[CONTRIBUTION FROM THE DIVISION OF PHYSICAL SCIENCES, UNIVERSITY OF CALIFORNIA AT RIVERSIDE]

Optically Active Butane-2-*d*. III. Verification of Configuration by Elimination Reactions[1]

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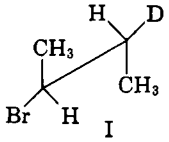
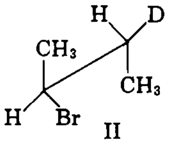
In the reaction sequence 2,3-epoxybutane → 2-butanol → 2-bromobutane → butane, a deuterium atom can be introduced stereospecifically at the first or last step by means of reduction with lithium aluminum deuteride. The anticipated inversion which should accompany these two steps has been further verified by the behavior of both *erythro*- and *threo*-2-bromobutane-3-*d* in a typical *trans*-elimination reaction. The *trans/cis* ratio of products from the dehydrobromination of halides were: *threo*-deuterohalide from active epoxide, 5.3; *erythro*-deuterohalide from meso epoxide, 1.2; undeuterated 2-bromobutane, 3.1. Mass spectral data are given for reaction products. Samples of monodeuterobutenes were prepared by three independent methods.

It has been demonstrated[2] that the lithium aluminum deuteride reduction of 2-bromobutane, 2,3-epoxybutane, and 2-methanesulfonoxybutane all show the same stereochemical result, namely, inversion of configuration if analogy is drawn to a comparable opening of bicyclic epoxides.[3] Each reduction can lead directly or indirectly to optically active butane-2-*d* which exhibits a sign of rotation of the plane of polarized light in agreement with that calculated for this simplest monodeuteroalkane.[4] However, further confirmation of the configuration of butane-2-*d* has been obtained here by the observation of the distribution of isomeric butenes resulting from elimination reactions of 2-bromobutane-3-*d*. Thus the levorotatory butane-2-*d* has the D configuration.

Two enantiomorphic monodeuterated 2-bromobutane derivatives were prepared from *meso*- and D-2,3-epoxybutane by reduction to 2-butanol-3-*d* with lithium aluminum deuteride followed by conversion to 2-bromobutane-3-*d* with PBr_3.[5] With inversion accompanying each reaction the products were respectively the *dl-erythro* (I) and *threo* (II) isomers. The *dl*-isomers of both I and II were obtained by Skell[6] in a study of addition reactions, and, as in this instance, the structure determination was based on elimination reactions comparable to those applied by Curtin and Kellom[7] to diastereomeric forms of 1,2-diphenylethanol-2-*d*.



I



II

Elimination reactions. The elimination of hydrogen bromide from 2-bromobutane with alcoholic potassium hydroxide under conditions favorable for an E_2 reaction leads to a mixture of 1-butene and *cis*- and *trans*-2-butene. If the halide contained a deuterium atom situated *trans* with respect to the bromine atom, as in I, an elimination reaction under identical conditions should lead to a product containing a smaller percentage of the *trans*-isomer because of the higher energy requirements in the transition state in which the C-D bond is broken. Also, in the absence of isomerization during or after the reaction, the *trans*-isomer should be free of deuterium. Conversely, the *threo*-isomer, II, should give a higher percentage of *trans*-2-butene and this should retain deuterium.

The results of elimination reactions carried out in 17.5% ethanolic potassium hydroxide at 65° are given in Table I. In each instance the distribution of isomers indicated an isotope effect which was in accord with a pattern of inversion during epoxide opening. Under the conditions of the reaction, no isomerization of butenes was found to occur.

TABLE I

PRODUCTS OF ELIMINATION REACTIONS OF 2-BROMOBUTANE AND DEUTERATED 2-BROMOBUTANES WITH 17.5% ETHANOLIC KOH

	Butene Distributions, %			*trans*/ *cis*
Isomer	1-	*cis*- 2-	*trans*- 2-	Ratio
2-Bromobutane	23	19	58	3.1
erythro-2-Bromobutane-3-*d* (I)	35	29	36	1.2
threo-2-Bromobutane-3-*d* (II)	24	12	64	5.3

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(1) This research was supported by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the donors of said fund.

(2) G. K. Helmkamp and B. F. Rickborn, *J. Org. Chem.*, **22**, 479 (1957).

(3) L. W. Trevoy and W. G. Brown, *J. Am. Chem. Soc.*, **71**, 1675 (1949).

