[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Peroxide Effect in the Addition of Reagents to Unsaturated Compounds. XX. The Addition of Hydrogen Bromide to 2-Butyne and 2-Bromo-2-butene

BY CHEVES WALLING,[1] M. S. KHARASCH AND F. R. MAYO

Since the report in 1933 of the reversal by certain catalysts, notably oxygen and organic peroxides, of the direction of addition of hydrogen bromide to olefins,[2] investigation in this Laboratory and elsewhere has disclosed some thirty olefins which undergo such a reversal of the direction of addition.[3] In all of these, addition occurs to a terminal double bond, while with a number of other olefins with non-terminal double bonds, no such reversal has been observed. Accordingly, it has become of increasing interest to know whether the presence of a terminal double bond is essential for this phenomenon.

The addition of the second of two molecules of hydrogen bromide to 2-butyne[4] appeared as a likely subject for investigation for two reasons. In the first place, the unsymmetrical distribution of substituents about the double bond in 2-bromo-2-butene would be expected to yield only one product of normal addition. Secondly, it has been observed in this Laboratory that halogen atoms attached to a molecule favor abnormal addition by retarding the normal reaction.

Addition of hydrogen bromide was carried out under the conditions specified in Table I, 5.4 g. of butyne being used in every instance. In the experiments marked "vacuum" the usual technique developed in this Laboratory was employed,[2] with evacuation to a pressure of 10^{-4} to 10^{-5} mm. After addition, the reaction mixture was first distilled at 5–10 mm. directly from the tubes in which the reaction took place into a trap at $-80°$, and the yield was determined at this point. In the case of additions in pentane the solvent was evaporated before distillation, while in experiments carried out in acetic acid the products were washed with water. All products were then distilled at 30 mm. in a Podbielniak column, and the index of the main fraction was taken. The first few drops of distillate and material which did not distill were rejected, but loss by this method rarely exceeded 2 g.

(1) Du Pont Fellow, 1938–1939.

(2) Kharasch and Mayo, THIS JOURNAL, **55**, 2468 (1933).

(3) See Kharasch, Engelmann and Mayo, *J. Org. Chem.*, **2**, 288 (1937), for references to the subject.

(4) As the product of the addition of one molecule of hydrogen bromide to 2-butyne is necessarily 2-bromo-2-butene under all conditions, no necessity of isolating this intermediate arises. There is no reason to expect that the *cis* and *trans* isomers would give rise to different products (see ref. 7).

Experimental Part

2-Butyne was prepared from sodium acetylide, sodamide, and dimethyl sulfate in liquid ammonia by the method of Bried and Hennion[5] except that the reaction was carried out in a flask cooled in a bath of solid carbon dioxide and acetone. In this way the temperature of the reaction mixture was held at -70 to $-60°$ during the addition of the dimethyl sulfate. The products were distilled through water to remove ammonia, and collected in a vessel cooled in ice water. Loss of product from the receiver was prevented by a trap maintained at $-80°$. With the use of a 2-liter flask containing about 1 liter of ammonia, 2 moles of sodium acetylide and other reagents in proportion could be handled with ease. The product was fractionated through a Podbielniak column. The yield from four moles of sodium acetylide was 88 g. (41%) of 2-butyne; b. p. 27.0–4° (754 mm.); m. p. $-28°$ to $-27°$; $n^{20}D$ 1.3920.

Identification of Products.—Analysis was by index of refraction, checked by the boiling range of the products. The wide difference in index and boiling point of the two products makes the analyses certain to at least 5%. The most probable index of 2,2-dibromobutane was determined as $n^{20}D$ 1.5015 by measurements, after another fractionation, on the combined products of the experiments showing normal addition. The material was definitely identified by conversion to the 2,4-dinitrophenylhydrazone of methyl ethyl ketone (m. p. 111–112°; melting point of mixture with known sample 111–112°). The racemic 2,3-dibromobutane was identified by boiling point and index of refraction.

As the meso and racemic forms of 2,3-dibromobutane have different indices of refraction ($n^{20}D$ 1.5116 and 1.5147, respectively),[6] the question naturally arises as to whether variations in the index of the abnormal products are due to variations in the ratios of the isomeric 2,3-dibromobutanes or to the presence of small quantities of 2,2-dibromobutane. To answer this question, the products of all experiments giving the abnormal product were combined and carefully fractionated through a Podbielniak column.[7] While the first portion had an index of 1.5108, indicating it to be largely 2,2-dibromobutane, the remaining 80% had an index of 1.5145–7. Thus, the abnormal product appears to be entirely the racemic isomer, and the percentages of normal and abnormal product are calculated on this basis.

