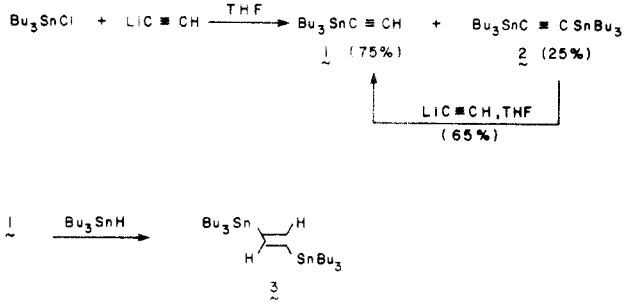
Scheme I



for 1 h at which time 60.0 g (180 mmol) of tri-*n*-butyltin chloride were added dropwise over a period of 30 min. The reaction mixture was warmed to room temperature and stored under a closed acetylene atmosphere for 12 h. Water (10 mL) was added, and the reaction mixture was concentrated in vacuo. Heptane (250 mL) was added, and the reaction mixture was washed with one 100-mL portion of water, dried over $MgSO_4$, and concentrated in vacuo to furnish an oil. Distillation afforded 43 g (75%) of tri-*n*-butylethynylstannane (1): bp 200 °C (2 mm) [lit.[11] bp 76 °C (0.2 mm)]. The NMR and IR spectra of 1 were identical with those of material previously reported.[12]

Conversion of Bis(tri-*n*-butylstannyl)acetylene (2) to Tri-*n*-butylethynylstannane (1). A solution of 80.0 mL (124 mmol) of *n*-butyllithium in hexane in 250 mL of dry tetrahydrofuran was stirred under an acetylene atmosphere at 0 °C for 1 h at which time 30.0 g of the accumulated residues, consisting largely of 2, was added dropwise over a period of 30 min. The reaction mixture was warmed to room temperature and stored under a closed acetylene atmosphere for 15 h. The isolation and purification procedure described above gave 22 g (65%) of 1. The remaining residue may be recycled for the preparation of more 1.[1c]

Registry No. 1, 994-89-8; 2, 994-71-8; 3, 14275-61-7; Bu_3SnCl, 1461-22-9.

(11) Zavgorodnii, V. S.; Sharanina, L. G.; Petrov, A. A. *J. Gen. Chem. USSR.* (*Engl. Transl.*) **1967**, *37*, 1469.
(12) Wollenberg, R. H. Ph. D. Thesis, Harvard University, 1976.

Nonprotic Procedure for Transesterification of Methyl Esters[1]

Dante Bencivengo and Joseph San Filippo, Jr.*

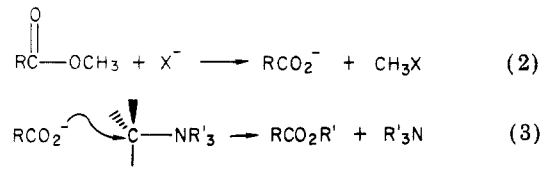
Department of Chemistry, Rutgers University, New Brunswick, New Jersey 08903

Received June 16, 1981

In the course of an unrelated investigation in our laboratory if became necessary to carry out a series of transesterifications under rigorously neutral conditions. A survey of the literature produced only an isolated example which remotely met these needs.[2] We report here our development of one procedure which does meet these qualifications and whose general synthetic applicbility appears to be moderate to good.

Treatment of the methyl ester of various carboxylate acids with tetra-*n*-alkylammonium halide at elevated

Scheme I



temperature leads to the production of the corresponding *n*-alkyl ester (eq 1). Thus, reaction of methyl cinnamate

$$\underset{\mathbf{1}}{RCO_2CH_3} + n\text{-}R'_4N^+X^- \rightarrow \underset{\mathbf{2}}{RCO_2R'} + CH_3X \quad (1)$$

with tetra-*n*-butylammonium bromide at 140 °C for 72 h under anhydrous conditions results in its quantitative conversion to *n*-butyl cinnamate (3). The same reaction repeated with the corresponding tetra-*n*-alkylammonium chloride or iodide under optimized conditions produces, respectively, 78% and 69% yields of 3.