(4) W. Fickett, *J. Am. Chem. Soc.*, **74**, 4204 (1952).

(5) G. K. Helmkamp, C. D. Joel, and H. Sharman, *J. Org. Chem.*, **21**, 844 (1956).

(6) P. S. Skell and R. G. Allen, from abstracts of papers presented at the September 1958 meeting of the American Chemical Society at Chicago, Ill.

(7) D. Y. Curtin and D. B. Kellom, *J. Am. Chem. Soc.*, **75**, 6011 (1953).

The component fractions of products of all elimination reactions were isolated by gas chromatographic methods for mass spectra determinations. In instances where deuterium should have been retained, such as the *cis*-2-butene from the *erythro*-isomer or the *trans*-2-butene from the *threo*-isomer, a major change was observed in the mass spectral pattern in the *m/e* region corresponding to 41 and 40 for undeuterated 2-butene. The 40/41 relative peak intensity for *trans*-2-butene was about 0.06 but the corresponding 41/42 ratio for deuterated analogs was never below 0.58. Several of these intensity values, along with those from the products of 2-bromobutane-2-*d*, III, are given in Table II.

TABLE II

RELATIVE PEAK INTENSITIES FOR MASS SPECTRA OF PRODUCTS OF ELIMINATION REACTIONS

Isomer and Source	Relative Peak Intensities[a]	
	41/42	40/41
cis, I	0.58	
trans, I		0.09
cis, II		0.20
trans, II	0.68	
cis, III	0.60	
trans, III	0.54	

[a] Consolidated Mass Spectrometer Model 21-620, ionizing current 20 microamperes.

The high 41/42 ratios can be accounted for by assuming isomerization, contamination with undeuterated alkene, or hydrogen migration in the mass spectrometer. The first was eliminated because neither *cis*-nor *trans*-2-butene showed measureable isomerization under the conditions of the reaction. The second and third could not be distinguished completely from one another, but deuterobutenes were prepared by independent methods for comparison of spectra.

The synthesis of a stereospecific isomer of 2-butene-2-*d* was carried out by two methods other than through the elimination reactions of deuterohalides.

The successive treatment of *cis*-2-bromo-2-butene with lithium metal (in ethyl ether) and D_2O according to the method of Curtin and Crump,[8] yielded a mixture of *cis*- and *trans*-2-butene-2-*d* (predominately *cis*) free of more than a trace of 1-butene. The 41/42 ratio of peak intensities was 0.56 for the total sample, and slightly higher for chromatographed samples.

The tiglic acid procedure for the preparation of *trans*-2-butene[9,10] applied to the synthesis of *trans*-2-butene-2-*d* yielded a product which contained no 1-butene and less than 0.5% *cis*-2-butene. The 41/42 ratio was 0.48 ,the lowest value encountered for any monodeuterobutene. Infrared analysis indicated less than 2% *trans*-2-butene was present, and the strong 960 cm.$^{-1}$ band was replaced by another strong band at about 875 cm.$^{-1}$

Although further work is being carried out on the mass and infrared spectra of deuterated butenes and precise analyses of deuterium contents will be deferred, a tentative assignment of deuterium content of isomers, based on the assumption of 98% isomeric purity of the tiglic acid butene, is given in Table III.

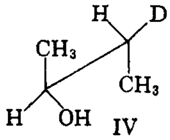
TABLE III

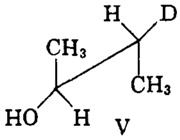
DEUTERIUM CONTENT OF VARIOUS ISOMERS OF 2-BUTENE FRACTION OF MOLECULES CONTAINING D

Sample Source	*cis*	*trans*
Dehydrobromination of I	0.90	0.14
Dehydrobromination of II	0.43	0.86
Dehydrobromination of III	0.90	0.95
Vinyl lithium procedure	0.94	0.93
Tiglic acid procedure		0.98[a]

[a] *Determined from infrared spectrum;* all others from mass spectra based on this isomer.

Since the deuteroalcohols, IV and V, showed 0.95 atom of deuterium per molecule, the lower deuterium contents of the *cis*-2-butene from I or the *trans*-2-butene from II indicate that racemization had taken place in the reaction sequence from epoxide to halide. In the case of the optically active series (involving deuterohalide II) this racemization could account for only a small part of the discrepancy in optical rotatory power between calculated[4] and experimental[5] values.


