Table I
Reduction of Quaternary Ammonium Iodides with Lithium Triethylborohydride ^a

Quaternary Salts	Registry no.	Temp, °C	Time, hr	Product(s) ⁶ (% yield) ⁶			
C ₆ H ₅ N(CH ₃) ₃ I	98-04-4	25	0.75	$C_{g}H_{5}N(CH_{3})_{2}$ (100, 92 ^d)			
		65	0.25	(100)			
$C_6H_5N(C_2H_5)(CH_3)_2I$	1006-07-1	25	0.75	$C_{g}H_{5}N(C_{2}H_{5})CH_{3}$ (96) + $C_{g}H_{5}N(CH_{3})_{2}$ (4)			
$C_6H_5N(C_2H_5)_2CH_3I$	1007-67-6	25	0.75	$C_{e}H_{5}N(C_{2}H_{5})_{2}$ (66) + $C_{e}H_{5}N(C_{2}H_{5})CH_{2}$ (33)			
$C_6H_5CH_2N(CH_3)_3I$	4525-46-6	65	7.0	$C_{2}H_{5}CH_{2}N(CH_{2})_{3}$ (100, 85 ^d)			
		25	2.0	(< 5)			
$CH_3(CH_2)_5N(CH_3)_3I$	15066-77-0	65	4.0	$CH_{2}(CH_{2})_{E}N(CH_{2})_{2}$ (100, 88 ^d)			
		25	2.0	(<5)			
$CH_3C(CH_3)_2CH_2C(CH_3)_2N(CH_3)_3I$	53624-41-8	65	1.0	$CH_{3}C(CH_{3})_{2}CH_{2}C(CH_{3})_{2}N(CH_{3})_{2}$ (100)			

^a Reductions were performed using 1.0 mmol of salt and 1.5 mmol of LiEt₃BH in 5 ml of dry THF under nitrogen.^b All products identified by comparison with authentic samples or through preparation of known derivatives of isolated products. ^c Yields were determined by glpc analysis with the aid of an internal standard unless otherwise noted. d Yield of isolated picrate salt.

pentyltrimethylammonium iodide suffers less than 5% reduction.

Quaternary ammonium salts of aliphatic amines are much less readily reduced, however, owing to the increased basicity of the tertiary amine and require longer reaction times at elevated temperatures for the quantitative liberation of the dealkylated tertiary amine. The addition of hexamethylphosphoric triamide, which often accelerates the rate of SN2 processes,³ does not affect a noticeable increase in the rate of the reaction with these substrates.

Thus, lithium triethylborohydride is an excellent reagent for the selective demethylation of quaternary ammonium salts containing methyl groups. It seems likely that this remarkable reagent will find use in other reductions involving the displacement of poor leaving groups by hydride ion.

Experimental Section

Materials. The quaternary ammonium salts employed in this work were prepared by the treatment of the corresponding tertiary amines with excess methyl iodide in benzene. The N,N-dimethyl amines were obtained from commercial sources or by the methylation of the corresponding primary amines.⁴ Physical properties of all materials were in agreement with published values. A 1 M stock solution of lithium triethylborohydride in THF was prepared as previously described.1

General Procedure for the Dealkylation of Quaternary Ammonium Salts. N,N-Dimethylaniline from Phenyltrimethylammonium Iodide. The following procedure illustrates the general procedure used for the reduction of all of the quaternary ammonium iodides reported in Table I. Variations in reaction time and temperature for specific salts are shown in Table I. To a suspension of 0.265 g (1.0 mmol) of phenyltrimethylammonium iodide in 5 ml of dry THF under a nitrogen atmosphere was added 1.5 ml of 1 M lithium triethylborohydride stock solution. The mixture was stirred at room temperature for 0.75 hr. The resulting homogeneous mixture was treated with 1.0 ml of 10% aqueous hydrochloric acid and the THF was removed under reduced pressure. The aqueous solution was made basic by the addition of sodium hydroxide and the tertiary amine was obtained by extraction of the aqueous phase with several small portions of ether. Addition of the ethereal solution of N,N-dimethylaniline to 5 ml of saturated picric acid in ethanol gave 0.322 g (92%) of N,N-dimethylaniline picrate, mp 161–162° (lit.⁵ mp 163°).

