Reduction of Some Bridgehead Bromides and *cis*- and *trans*-α-Bromostilbene with Triphenyltin Hydride[1]

EUGENE J. KUPCHIK AND ROBERT J. KIESEL

Department of Chemistry, St. John's University, Jamaica 32, New York

Received September 3, 1963

Organotin hydrides can bring about replacement of the halogen in alkyl,[2,3] aryl,[2,4,5] benzoyl,[6] and acyl,[7] halides by hydrogen. Stepwise reduction of chloromethanes with triphenyltin hydride[8] and of benzotrichloride[9,10] and *gem*-dihalocyclopropanes[11] with tri-*n*-butyltin hydride has been accomplished.

In a mechanistic study of the reduction of alkyl halides by organotin hydrides, Kuivila, *et al.*,[9,10] have shown that the reaction is not of the SN1 or SN2 type. Very importantly they found that the reduction is catalyzed by azobisisobutyronitrile which suggests a radical chain mechanism.

We also have found that an SN1 or SN2 mechanism is unlikely by observing that triphenyltin hydride can reduce 1-bromonorbornane,[1] a bridgehead halide which does not readily undergo SN1 or SN2 type reactions.[12] For example, triphenyltin hydride reacted with 1-bromonorbornane in cyclohexane at the reflux temperature to give norbornane in 55% yield and triphenyltin bromide in 49% yield. The yield of norbornane in this reaction is based on gas–liquid chromatography data, whereas the yield of triphenyltin bromide is based on product isolation. The lower value for the triphenyltin bromide is probably due, at least in part, to losses during purification. There is strong, but not entirely conclusive, evidence that benzene also is formed in this reaction. The vapor phase chromatogram of the cyclohexane solution of the reaction mixture contained an extra band whose retention time was identical to that for benzene. Also, the infrared spectrum of the cyclohexane solution of the reaction mixture contained a small band at 14.87 μ which also suggests the presence of benzene. Although we have no conclusive proof, the benzene may have arisen *via* the decomposition of the triphenyltin hydride. Benzene is also one of the products of the reaction between triphenyltin hydride and benzylamine[13,14] and between triphenyltin hydride and 2-thenoic acid.[15]

Triphenyltin hydride also can reduce other bridgehead bromides, namely 1-bromotriptycene and 1-bromoapocamphane. The results are summarized in Table I. In the case of the bridgehead bromides the yield of reduction product, especially when based on product isolation, is often less than the yield of triphenyltin bromide. We tentatively attribute this to the difficulty in separating the reduction product from the starting bromide and to losses owing to the high volatility of the reduction product.

It should be noted that in some cases hexaphenylditin and tetraphenyltin were isolated from the reaction mixture. The precise origins of these by-products were not investigated. The hexaphenylditin may have arisen *via* the decomposition of triphenyltin hydride, a reaction which is known to occur.[13,16]

We have found triphenyltin hydride to be very reactive towards *cis*- and *trans*-α-bromostilbene. For example, when triphenyltin hydride and *cis*-α-bromostilbene are mixed at *ca.* 26°, an exothermic reaction occurs, the temperature rising to 42°. The products isolated from this reaction were *trans*-stilbene (98.0%) and triphenyltin bromide (73.8%). When this reaction was carried out at *ca.* 26 to 29°, the products were *trans*-stilbene (61.1%), *cis*-stilbene (30.5%), and triphenyltin bromide (72.0%). Triphenyltin hydride also reacted readily with *trans*-α-bromostilbene at *ca.* 26 to 30° to give triphenyltin bromide in 71.7% yield, *trans*-stilbene in 54.1% yield, and *cis*-stilbene in 38.6% yield. No isomerization of the starting bromide or of the initially formed stilbenes would be expected to occur under the mild reaction conditions employed or during the isolation procedure employed. Furthermore, although the percentages of *cis*-stilbene and *trans*-stilbene are based on product isolation, the values are probably quite close to the actual amounts of these stilbenes formed in the reaction. The isolation procedure was similar to that employed by Curtin and Harris[17] to separate *cis*-stilbene from *trans*-stilbene. The effectiveness of the procedure in the present case was demonstrated by applying it to a known mixture of *trans*-stilbene, *cis*-stilbene, and triphenyltin bromide. These three compounds were recovered in yields of 98.7%, 100%, and 79.0%, respectively.

