water gave an analytical sample which melted at 281–282°: ν_{max}^{KBr} (cm^{-1}) 3200 (w), 1680 (s), 1625 (m), 1440 (w), 775 (w); $\tau^{CF_3CO_2H}$ (ppm) 2.98 (5 H, s), 3.05 (1 H, s), 5.92 (2 H, s). *Anal.* Calcd for $C_{11}H_{10}N_2O_2$: C, 65.34; H, 4.99; N, 13.86. Found: C, 65.18; H, 4.97; N, 13.87.

Hydrolysis of 3-Benzylidene-2,5-diketopiperazine (6).—A slurry of 0.30 g (0.0015 mol) of 3-benzylidene-2,5-diketopiperazine (5) in 4 ml of 0.5 *N* hydrochloric acid and 2 ml of glacial acetic acid was refluxed for 2 hr. On cooling in a refrigerator overnight, 0.10 g of a precipitate which was identified as starting material formed. After filtration crystals appeared in the filtrate on standing at room temperature and after cooling another filtration gave 0.20 g (60%) of a colorless solid which melted at 164–166° (lit. mp 166–167°). This material was the same by a mixture melting point test as phenylpyruvylglycine (7) prepared by hydrolysis of acetyldehydrophenylalanylglycine (**2**, R = H).[4]

Registry No.—2 (R = H), 19459-01-9; **5**, 19459-02-0; **6**, 19459-03-1.

A Simple Technique for Performing Reactions with Organotin Hydrides

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The most useful reactions of organotin hydrides include additions to unsaturated systems and reductions of functional groups such as halides.[1] Preparation of the organotin hydride usually involves reduction of an organotin halide or oxide with a reducing agent such as lithium aluminum hydride. The hydride is then isolated and used immediately or stored until needed in an air-tight container.

It has been recently reported that organotin hydrides can be prepared by the reaction of the appropriate oxides with polymethylsiloxane, eq 1.[2] The reactants

$$(R_3Sn)_2O + [CH_3SiHO]_n \rightarrow\rightarrow\rightarrow 2R_3SnH + [CH_3SiO_{1.5}]_n \quad (1)$$

are simply mixed without solvent and the hydride separated from the cross-linked silicone polymer by distillation. Since the polymer is nonvolatile it appeared to us that a substance which would react with the hydride could be added to the mixture without the necessity for isolating the hydride. Furthermore, silanes do not react readily with unsaturated and reducible functions. This suggested further that the desired reaction of the organotin hydride could be effected by simply mixing the polysiloxane, organotin oxide and substrate, as illustrated in eq 2 for an organic

$$2RX + (R'_3Sn)_2O + [CH_2SiHO]_n \longrightarrow 2RH + 2R'_3SnX + [CH_3SiO_{1.5}]_n \quad (2)$$

halide. A preliminary experiment with *n*-heptyl bromide yielded 70% of *n*-heptane indicating that the method was promising and as effective as the conventional method.[3] Further experiments were then carried out to determine whether yields were generally good with simple halides and whether other reducible functions were reduced in competition with the halides.

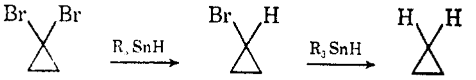
TABLE I

REDUCTION OF GEMINAL DIBROMOCYCLOPROPANES WITH TRI-*n*-BUTYLTIN HYDRIDE GENERATED *in Situ*

Halide	Conditions	% yield of monobromide[a]
1,1-Dibromo-*trans*-2,3-dimethyclyclopropane[b]	0°, 1.5 hr	85
1,1-Dibromo-2,2,3,3-tetramethylcyclopropane[c]	Room temperature, 1.5 hr	73 (78)
7,7-Dibromobicyclo-[4.1.0]heptane[d]	50°, 3 hr	79 (82)

[a] Figures in parentheses are from ref 4. [b] P. S. Skell and A. Y. Gardner, *J. Amer. Chem. Soc.*, **78**, 3409 (1956). [c] P. S. Skell and A. Y. Gardner, *ibid.*, **78**, 5430 (1956). [d] W. von E. Doering and A. K. Hoffman, *ibid.*, **76**, 6162 (1954).

