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of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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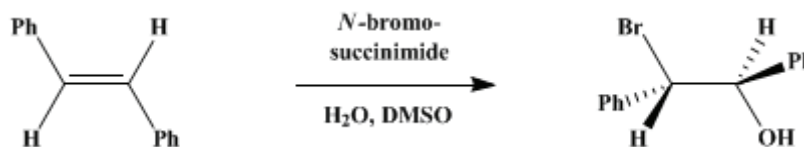
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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BROMOHYDRINS FROM ALKENES AND *N*- BROMOSUCCINIMIDE IN DIMETHYL SULFOXIDE: *erythro*-2- BROMO-1,2-DIPHENYLETHANOL

[Ethanol, 2-bromo-1,2-diphenyl-, *erythro*-]



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1. Procedure

A 500-ml., round-bottomed flask equipped with a magnetic stirring bar and a thermometer is charged with 18.0 g. (0.100 mole) of (*E*)-stilbene (Note 1), 5.0 ml. (0.28 mole) of water, and 300 ml. (4.23 moles) of dimethyl sulfoxide (Note 2). The resulting suspension is stirred for 5 minutes at room temperature (20–25°) (Note 3). Stirring is continued as 35.6 g. (0.200 mole) of *N*-bromosuccinimide (Note 4) is added in small portions over *ca.* 10 minutes. A yellow color appears when the first portion of *N*-bromosuccinimide is added, and by the time the addition is complete, the solution is bright orange. During the addition the temperature of the mixture rises to 50–55°, and all the (*E*)-stilbene dissolves. The contents of the flask are stirred for another 15 minutes and poured into 1 l. of ice water; the product separates immediately as a white solid (Note 5). The aqueous slurry is transferred to a separatory funnel with the aid of 50-ml. portions of water and diethyl ether, and extracted with four 200-ml. portions of ether. The combined ethereal extracts are washed with 250 ml. of water and 250 ml. of sodium chloride solution, dried over anhydrous magnesium sulfate, and evaporated with a rotary evaporator at a water bath temperature of *ca.* 30°. The pale yellow, crystalline residue is dissolved, to the extent possible, in 600 ml. of hot hexane, and the resulting suspension is filtered while hot, removing a small amount of an insoluble impurity. Cooling the filtrate provides colorless fibers of analytically pure *erythro*-2-bromo-1,2-diphenylethanol, m.p. 83–84° (Note 6); a second crop of crystals is obtained by concentrating the mother liquor to 200 ml. (Note 7). The combined yield is 22.0–24.9 g. (80–90%) (Note 8).

2. Notes

1. (*E*)-Stilbene, m.p. 123–126°, was purchased from Aldrich Chemical Company, Inc., and used as received. It is also available from J. T. Baker Chemical Company and from Eastman Organic Chemicals.
2. Reagent grade dimethyl sulfoxide was used without purification. The amount of dimethyl sulfoxide can be varied. A large excess is employed in this case to facilitate dissolution of the stilbene.
3. The suspension may be warmed to dissolve the alkene more rapidly; (*E*)-stilbene dissolves completely at *ca.* 65°. If the suspension is warmed, it *must* be cooled below 30° before proceeding further to prevent a vigorous reaction when the *N*-bromosuccinimide is added. The submitters recommend that the warm suspension be cooled under an atmosphere of nitrogen. If a volatile alkene is used, the mixture should be cooled prior to and during the addition of *N*-bromosuccinimide to prevent losses by evaporation.
4. *N*-Bromosuccinimide purchased from Arapahoe Chemical Company was used without purification. If the purity of the *N*-bromosuccinimide is in doubt, it should be titrated before use by the standard iodide–thiosulfate method and purified, if necessary, by recrystallization from 10 times its weight of water.² Solutions of *N*-bromosuccinimide in dimethyl sulfoxide cannot be stored, since the solvent is oxidized by the brominating reagent.
5. The product does not appear to deteriorate if allowed to stand at this point.

6. The submitters recrystallized the product from 600 ml. of petroleum ether (b.p. 30–60°) and reported a melting point of 84–84.5° (lit., m.p. 84.5–85.5°³ and 86°⁴).
7. The submitters found that the residue (2.8 g.) obtained upon evaporation of the mother liquor was largely *erythro*-2-bromo-1,2-diphenylethanol contaminated with a small amount of succinimide. Absorptions for the *threo* isomer could not be detected in the IR and ¹H NMR spectra of this material.
8. The product obtained by the checkers was analyzed. Analysis calculated for C₁₄H₁₃BrO: C, 60.67; H, 4.73. Found: C, 60.74; H, 4.77. The spectral properties of the product are as follows: IR (CCl₄) cm.⁻¹: 3610, 1500, 1460, 700; ¹H NMR (CDCl₃), δ (multiplicity, coupling constant *J* in Hz., number of protons, assignment): 5.06 and 5.16 (AB doublet, *J* = 6.5, 2H, CHBrCHOH), 7.35 (m, 10H, aryl H).

3. Discussion

The present procedure affords a simple, general method for preparing bromohydrins from alkenes and avoids the heterogeneous solvent systems often used in such reactions. Labeling experiments have demonstrated that the oxygen from the dimethyl sulfoxide appears in the hydroxyl group of the bromohydrin;⁵ therefore, the role of the water is to hydrolyze the intermediate β-bromodimethylsulfoxonium ion.

