C_2H_5–	$NaHSO_4$	138–148	0.6	63	1.5005
Alkyl β,β-Dialkylthiopropionates $(RS)_2CH{-}CH_2CO_2R'$						
n-C_4H_9–	C_2H_5–	$Et_2O{\cdot}BF_3$	138–143	1	79	1.4866
Alkyl Alkoxymaleates $R'O_2CC(OR){=}CHCO_2R'$						
n-C_4H_9–	n-C_4H_9–	H_2SO_4	138–145	0.3	79	1.4570
C_8H_{17}–[a]	C_8H_{17}–[a]	H_2SO_4	150–164	0.05	54	1.4621
t-$C_4H_9OC_2H_5$–	t-$C_4H_9OC_2H_5$–	$Mg(OR)_2$	187–195	2.0	83	1.4540
n-$C_4H_9OC_2H_5$–	n-$C_4H_9OC_2H_5$–	$Mg(OR)_2$	190–205	1.0	63	1.4550
Alkyl α,α-Dialkoxysuccinates $R'O_2CC(OR)_2CH_2CO_2R'$						
$CH_2{=}CH{-}CH_2$–	C_2H_5–	$Et_2O{\cdot}BF_3$	107–112	0.4	71	1.4501
$(C_2H_5)_2CHCH_2$–	C_2H_5–	$Et_2O{\cdot}BF_3$	125–128	0.1	11	1.4410
n-C_4H_9–	n-C_4H_9–	$Mg(OR)_2$	159	1	88	1.4409
n-C_4H_9–	n-C_4H_9–	NaOR	147–152	0.7	47	1.4410
C_3H_{17}–[a]	C_8H_{17}–[a]	$Mg(OR)_2$	148	0.02	79	1.4551

alkoxide ion on the diethoxypropionate (I) to produce a carbanion $((C_2H_5O)_2CH\overset{\ominus}{C}HCOOC_2H_5)$ which by loss of an ethoxide ion yields the acrylate. When a higher boiling alcohol is present, addition to the acrylate occurs, and elimination of ethanol gives the β-alkoxyacrylate. Repetition of this process then yields the dialkoxypropionates. Transesterification appears to occur simultaneously with transetherification since no ethyl β-alkoxy or alkyl β-ethoxy esters are isolated.

Acknowledgment.—The analyses were carried out under the direction of Mr. C. W. Nash and Dr. E. L. Stanley. Mrs. R. Albert and Mr. C. Gianotti carried out a number of the experiments herein reported.

Experimental

Ethyl β-Ethoxy-β-butoxypropionate.—A mixture of 72 g. (0.5 mole) of ethyl β-ethoxyacrylate, 37 g. (0.5 mole) of 1-butanol and 5 ml. of a boron trifluoride–ethyl ether complex (1:1) was allowed to stand overnight, washed with an aqueous 5% sodium bicarbonate solution, then with water and dried over anhydrous potassium carbonate. Fractionation gave, after removal of a small forerun, 86 g. (79%) of the pure propionate, b. p. 80–85° (0.45 mm.); $n^{20}D$ 1.4200. *Anal.* Calcd. for $C_{12}H_{22}O_4$: C, 60.55; H, 10.09. Found: C, 60.60; H, 10.20; saponification equivalent 215 (calcd. 218).

Repeating the above experiment with ethanol gave 64 g. (72%) of ethyl β,β-diethoxypropionate; 1 g. of concd. sulfuric acid gave a 41% yield of the propionate; and 1 g.

TABLE I (*Continued*)

