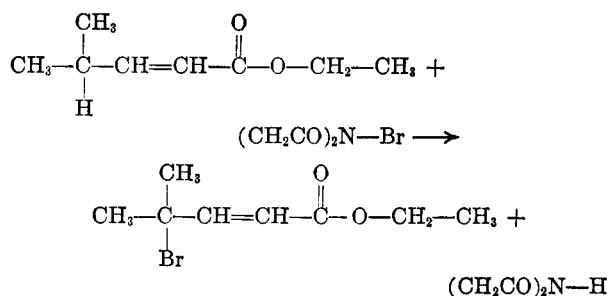


## N-Bromosuccinimide. II. Allylic Bromination of Tertiary Hydrogens<sup>1</sup>

HYP J. DAUBEN, JR., AND LAYTON L. MCCOY<sup>2</sup>

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In a number of textbooks and reference books on organic chemistry it is stated that allylic brominations of tertiary hydrogens by NBS is not possible under Ziegler's original conditions (in refluxing carbon tetrachloride without irradiation or addition of initiators) but may be effected when initiators, such as benzoyl peroxide, are added; reference is usually made to the NBS review article by Djerassi,<sup>3</sup> to the paper of Schmid and Karrer in which they introduced the use of benzoyl peroxide,<sup>4</sup> or to the original paper by Ziegler and co-workers.<sup>5</sup> Careful perusal of the latter two papers indicates that this conclusion rests not on experimental grounds but, presumably, on a repeated, misconstrued statement in the original Ziegler paper.<sup>3-5</sup> Consequently, it was a matter of interest to determine if tertiary allylic hydrogens would undergo bromination by NBS under the original Ziegler reaction conditions. For this purpose, a study was made on the effect of environmental factors (performed peroxides, light, oxygen) on the course and the reaction time of the reaction of NBS with ethyl 4-methyl-2-pentenoate, the same alkenic component used by Schmid and Karrer to demonstrate that benzoyl peroxide was needed to effect bromination of a tertiary allylic hydrogen. Previous studies<sup>6</sup> had clearly shown that these



(1) (a) Taken from the Ph.D. Thesis of Layton L. McCoy, University of Washington, 1951. (b) Supported in part by research contract No. N8-onr-52007 with the Office of Naval Research, U. S. Navy.

(2) Predoctoral Fellow, Atomic Energy Commission, 1950-1951.

(3) C. Djerassi, *Chem. Revs.*, **43**, 271 (1948).

(4) H. Schmid and P. Karrer, *Helv. Chim. Acta*, **29**, 573 (1946).

(5) K. Ziegler, A. Späth, E. Schaaf, W. Schumann, and E. Winklemann, *Ann.*, **551**, 80 (1942), reported that both primary and secondary allylic hydrogens undergo bromination with NBS, the latter more rapidly, but made no specific statement that tertiary allylic hydrogens will not react; in fact, this paper contains no mention of any attempt to effect allylic brominations of alkenes containing tertiary allylic hydrogens.

(6) H. J. Dauben, Jr., and L. L. McCoy, *J. Am. Chem. Soc.*, **81**, 4863 (1959).

environmental factors were responsible for initiation of the allylic bromination of the secondary allylic hydrogen in cyclohexene by NBS under the original Ziegler reaction conditions.

Ethyl 4-methyl-2-pentenoate when freshly distilled gives a negative test for peroxides but peroxidic impurities are formed, presumably by autoxidation, when this material is allowed to stand in a glass-stoppered bottle. Under the ordinary conditions (refluxing carbon tetrachloride, diffuse laboratory light, air access through top of condenser) stale ethyl 4-methyl-2-pentenoate reacts completely with NBS in <20 min. to give an 81% yield of ethyl 4-bromo-4-methyl-2-pentenoate (Table I, Run 1); with 0.5 mole % benzoyl peroxide Schmid and Karrer obtained, after several hours reflux, a 67% yield of the same product. When preformed peroxides or light are excluded, the reaction times are lengthened about 3-fold but the yields remain about the same (Table I, Runs 2 and 3); these results indicate that either preformed peroxides or light catalyze the allylic bromination of this tertiary hydrogen compound. When preformed peroxides and oxygen are both excluded, reaction times either in the presence or the absence of diffuse light are about the same and about 10-fold longer than for the ordinary run, and the yields are somewhat lower (Table I, Runs 4 and 5); these results indicate that even atmospheric oxygen, possibly by the *in situ* formation of tertiary hydroperoxides, exerts a catalytic action. The pattern for the effects of environmental factors (catalysis by preformed peroxides, light, and oxygen) on the bromination of tertiary allylic hydrogens by NBS qualitatively resembles those obtained earlier<sup>6</sup> for reaction with secondary allylic hydrogens.<sup>7</sup> These results establish beyond doubt