One of the more important applications of organotin hydrides in organic synthesis is in the stepwise reduction of geminal polyhalides.[3] This feature has been exploited in the reduction of the adducts of dibromocarbene to simple olefins[4] and to allenes,[5] eq 3.[6] Results of



(3)

the reduction of three dibromocyclopropanes to the corresponding monobromo derivatives are given in Table I, and can be seen to be comparable with those obtained by the conventional procedure.

A survey of the reduction of several aromatic and aliphatic chlorides and bromides was made with the results shown in Table II. Some of the reactions were carried out thermally. Others were initiated photochemically in Pyrex vessels and were found to provide improved yields at lower temperatures. The reactions carried out at 100° or higher were usually accompanied by the formation of a grayish precipitate which was not observed in the photochemical reductions.

It appears that reductions of aromatic bromides by this method are very slow in the presence of a ketone, aldehyde or amino group. Aliphatic carbonyl compounds with α halogens have been shown to be reduced in good yield.[3] Decomposition of organotin hydrides catalyzed by amines is a well-documented process.[1a] When the reduction of *p*-bromo-N,N-dimethylaniline was carried out thermally, the amount of decomposition appeared to be quite large, as reflected in the low yield of reduction product. Although the yield of product was larger in the case of the photochemically induced reduction, the reaction was quite slow.

It is interesting to note that *m*-chlorotoluene was not reduced at all even after irradiation for 5 days, while aliphatic chlorides were reduced in good yield under these conditions. In contrast to this, *o*-bromotoluene

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(1) For recent reviews, see (a) H. G. Kuivila in "Advances in Organometallic Chemistry," Vol. I, F. G. A. Stone and R. West, Ed., Academic Press, New York, N. Y., 1964, p 47; (b) W. P. Neumann, *Angew. Chem.*, **76**, 849 (1964); (c) W. P. Neumann, "Die Organishe Chemie Des Zinns," Enke Verlag, Stuttgart, West Germany, 1967; (d) H. G. Kuivila, *Accounts Chem. Res.*, **1**, 299 (1968).

(2) K. Hayashi, J. Iyoda, and I. Shiihara, *J. Organometal. Chem.*, **10**, 81 (1967).

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

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

(5) W. Rahman and H. G. Kuivila, *ibid.*, **31**, 772 (1966).

(6) Other methods which are available for this reduction involve strongly basic conditions to which functional groups such as esters and nitriles are sensitive; see D. Seyferth and D. Prokai, *ibid.*, **31**, 1702 (1966); A. J. Frey and R. H. Moore, *ibid.*, **33**, 1283 (1968).

TABLE II

REDUCTION OF SOME ORGANIC HALIDES WITH TRI-*n*-BUTYLTIN HYDRIDE GENERATED *in Situ*

Halide	Temp,[a] °C	Time, hr	Product	% yield
n-Bromoheptane	50	1	*n*-Heptane	70
4-Bromovaleronitrile	50	1	Valeronitrile	60
2-Bromoethyl acetate	50	1	Ethyl acetate	63
o-Bromotoluene	110	14	Toluene	93
β-Bromoethylbenzene	110	4	Ethylbenzene	69
2-Chlorooctane	110	16	*n*-Octane	63
p-Bromoanisole	110	4	Anisole	34
	110	16		64
2-Bromopyridine	110	14	Pyridine	91
p-Bromo-N,N-dimethylaniline	110	14	N,N-Dimethylaniline	10
o-Bromotoluene	*h*ν	5	Toluene	100
p-Bromo-N,N-dimethylaniline	*h*ν	14	N,N-Dimethylaniline	25
2-Chlorooctane	*h*ν	7	*n*-Octane	70
	*h*ν	19		100
2-Chloroethyl acetate	*h*ν	20	Ethyl acetate	91
3-Chlorobutyronitrile	*h*ν	20	Butyronitrile	93
m-Chlorotoluene	*h*ν	120	Toluene	0
p-Bromoacetophenone	*h*ν	5	Acetophenone	30
p-Bromobenzaldehyde	*h*ν	5	No reduction	0
p-Bromobenzenethiol	*h*ν	5	No reduction	0

[a] Photoinitiated reaction at 35–40°.

was reduced in quantitative yield after only 5 hr of irradiation. It has been reported that chlorobenzene was reduced to benzene in 64% yield when heated for 21 hr at 80° in the presence of AIBN.[3] Perhaps the lower temperature employed in the photochemical reactions results in more selective reductions.