IV


V

Vapor phase dehydrohalogenation over calcium oxide. Samples of various 2-bromobutanes were passed over calcium oxide at elevated temperatures during the search for an elimination reaction which would yield stereospecific isomers with complete loss or retention of deuterium. This reaction yielded predominately *cis*-2-butene when carried out just above the minimum temperature for reaction, and as the temperature increased the *cis-trans* ratio dropped. These ratios, given in Table IV, are due in part to an increased rate of isomerization at elevated temperatures. Also, the ratios were dependent on the length of time a packing was in use.

In the reaction of a series of compounds including 2-bromobutane, *erythro*-2-bromobutane-3-*d*, and *threo*-2-bromobutane-3-*d*, the respective ratios of 1-butene/*cis*-2-butene/*trans*-2-butene at 200° were 11/56/33, 17/51/32 and 21/40/39. Deuterium

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(8) D. Y. Curtin and J. W. Crump, *J. Am. Chem. Soc.*, **80**, 1922 (1958).

(9) J. Wislicenus, H. P. Talbot, and M. Henze, *Ann.*, **313**, 228 (1900).

(10) W. G. Young, R. T. Dillon, and H. J. Lucas, *J. Am. Chem. Soc.*, **51**, 2528 (1929).

TABLE IV

EFFECT OF TEMPERATURE ON VAPOR PHASE DEHYDROHALOGENATION OF 2-BROMOBUTANE OVER CALCIUM OXIDE

	Composition of Products, %		
T, °C.	1-Butene	*cis*-2-Butene	*trans*-2-Butene
150	11	61	28
200	13	50	37
250	16	45	39
300	18	42	41

analyses on the products are given in Table V. It is of interest to note that the *threo*-isomer showed the major isotope effect and the deuterium retention was lowest. Although this might be a *cis*-elimination the equal distribution of deuterium between *cis*- and *trans*-2-butenes rules out any straightforward interpretation. Hydride shifts must be involved because the 1-butene from the *threo*, deuterohalide contained only 60% as much deuterium as that obtained through dehydrobromination with alcoholic potassium hydroxide. The 1-butene from the *erythro*-isomer contained 90% of the maximum observed deuterium.

TABLE V

DEUTERIUM CONTENTS OF PRODUCTS OF CALCIUM OXIDE DEHYDROBROMINATION REACTIONS AT 200°

Butene and Source	Deuterium Retention, %
cis, From I (*erythro*)	62
trans, From I	63
cis, From II (*threo*)	51
trans, From II	51

EXPERIMENTAL

D(−)-*2,3-Butanediol* was prepared from the fermentation of "Karo" corn syrup by *Aerobacillus polymyxa*[11] by a method adapted from that of Rose and King.[12] The observed rotation of the diol, α^{25}_{D} −12.90° (lit.,[13] α^{29}_{D} −13.08°), was somewhat lower than previous values because no attempt was made to remove the last traces of water from the compound. The criterion of optical purity was the L-2-butanol prepared according to the method of Leroux and Lucas[14]; $[\alpha]^{25}_{D}$ −13.50° (lit.,[14] −13.51°).

D(+)-*2,3-Epoxybutane*, D(−)-*erythro-3-butanol-2-d*, L(+)-*threo-3-bromobutane-2-d*. These compounds were products from previously reported syntheses.[5] The deuterobutanol contained 0.95 atom of deuterium per molecule.

meso-2,3-Epoxybutane, DL-*threo-3-butanol-2-d*, DL-*erythro-3-bromobutane-2-d*. This series of compounds was prepared from recrystallized *meso*-2,3-butanediol, m.p. 33.5–34.0°, by the same sequence of reactions used for the active isomers.[5]

2-Butanol-2-d. This was prepared according to the procedure given for 2-propanol-2-*d*[15]; b.p. 98–99° (740 mm.); n^{25}_{D} 1.3944.

2-Bromobutane-2-d. The PBr_3 method for other deuterohalide syntheses[5] was used to prepare this from the alcohol: b.p. 89.5–90.0°; n^{25}_{D} 1.4335.

cis-2-Butene-2-d via the organolithium reagent. With the exception of the reduction step, this reaction sequence is analogous to that used by Hoff, Greenlee, and Boord[16] for the quantitative inversion of the configuration about the carbon-carbon double bond in normal alkenes. *trans*-2-Butene was converted to the dibromide with Br_2 in CCl_4 at −5°[10] and the product was dehydrobrominated with 10 molar KOH in ethylene glycol at 150°: crude yield from butene, 93%. Fractional distillation yielded 2-bromo-2-butene: b.p. 90.6–91.6° (737 mm.); $n^{19.3}_{D}$ 1.4631 (lit.,[17] for *cis*-isomer: b.p. 93.9°; $n^{19.2}_{D}$ 1.4631). The lithium derivative was prepared from 13.5 g. (0.10 mole) of halide and 1.4 g. (0.20 g. atom) of lithium in 50 ml. of ether according to the method of Curtin and Crump.[8] The gases formed on addition of D_2O were fractionally distilled through a 25 cm. helices column; b.p. 0° ± 0.5° (735 mm.); yield 3.3 g., 58%.