TABLE I  
EFFECT OF ENVIRONMENTAL FACTORS ON REACTION OF NBS WITH ETHYL 4-METHYL-2-PENTENOATE

Run No.	Pre-formed <sup>a</sup> Peroxides	Light <sup>b</sup>	Oxygen <sup>c</sup>	Time for Complete <sup>d</sup> Reaction (min.)	Yield of Tertiary Bromide (%)
1	+	+	+	<20	81
2	-	+	+	55-70	86
3	+	-	+	60-75	83
4	-	+	-	205-320	66
5	-	-	-	215-240	65

<sup>a</sup> Presence or absence of preformed peroxides, qualitatively determined by color test with ammonium thiocyanate and ferrous ammonium sulfate; since sensitivity of this test was not determined, minute amounts of peroxides may be present in samples giving a negative color test. <sup>b</sup> Presence or absence of diffuse laboratory light. <sup>c</sup> Presence or absence of atmospheric oxygen. <sup>d</sup> Times for last positive and first negative tests for positive bromine with moistened starch-iodide paper.

(7) The major difference appears to be that light in the absence of peroxides and oxygen acts as a catalyst for the reaction with secondary hydrogens but not with tertiary hydrogens.

that the tertiary hydrogen in ethyl 4-methyl-2-pentenoate reacts with NBS under Ziegler's original conditions.

A number of other examples have been reported in which allylic bromination reactions have been conducted on alkenes containing allylic tertiary hydrogens, either alone<sup>8a</sup> or along with primary<sup>8b-d</sup> or secondary<sup>8e-i</sup> allylic hydrogens, available for substitution; with one exception, 3-methylcyclohexene,<sup>8i</sup> all of these compounds belong to the steroid or triterpenoid series. In none of the cases was an initiator added to the reaction<sup>9</sup> but several of these examples were strongly irradiated.<sup>8a,b,d-f</sup> Even though tertiary allylic bromides were not isolated from any of these reactions, in four cases unsaturated products were obtained which probably arose by bromination at the tertiary position and subsequent dehydrobromination,<sup>8c,e,g,h,10</sup> and in three cases where primary or secondary bromides, or the corresponding dehydrobromination products, were obtained in only 30-70% yields,<sup>8b,f,i</sup> tertiary bromination products or the resultant alkenes might have been formed but not isolated; the one compound that failed to react with NBS contained only a tertiary allylic hydrogen.<sup>8a</sup> The collective evidence indicates that most, if not all, tertiary allylic hydrogens undergo bromination by NBS and, in at least several cases, without deliberate addition of initiating substances or the use of strong irradiation.

Adequate experimental evidence is lacking at the present time to decide definitely about the relative reactivity of tertiary allylic hydrogens with respect to secondary or primary allylic hydrogens in the NBS-allylic bromination reaction. In their original work on this reaction, Ziegler and coworkers<sup>8</sup> showed that secondary allylic hydrogens reacted faster than primary ones, in comparable systems the latter requiring 10- to 100-fold longer reaction