It is clear that organotin hydride reductions of halides can be carried out in the presence of a variety of functional groups which are sensitive to the basic conditions encountered when other reducing agents are used.

Carbonyl compounds are reduced to alcohols by organotin hydrides,[1a] eq 4. One advantage of this

$$R_2CO = 2SnH \longrightarrow R_2CHOH + Sn\text{-}Sn \qquad (4)$$

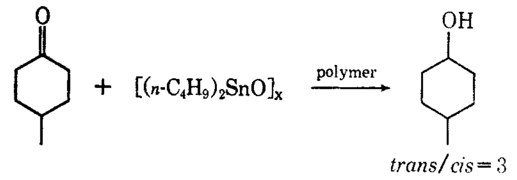
reduction is that hydrolysis is not necessary. Ketones are reduced less readily than halides by tri-*n*-butyltin hydride.[3]

Simple carbonyl compounds are reduced in an exothermic reaction at room temperature by the dihydrides. However, tri-*n*-butyltin hydride required a temperature of 140° for reduction at a convenient rate. Irradiation of a mixture of 4-methylcyclohexanone, silicone polymer and bistri-*n*-butyltin oxide for the 3 days resulted in only 10% reduction of the ketone to a mixture of *cis*- and *trans*-4-methylcyclohexanol.

The hydride exchange reaction between the silicone polymer and organotin oxides has also been used to prepare organotin dihydrides, eq 5. Hydrolysis of

$$\frac{1}{x}(R_2SnO)_x + \frac{2}{n}[MeSiHO]_n \longrightarrow \frac{1}{x}R_2SnH_2 + \frac{2}{n}[MeSiO_{1.5}]_n \qquad (5)$$

di-*n*-butyltin dichloride with sodium hydroxide solution produced di-*n*-butyltin oxide. When the silicone polymer, organotin oxide and ketone were mixed together, an exothermic reaction took place which resulted in extensive decomposition. By slow addition of the ketone and silicone polymer to a slurry of the oxide in toluene, the reaction could be easily controlled. In this manner, 4-methylcyclohexanone was reduced to a mixture of *cis*- and *trans*-4-methylcyclohexanol in 75% yield, eq 6.



(6)

Several unsuccessful attempts were made to add organotin hydride, generated *in situ*, to double bonds. Even addition to 1-hexene could not be effected in satisfactory yield after irradiation with the silicone polymer and bistri-*n*-butyltin oxide for 3 days.

Experimental Section

General.—Infrared spectra were determined on a Beckman IR-7 spectrophotometer. Determinations of nmr spectra were carried out with a Varian Model A-60A spectrometer using carbon tetrachloride as solvent and tetramethylsilane as the internal standard. Gas–liquid partition chromatography analysis was carried out on a F & M Model 5750 research gas chromatograph equipped with a dual flame detector. For analysis of starting materials and products of halide reductions, a 6-ft, ⅛-in. Apiezon L on 60–80 Chromosorb W column was used. For analysis of the starting material and products from reduction of 4-methylcyclohexanone, a 15-ft, 0.25-in. 1,2,3-triscyanoethoxypropane on 60–80 Chromosorb P column at 150° was used.

Reduction of 1,1-Dibromo-*trans*-2,3-dimethylcyclopropane.—To a 250-ml round-bottomed one-necked flask, equipped with a powerful magnetic stirrer, pressure-equalizing addition funnel and drying tube, was added 45.6 g (0.2 mol) of dibromide and 18 g (0.3 equiv) of silicone polymer (General Electric Dri-Film 1040). While stirring at 0°, 67.2 g (0.112 equiv) of bistri-*n*-butyltin oxide was added dropwise. After the addition was complete, the reaction mixture was stirred at 0° for 1.5 hr. The flask was then fitted with a condenser and stirring continued at room temperature until the reaction was no longer exothermic or until the mixture set into a gel. The product was distilled through a short column into an efficient Dry Ice trap under reduced pressure, yield 85% based on starting dibromide.

Reduction of 7,7-Dibromobicyclo[4.1.0]heptane.—The above procedure was followed except the reaction mixture was stirred for 3 hr at 50° instead of room temperature.