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Registry No.-Lithium triethylborohydride, 22560-16-3.

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Carboalkoxylation of Aryl and Benzyl Halides Catalyzed by Dichlorobis(triphenylphosphine)palladium(II)

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With the exception of allyl halides, the carbonylation of organic halides using palladium catalysts has received little attention because of the severe reaction conditions.¹⁻⁴ A recent study⁵ of the carbonylation of dichlorobis(triphenylphosphine)palladium(II) (1) suggests it as a potential catalyst for the carbonylation of organic halides. Carbonylation of 1 in methanol in the presence of primary or secondary amines affords a mixture of carbonylpalladium(0) complexes 2 and 3, whereas in the presence of tertiary amines, chlorocarbomethoxybis(triphenylphosphine)palladium(II) (4) is formed. Treatment of 4 with methyl iodide or benzyl bromide yields the corresponding methyl ester.⁵

Since aryl, benzyl, and vinyl halides readily react with either finely divided palladium metal^{6,7} or organophosphinepalladium(0) complexes^{8,9} to form organopalladium(II) complexes, it appeared likely that the palladium(0) complexes 2 and 3 would react with organic halides via oxi-

$$L_2 PdCl_2 + CO + CH_3 OH \xrightarrow{RR'NH}_{RNH_2} Pd(CO)L_3 + Pd_3(CO)_3L_4$$

$$I, L = PPh_3 \qquad 2 \qquad 3$$

$$1 + CO + CH_3 OH \xrightarrow{RR'R'N}_{L_2} PdCl(CO_2CH_3)$$

$$4$$

dative addition to afford organopalladium complexes which upon carbonylation would give acylpalladium(II) derivatives. Alcoholysis of the acylpalladium(II) compounds would afford esters and regenerate a palladium(0) complex in the presence of a base.¹⁰ A catalytic cycle for the carbonvlation of organic halides could also be achieved with the carbomethoxypalladium complex 4 if dihalobis(triphenyl-

 Table I

 Carboalkoxylation of Aryl and Benzyl Halides^a

RX	R'OH	Base	Reaction	Reaction time, hr	% conversion		
			temp, °C		RCO ₂ R'	ROR'	ROAc
PhI ^b	CH ₃ OH	NaOAc	60	48	80		
PhI^{b}	CH ₃ OH	Et_3N	60	48	85		
$PhCH_{2}Cl^{o}$	CH ₃ OH	NaOAc	80	24	61	19	13
PhCH ₂ Cl ^c	n-BuOH	NaOAc	80	36	68	Trace	Trace
$PhCH_2Cl^{c}$	<i>n</i> -BuOH	NaOAc	60	36	50	Trace	Trace
$PhCH_2Cl^{c}$	CH ₃ OH	Na_2CO_3	80	24	49	35	
PhCH ₂ Cl ^c	CH ₃ OH	Et ₃ N	80	24	36	4	
$PhCH_2Cl^{c}$	CH ₃ OH	1,8-Bis(dimethylamino)naphthalene	80	20	91	3	
$PhCH_2Cl^{c}$	CH ₃ OH	2,6-Lutidine	80	40		36	
$PhCOCH_2Br^d$	CH ₃ OH	1,8-Bis(dimethylamino)naphthalene	80	48	64		

 ${}^{a}p(CO) = 200 \text{ psi at room temperature. } PdCl_{2}(PPh_{3})_{2}-PhI = 1:100; PhI = 30 \text{ mmol}; \text{ base} = 50 \text{ mmol}; CH_{3}OH = 100 \text{ ml}. {}^{c}PdCl_{2}(PPh_{3})_{2}-PhCH_{2}Cl = 1:100; PhCH_{2}Cl = 40 \text{ mmol}; \text{ base} = 60 \text{ mmol}; R'OH = 100 \text{ ml}. {}^{d}PdCl_{2}(PPh_{3})_{2}-PhCOCH_{2}Br = 1:58; PhCOCH_{2}Br = 25 \text{ mmol}; \text{ base} = 29 \text{ mmol}; CH_{3}OH = 100 \text{ ml}.$

phosphine)palladium(II) (1a) is produced from the reaction of 4 with organic halides to afford esters.