times for complete reaction. Some evidence has also been obtained that tertiary hydrogens in benzylic<sup>11a,b</sup> and saturated<sup>11c</sup> systems are quite reactive toward NBS. It would be expected, however, on mechanistic and energetic grounds that allylic hydrogens would show the usual reactivity order of primary < secondary < tertiary in the NBS reaction. Kinetic studies<sup>12</sup> have shown that the rate-determining step in the allylic bromination reaction involves abstraction of an allylic hydrogen atom by the succinimidyl radical and the ease of abstraction of different types of allylic hydrogens will be determined, in the first approximation, by their bond dissociation energies and by stabilization due to introduction of polar structures in the transition states of their reactions with succinimidyl radicals. Since both bond dissociation energies of the allylic C-H bonds and ionization potentials of the substituted allyl radicals (which will determine the amount of polar character in their transition states) would be expected to decrease in order primary > secondary > tertiary,<sup>13</sup> the reactivity order for the reaction of different types of allylic hydrogens toward succinimidyl radicals, and consequently in the NBS reaction, should be: primary < secondary < tertiary. Steric factors may reduce the relative reactivity of tertiary allylic hydrogens and the apparent lack of reactivity of certain highly hindered hydrogens of this type in steroid and triterpenoid compounds<sup>10a,b,c</sup> may be due to this factor.

#### EXPERIMENTAL

*Ethyl 4-methyl-2-pentenoate.* 4-Methyl-2-pentenoic acid (b.p. 111.5-112.0° (19 mm.),  $n_D^{25}$  1.4481; reported,<sup>14b</sup> b.p. 115-116° (20 mm.),  $n_D^{25}$  1.4489), prepared by the method of Goldberg and Linstead,<sup>14a</sup> on direct esterification according to the method of Linstead<sup>14b</sup> yielded ethyl 4-methyl-2-pentenoate (b.p. 68-69.5° (19 mm.),  $n_D^{25}$  1.4340; re-

(8) (a) C. Meystre, L. Ehrmann, R. Neber, and K. Miescher, *Helv. Chim. Acta*, **28**, 1252 (1945); (b) C. Meystre and A. Wettstein, *Helv. Chim. Acta*, **30**, 1037, 1256 (1947); (c) L. Ruzicka, P. A. Plattner, and J. Pataki, *Helv. Chim. Acta*, **28**, 1360 (1945); (d) A. Wettstein and C. Meystre, *Helv. Chim. Acta*, **30**, 1262 (1945); (e) L. Ruzicka, P. A. Plattner, and H. Heusser, *Helv. Chim. Acta*, **29**, 473 (1946); (f) P. A. Plattner, L. Ruzicka, H. Heusser, J. Pataki, and K. Meier, *Helv. Chim. Acta*, **29**, 942 (1946); (g) L. Ruzicka, O. Jeger, and J. Redel, *Helv. Chim. Acta*, **26**, 1235 (1943); (h) M. Rubin and B. H. Ambrecht, *J. Am. Chem. Soc.*, **75**, 3513 (1943); (i) M. Mousseron and R. Jacquier, *Bull. soc. chim. France*, 106 (1951).

(9) Mousseron and Jacquier<sup>8i</sup> state that benzoyl peroxide was useless in their studies of the reaction of NBS with substituted cyclohexenes.

(10) It is not surprising that most tertiary allylic bromide products are not stable with respect to elimination under these reaction conditions since it has been shown that even a secondary allylic bromide product, 3-bromocyclohexene, undergoes slow dehydrobromination during the NBS reaction.<sup>6</sup> Ethyl 4-methyl-2-pentenoate, isolated in the present work, is more stable than the other tertiary bromide products but it evolves hydrogen bromide slowly on standing at room temperature.

(11) (a) R. A. Barnes and G. R. Buchwalter, *J. Am. Chem. Soc.*, **73**, 3858 (1951), found that *p*-cymene with NBS and benzoyl peroxide catalyst brominates preferentially in the tertiary benzylic position; (b) J. Klein and E. D. Bergmann, *J. Org. Chem.*, **22**, 1019 (1957); (c) J. Cason, N. L. Allinger, and D. E. Williams, *J. Org. Chem.*, **18**, 842 (1953).

(12) E. A. Youngman, Ph.D. Thesis, University of Washington, 1952; cf. ref. (6).