The stereochemical results obtained with the α-bromostilbenes are consistent with a free radical mechanism. It is hoped that a study of the effect of substituents on the kinetics of this reaction will provide more detailed information concerning the mechanism.

Experimental

Melting points were determined in open capillaries using an electrically heated aluminum block and are uncorrected. Each triphenyltin hydride reduction was carried out in a nitrogen atmosphere. The triphenyltin bromide obtained in each reduction was identified by mixture melting point determination and infrared spectral comparison with a known sample.

1-Bromonorbornane.—This compound was prepared from norbornane-1-carboxylic acid[18] by a procedure similar to that described for the preparation of 1-bromoapocamphane.[19] The silver salt of norbornane-1-carboxylic acid (17.7 g.) afforded 8.3 g. (65.0%) of 1-bromonorbornane, b.p. 56° (18 mm.), $n^{25}\text{D}$ 1.5065, lit.[20] b.p. 57–58° (21 mm.).

---

[1] Published in part as a Communication in *Chem. Ind.* (London), 1654 (1962).

[2] J. G. Noltes and G. J. M. van der Kerk, *ibid.*, 294 (1959).

[3] E. J. Kupchik and R. E. Connolly, *J. Org. Chem.*, **26**, 4747 (1961).

[4] L. A. Rothman and E. I. Becker, *ibid.*, **24** (1959); **25**, 2203 (1960).

[5] D. H. Lorenz, P. Shapiro, A. Stern, and E. I. Becker, *ibid.*, **28**, 2332 (1963).

[6] G. J. M. van der Kerk, J. G. Noltes, and J. G. A. Luijten, *J. Appl. Chem.* (London), **7**, 356 (1957).

[7] H. G. Kuivila, *J. Org. Chem.*, **25**, 284 (1960).

[8] D. H. Lorenz and E. I. Becker, *ibid.*, **27**, 3370 (1962).

[9] H. G. Kuivila, L. W. Menapace, and C. R. Warner, *J. Am. Chem. Soc.*, **84**, 3584 (1962).

[10] H. G. Kuivila and L. W. Menapace, *J. Org. Chem.*, **28**, 2165 (1963).

[11] D. Seyferth, H. Yamazaki, and D. L. Alleston, *ibid.*, **28**, 703 (1963).

[12] U. Schöllkopf, *Angew. Chem.*, **72**, 147 (1960).

[13] A. Stern and E. I. Becker, *J. Org. Chem.*, **27**, 4052 (1962).

[14] E. J. Kupchik and R. J. Kiesel, unpublished results.

[15] S. Weber and E. I. Becker, *J. Org. Chem.*, **27**, 1258 (1962).

[16] G. J. M. van der Kerk, J. G. Noltes, and J. G. A. Luijten, *Rec. trav. chim.*, **81**, 853 (1962).

[17] D. Y. Curtin and E. E. Harris, *J. Am. Chem. Soc.*, **73**, 4519 (1951).

[18] W. H. Boehme, *ibid.*, **81**, 2762 (1959).

[19] P. Wilder, Jr., and A. Winston, *ibid.*, **75**, 5370 (1953).

[20] W. P. Whelan, Jr., dissertation, Columbia University, 1952.

TABLE I

REDUCTION OF BRIDGEHEAD BROMIDES AND α-BROMOSTILBENES BY TRIPHENYLTIN HYDRIDE

			% yield[a]	
Reduction no.	Bromide	Conditions	Reduction product	Triphenyltin bromide
1[b]	1-Bromonorbornane	80°, neat, 24 hr.	*c*	10.0
2[b]	1-Bromonorbornane	benzene, reflux, 24 hr.	*c*	45.1
	1-Bromonorbornane	diethyl ether, reflux, 24 hr.	*c*	43.0
	1-Bromonorbornane	cyclohexane, reflux, 24 hr.	*c*	48.8
3[b]	1-Bromonorbornane	80°, neat, 24 hr.	9.3	17.2
4[d]	1-Bromonorbornane	cyclohexane, reflux, 24 hr.	55[e]	*c*
5	1-Bromotriptycene	benzene, reflux, 24 hr.	26.3	51.8
6	1-Bromotriptycene	*ca.* 26°, neat, 24 hr.	8.8	7.8
7	1-Bromoapocamphane	benzene, reflux, 20 hr.	*c*	35.1
8[f]	1-Bromoapocamphane	80°, neat, 24 hr.	6.8	26.5
9	1-Bromoapocamphane	benzene, reflux, 20 hr.	22[e]	*c*
10	*cis*-α-Bromostilbene	*ca.* 26 to 42°, neat	98.0 (*trans*)	73.8
	cis-α-Bromostilbene	*ca.* 26 to 29°, neat	30.5 (*cis*) 61.1 (*trans*)	72.0
11	*trans*-α-Bromostilbene	*ca.* 26 to 30°, neat	38.6 (*cis*) 54.1 (*trans*)	71.7