Many alkenes have been converted into their respective bromohydrins by this procedure, usually with high regio- and stereoselectivity (Table I).^{5,6} Although the regioselectivity of the addition generally follows Markovnikov's rule, the opposite orientation is observed with alkenes bearing the bulky *tert*-butyl substituent (entries 7–9). The reaction of conjugated dienes with *N*-bromosuccinimide in aqueous dimethyl sulfoxide also occurs in a regio- and stereoselective manner, leading exclusively to vicinal bromohydrins in high yield.⁷

TABLE I BROMOHYDRINS FROM ALKENES WITH *N*-BROMOSUCCINIMIDE IN AQUEOUS DIMETHYL SULFOXIDE

Entry	Alkene	Bromohydrin	Yield (%) ^a
1	(<i>Z</i>)-C ₆ H ₅ CH=CHC ₆ H ₅	<i>threo</i> -C ₆ H ₅ CH(OH)CH(Br)C ₆ H ₅	82
2	(<i>E</i>)-C ₆ H ₅ CH=CHCH ₃	<i>erythro</i> -C ₆ H ₅ CH(OH)CH(Br)CH ₃	92
3	(<i>Z</i>)-C ₆ H ₅ CH=CHCH ₃	<i>threo</i> -C ₆ H ₅ CH(OH)CH(Br)CH ₃	95
4	C ₆ H ₅ CH=CH ₂	C ₆ H ₅ CH(OH)CH ₂ Br	76
5	C ₆ H ₅ -C(CH ₃)=CH ₂	C ₆ H ₅ C(CH ₃)(OH)CH ₂ Br	89
6	C ₆ H ₅ CH ₂ CH=CH ₂	C ₆ H ₅ CH ₂ CH(OH)CH ₂ Br	83
7	(<i>E</i>)-(CH ₃) ₃ CCH=CHCH ₃	<i>erythro</i> -(CH ₃) ₃ CCH(Br)CH(OH)CH ₃	90
8	(<i>Z</i>)-(CH ₃) ₃ CCH=CHCH ₃	<i>threo</i> -(CH ₃) ₃ CCH(Br)CH(OH)CH ₃	90
9	(CH ₃) ₃ CCH=CH ₂	(CH ₃) ₃ CCH(Br)CH ₂ OH	89
10	(CH ₃) ₃ CC(CH ₃)=CH ₂	(CH ₃) ₃ CC(CH ₃)(OH)CH ₂ Br	60 ^b

^aAverage yield from two or more runs.

^bAccompanied by 24% dibromide.

When electron-withdrawing groups are attached to the double bond, the reaction is strongly inhibited and may fail completely. In such cases, the bromide anion, produced by the reaction of dimethyl sulfoxide with *N*-bromosuccinimide, competes with the dimethyl sulfoxide for the bromonium (or bromo carbonium) ion intermediate. Thus, dibromide may accompany recovered alkene or any bromohydrin formed. Similarly, exogenous anions often compete with dimethyl sulfoxide for the cation.⁶

erythro-2-Bromo-1,2-diphenylethanol has been prepared by reaction of (*E*)-stilbene with *N*-bromoacetamide in buffered aqueous acetone,³ by addition of hydrogen bromide to (*E*)-stilbene oxide,⁴ and by reaction of (*E*)-stilbene with bromotrinitromethane in dimethyl sulfoxide followed by hydrolysis.⁸

References and Notes

1. Department of Chemistry, Temple University, Philadelphia, Pennsylvania 19122.
 2. L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Vol. 1, Wiley, New York, 1967, p. 78.
 3. H. O. House, *J. Am. Chem. Soc.*, **77**, 3070 (1955).
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 5. D. R. Dalton, V. P. Dutta, and D. C. Jones, *J. Am. Chem. Soc.*, **90**, 5498 (1968).
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 8. K. Torssell, *Ark. Kemi*, **23**, 543 (1965).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

petroleum ether

erythro-2-Bromo-1,2-diphenylethanol

Ethanol, 2-bromo-1,2-diphenyl-, erythro-

(Z)-C₆H₅CH=CHC₆H₅

threo-C₆H₅CH(OH)CH(Br)C₆H₅

(E)-C₆H₅CH=CHCH₃

erythro-C₆H₅CH(OH)CH(Br)CH₃

(Z)-C₆H₅CH=CHCH₃

threo-C₆H₅CH(OH)CH(Br)CH₃

C₆H₅CH=CH₂

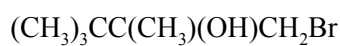
C₆H₅CH(OH)CH₂Br

C₆H₅-C(CH₃)=CH₂

C₆H₅C(CH₃)(OH)CH₂Br

C₆H₅CH₂CH=CH₂

C₆H₅CH₂CH(OH)CH₂Br



ether,
diethyl ether (60-29-7)

sodium chloride (7647-14-5)

hydrogen bromide (10035-10-6)

oxygen (7782-44-7)

nitrogen (7727-37-9)

acetone (67-64-1)

magnesium sulfate (7487-88-9)

N-bromosuccinimide (128-08-5)

hexane (110-54-3)

N-Bromoacetamide (79-15-2)

dimethyl sulfoxide (67-68-5)

bromotrinitromethane (560-95-2)

(E)-stilbene (103-30-0)

(E)-stilbene oxide