(13) Bond dissociation energies for all of the different types of allylic C-H bonds have not been determined but will probably differ from those for the corresponding types of bonds in alkanes (D(I°C-H) = 98, D(II°C-H) = 94, D(III°C-H) = 90 kcal. mole<sup>-1</sup>) by the allyl radical resonance energy (18-22 kcal. mole<sup>-1</sup>). Assuming comparable bond distances in the transition states, the amount of polar character in the transition states will be determined by the electron affinity of the succinimidyl radical and the relative magnitudes of the ionization potentials of the different types of allyl radicals; the latter would be expected to decrease in the same manner as found for the ionization potentials of the corresponding types of saturated radicals (I°(I°R·) ≈ 200, I°(II°R·) ≈ 182, I°(III°R·) ≈ 171 kcal. mole<sup>-1</sup>; F. P. Lossing and J. B. deSousa, *J. Am. Chem. Soc.*, **81**, 281 (1959).

(14) (a) A. A. Goldberg and R. P. Linstead, *J. Chem. Soc.*, 2343 (1928); (b) R. P. Linstead, *J. Chem. Soc.*, 2498 (1929).

ported:<sup>14b</sup> for the  $\alpha,\beta$ -unsaturated ester, b.p. 60° (13 mm.),  $n_D^{25}$  1.4341; for the  $\beta,\gamma$ -unsaturated ester, b.p. 58° (11 mm.),  $n_D^{25}$  1.4329).

**Reaction of ethyl 4-methyl-2-pentenoate with NBS.** Ethyl 4-methyl-2-pentenoate (7.1 g., 0.05 mole; contained peroxides (ammonium thiocyanate-ferrous ammonium sulfate color test) formed by autoxidation on standing in a glass-stoppered bottle), NBS (7.3 g., 0.04 mole; purified by method Aa<sup>6</sup>) and carbon tetrachloride (30 ml.) were refluxed until a test with starch-iodide paper showed the absence of positive bromine; time for complete reaction, <20 min. The reaction mixture was cooled in an ice bath, filtered, and the succinimide (4.1 g., 100%) washed twice with 5-ml. portions of carbon tetrachloride. The washings and filtrate were combined and concentrated under reduced pressure (water aspirator). Distillation of the residue gave ethyl 4-bromo-4-methyl-2-pentenoate [7.1 g., 81%, b.p. 108–111° (18 mm.),  $n_D^{25}$  1.4848]; reported<sup>4</sup> (same general procedure except benzoyl peroxide initiator present), 67%, b.p. 105–110° (13 mm.); the bromo product is unstable, slowly evolving hydrogen bromide and becoming dark colored.

Runs in which preformed peroxides, light, and oxygen were singly or collectively excluded were performed by essentially the same technique as employed earlier in the study of effects of these environmental factors on the reaction of cyclohexene with NBS.<sup>6</sup> Freshly distilled ester gave a negative test for peroxides and was used in Runs 2, 4 and 5; addition of any material to decompose peroxides was omitted to avoid possible isomerization of the  $\beta,\gamma$ -isomer during the distillation. In Runs 4 and 5 oxygen was excluded by flushing the apparatus with deoxygenated nitrogen before distillation of the ester into it and a slight positive pressure of nitrogen was maintained in the system throughout the run. Results of these runs are summarized in Table I.

DEPARTMENT OF CHEMISTRY  
UNIVERSITY OF WASHINGTON  
SEATTLE 5, WASH.

## Preparation of Propene-d-1

WILLIAM P. NORRIS

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Propene-d-1 has been prepared previously in poor yield and of undisclosed deuterium content by reduction of propyne-d-1.<sup>1</sup>