[a] Unless otherwise noted, the yields are based on product isolation. [b] Hexaphenylditin and tetraphenyltin also were isolated. [c] Not isolated. [d] Benzene also probably was formed. [e] Based on g.l.c. data. [f] Hexaphenylditin also was isolated.

Reduction of 1-Bromonorbornane with Triphenyltin Hydride. Reduction No. 3.—Triphenyltin hydride (35.1 g., 0.10 mole) and 17.5 g. (0.10 mole) of 1-bromonorbornane were heated at 80 ± 5° with stirring for 24 hr. after which time the mixture had become a thick cream-colored paste. Distillation of the reaction mixture gave 10.0 g. (57.0%) of unchanged 1-bromonorbornane, b.p. 61–62° (25 mm.), $n^{25}\mathrm{D}$ 1.5065. In a Dry Ice trap connected to the distillation receiver was found 0.900 g. (9.3%) of norbornane, m.p. 70–74°. After sublimation, the melting point was 85–87°, lit.[21] m.p. 86–87°, and was undepressed on admixture with an authentic sample of norbornane. The infrared spectrum (5% solution in carbon tetrachloride) was superimposable upon that of an authentic sample of norbornane (5% solution in carbon tetrachloride).

The residue from the distillation, which solidified on cooling, was extracted with two 100-ml. portions of diethyl ether. Distillation of the ether left a solid which was extracted with 50 ml. of hot methanol. The residue (0.50 g.) was not identified. Distillation of the methanol *in vacuo* left a solid which was recrystallized from *n*-propyl alcohol to give 7.4 g. (17.2%) of triphenyltin bromide, m.p. 119–121°.

The residue from the ether extraction was recrystallized from 50 ml. of chloroform to give 12.5 g. of hexaphenylditin, m.p. 232–234°, melting point undepressed on admixture with a known sample of hexaphenylditin. The mother liquor was evaporated to dryness, and the residue was fractionally crystallized to give an additional 4.5 g. of hexaphenylditin, m.p. 232–234°, no depression on admixture with a known sample of hexaphenylditin. Also obtained was 3.0 g. of tetraphenyltin, m.p. 222–224°, no depression on admixture with an authentic sample of tetraphenyltin.

Another run using 3.5 g. (0.02 mole) of 1-bromonorbornane and 7.0 g. (0.02 mole) of triphenyltin hydride gave 1.75 g. (50.0%) of unchanged 1-bromonorbornane, 1.9 g. (22.0%) of triphenyltin bromide, and 0.075 g. of impure norbornane, m.p. 85–86°, after sublimation.

Reduction No. 4.—Reduction no. 2 was repeated using refluxing cyclohexane. A portion (10 μl.) of the solution remaining after reaction was subjected to gas–liquid chromatography using a diisodecyl phthalate column at 100° and a flow rate of 95 cc. helium/min. The estimated per cents of norbornane and 1-bromonorbornane were 55 and 45%, respectively. The per cents were estimated by comparison with standard chromatograms. An additional band was present whose retention time was identical to that for benzene. The infrared spectrum of the solution remaining after reaction contained a small band at 14.87 μ.