The applicability of this procedure to a representative series of methyl ethers is summarized in Table I. Several aspects about this data deserve brief comment. For example, the rate of reaction, in HMPA solution, exhibits the following dependence on halogen: $Cl^- > Br^- > I^-$. No reaction is observed with $n\text{-}Bu_4N^+BF_4^-$.

Second, higher concentrations of tetra-*n*-butylammonium halide promote higher product yields, a fact which may be related to the further observation that, in general, most solvents have a deleterious effect on the course of this reaction.[3] Thus, in general, optimum results are obtained in the absence of any solvent. Although the use of hexamethylphoshoramide (HMPA) seems to cause little or no diminution in product yield, the workup, isolation, and purification of products obtained from reactions performed in HMPA are generally more difficult.

Third, entries 31 and 32 summarize the influence which the structure of the alkyl group in the tetra-*n*-alkylammonium halide has on the transesterification. Lower yields appear to obtain with tetra-*n*-propyl- than with tetra-*n*-butylammonium halide. In general, the influences of time, solvent, and reactant ratios parallel those presented in Table I.

Mechanistically, we believe the transformation defined by eq 1 is occurring by the pathway outlined in Scheme I. Thus, eq 2 defines the well-known *O*-alkyl cleavage of a methyl ester by nucleophilic displacement while eq 3 presents the alkylation of a carboxylate anion by an onium ion. This scheme is consistent with (i) the previously observed influence which the nature of the group R in the OR functionality has on the *O*-alkyl cleavages of esters,[4,5] (ii) an increasing recognition of the moderately nucleophilic nature of carboxylate ions under *aprotic* conditions,[6] and (iii) the influence exerted by the nature of the alkyl group

(1) This work was supported by the National Science Foundation, Grant 80-17045.
(2) Brasen, W. R.; Hauser, C. R. *Org. Synth.* **1954**, *34*, 58.

(3) Experiments performed in dimethylformamide (DMF) and *N*-methylpyrrolidone produced no significant yield of transesterification product. Transesterification can be effected by using ether tri- or tetraglyme solvent; however, the yields are 20–30% less than those observed for the equivalent reactions performed neat or in HMPA.
(4) Consistent with earlier observations[5] that *O*-alkyl cleavage of esters by nucleophilic displacement is effective only when the alkyl group is methyl, we have observed that treatment of *ethyl* octanoate with 4 equiv of $(n\text{-}C_4H_9)_4N^+Cl^-$ at 140 °C for 36 h produced a 9% yield of *n*-butyl octanoate. Similar treatment of *n*-propyl octanoate failed to yield any (<1%) *n*-butyl octanoate.
(5) Taschner, E.; Liberek, B. *Rocz. Chem.* **1956**, *30*, 323. Elsinger, F.; Schreiber, J.; Eschenmoser, A. *Helv. Chim. Acta* **1960**, *43*, 113. Meyer, W. L.; Levinson, A. S. *J. Org. Chem.* **1963**, *28*, 2184. Krakower, G. W.; Brown, J. W.; Fried, J. *Ibid.* **1962**, *27*, 4710. Bartlett, P. A.; Johnson, W. S. *Tetrahedron Lett.* **1970**, 4459. McMurry, J. E.; Wong, G. B. *Syn. Commun.* **1972**, *2*, 389 and references therein.
(6) San Filippo, J., Jr.; Romano, L. J. *J. Org. Chem.* **1975**, *40*, 1514 and references therein.

0022-3263/81/1946-5222$01.25/0

Table I. Reaction of Selected Methyl Esters with Tetra-*n*-alkylammonium Halides[a]