In the present work propene-d-1 was prepared by treating propenyl-1-magnesium bromide with deuterium oxide. The yield of product was 70% based on 1-bromo-1-propene and, according to parent peak analysis on the mass spectrometer, was at least 99% mono-deuterated propylene. The infrared spectrum of this propene-d-1 exhibited absorption peaks at 10.26  $\mu$  (*trans* isomer) and 12.52  $\mu$  (*cis* isomer).<sup>2</sup> By comparing the relative intensities of the two peaks, the propene-d-1 prepared is judged to be 60% *cis* and 40% *trans* isomer. Very small peaks appeared at 10.09  $\mu$  and 11.00  $\mu$  which

are probably due to undeuterated propene.<sup>3</sup> From the work of Normant,<sup>4</sup> it may be assumed that position isomerization did not occur either in the preparation of the Grignard or in the reaction of the Grignard reagent with deuterium oxide. Geometric isomerization did occur in the reaction sequence, as the Grignard reagent was prepared from 1-bromopropene which was 98% *cis* isomer.

The 1-bromo-1-propene used in the preparation of the propenylmagnesium bromide was prepared by a modification of an existing method.<sup>5</sup> Instead of treating *trans*-crotonic acid dibromide with sodium carbonate in hot water or with refluxing pyridine, both of which reportedly gave yields of *cis*-1-bromo-1-propene in the range of 16–20%, the acid was treated with an excess of sodium bicarbonate in dimethylformamide at 70°. A 38% yield of 1-bromo-1-propene was obtained which was at least 99% *cis*-1-bromo-1-propene as determined by vapor phase chromatography and infrared analysis. By raising the temperature to 90° and distilling under reduced pressure, it is possible to obtain another 38% yield of 1-bromo-1-propene which analyzes for 96% *cis* and 4% *trans*-1-bromo-1-propene. This gives a total yield of 76% of 1-bromo-1-propene.

The infrared spectrum of the first fraction was identical with the spectrum of *cis*-1-bromo-1-propene prepared by Skell and Allen<sup>6</sup> by the *trans* radical addition of hydrogen bromide to propyne.

The *cis*-1-bromo-1-propene is the isomer expected from this series of reactions because of the stereochemistry involved.<sup>7,8</sup> *Cis*-1-bromo-1-propene is easily isomerized to the *trans* isomer. When a portion of the first fraction was redistilled, b.p. 55–55.2°, without protection from light, analysis by vapor phase chromatography showed the composition to be 90% *cis* and 10% *trans* isomer.

## EXPERIMENTAL

**Preparation of 1-bromo-1-propene.** Three hundred and seventeen g. (1.20 mole) of *trans*-crotonic acid dibromide, m.p. 85–87°, was dissolved in the minimum amount of dimethylformamide. This solution was added, over a 20 minute period, to a reaction vessel which contained 163 g. (1.29 mole) sodium bicarbonate suspended in 500 ml. of dimethylformamide and which was connected to a Dry Ice trap. The reaction mixture was held at 70° during the addition. When

(1) B. S. Rabinovitch and F. S. Looney, *J. Am. Chem. Soc.*, **75**, 2652 (1953).

(2) Infrared spectra of essentially pure *cis*- and *trans*-propene-d-1 were provided by B. S. Rabinovitch of the University of Washington, Seattle, Washington.

(3) R. S. Rasmussen and R. R. Brattain, *J. Chem. Phys.*, **15**, 120 (1947). R. H. Pierson, A. N. Fletcher and E. Gantz, *Anal. Chem.*, **28**, 1218 (1956).

(4) H. Normant, *Compt. rend.*, **239**, 1510, 1811 (1954); **240**, 314, 440, (1955).

(5) E. A. Braude and J. A. Coles, *J. Chem. Soc.*, 2078 (1951). J. Wislicenus, *Ann.*, **248**, 281 (1888).

(6) P. S. Skell and R. G. Allen, Abstracts of Papers Presented at Chicago, Illinois, September 7–12, 1958, p. 27P. The infrared spectra of *trans* and *cis*-1-bromo-1-propene were kindly provided by Skell and Allen.

(7) A. McKenzie, *J. Chem. Soc.*, 101, 1196 (1912).

(8) S. J. Cristol and W. P. Norris, *J. Am. Chem. Soc.*, **75**, 2645 (1953). E. Grovenstein, Jr., and D. E. Lee, *J. Am. Chem. Soc.*, **75**, 2639 (1953).