d^{20}_{20}	*MR.* Calcd.	Obs.	Formula	Analyses, % Calcd. Carbon	Calcd. Hydrogen	Found Carbon	Found Hydrogen	Sapon. equiv. Calcd.	Sapon. equiv. Found
0.9715	46.59	47.55	$C_9H_{16}O_3$	62.78	9.36	63.11	9.26	172	171
0.9780	46.59	46.57	$C_9H_{16}O_3$	62.78	9.36	62.63	7.90	172	170
0.9357	65.06	65.72	$C_{13}H_{24}O_3$	68.40	11.04	68.69	10.44	228	228
1.018	53.53	55.44	$C_{11}H_{18}O_3$	66.62	9.15	66.58	9.00	196	186
1.043	48.24	49.30	$C_9H_{16}O_4$	57.44	8.54	56.14	8.31	188	186
1.212	40.01	41.42	$C_7H_{11}O_3Cl^c$						
1.022	64.89	64.00	$C_8H_{12}O_3Cl_2$	42.29	5.29	41.40	6.28		
0.9465	55.83	56.93	$C_{11}H_{20}O_3$	65.96	10.07	66.17	9.02	200	196
0.9390	55.83	57.05	$C_{11}H_{20}O_3$	65.96	10.07	65.96	9.41	200	197
0.908	92.77	93.72	$C_{19}H_{36}O_3$	73.02	11.61	72.84	11.21	313	313
			$C_{23}H_{44}O_3$	75.00	11.95	74.99	11.91	369	364
0.9950	63.61	64.84	$C_{11}H_{22}N_2O_2$	57.36	9.64	57.63	9.44	[e]	
1.139	75.33	77.06	$C_{17}H_{16}O_3$	76.11	6.01	75.52	6.10	268	268
0.990	77.59	79.04	$C_{15}H_{28}O_5$	62.48	9.79	62.16	9.74	288	286
0.9257	67.17	67.67	$C_{13}H_{26}O_4$	63.41	10.57	63.27	10.53	246	244
0.9322	76.41	76.49	$C_{15}H_{30}O_4$	65.69	10.95	66.01	11.18	274	268
0.9268	76.41	76.23	$C_{15}H_{30}O_4$	65.69	10.95	66.04	11.46	274	274
1.038	97.52	97.00	$C_{21}H_{36}O_4$	71.59	10.23	71.31	10.23	352	340
0.899	131.83	131.41	$C_{27}H_{54}O_4$	73.30	12.21	73.20	12.16	442	438
0.996	57.00	56.83	$C_{11}H_{18}O_4$	61.64	8.50	61.66	8.67	214	212
1.001	54.65	55.20	$C_9H_{16}O_2S$	57.4	8.55	57.8	8.66	188	187
0.9568	71.39	74.24	$C_{13}H_{24}O_2S$	63.94	9.84	64.40	10.10	[f]	
0.9653	87.86	91.48	$C_{17}H_{32}O_2S$	68.00	10.67	67.83	10.76	[h]	
1.003	79.83	79.65	$C_{13}H_{26}O_2S_2$	56.11	9.36	56.39	9.48	[i]	
0.9961	80.57	82.05	$C_{16}H_{28}O_5$	63.95	9.39	63.80	9.50	150	152
0.9373	135.99	137.56	$C_{28}H_{52}O_5$	71.74	11.20	71.66	11.20	234	233
1.023	113.21	114.40	$C_{22}H_{40}O_8$	61.11	9.26	60.94	9.42	216	222
1.020	113.21	115.04	$C_{22}H_{40}O_8$	61.11	9.26	60.95	9.16		
1.060	72.51	72.61	$C_{14}H_{22}O_6$	58.71	7.75	58.05	7.71	140	143
1.001	101.15	98.80	$C_{20}H_{38}O_6$	64.17	10.22	64.20	10.31	187	182
0.986	101.15	100.29	$C_{20}H_{38}O_6$	64.17	10.22	64.03	10.01	187	179
0.9024	175.04	179.80	$C_{36}H_{70}O_6$	72.24	11.70	71.98	11.64	300	274

[a] 2-Ethylhexyl. [b] Cyclohexyl. [c] Calcd.: Cl, 19.8. Found: Cl, 21.0. [d] Calcd.: Cl, 31.2. Found: Cl, 30.1. [e] Calcd.: N, 12.17. Found: N, 12.00. [f] Calcd.: S, 13.11. Found: S, 13.22. [g] *t*-Dodecylmercaptans obtained from Phillips Petroleum. [h] Calcd.: S, 10.67. Found: S, 11.22. [i] Calcd.: S, 23.02. Found: S, 22.79.

of sodium bisulfate as catalyst gave, after heating at 80–90° for two hours, an 84% yield of the propionate.