Ethanol-1,1-d_2. A 3-neck, one-liter flask equipped with a mechanical stirrer, Friedrichs condenser, and dropping funnel was flame-dried and flushed with dry nitrogen. After the addition of 10 g. (0.24 mole) of lithium aluminum deuteride, about 300 ml. of ether was distilled into the apparatus from a 500-ml. flask containing lithium aluminum hydride. Over a period of 2 hr., 40 g. (0.183 mole) of triacetin in 60 ml. of dry ether was added; then the mixture was refluxed for 2 hr. and allowed to stand overnight. This was hydrolyzed with dilute sulfuric acid, dried with K_2CO_3, and distilled. The fraction boiling from 75–80° was collected. This contained 21.7 g. (0.45 mole, 82%) of ethanol-1,1-d_2, calculated from the refractive index. No further purification was made.

Ethanal-1-d. The procedure for oxidation of ethanol as described by Wertheim[18] was modified by omission of nitric acid from the oxidizing mixture. When nitric acid was present the ethanal contained a contaminant which inhibited initiation of the subsequent Reformatsky reaction. The ethanal-1-*d*-was collected in benzene then dried over $MgSO_4$. This dry solution was used directly in the Reformatsky reaction. The yields in preliminary runs using ethanol were 40–50%.

Ethyl 2-methyl-3-hydroxybutanoate-3-d and ethyl 2-methyl-3-acetoxybutanoate-3-d. Using a general Reformatsky reaction as described in "Organic Reactions,"[19] the deuteroester was prepared from 16.7 g. (0.26 g. atoms) mossy zinc, 7.3 g. (0.16 mole) ethanal-1-*d*, and 36 g. (0.20 mole) ethyl 2-bromopropanoate. The hydroxyester was not isolated but was converted directly into the acetoxyester with ketene: b.p. 84° (10 mm.); yield 20.4 g., 60% from ethanal-1-*d* (lit.[20] b.p. 97.5° at 15 mm.).

Tiglic acid-3-d. Pyrolysis of ethyl 2-methyl-3-acetoxybutanoate-3-*d* at 500°[21] yielded a mixture of methylbutenoic acids with a major portion unconjugated according to infrared spectra: b.p. 88–91° (14 mm.); yield 3.3 g., 34%. This mixture was refluxed for 5 hr. with 4 g. NaOH in 20 ml. of water-ethanol. The reaction mixture was acidified

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(11) The authors are indebted to Dr. R. W. Watson of the National Research Council of Canada for a culture of N.R.C. No. 42 (3) *Bacillus polymyxa*.

(12) D. Rose and W. S. King, *Can. J. Research*, **23F**, 78 (1945).

(13) A. C. Neish, *Can. J. Research*, **23B**, 10 (1945).

(14) P. J. Leroux and H. J. Lucas, *J. Am. Chem. Soc.*, **73**, 41 (1951).

(15) A. Leo and F. H. Westheimer, *J. Am. Chem. Soc.*, **74**, 4383 (1952).

(16) M. C. Hoff, K. W. Greenlee, and C. E. Boord, *J. Am. Chem. Soc.*, **73**, 3329 (1951).

(17) M. Lepingle, *Bull. soc. chim.*, **39**, 741 (1926).

(18) E. Wertheim, *J. Am. Chem. Soc.*, **44**, 2658 (1922).

(19) R. L. Shriner, *"Organic Reactions,"* Vol. 1, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 16.

(20) E. Blaise and I. Herman, *Ann. chim. et phys.*, **20**, 190 (1910).