Treatment of iodobenzene with carbon monoxide (200 psi) and bases in methanol in the presence of a catalytic amount of 1 at 60° afforded good yields of methyl benzoate (Table I). The palladium catalyst was recovered as halocarbomethoxybis(triphenylphosphine)palladium(II) (4a) in >90% yield. Carboalkoxylation of benzyl chloride was achieved under similar conditions in the presence of a variety of bases. The best yield of ester product was obtained with 1,8-bis(dimethylamino)naphthalene, a strong base with low nucleophilicity. By-products such as benzyl methyl ether and benzyl acetate probably arose from nucleophilic displacements at either benzyl chloride or a benzylpalladium species. In the reactions of benzyl chloride which yielded esters, the palladium catalyst 1 was converted to either palladium black or an air-sensitive complex, probably a palladium(0) material. No ester was obtained in the presence of 2,6-lutidine and a 70% yield of 4 was obtained, thus suggesting a palladium(0) species as the active catalyst in the carboalkoxylation of benzyl chloride.

Carbonylation of equimolar amounts of 1 and iodobenzene afforded a 34% yield of methyl benzoate after 12 hr. Treatment of iodobenzene with an equimolar amount of 4 under similar conditions resulted in a 25% conversion to methyl benzoate. Allowing for the variation in reaction temperature, these results as well as the isolation of 4a from the catalytic carbomethoxylation of iodobenzene are compatible with 4a being the actual catalyst. However, the possibility that the active catalyst is a palladium(0) species present in a trace amount in the reaction mixture cannot be eliminated.

$$1 + PhI + CO + CH_{3}OH \xrightarrow{NaOAc, 12 hr} PhCO_{2}CH_{3} + L_{2}PdX(CO_{2}CH_{3})$$

$$34\% \qquad 4a, X = Cl \text{ or } I$$

$$L = PPh_{3}$$

$$4 + PhI \xrightarrow{CH_{3}OH} PhCO_{2}CH_{3} + L_{2}PdXCl$$

$$25\% \qquad 1a, X = Cl \text{ or } I$$

$$L = PPh_{3}$$

The carbonylation of α -bromoacetophenone (5) in methanol in the presence of 1,8-bis(dimethylamino)naphthalene was effected by treatment with a catalytic amount of 1 and carbon monoxide (200 psi) at 80°. The reaction afforded a



64% yield of α -carbomethoxyacetophenone. Carbonylation of 2-bromobutane in benzene, methanol or dimethyl sulf-oxide gave no carboxylic acid derivatives.

Experimental Section

General Procedure for the Catalytic Carbonylation of Phenyl Iodide and Benzyl Chloride. In a 500-ml autoclave was placed a mixture of the organic halide, the base, dichlorobis(triphenylphosphine)palladium(II) (1), and alcohol. The mixture was heated at 60 or 80° under 200 psi of carbon monoxide until gas absorption stopped. The palladium catalyst was removed by gravity filtration and washed with 50 ml of methanol. The combined filtrates were concentrated by distillation through a 10 cm Vigreux column. The residue was diluted with 100 ml of water and extracted with several small portions of pentane. The combined pentane extracts were washed with 2N hydrochloric acid, aqueous sodium bicarbonate, and saturated aqueous sodium chloride successively. The pentane solution was dried over magnesium sulfate, concentrated by evaporation through a 10 cm Vigreux column, and then distilled under reduced pressure using a short path distillation apparatus to give the organic products. The products were characterized by nmr and vpc. Separation and quantitative analysis of organic products were achieved by vpc using a 10 ft \times % in. 30% DEGS-Chromosorb W column. The results are given in Table I.