entry	R of RCO_2CH_3	$R'_4N^+X^-$[b]	solvent	time, h	product,[f] %	
1	n-C_7H_{15}	$(n$-$C_4H_9)_4N^+Cl^-$[c]	HMPA	24	n-$C_7H_{15}CO_2$-n-C_4H_9	10
2		[d]		24		24
3		[e]		24		37
4				24		42
5	n-C_7H_{15}	$(n$-$C_4H_9)_4N^+Cl^-$	HMPA	12	n-$C_7H_{15}CO_2$-n-C_4H_9	30
6				24		40
7				36		56
8				48		38
9	n-C_7H_{15}	$(n$-$C_4H_9)_4N^+Cl^-$	neat	12	n-$C_7H_{15}CO_2$-n-C_4H_9	30
10				24		45
11				36		49
12				48		52
13				72		53
14	2-$CH_3C_7H_{14}$	$(n$-$C_4H_9)_4N^+Cl$	HMPA	24	2-$CH_3C_7H_{14}CO_2$-n-C_4H_9	45
15	2-$CH_3C_7H_{14}$	$(n$-$C_4H_9)_4N^+Cl^-$	HMPA	36	2-$CH_3C_7H_{14}CO_2$-n-C_4H_9	70
16	2-$CH_3C_7H_{14}$	$(n$-$C_4H_9)_4N^+Cl^-$	neat	72	2-$CH_3C_7H_{14}CO_2$-n-C_4H_9	52
17	2,2-$(CH_3)_2C_7H_{13}$	$(n$-$C_4H_9)_4N^+Cl^-$	HMPA	48	2,2-$(CH_3)_2C_7H_{13}CO_2$-n-C_4H_9	50
18	2,2-$(CH_3)_2C_7H_{13}$	$(n$-$C_4H_9)_4N^+Cl^-$	neat	72	2,2-$(CH_3)_2C_7H_{13}CO_2$-n-C_4H_9	54
19	n-C_7H_{15}	$(n$-$C_4H_9)_4N^+Br^-$	HMPA	72	n-$C_7H_{15}CO_2$-n-C_4H_9	25
20	n-C_7H_{15}	$(n$-$C_4H_9)_4N^+Br^-$	neat	72	n-$C_7H_{15}CO_2$-n-C_4H_9	57
21	2-$CH_3C_7H_{14}$	$(n$-$C_4H_9)_4N^+Br^-$	HMPA	72	2-$CH_3C_7H_{14}CO_2$-n-C_6H_9	51
22	2-$CH_3C_7H_{14}$	$(n$-$C_4H_9)_4N^+Br^-$	neat	72	2-$CH_3C_7H_{14}CO_2$-n-C_4H_9	60
23	2,2-$(CH_3)_2C_7H_{13}$	$(n$-$C_4H_9)_4N^+Br^-$	neat	72	2,2-$(CH_3)_2C_7H_{13}CO_2$-n-C_4H_9	60
24	n-C_7H_{15}	$(n$-$C_4H_9)_4N^+I$	HMPA	48	n-$C_7H_{15}CO_2$-n-C_4H_9	15
25	C_6H_5CH=CH[d]	$(n$-$C_4H_9)_4N^+Cl^-$	neat	72	C_6H_5CH=$CHCO_2$-n-C_4H_9	78
26	C_6H_5CH=CH[d]	$(n$-$C_4H_9)_4N^+Br^-$	neat	72	C_6H_5CH=$CHCO_2$-n-C_4H_9	100
27	C_6H_5CH=CH[d]	$(n$-$C_4H_9)_4N^+I^-$	neat[g]	72	C_6H_5CH=$CHCO_2$-n-C_4H_9	69
28	C_6H_5[d]	$(n$-$C_4H_9)_4N^+Cl^-$	neat	24	$C_6H_5CO_2$-n-C_4H_9	34
29	[d]			36		60
30	[d]			72		74
31	p-$(CH_3O)_2CHC_6H_4$			72	p-$(CH_3O)_2CHC_6H_4CO_2$-n-C_4H_9	90
32	C_6H_5CH=CH[d]	$(n$-$C_4H_9)_4N^+Br^-$	HMPA	72	C_6H_5CH=$CHCO_2$-n-C_4H_9	91
33	C_6H_5CH=CH[d]	$(n$-$C_3H_7)_4N^+Br^-$	HMPA	72	C_6H_5CH=$CHCO_2$-n-C_3H_7	69

[a] Unless otherwise indicated, all reactions were carried out at 140 °C. [b] Unless otherwise indicated, a 4:1 molar ratio of $R'_4N^+X^-$ to RCO_2CH_3 was employed. [c] A 1:1 ratio of RCO_2CH_3 to $R'_4N^+X^-$ was employed. [d] A 1:2 ratio of RCO_2CH_3 to $R'_4N^+X^-$ was employed. [e] A 1:3 ratio of RCO_2CH_3 to $R'_4N^+X^-$ was employed. [f] Yields were determined by GLC using the internal standard technique and are based on starting ester. [g] Reaction carried out at 150 °C.