Reduction of 1-Bromotriptycene with Triphenyltin Hydride. Reduction No. 5.—A solution of 1.5 g. (0.0045 mole) of 1-bromotriptycene[22] and 1.58 g. (0.0045 mole) of triphenyltin hydride in 10 ml. of benzene was refluxed for 24 hr. Distillation of the benzene at 60–70° *in vacuo* left a residue which solidified on cooling. The residue was extracted with 25 ml. of hot methylene chloride. The residue from the extraction (40 mg.) was a grey-black solid. Distillation of the methylene chloride *in vacuo* left a solid residue which was sublimed at 130° (1 mm.) to give 2.0 g. of solid material. Recrystallization from cyclohexane–methylene chloride gave white needles, m.p. 245–248°. The solvent was evaporated from the mother liquor, and the residue was extracted with three 10-ml. portions of hot methanol. Distillation of the methanol *in vacuo* left a residue which was recrystallized from *n*-propyl alcohol to give 1.0 g. (51.8%) of triphenyltin bromide, m.p. 112–114°.

The residue from the methanol extraction was recrystallized from cyclohexane–methylene chloride to give 100 mg. of solid material, m.p. 242–245°. This material was combined with the previous solid having m.p. 245–248° and was recrystallized from cyclohexane–methylene chloride to give 300 mg. (26.3%) of triptycene, m.p. 252–254°, lit.[23] m.p. 255–256°, no depression on admixture with a known sample of triptycene, infrared spectrum superimposable on that of a known sample of triptycene.

The residue which remained after the initial sublimation was recrystallized from methanol to give 50 mg. (3.3%) of 1-bromotriptycene, m.p. 240–244°.

Reduction of 1-Bromoapocamphane with Triphenyltin Hydride. Reduction No. 8.—1-Bromoapocamphane[19] (14.46 g., 0.071 mole) and 24.92 g. (0.071 mole) of triphenyltin hydride were stirred at 80 ± 5° for 24 hr. The reaction flask was connected to an ice–water trap which lead to a Dry Ice trap and then was heated at 90° (1 mm.). From the ice–water trap was recovered 10.2 g. (70.5%) of unchanged 1-bromoapocamphane, m.p. 161–163°. From the Dry Ice trap was obtained 720 mg. of impure apocamphane, m.p. 70–75°. This material was sublimed twice to give 605 mg. (6.8%) of apocamphane, m.p. 82–84°, lit.[19] m.p. 86–92°, no depression on admixture with a known sample of apocamphane, infrared spectrum superimposable on that of a known sample of apocamphane.

The residue remaining in the reaction flask after sublimation was extracted with three 40-ml. portions of diethyl ether. Distillation of the ether left a residue which was extracted with 40 ml. of hot methanol. Distillation of the methanol *in vacuo* left a solid which was recrystallized twice from *n*-propyl alcohol to give 8.1 g. (26.5%) of triphenyltin bromide, m.p. 116–118°.

The residue from the methanol extraction (3.2 g.) was not identified.

The residue from the ether extraction (8.5 g.) was recrystallized from chloroform to give 6.87 g. of hexaphenylditin, m.p. 232–234°, no depression on admixture with a known sample of hexaphenylditin.

Reduction No. 9.—Reduction No. 7 was repeated. A portion (10 μl.) of the solution remaining after reaction was subjected to gas–liquid chromatography using a diisodecyl phthalate column

---

[21] G. Kamppa and S. Beckmann, *Ann.*, **512**, 183 (1934).

[22] W. Thielocker, U. Berger-Brose, and K. H. Beyer, *Chem. Ber.*, **93**, 1658 (1960).

[23] G. Wittig, *Org. Syn.*, **39**, 75 (1959).

at 140° and a flow rate of 55 cc. helium/min. The estimated per cents of apocamphane and 1-bromoapocamphane were 22% and 78%, respectively. The per cents were estimated by comparison with standard chromatograms.

Reduction of *cis*-α-Bromostilbene with Triphenyltin Hydride. Reduction No. 10.—A mixture of 5.18 g. (0.02 mole) of *cis*-α-bromostilbene[24] and 7.02 g. (0.02 mole) of triphenyltin hydride was stirred at *ca.* 26°. During 10 min. the reaction temperature rose to 42°, remained at this temperature for 5 min., and then gradually decreased to *ca.* 26°. After 1 hr. the reaction mixture had completely solidified. The mixture was allowed to remain at *ca.* 26° overnight before processing. It was then slurried with 25 ml. of petroleum ether (b.p. 30-60°) and poured onto 100 g. of Woelm neutral alumina (activity I-II). The column was eluted with petroleum ether until 700 ml. of eluate was obtained. Distillation of the petroleum ether *in vacuo* left 6.2 g. of solid material which was recrystallized from 95% ethanol to give 3.18 g. of *trans*-stilbene, m.p. 120-122°, no depression on admixture with a known sample of *trans*-stilbene, infrared and ultraviolet spectra superimposable on that of a known sample of *trans*-stilbene.