Stoichiometric Carbonylation of Iodobenzene. A mixture of 0.3 g (1.43 mmol) of iodobenzene, 0.24 g (2.9 mmol) of sodium acetate, and 1.0 g (1.43 mmol) of dichlorobis(triphenylphosphine)palladium(II) (1) in 15 ml of methanol was heated at 60° in a heating mantle with stirring in an autoclave which was pressurized with carbon monoxide at 200 psi. After 12 hr, the reaction mixture was filtered gravimetrically and washed with 50 ml of Skelly B to afford 1.0 g of a grayish-white complex which was identified by ir and nmr analyses as halocarbomethoxybis(triphenylphosphine)palladium(II) (4a): (KBr) 1665 cm⁻¹ (C=): nmr $(CDCl_3)$ δ 2.39 (s, 3, CO_2CH_3), and 7.2-8.0 ppm (30). The combined filtrates were concentrated under reduced pressure and the residue was extracted with several small portions of pentane. The combined pentane extracts were washed with aqueous sodium bicarbonate and saturated aqueous sodium chloride, dried over magnesium sulfate, and concentrated under reduced pressure. Quantitative vpc analysis showed a 34% yield of methyl benzoate.

Reaction of Iodobenzene with Chlorocarbomethoxybis(triphenylphosphine)palladium(II) (4). A mixture of 0.29 g (1.38 mmol) of iodobenzene and 1.0 g (1.38 mmol) of 4 in 15 ml of methanol was heated at 60° in an oil bath for 12 hr. (*Anal.* Calcd for $C_{38}H_{33}ClO_2P_2Pd$: C, 62.91; H, 4.58. Found: C, 63.01; H, 4.57.) The yellow solid was collected by gravity filtration and washed with 50 ml of Skelly B to afford 1.0 g of a mixture of 1a and 4a as determined by ir analysis. The combined filtrates were concentrated under reduced pressure and analyzed by vpc. The yield of methyl benzoate was 25%

Carbonylation of α -Bromoacetophenone (5). A mixture of 5.0 g (25 mmol) of 5, 0.3 g (0.43 mmol) of 1, 6.0 g (29 mmol) of 1,8-bis-(dimethylamino)naphthalene, and 50 ml of methanol was heated at 80° with stirring in a 500 ml autoclave which was pressurized with carbon monoxide at 200 psi. After 48 hr, the reaction mixture was filtered gravimetrically and washed with 50 ml of methanol. The combined filtrates were concentrated under reduced pressure and the residue was extracted with three 50-ml portions of dichloromethane. The combined extracts were washed with 2 N hydrochloric acid, aqueous sodium bicarbonate, and saturated aqueous sodium chloride successively. The dichloromethane solution was concentrated under reduced pressure and the residue was distilled using a short path distillation apparatus to afford 3.0 g (16 mmol, 64%) of a liquid which was identified as α -carbomethoxyacetophenone by comparison of its nmr spectrum with that reported for an authentic sample:¹¹ bp 90–94° (0.4 mm); nmr (CDCl₃) δ 3.72 (s, 3), 3.98 (s, 1.7), 5.64 (s, 0.3), 7.2-8.0 (m, 5), and 12.51 ppm (s, 0.3).

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Cleavage-Elimination of 2,3-Decalindione Monothioketals Leading to Vinylic Ester and Lactone **Prototypes of Vernolepin**

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A number of years ago we described a new method for the nonoxidative cleavage of carbon-carbon bonds which involved treatment of α -diketone monothioketals with nucleophilic bases.¹ In the course of subsequent studies aimed at clarifying the reaction pathway we discovered that cleavage of decalone 1 followed by the addition of methyl iodide to the basic reaction mixture led to the vinyl sulfide $4.^2$ This intermediate was smoothly converted to the vinvl compound 5 upon desulfurization with Raney nickel. Alternatively, the intermediate dithianyl acid 2 could be isolated, esterified, and then converted to the sulfonium salt with various methylating agents. Base cleavage was then best effected with sodium hydride. These facile transformations seemed well suited as a potential synthetic entree to the recently discovered growth-inhibitory elemanolide sesquiterpene dilactones vernolepin, vernodalin, and vernomenin.³ With such goals in mind we directed our atten-



tion to the prototype lactone 13 (Scheme I) as our initial synthetic objective.⁴



Attempts at dithianylation of hydroxy ketone 6^5 via the hydroxymethylene derivative⁶ were unsuccessful presumably because of interactions between the hydroxyl and carbonyl groupings. We therefore examined a number of hydroxyl-protected derivatives of which the mixed acetal 7 proved most suitable.⁷ Basic cleavage of the derived thicketal ketone 8 followed by acid hydrolysis yielded the crystalline lactone $9.^1$

We next explored the conversion of lactone thioacetal 9