Discussion of Results

The results of our experiments are summarized in Table I. It will be noted that under most con-

(5) Bried and Hennion, THIS JOURNAL, **59**, 1310 (1937).

(6) Dillon, Young and Lucas, *ibid.*, **52**, 1953 (1930).

(7) Podbielniak, *Ind. Eng. Chem., Anal. Ed.*, **5**, 119 (1933).

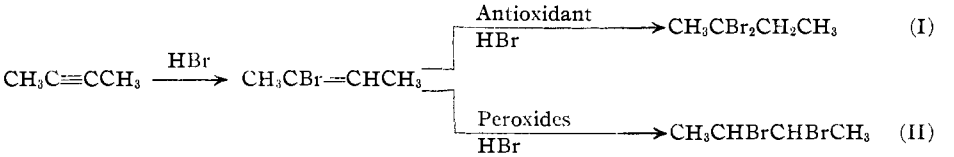
TABLE I

ADDITION OF HYDROGEN BROMIDE TO 2-BUTYNE

Expt.	Conditions of addition: Mol. HBr[a]	Temp., °C.	Time, hr.	Substance Added	Mol.[a]	Vacuum technique	Product[e]: Yield, %	B. p. (30 mm.) °C.	$n^{20}D$	% 2,2-dibromide
III	2.4	20	2	Catechol	0.04	(+)	60[d]	52	1.5022	95
V	2.0	20	12	Diphenylamine	.02	(+)	60[b,d]	30–53	1.4947	(100)
VI	2.2	20	2	Diphenylamine	.02	(+)	65[d]	51–52	1.5012	100
IV	3.0	−80	12	$FeBr_3$	.01	(−)	50[d]	51	1.5018	98
XI	2.4	20	22	.....	...	(−)	75	51–53	1.5013	100
X	2.4	20	22	Acetic acid	2.0	(+)	85	51–53	1.5012	100
II	2.5	20	12	Acetic acid[c]	2.00	(−)	98	62	1.5139	6
VII	2.5	20	2	Acetic acid[c]	2.0	(−)	95	62–63	1.5132	11
VIII	2.6	20	5	Ascaridole	0.04	(−)	90	51–60	1.5022	95
I	2.6	20	24	Ascaridole	.03	(−)	100	52–64	1.5070	58
IX	2.4	20	4	Ascaridole	.04	(−)	85	62–65	1.5134	10
				Pentane	6.0					
XII	2.5	20	12	Ascaridole	.04	(−)	90	62–64.5	1.5142	4
				Pentane	6.0					

[a] In moles per mole of 2-butyne. [b] Considerable 2-bromo-2-butene in product. [c] Sample of 2-butyne employed gave very strong test for peroxide. [d] Not including 10–20% of dark, non-volatile material obtained. [e] Indices used in analysis: 2,2-dibromobutane, $n^{20}D$ 1.5015; racemic 2,3-dibromobutane $n^{20}D$ 1.5147.

ditions described in Table I the product is exclusively normal, namely, 2,2-dibromobutane,[8] and that even the addition of 3 mole per cent. of ascaridole fails to reverse the addition completely. However, when the normal addition is retarded by dilution with pentane, the product is almost exclusively abnormal. In acetic acid solution, addition is normal (expt. X) except when the 2-butyne has a high peroxide content (expts. II and VII).



The discovery of a case of abnormal addition to a non-terminal double bond considerably increases the number of compounds which may be expected to undergo this reaction. In fact, it now seems likely that, with certain exceptions, abnormal addition to any ethylenic bond may be observed. The exceptions appear to be as follows. (1) Compounds in which symmetrical substitution by groups of the same order of electronegativity results in a double bond of low polarity. Compounds such as 2-pentene[9] and 9-undecenoic acid[10] give an equimolecular mixture of two addition products in the presence or absence of peroxides, and it cannot be determined whether or not reversal takes place. A border-line case is that of 2-bromopropene, which gives a 2:1 mixture on normal addition and a single product in the presence of oxygen or peroxides.[3] (2) Compounds in which double bonds are conjugated with carboxyl and similar groups. (3) Compounds for which abnormal addition is masked by a very rapid normal reaction. All known cases of failure to obtain a reversal of the direction of addition of hydrogen bromide in the presence of peroxides seem to fall into one of these three classes.

The effect of a rapid normal addition in the abnormal reaction is clearly demonstrated in the case of 2-butyne. Here, the normal reaction is comparatively rapid (almost complete in two hours at 0°), with the result that only upon dilution does the abnormal reaction become important. The abnormal reaction, being presumably a chain reaction,[3] is not retarded greatly by dilution with an inert solvent.