(21) W. J. Bailey and C. King, *J. Am. Chem. Soc.*, **77**, 75 (1955).

and the organic material was extracted with ether, dried, and distilled. This isomerization yielded some angelic acid but principally tiglic acid: b.p. 195–200°; m.p. 62–64° (lit., b.p. 198.5°[22]; m.p. 63.5–64.0°[10]).

trans-2-Butene-2-d. Tiglic acid-3-*d* was converted to the alkene by the method of Young, Dillon, and Lucas.[10] The tiglic acid hydriodide intermediate melted at 86–87.5° (lit.,[10] 86.2–86.3°). Treatment of the hydriodide with aqueous sodium carbonate at 75° yielded *trans*-2-butene-2-*d* in 67% yield. The product was at least 99.5% pure according to chromatographic analysis. The major contaminant was a trace of *cis*-2-butene-2-*d*.

RIVERSIDE, CALIF.

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(22) R. Fittig and H. Kopp, *Ann.*, **195**, 81 (1879).

[CONTRIBUTION FROM THE MONSANTO CHEMICAL CO., PLASTICS DIVISION]

Mechanism of the Michaelis-Arbuzov Reaction: Olefin Formation

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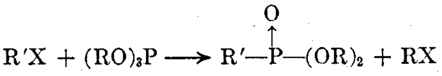
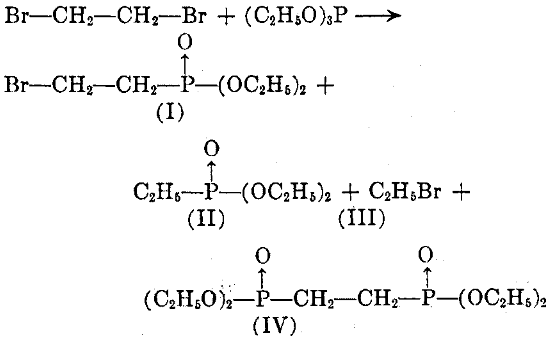
Support is given for the mechanism of the Michaelis-Arbuzov reaction in terms of the formation of a quasiphosphonium salt intermediate. The production of olefin and dialkyl phosphonate, $(RO)_2\overset{O}{\overset{\uparrow}{P}}—H$, is shown to be a general phenomenon when an *alpha*-haloalkane which has an activating group on the *beta* carbon is treated with a trialkyl phosphite. The formation of these products is explained in terms of an intramolecular *beta*-elimination involving the quasiphosphonium salt intermediate.

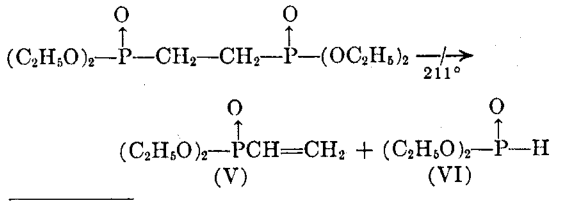
Introduction. During the preparation of diethyl β-bromoethylphosphonate (I) by the Michaelis-Arbuzov Reaction (1) using triethyl phosphite and 1,2-dibromoethane (2), it was found through the use of infrared spectroscopy and vapor phase chromatography that diethyl vinylphosphonate (V) and diethyl phosphonate (VI) are formed. In addition, diethyl β-bromoethylphosphonate (I), diethyl ethylphosphonate (II), ethyl bromide (III), and tetraethyl ethylenediphosphonate (IV) are found as reported previously by Ford-Moore and Williams[1a] and Kosolapoff.[1b] The most obvious explanation for the formation of these products is that the tetraethyl ethylenediphosphonate (IV) decomposes under the conditions of the reaction. This decomposition, however, has been shown not to take place. The diphosphonate (IV) is stable at 211° over a period of 5 hr., and the initial reaction was run at 150° to 170°.



$$R'X + (RO)_3P \longrightarrow R'—\overset{O}{\overset{\uparrow}{P}}—(OR)_2 + RX \qquad (1)$$