Ethyl β-Butoxyacrylate.—A mixture of 50 g. (0.26 mole) of ethyl β,β-diethoxypropionate, 74 g. (1 mole) of 1-butanol and 0.1 g. of sodium bisulfate was fractionated through a short packed column. There was obtained 24 g. of an ethanol–butanol mixture, b. p. 78–114°, 48 g. of recovered butanol, b. p. 114–115°, and 29 g. (65%) of ethyl β-butoxyacrylate, b. p. 87° (3 mm.). The residue remaining in the distilling flask amounted to 11 g. It was distilled from a Claisen flask to give 5 g. of butyl β-butoxyacrylate, b. p. 113° (4 mm.). When ethyl β-ethoxyacrylate was used in place of the propionate similar results were obtained.

In a similar experiment from 48 g. (0.25 mole) of ethyl β,β-diethoxypropionate, 111 g. (1.5 moles) of 1-butanol and 0.5 ml. of concd. sulfuric acid there was obtained 4 g. (8%) of butyl β-butoxyacrylate, b. p. 92–100° (2 mm.); n^{20}_D 1.4505 and 16 g. of higher boiling material, b. p. 110–185° (2 mm.).

Ethyl β-Butoxypropionate.—Hydrogenation of ethyl β-butoxyacrylate (0.35 mole) over 6 g. of ethanol-moist Raney nickel at 1400 p. s. i. gage pressure and 50° gave the propionate (0.29 mole) (79%), b. p. 45° (1 mm.); n^{20}_D 1.4147. *Anal.* Calcd. for $C_9H_{18}O_3$: C, 62.04; H, 10.04; sapn. equiv., 174. Found: C, 62.17; H, 10.48; saponification equivalent, 174.

β-Butoxypropionic Acid.—To a stirred solution of 24 g. (0.6 mole) of sodium hydroxide in 220 ml. of water there was added 87 g. (0.5 mole) of ethyl β-butoxypropionate.

The two-phase mixture was refluxed for twenty minutes and distilled to give 148 g. of an ethanol–water mixture, b. p. 90–100°. The distillate was saturated with potassium carbonate, the upper layer separated and dried over anhydrous magnesium sulfate. Distillation gave 19 g. (82.6%) of ethanol, b. p. 77–78°; $n^{15}\mathrm{D}$ 1.3660. The saponification residue was acidified with 60 ml. of concd. hydrochloric acid, extracted with ether, dried over anhydrous magnesium sulfate and distilled. There was obtained, after removal of ether, 62 g. (85%) of crude β-butoxypropionic acid, b. p. 100–115° (3 mm.) which on redistillation boiled at 93.5–95° (2 mm.); $n^{20}\mathrm{D}$ 1.4264; neutral equivalent 146 (calcd. 146).

Ethyl β,β-Dibutoxypropionate.—In a similar trans-etherification experiment there was obtained from 190 g. (1 mole) of ethyl β,β-diethoxypropionate, 288 g. (4 moles) of 1-butanol and 0.2 g. of sodium bisulfate 89 g. of ethanol. The distillation was stopped at this point, the residue cooled to room temperature, washed with an aqueous 5% sodium carbonate solution and dried over anhydrous potassium carbonate. Distillation gave 153 g. (62%) of ethyl β,β-dibutoxypropionate. There was 25 g. of higher boiling material, b. p. 94–121° (0.3 mm.) which consisted of a mixture of butyl β-butoxyacrylate and butyl β,β-dibutoxypropionate.

Similar results were obtained when 2 ml. of boron trifluoride–ethyl ether complex (1:1) was used. Ethyl β-ethoxyacrylate with butanol and ether catalyst gave the same results.