Thermally Induced Reductions of Halides.—The same procedure was used for all reductions. To a 50-ml flask, equipped with magnetic stirrer, condenser and drying tube, was placed 0.05 mol of halide, 0.075 equiv of silicone polymer (4.6 g) and 0.038 equiv of bistri-*n*-butyltin oxide (22.8 g). The reaction mixture was stirred for the time at the temperature indicated in Table II. The product was distilled into a Dry Ice trap at reduced pressure (15–20 mm). The infrared spectrum of each product reported was identical with that of an authentic sample.

Photochemically Induced Reduction of Halides.—To a 50-ml Pyrex tube fitted with a glass stopper was added 0.05 mol of halide, 0.075 equiv of polymer (4.6 g), and 0.038 equiv of bistri-*n*-butyltin oxide (22.8 g). The reaction mixture was irradiated in a Rayonet photochemical reactor for the time indicated in Table II. Transfer of the reaction mixture to a 50-ml flask followed by distillation at reduced pressure (15–20 mm) gave pure product. The infrared spectrum of each product reported was identical with that of an authentic sample.

Reduction of 4-Methylcyclohexanone.—To a 100-ml three-necked flask equipped with a Hershberg stirrer, condenser and addition funnel was added 30 g of di-*n*-butyltin oxide (0.12 mol) and 35 ml of toluene. While stirring at 25°, there was added dropwise a mixture of 11.2 g of ketone (0.1 mol) and 18 g of silicone polymer (0.3 equiv). After addition was complete, the reaction mixture was stirred at 25° for 3 hr. Distillation at reduced pressure have a mixture of *cis*- and *trans*-4-methylcyclohexanol: bp 55° (20 mm); yield 75% based on starting ketone.

Registry No.—Tri-*n*-butyltin hydride, 688-73-3; 1,1-dibromo-*trans*-2,3-dimethylcyclopropane, 3591-58-0; 7,7-dibromobicyclo[4.1.0]heptane, 2415-79-4; 4-methylcyclohexanone, 589-92-4.

Acknowledgment.—The authors gratefully acknowledge generous gifts of Dri-Film 1040 from the General Electric Co. Silicone Products Division and bistri-*n*-butyltin oxide from the M & T Chemicals, Inc.

Nitrile Oxides. XII. Cycloaliphatic and Aliphatic Stable Nitrile Oxides[1]

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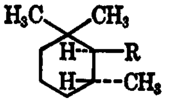
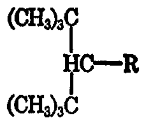
Simple aliphatic nitrile oxides are extremely unstable and isomerize even at 0° in dilute solutions within seconds or, at best, minutes to the corresponding dialkylfurazan oxides (furoxans, 1,2,5-oxadiazole 1-oxides).[2,3] Only recently a few representatives of aliphatic nitrile oxides have been obtained as monomers by working at temperatures of approximately −40°.[4] Trimethylacetonitrile oxide [**1**, $(CH_3)_3C—C\equiv N\rightarrow O$] is the only member of the series reported so far to be stable enough to be distilled *in vacuo* and to require several days at room temperature to dimerize completely.[2,4,5] In the light of our recent success in completely stabilizing aromatic and heterocyclic nitrile oxides by controlled steric hindrance,[6] the relative stability of **1** may be attributed to the bulky *t*-butyl group. Aromatic and heterocyclic nitrile oxides are adequately protected against dimerization by two methyl groups in *o,o'* position to the CNO group, but the limited lifetime of **1** indicated that a higher degree of steric hindrance than that provided by one *t*-butyl group would be necessary for the stabilization of an aliphatic or cycloaliphatic nitrile oxide, probably because of the greater conformational freedom of these structures.