The mother liquor was evaporated to dryness, slurried with 25 ml. of petroleum ether and poured onto 70 g. of Woelm neutral alumina (activity I-II). The column was eluted with petroleum ether until 500 ml. of eluate was obtained. Evaporation of the petroleum ether followed by recrystallization of the solid residue from 95% ethanol gave 350 mg. of *trans*-stilbene, m.p. 120-122°, total yield of *trans*-stilbene 3.53 g. (98.0%).

The first column (100 g. of alumina) was eluted with methylene chloride-methanol (9:1) until 700 ml. of eluate was obtained, and the second column was eluted with methylene chloride-methanol (9:1) until 500 ml. of eluate was obtained. The two fractions were combined, and the solvent was distilled *in vacuo*. There remained 6.6 g. of solid material, m.p. 95-98°, which upon recrystallization from *n*-propyl alcohol gave 6.35 g. (73.8%) of triphenyltin bromide, m.p. 116-118°.

In another run using 2.59 g. (0.01 mole) of *cis*-α-bromostilbene and 3.51 g. (0.01 mole) of triphenyltin hydride there was obtained, using essentially the same isolation procedure as above, *trans*-stilbene (88.8%) and triphenyltin bromide (72.1%).

In another run using 5.18 g. (0.02 mole) of *cis*-α-bromostilbene and 7.02 g. (0.02 mole) of triphenyltin hydride and carried out at *ca.* 26 to 29°, there was obtained *trans*-stilbene (61.1 %), *cis*-stilbene (30.5%), and triphenyltin bromide (72.0%).

Reduction of *trans*-α-Bromostilbene with Triphenyltin Hydride. Reduction No. 11.—A mixture of 7.0 g. (0.027 mole) of *trans*-α-bromostilbene[24] and 9.47 g. (0.027 mole) of triphenyltin hydride was stirred at *ca.* 26°. During the course of 10 min. the temperature rose to 30°, remained at that temperature for 15 min., and then returned to *ca.* 26°. After 24 hr. the reaction mixture had become a thick paste. The mixture was slurried with 25 ml. of petroleum ether and poured onto 70 g. of Woelm neutral alumina (activity I-II, column I). The column was eluted with petroleum ether. The first 250-ml. portion of eluate yielded no residue. The next two 500-ml. portions of eluate were combined and yielded, after removal of the solvent, 7.4 g. of a semisolid, which was slurried with 20 ml. of *n*-hexane and cooled overnight in a refrigerator. The crystals which were present were collected on a filter (1.65 g.), m.p. 112-114°. Recrystallization from 95% ethanol gave 1.60 g. of *trans*-stilbene, m.p. 120-122°, no depression on admixture with an authentic sample of *trans*-stilbene.

The hexane was removed from the first mother liquor *in vacuo*, and the residue was distilled to give 1.87 g. (38.6%) of *cis*-stilbene, b.p. 93-97° (2 mm.); authentic *cis*-stilbene had b.p. 93-96° (2 mm.). The infrared and ultraviolet spectra were superimposable upon that of an authentic sample of *cis*-stilbene.

The residue from the distillation was slurried with 25 ml. of petroleum ether and poured onto 70 g. of Woelm neutral alumina (activity I-II, column II). The column was eluted with petroleum ether until 250 ml. of eluate was obtained. Removal of the petroleum ether *in vacuo* gave 1.5 g. of a semisolid which yielded after two recrystallizations from 95% ethanol 1.03 g. of *trans*-stilbene, m.p. 120-122°. The total yield of *trans*-stilbene was 2.63 g. (54.1%).

Column I was further eluted with methylene chloride-methanol (98:2) until 1 l. of eluate was obtained. Column II was eluted with methylene chloride-methanol (98:2) until 250 ml. of eluate was obtained. The two eluates were combined, and the solvent was removed *in vacuo* leaving 8.65 g. of solid material which afforded after recrystallization from *n*-propyl alcohol 8.32 g. (71.7 %) of triphenyltin bromide, m.p. 116-118°.