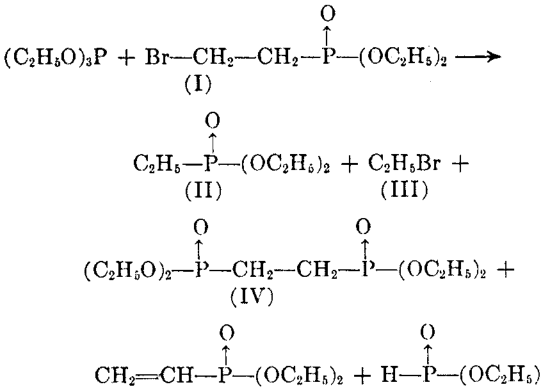


$$\begin{aligned}&Br—CH_2—CH_2—Br + (C_2H_5O)_3P \longrightarrow\\ &\underset{\text{(I)}}{Br—CH_2—CH_2—\overset{O}{\overset{\uparrow}{P}}—(OC_2H_5)_2} +\\ &\qquad \underset{\text{(II)}}{C_2H_5—\overset{O}{\overset{\uparrow}{P}}—(OC_2H_5)_2} + \underset{\text{(III)}}{C_2H_5Br} +\\ &\qquad \underset{\text{(IV)}}{(C_2H_5O)_2—\overset{O}{\overset{\uparrow}{P}}—CH_2—CH_2—\overset{O}{\overset{\uparrow}{P}}—(OC_2H_5)_2} \qquad (2)\end{aligned}$$

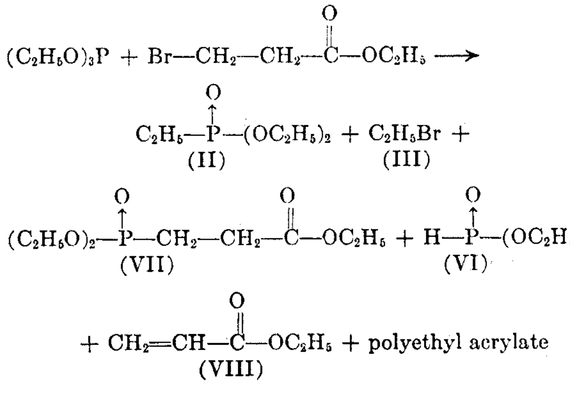


$$\begin{aligned}&(C_2H_5O)_2—\overset{O}{\overset{\uparrow}{P}}—CH_2—CH_2—\overset{O}{\overset{\uparrow}{P}}—(OC_2H_5)_2 \underset{211^\circ}{\not\longrightarrow}\\ &\qquad \underset{\text{(V)}}{(C_2H_5O)_2—\overset{O}{\overset{\uparrow}{P}}CH{=}CH_2} + \underset{\text{(VI)}}{(C_2H_5O)_2—\overset{O}{\overset{\uparrow}{P}}—H} \qquad (3)\end{aligned}$$

The following reactions were run to determine the generality of this reaction as an olefin-forming



$$\begin{aligned}&(C_2H_5O)_3P + \underset{\text{(I)}}{Br—CH_2—CH_2—\overset{O}{\overset{\uparrow}{P}}—(OC_2H_5)_2} \longrightarrow\\ &\qquad \underset{\text{(II)}}{C_2H_5—\overset{O}{\overset{\uparrow}{P}}—(OC_2H_5)_2} + \underset{\text{(III)}}{C_2H_5Br} +\\ &\qquad \underset{\text{(IV)}}{(C_2H_5O)_2—\overset{O}{\overset{\uparrow}{P}}—CH_2—CH_2—\overset{O}{\overset{\uparrow}{P}}—(OC_2H_5)_2} +\\ &\qquad \underset{\text{(V)}}{CH_2{=}CH—\overset{O}{\overset{\uparrow}{P}}—(OC_2H_5)_2} + \underset{\text{(VI)}}{H—\overset{O}{\overset{\uparrow}{P}}—(OC_2H_5)_2} \qquad (4)\end{aligned}$$



$$\begin{aligned}&(C_2H_5O)_3P + Br—CH_2—CH_2—\overset{O}{\overset{\|}{C}}—OC_2H_5 \longrightarrow\\ &\qquad \underset{\text{(II)}}{C_2H_5—\overset{O}{\overset{\uparrow}{P}}—(OC_2H_5)_2} + \underset{\text{(III)}}{C_2H_5Br} +\\ &\underset{\text{(VII)}}{(C_2H_5O)_2—\overset{O}{\overset{\uparrow}{P}}—CH_2—CH_2—\overset{O}{\overset{\|}{C}}—OC_2H_5} + \underset{\text{(VI)}}{H—\overset{O}{\overset{\uparrow}{P}}—(OC_2H_5)_2}\\ &\qquad + \underset{\text{(VIII)}}{CH_2{=}CH—\overset{O}{\overset{\|}{C}}—OC_2H_5} + \text{polyethyl acrylate} \qquad (5)\end{aligned}$$

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(1) (a) A. H. Ford-Moore and J. W. Williams, *J. Chem. Soc.*, 1467 (1945). (b) G. M. Kosolapoff, *J. Am. Chem. Soc.*, **66**, 109 (1944).