The principle of preferential retardation of the normal reaction by dilution appears to be a valuable tool, and it is now being employed in this Laboratory in attempts to detect abnormal addition in the addition of hydrogen bromide to several olefins which show a rapid normal reaction.

(8) This is the product reported by Wislicenus and Hölz, *Ann.*, **250**, 232 (1889).

(9) Kharasch, Walling and Mayo, THIS JOURNAL, **61**, 1559 (1939).

(10) Abraham, Mowat and Smith, *J. Chem. Soc.*, 948 (1937).

Summary

1. 2-Butyne adds hydrogen bromide in the

absence of oxygen and peroxides to give 2,2-dibromobutane.

2. Under the influence of peroxide catalysis racemic 2,3-dibromobutane is obtained. This product is most easily obtained by retarding the normal reaction through dilution with an inert solvent.

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Local Anesthetics from β-(2-Piperidyl)-ethanol

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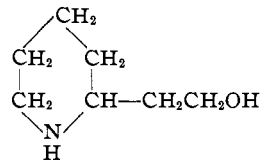
The recent publication of Tullock and MacElvain[1] on anesthetics derived from α-picoline prompts submission of the following paper.

A series of substituted benzoic esters of β-



(2-piperidyl)-ethanol was prepared by refluxing one equivalent of the hydrochloride of the amino alcohol with one equivalent of acid chloride in dry chloroform. The amino ester hydrochlorides were purified by crystallization from absolute alcohol or from absolute alcohol–ether mixture. The N-phenylurethan and the cinnamate were prepared similarly from phenyl isocyanate and cinnamoyl chloride, respectively. The hydrochlorides of the nitro esters were reduced to the amino compounds with platinum and hydrogen in glacial acetic acid.

Pure β-(2-pyridyl)-ethanol is best prepared by heating α-picoline with twice its weight of 40% formaldehyde in a sealed tube at 120° for sixteen to twenty hours. The mixture is then fractionally distilled at a pressure sufficiently reduced so that the temperature of the mixture never rises above 130°. The yields are only 15 to 20% but the product is not contaminated with the β-(2-pyridyl)-allyl alcohol which is formed by dehydration of β-(2-pyridyl)-propylene glycol at higher temperatures. Some of the latter compound is formed from two moles of formaldehyde and one of picoline even at 120°.

The pyridyl alcohol was reduced to the piperidyl alcohol with sodium and absolute alcohol.[2]

The properties of the compounds are recorded in the following table. They are all nicely crystalline and non-hygroscopic without exception.

TABLE I

	β-(2-Piperidyl)-ethanol ester hydrochloride	Formula	M. p., °C., corr.	Analyses, %Cl Calcd.	Found
I	Benzoate	$C_{14}H_{20}O_2NCl$	189–191[a]	13.14	13.08
II	*p*-Nitrobenzoate	$C_{14}H_{19}O_4N_2Cl$	209–210	11.26	11.15
III	*m*-Nitrobenzoate	$C_{14}H_{19}O_4N_2Cl$	170–172	11.26	10.96
IV	*o*-Nitrobenzoate	$C_{14}H_{19}O_4N_2Cl$	148–150	11.26	11.46
V	*p*-Aminobenzoate	$C_{14}H_{21}O_2N_2Cl$	249–251	12.44	12.20
VI	*m*-Aminobenzoate	$C_{14}H_{21}O_2N_2Cl$	177–180	12.44	12.28
VII	*o*-Aminobenzoate	$C_{14}H_{21}O_2N_2Cl$	209–211	12.44	12.30
VIII	*p*-Ethoxy, *m*-nitrobenzoate	$C_{16}H_{23}O_5N_2Cl$	150–155	9.87	10.21
IX	*p*-Ethoxy, *m*-aminobenzoate	$C_{16}H_{25}O_3N_2Cl$	173–175	10.78	10.61
X	*p*-Ethoxybenzoate	$C_{16}H_{24}O_3NCl$	146–148	11.29	11.44
XI	Cinnamate	$C_{16}H_{22}O_2NCl$	180–182	11.98	11.95
XII	N-Phenylurethan	$C_{14}H_{21}O_2N_2Cl$	200–202	12.44	12.54

[a] Ladenburg, *Ann.*, **301**, 124 (1898), gives m. p. 182–183°.

TABLE II

Compound	Duration of anesthesia rabbit cornea, min., 2% solution	Subcutaneous toxicity to mice M. L. D. 50% mg./kg.
I	6	85
V	47	20
VI	27	87
VII	100	23
IX	10	..
X	15	..
XI	0	..
XII	9	40
Cocaine	56	10

(1) Tullock and MacElvain, THIS JOURNAL, **61**, 961 (1939).

(2) Marvel and Shelton, *ibid.*, **51**, 915 (1929).