bonded to the onium center on the course of such reactions (eq 2). Moreover, we have examined the reaction of a typical carboxylate anion, *n*-octanoate, with tetra-*n*-butylammonium bromide under conditions comparable to

$$n\text{-}C_7H_{15}CO_2^-Na^+ \xrightarrow[140\ °C,\ 72\ h]{n\text{-}Bu_4N^+Br^-} n\text{-}C_7H_{15}CO_2\text{-}n\text{-}Bu\ 78\%$$

those employed in transesterification and have observed its facile alkylation. Finally, in an effort to further establish the participation of eq 2, we treated the effluent from the reaction of methyl cinnamate and tetra-*n*-butylammonium iodide with tri-*n*-butylamine. Characterization of the resulting white precipitate showed it to be the expected quaternary salt $[(n\text{-}C_4H_9)_3NCH_3]^+I^-$.

Taken together, these facts are consistent with the general reaction outlined in eq 1 as proceeding by the pathway shown in Scheme I. Our results suggest that such a procedure can provide a synthetically satisfactory method for the transesterification of methyl esters under neutral conditions, and thus could be especially useful in those systems where the presence of acid-sensitivie functionalities preclude classical procedures for transesterification (cf. entry 31, Table I).

Experimental Section

All glassware was flame dried and allowed to cool under a purge of dry nitrogen prior to use. Hexamethylphosphoramide (HMPA) was obtained commercially and distilled from sodium shot [bp 76–78 °C (1 torr)] immediately prior to use.

Quantitative GLC determinations were carried out on either a Hewlett-Packard Model 5750 or a Varian Model 1400 gas chromatograph equipped with an FID. The internal standard technique was employed, and areas were determined electronically by using a Hewlett-Packard Model 3380A integrator. Qualitative GLC determination was performed on a Varian Model 90-P chromatograph equipped with a thermal-conductivity detector. ^1H NMR spectra were determined on a Varian Model T-60 spectrometer; mass spectra were obtained on a Hewlett-Packard Model 5985B GC/MS.

n-$Bu_4N^+Cl^-$, *n*-$Bu_4N^+Br^-$, and *n*-$Bu_4N^+I^-$ were purchased from Aldrich Chemical Co. *n*-$Bu_4N^+Cl^-$ was purified before use as described below. *n*-$Bu_4N^+BF_4^-$ was used as received from Southwestern Technical Products.

Preparation of Esters. Most esters were prepared by well-established literature procedures.

2-Methyl octanoic acid, prepared by the reaction of 2-octylmagnesium bromide with excess dry ice in diethyl ether, was converted to the corresponding acid chloride and subsequently to methyl 2-methyloctanoate by reaction with dry methanol; bp 35 °C (0.7 torr) [lit.[7] bp 42–43 °C (3 torr)].

Preparation of Methyl 2,2-Dimethyloctanoate. The procedure used was analogous to that reported by Rathke and Lindert[8] for the preparation of sterically hindered methyl esters; bp 56–60 °C (4.0 torr) [lit.[9] bp 51–53 °C (3 torr)].

Purification of Tetra-*n*-butylammonium Chloride ($Bu_4N^+Cl^-$). Into a 500-mL round-bottomed flask were placed tetra-*n*-butylammonium chloride (100 g) and benzene (250 mL). The flask was fitted with a Dean–Stark apparatus and water removed by azeotropic distillation. After the mixture was cooled, crystallization was induced by shaking. Dry hexane was added, and the white crystals were filtered with suction in a nitrogen-filled drybox. The isolated solid was washed twice with 50-mL portions

(7) Belskii, I. F.; Shotakowski, V. M.; Vol'nova, Z. K.; Ishchenko, S. I.; Glukhovtsev, V. G., *Izv. Akad. Nauk. SSSR, Khim.* **1967**, *2*, 420.
(8) Rathke, M. W.; Lindert, A. *J. Am. Chem. Soc.* **1971**, *93*, 2318.
(9) Shutikova, L. A.; Puzitskii, K. V.; Cherkaev, V. G.; Eidus, Y. T. *Tr. Uses, Nauchno-Issled. Sint. Natur. Dunshist. Veshchestv.* **1965**, *No. 7*, 16.

of hexane and the remaining solvent removed under reduced pressure. n-$Bu_4N^+Cl^-$ is exceedingly hygroscopic and should be handled accordingly.