The above dibutoxypropionate was characterized as follows: Saponification of 98.4 g. (0.4 mole) of the propionate with 200 g. (0.5 mole) of aqueous 10% sodium hydroxide solution gave 8 g. (45%) of ethanol, b. p. 76–81; $n^{20}\mathrm{D}$ 1.3660. The aqueous residue on acidification yielded an oil which was taken up in ether and dried over Drierite. Distillation of the oil, after removal of ether, produced 6.4 liters of carbon dioxide and 25 g. (35%) of dibutyl acetal, b. p. 186–188°; $n^{20}\mathrm{D}$ 1.4087.[4]

Butyl β,β-Dibutoxypropionate.—A mixture of 190 g. (1 mole) of ethyl β,β-diethoxypropionate, 296 g. (4 moles) of 1-butanol and 5 g. of magnesium butoxide was fractionated to give 135 g. of ethanol, b. p. 78–81 and 60 g. of recovered 1-butanol, b. p. 40–50° (50 mm.). The residue was cooled to room temperature and an equal volume of ether was added. The ether solution was washed with aqueous 10% hydrochloric acid and then with water until the washings were neutral, dried over anhydrous calcium sulfate and fractionated. After removal of ether and excess butanol there was obtained 21 g. of a forerun, b. p. 32–112° (0.4 mm.); $n^{20}\mathrm{D}$ 1.4480, 131 g. of a mixture consisting of 28% butyl β-butoxyacrylate and 72% butyl β,β-dibutoxypropionate (calcd. from index of refraction curve), b. p. 112–121° (0.5 mm.); $n^{20}\mathrm{D}$ 1.4344; and 89 g. of pure butyl β,β-dibutoxypropionate.[2] The yield of acrylate was 32% and the combined yield of propionate as determined from index of refraction of the mixture plus the pure material was 67%. Similar results were obtained using sodium ethoxide.

If the alkaline catalyst was not removed by neutralization and washing and the fractionation continued so as to remove excess butanol, butyl β-butoxyacrylate was isolated.

Butyl α,α-Dibutoxysuccinate.—When ethyl α,α-diethoxysuccinate or ethyl ethoxymaleate was substituted for the propionate in the above experiment there was obtained butyl α,α-dibutoxysuccinate.

If the alkaline catalyst was not removed by neutralization and washing and the fractionation continued so as to remove excess butanol, butyl butoxymaleate was the isolated product.

Butyl Butoxymaleate.—A mixture of 103 g. (0.5 mole) of methyl α,α-dimethoxysuccinate, 148 g. (2.0 moles) of 1-butanol and 0.5 ml. of concd. sulfuric acid was fractionated through a short packed column to give 60.5 g. (1.9 moles) of methanol, b. p. 64–70°. The excess butanol was removed under reduced pressure, the residue taken up in chloroform, washed with water, dried over anhydrous potassium carbonate and distilled. After removal of chloroform, there was obtained 93 g. (62%) of butyl butoxymaleate.

If 1 g. of sodium bisulfate was used in place of the sulfuric acid no reaction occurred. However, 2-ethyl-1-butanol, the above succinate and sodium bisulfate reacted to give 2-ethylbutyl-2-ethylbutoxymaleate, b. p. 163–169° (0.5 mm.), $n^{20}\mathrm{D}$ 1.4630, saponification equivalent 379 (calcd. 384).

Ethyl α,α-Dialloxysuccinate.—The ester (85.8 g.) (0.3 mole) obtained from a boron trifluoride catalyzed reaction was saponified by heating for three hours with 200 ml. of an aqueous 15% solution of sodium hydroxide. There was obtained 24 g. (90%) of ethanol, b. p. 74–80°, $n^{20}\mathrm{D}$ 1.3680. Acidification of the saponification residue produced an oily acid which was not purified.

Summary

1. The system ethyl β-ethoxyacrylate–ethyl β,β-diethoxypropionate has been shown to be reversible in the presence of some acidic type catalysts.

2. A selective exchange reaction between ethyl β-ethoxyacrylate (IV), ethyl β,β-diethoxypropionate (I), ethyl ethoxymaleate, ethyl α,α-diethoxysuccinate and alcohols has been demonstrated to occur in the presence of certain acid type catalysts to produce ethyl β-alkoxyacrylates, ethyl β,β-dialkoxypropionates and ethyl α,α-dialkoxysuccinates.

3. Certain other catalysts with the above esters give the alkyl β-alkoxyacrylates, alkyl β,β-dialkoxypropionates, alkyl alkoxymaleates and alkyl α,α-dialkoxysuccinates.

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[4] Croxall, Glavis and Neher, THIS JOURNAL, **70**, 2805 (1948).