Separation of a Known Mixture of *trans*-Stilbene, *cis*-Stilbene, and Triphenyltin Bromide.—A known mixture consisting of 1.62 g. of *trans*-stilbene, 0.180 g. of *cis*-stilbene, and 4.30 g. of triphenyltin bromide was slurried with 25 ml. of petroleum ether and poured onto 70 g. of Woelm neutral alumina (activity I-II). The column was eluted with petroleum ether until 500 ml. of eluate was obtained. Removal of the solvent *in vacuo* left 1.85 g. of a semisolid which gave after recrystallization from 95% ethanol 1.55 g. of *trans*-stilbene, m.p. 120-122°.

The mother liquor was evaporated to dryness, and the residue was dissolved in 5 ml. of hexane and allowed to stand at −5° overnight. The crystals were collected on a filter giving 50 mg. of *trans*-stilbene, m.p. 120-122°. The total yield of *trans*-stilbene was 1.60 g. (98.7%).

Removal of the hexane from the filtrate followed by distillation of the residue gave 0.180 g. (100%) of *cis*-stilbene, b.p. 93-96° (2 mm.).

The column was further eluted with methylene chloride-methanol (9:1) until 500 ml. of eluate was obtained. Removal of the solvent *in vacuo* left 3.4 g. of solid material which afforded after recrystallization from *n*-propyl alcohol 3.4 g. (79.0%) of triphenyltin bromide, m.p. 116-118°.

---

[24] J. Wislicenus, *Ber. Verhandl. sachs. Akad. Wiss. Leipzig Math. phys. Kl.*, **52**, 117 (1900).

The Absolute Configuration of Citrinin[1]

RICHARD K. HILL AND LIBERO A. GARDELLA

Frick Chemical Laboratory,
Princeton University, Princeton, New Jersey

Received September 23, 1963

One of the first compounds with antibiotic activity isolated in Raistrick's classic investigations on fungal metabolites was the substance citrinin, obtained in 1931 from *Penicillium citrinum*.[2] Though it proved too toxic for medical use, the discovery of its activity intensified the search which subsequently led to practical antibiotics.

The structure of citrinin (I) was established in 1949, primarily by the investigations of Robertson and his co-workers,[3] and several syntheses have been recorded.[4] An ingenious suggestion of Cram[5] led to the assignment of relative stereochemistry. Hydrolysis of citrinin gives the levorotatory phenol (II) which is partially or wholly racemized by acid. Cram pointed out that if the methyl groups on the asymmetric carbons of citrinin were *trans*, participation of the aromatic ring in the formation of a carbonium ion from II would afford a symmetrical intermediate and consequently lead to racemization; his subsequent studies with model compounds confirmed this proposal.[6]

Further degradation of citrinin has now made it possible to complete the stereochemical assignment by showing the absolute configuration. The dimethyl

---

[1] This investigation was supported by a research grant (GM 06568-04) from the Public Health Service, to whom the authors express their appreciation.

[2] A. C. Hetherington and H. Raistrick, *Phil. Trans. Roy. Soc. London*, **220B**, 269 (1931).

[3] (a) J. P. Brown, N. J. Cartwright, A. Robertson, and W. B. Whalley, *J. Chem. Soc.*, 859 (1949); (b) J. P. Brown, A. Robertson, W. B. Whalley, and N. J. Cartwright, *ibid.*, p. 867.

[4] (a) N. J. Cartwright, A. Robertson, and W. B. Whalley, *ibid.*, 1563 (1949); (b) H. H. Warren, G. Dougherty, and E. S. Wallis, *J. Am. Chem. Soc.*, **71**, 3422 (1949); (c) T. S. Gore, R. V. Talavdekar, and K. Venkataraman, *Current Sci.* (India), **19**, 20 (1950); *Chem. Abstr.*, **44**, 7313 (1950).

[5] D. J. Cram, *J. Am. Chem. Soc.*, **70**, 4244 (1948).

[6] D. J. Cram, *ibid.*, **71**, 3863 (1949); **72**, 1001 (1950).