Preparation of Methyl 4-(Dimethoxymethyl)benzoate. A solution of 4-carboxybenzaldehyde (6.0 g, 40 mmol) in a 70/30 mixture of diethyl ether/methanol was esterified by treatment with 1.68 g of diazomethane. The resulting solution was concentrated and transferred into a 250-mL flask containing methanol (125 mL), trimethyl orthoformate (4.67 g, 10% excess), p-toluenesulfonic acid (0.38 g, 5 mol %), and a Teflon-coated stirring bar. The flask was fitted with a water-cooled condenser and heated at reflux for 24 h. A standard workup followed by microscale distillation afforded 5.75 g (70% yield based on starting acid) of clear colorless liquid, bp 100 °C (0.65 torr).

Transesterification. Reaction of Methyl Cinnamate with Tetra-*n*-butylammonium Bromide. Into a 50-mL flask were placed methyl cinnamate (4.00 g), tetra-n-butylammonium bromide (15.9 g, 2.00 equiv), and a Teflon-coated stirrer bar. The flask was fitted with a condenser and heated in an oil bath maintained at 140 °C under a static head of nitrogen. After 72 h the reaction was allowed to cool. The resulting semisolid mixture was partitioned between petroleum ether and water. The organic layer was separated and washed with two 250-mL portions of 0.1 M HCl, 200 mL of saturated aqueous sodium bicarbonate, and finally 200 mL of water before being dried ($MgSO_4$) and concentrated in vacuo. Microscale distillation under reduced pressure afforded 4.19 g (83%) of clear, colorless n-butyl cinnamate, bp 117 °C (0.7 torr) (lit.[10] bp 288–289 °C).

Registry No. n-$C_7H_{15}CO_2CH_3$, 111-11-5; 2-$CH_3C_7H_{14}CO_2CH_3$, 2177-86-8; 2,2-$(CH_3)_2C_7H_{13}CO_2CH_3$, 14250-74-9; $C_6H_5CH{=}CHCO_2CH_3$, 103-26-4; $C_6H_5CO_2CH_3$, 93-58-3; p-$(CH_3O)_2CHC_6H_4CO_2CH_3$, 42228-16-0; $(n\text{-}C_4H_9)_4N^+Cl^-$, 1112-67-0; $(n\text{-}C_4H_9)_4N^+Br^-$, 1643-19-2; $(n\text{-}C_4H_9)_4N^+I^-$, 311-28-4; $(n\text{-}C_3H_7)_4N^+Br^-$, 1941-30-6; n-$C_7H_{15}CO_2$-n-C_4H_9, 589-75-3; 2-$CH_3C_7H_{14}CO_2$-n-C_4H_9, 79420-98-7; 2,2-$(CH_3)_2C_7H_{13}CO_2$-n-C_4H_9, 79420-99-8; $C_6H_5CH{=}CHCO_2$-n-C_4H_9, 538-65-8; $C_6H_5CO_2$-n-C_4H_9, 136-60-7; p-$(CH_3O)_2CHC_6H_4CO_2$-n-C_4H_9, 79421-00-4; $C_6H_5CH{=}CHCO_2$-n-C_3H_7, 7778-83-8; 2-methyloctanoic acid, 3004-93-1; 2-methyloctanoyl chloride, 43152-88-1; 2-octylbromide, 557-35-7; 4-carboxybenzaldehyde, 619-66-9; 4-formylbenzoic acid methyl ester, 1571-08-0.

(10) Vorländer, D.; Walter, R. *Z. Phys. Chem.* **1925**, *118*, 1.