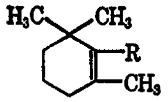
These speculations were confirmed by the preparation of the strongly hindered nitrile oxides, *trans*-2,2,6-trimethylcyclohexylfulmide (**2**) and di-*t*-butylacetonitrile oxide (**3**). Both compounds proved indefinitely stable at 25°. The parent carbon skeleton structures of **2** and **3** were chosen for their accessibility. The synthesis of both **2** and **3** started with the known aldehydes **4**[7] and **5**,[8] which were converted into the oximes and then dehydrogenated by the recently described improved procedure.[9] The remarkable degree of steric protection provided by the 2,2,6-trimethylcyclohexane moiety was impressively demonstrated by the preparation of 2,2,6-trimethylcyclohexen-1-ylfulmide (**6**) from the corresponding aldehyde **7** (β-cyclocitral). Compound **6** is the first known unsaturated nitrile oxide. Generally, ethylenic double bonds react quite readily with the nitrile oxide function, but their reactivity decreases sharply with increased substitution.[2a,10] No intermolecular reaction of the CNO and the ethylenic group of **6** could be enforced.



2, $R = C\equiv N\rightarrow O$
4, $R = CHO$
9, $R = N=C=O$



3, $R = C\equiv N\rightarrow O$
5, $R = CHO$
8, $R = CH_2OH$
10, $R = N=C=O$



6, $R = C\equiv N\rightarrow O$
7, $R = CHO$
11, $R = N=C=O$

In spite of the crowded vicinity of the CNO group in **2**, **3**, and **6**, they reacted as easily as unhindered nitrile oxides with a number of typical dipolarophiles and nucleophiles. Heating the nitrile oxides for 5 hr to 125–130° rearranged them neatly to the corresponding isocyanates **9–11** which were characterized by subsequent reaction with aniline to give the corresponding N-phenylureas. Data on the obtained products are listed in Table I.

Experimental Section[11]

***trans*-2,2,6-Trimethylcyclohexylfulmide (2).**—*trans*-2,2,6-Trimethylcyclohexane-1-aldehyde (IV) was obtained by the hydrogenation of the ethylene acetal of β-cyclocitral with platinum oxide in acetc acid.[7] The oxime of IV is best prepared by the following method. The aldehyde (5 g) was dissolved in methanol (100 ml) and a solution of hydroxylamine hydrochloride (5 g) and sodium carbonate (3.5 g) in water (15 ml) was added. The reaction mixture was heated to reflux for 5 hr, poured into water (500 ml), and extracted with ether. The ethereal extracts were dried over anhydrous sodium sulfate, the solvent was removed *in vacuo*, and the residue was fractionated. The fraction

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[1] Previous communication by C. Grundmann and R. Richter, *Tetrahedron Lett.*, 963 (1968).

[2] (a) C. Grundmann, *Fortschr. Chem. Forsch.*, **7**, 62 (1966); (b) T. Mukaiyama and T. Hoshino, *J. Amer. Chem. Soc.*, **82**, 5339 (1960).

[3] The parent member of this series, fulminic acid, $HC\equiv N\rightarrow O$, is apparently a little more stable in solution, but undiluted will explode at −20° (C. Grundmann in "The Chemistry of the Cyano Group," Z. Rappoport, Ed., Interscience Publishers, Inc., London, in press).

[4] G. Zinner and H. Günther, *Angew. Chem.*, **76**, 440 (1964).

[5] G. Speroni and A. Quilico in "The Chemistry of Heterocyclic Compounds," Vol. XVII, A. Weissberger, Ed., Interscience Publishers, Inc., N. Y., 1962, p 21, Table II.

[6] C. Grundmann and J. M. Dean, *Angew. Chem.*, **76**, 682 (1964); C. Grundmann and J. M. Dean, *J. Org. Chem.*, **30**, 2809 (1965); C. Grundmann and R. Richter, *ibid.*, **32**, 2308 (1967).

[7] L. Colombi, A. Bosshard, A. Schinz, and C. F. Seidel, *Helv. Chim. Acta*, **34**, 265 (1951).

[8] M. S. Newman, A. Arkell, and T. Fukunaga, *J. Amer. Chem. Soc.*, **82**, 2498 (1960).

[9] C. Grundmann and R. Richter, *J. Org. Chem.*, **33**, 476 (1968).

[10] R. Huisgen, *Angew. Chem.*, **75**, 604 (1963); C. Grundmann, H. D. Frommeld, K. Flory, and S. K. Datta, *J. Org. Chem.*, **33**, 1464 (1968).

[11] Melting points were determined with the Fisher-Johns melting point apparatus and are uncorrected. Microanalyses were by Galbraith Laboratories, Knoxville, Tenn. Molecular weights were determined by the osmometric method; the applied solvent is indicated in parentheses.