Reaction of Epoxides with 2,6-Di-*tert*-butylphenol

Robert W. Layer

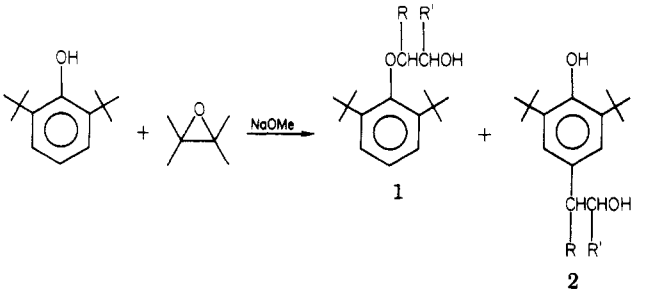
BFGoodrich Research and Development Center, Brecksville, Ohio 44141

Received July 21, 1981

The alkylation of phenols with epoxides under basic conditions is known to give the 2-hydroxyethyl ethers of the phenols and their hydroxyethyl oligomers.[1] Since it is well-known that 2,6-di-*tert*-butylphenol, in many cases, is alkylated at the 4-position rather than on the oxygen,[2] we investigated the reaction of this phenol with epoxides. We now report that both carbon and oxygen alkylation occur when epoxides react with 2,6-di-*tert*-butylphenol and that the relative amount of carbon alkylation increases with an increase in the number of substituents on the epoxide.

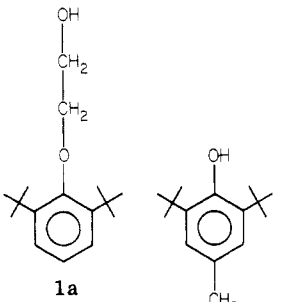
When equimolar amounts of 2,6-di-*tert*-butylphenol and ethylene oxide are heated with a small amount of sodium methoxide for 4 h at 220 °C, the primary product is the 2-hydroxyethyl ether of the phenol **1a** along with a smaller amount of 4-(2-hydroxyethyl)-2,6-di-*tert*-butylphenol (**2a**). GC analysis shows that the hydroxyethyl oligomers of these alcohols are also formed during the reaction. It is important to note that these oligomers are formed in the same ratio as their parent compounds from which they are derived. Thus, the ratio of **1a**:**2a** depends soley on their relative rates of formation rather than on subsequent reactions. Distillation of the crude product gives up to 44% yields of a mixture of 1 and **2**.

Table I. Formation of 1 and 2[b]



reaction	R	R'	2:1[d]	bp, °C (mm)[c]	% yield
a	H	H	4	125-127 (0.7)	44
b	H	CH_3	1.2	110-120 (0.5)	39
c	H	C_2H_5	0.97	122-137 (1.0)	43
d	H	n-C_8H_{17}	1	221-268 (1.4)	49
e	H	Ph	1.13[a]	134-165 (0.9)	19
f	H	CH_2OPh	1.22[a]	194-229 (1.0)	31
g	C_4H_8		all 2	150-170 (0.2)	28
h	C_3H_6		all 2	146-151 (0.7)	14

[a] From ^1H NMR ratios of $PhCH_2$ to $PhOCH_2$ areas. [b] All were analyzed by field desorption, atomic composition mass spectroscopy and found to have accurate masses with 3 ppm of the calculated values. [c] The boiling point range of the products, 1 and 2, used to establish the yield and product ratio. [d] From GC peak areas.



1a

2a

It can be seen from Table I that ethylene oxide alkylates the oxygen 4 times more readily than the carbon. When the more bulky propylene oxide, or other epoxides of terminal olefins, are used in this reaction, the relative amount of carbon alkylated products increases. With these epoxides, the oxygen and carbon are alkylated at equal rates. As would be expected under base-catalyzed conditions, the phenol reacts only at the least substituted (methylene) carbon of the epoxide to give a primary alkyl attachment.[3] Epoxides of cyclic olefins give only the carbon alkylation products. In these cases, the phenol

(1) Miller, S. A.; Bann, B.; Thrower, R. D. *J. Chem. Soc.* **1950**, 3623.
(2) Starnes, W. H., Jr.; Patton, T. L. U.S. Patent 3 526 668 (1970); *Chem. Abstr.* **1970**, *73*, 98589d.
(3) Chitwood, H. C.; Freure, B. T. *J. Am. Chem. Soc.* **1946**, *68*, 680.

0022-3263/81/1946-5224$01.25/0